The 28th Annual Meeting of KSBNS

K-Brain 2025 & The 3rd CJK Neuroscience Meeting

AUG 24SUN - 27WED, 2025

SONGDO CONVENSIA, INCHEON, KOREA

The Korean Society for Brain and Neural Sciences

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KSBNS 2025

The 28th Annual Meeting of
The Korean Society for Brain and Neural Sciences

K-Brain 2025 & The 3rd CJK Neuroscience Meeting

·Date August 24(Sun)- 27(Wed), 2025
·Venue Songdo Convensia, Incheon, Korea

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Woosung Cryotech Co,.LTD	Preclina Inc.	Chinese Neuroscience Society
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KOMABIOTECH	RAONBIO	VIVO Solutions
B2BIO,Inc.	Ajou University Medical Center	EVIDENT KOREA CO.,LTD
MDPI Korea	Neumous Inc.	KRIBB NPRC
Bioclone Corp.	Optic Solution	KB FINANCIAL GROUP
Daegu-Gyeongbuk Medical Innovation Foundation	VIUS Inc	Hanwha Life Financial Services
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Institute for Basic Science	Institute for Basic Science	Institute for Basic Science
Korea Institute of Oriental Medicine	BIOMEDBOOK	RWD Life Science Co., Ltd.
Sang Chung Commercial Co., Ltd.	Experimental Neurobiology	IBRO
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This work is supported by the 'Lottery Fund' of the 'Ministry of Strategy and Finance' and the 'Science and Technology Promotion Fund' of the 'Ministry of Science and ICT', contributing to the realization of social value and the development of national science and technology.

Welcome Address

Warm greetings and best wishes for a successful and prosperous year 2025

The Korean Society for Brain and Neural Sciences (KSBNS), with over 5,000 members, stands as Korea's leading neuroscience organization. We provide a dynamic platform for collaboration among neuroscientists, clinicians, and global experts, bridging basic science, applied research, and clinical practice. This success would not have been possible without our valued partners' unwavering support and interest, for which we are deeply grateful.

In 2025, we are proud to host the 28th Annual International Conference, K-Brain 2025 & The 3rd CJK Neuroscience Meeting, from August 24 to 27 at Songdo Convensia, Incheon. This event will bring together over 5,000 participants and feature over 50 symposia, including 20 CJK symposia. The conference will include top researchers from Korea and leading international scholars, particularly from China and Japan.

The conference, in collaboration with China and Japan (CJK), will feature a diverse and dynamic program, including Plenary and keynote lectures by distinguished scientists, Symposia on cutting-edge topics in neuroscience, Sessions led by and for early-career researchers, Editor's sessions including a Nature Masterclass and an extensive exhibition, fostering connections between researchers, industry, and clinicians.

We have developed sponsorship packages to support the conference and year-round society activities. By becoming a sponsor, you will play a vital role in advancing neuroscience research and innovation, both domestically and internationally. Your support will also provide unparalleled opportunities to connect with top researchers, institutions, and industry leaders in the neuroscience community.

Your continued engagement is crucial in enabling KSBNS to remain at the forefront of global neuroscience efforts. We invite you to join us in this exciting endeavor as a valued sponsor.

Thank you for your consideration and support.

Sincerely,

C. Justin Lee
President
Korean Society for Brain and Neural Sciences (KSBNS)

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Organizing Committee

Title	Name	Affiliation
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KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Science: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Program at a Glance

August 23

Time	Hall 1	Grand Ballroom	Premier Ballroom A	Premier Ballroom B	Premier Ballroom C	Rm.113-115	Rm.116-118	Rm.204-205	Rm.206-207	Rm.104-106	Rm.107-109	Rm.110-111
13:00-19:00				Satellite Meeting (The KSBNS Glia Section Satellite Symposium) Neuroglia in physiology and pathophysiology								

August 24

Time	Hall 1	Grand Ballroom	Premier Ballroom A	Premier Ballroom B	Premier Ballroom C	Rm.113-115	Rm.116-118	Rm.204-205	Rm.206-207	Rm.104-106	Rm.107-109	Rm.110-111
8:30-12:00				Satellite Meeting (The KSBNS Glia Section Satellite Symposium) Neuroglia in physiology and pathophysiology								
12:00-13:00	Registration											
13:00-14:55	**Poster Session 1** (13:00-18:00)	**Symposium 1** Molecular and circuit-level understanding of memory and memory related disorders	**Symposium 2** Mechanotransduction in the peripheral and central nerve system	**Symposium 3** Neuroglia in diseases of cognition	**Symposium 4** Novel insights in sleep regulation and function	**Symposium 5** The brainstem: a critical conduit for body-brain signaling	**Symposium 6** Exploring the neuroscience of general anesthesia					
14:55-15:00		Break										
15:00-16:35									**Special Session 1** Cutting-edge approaches to decoding dementia: from genomics to neuropathology			
16:35-16:40		Break										
16:40-16:55		Opening Ceremony										
16:55-17:35		**Award Lecture 1**										
17:35-17:40		Break										
17:40-18:30		**KSBNS Plenary Lecture 1** Matteo Carandini										
18:30-19:00		Break										
19:00-20:30		Presidential Dinner (Grand ballroom C)										

August 25

Time	Hall 1	Grand Ballroom	Premier Ballroom A	Premier Ballroom B	Premier Ballroom C	Rm.113-115	Rm.116-118	Rm.204-205	Rm.206-207	Rm.104-106	Rm.107-109	Rm.110-111
8:30-10:25	**Poster Session 1** (8:30-12:30)	**Symposium 7** Neuromodulation in psychiatry: from circuit to psychopharmacology			**Symposium 8** Gene delivery to the brain: applications in life sciences and gene therapy		**Symposium 9** Translational and clinical neuroscience: precision convergent medicine for treating intractable diseases, pain, and central nervous system trauma	**Symposium 10** Synaptic balance in memory, homeostasis, and network stability		**Special Session 2** (9:15-10:25) INSCOPIX 2P miniature microscope seminar	**Symposium 11** Neural codes across sensory systems: insights into perception and behavior	
10:25-10:35		Break										
10:35-12:30		**Special Lecture 1** (11:45-12:35) Won Do Heo	**Symposium 12** Diverse aspects of social behaviors: recognition, remembering, and reacting	**Symposium 13** Synapse function and diseases	**Symposium 14** Decoding the cerebellum in health and disease	**Symposium 15** Integrative approaches to neurodegeneration: insights from multiomics, inflammation, and cellular pathways	**Symposium 16** Recent advances in functional observation of ion channels and synaptic transmission	**Symposium 17** Transforming brain networks - neuromodulation strategies for neuropsychiatric disorders		**Educ. Session 1** (10:35-13:00) Optical techniques in neuroscience		
12:30-13:30			Luncheon Seminar ZEISS (12:35:13:05)	Luncheon Seminar Noldus Information Technology - Scitech Korea (12:35:13:05)	Luncheon Seminar CrestOptics S.p.A. (12:35:13:05)	Luncheon Seminar IVIM Technology, Inc. (12:35:13:05)	Luncheon Seminar Korea Otsuka Pharmaceutical (12:35:13:05)					
13:30-14:20	**Poster Session 2** (13:30-18:00)	**CJK Plenary Lecture 1** Hailan Hu									**Special Session 4** (13:00-17:55)	
14:20-14:30		Break										

Program at a Glance

14:30-16:25	**Poster Session 2** (13:30-18:00)	**Symposium 18** The brain-body-microbiome axis: a key to regulate ingestion and beyond	**Symposium 19** Taste sensing from the tongue to the brain	**Symposium 20** Updates on autism models and potential rescue strategies	**Educ. Session 2** (15:30-17:30) History of neuroscience	**Symposium 21** Innovations in imaging- and sequencing-based approaches in neurosciences	**Special Session 3** Parkinson's disease: Unmet needs between clinical practice and basic research	**Symposium 22** Hurting inside and out: sensing pain and nausea	**Symposium 23** Neuromodulation in the brain: new understanding and emerging methods		**Special Session 4** (13:00-17:55)
16:25-17:40											
17:40-18:30		**Presidential Lecture 1** Benjamin Deneen									

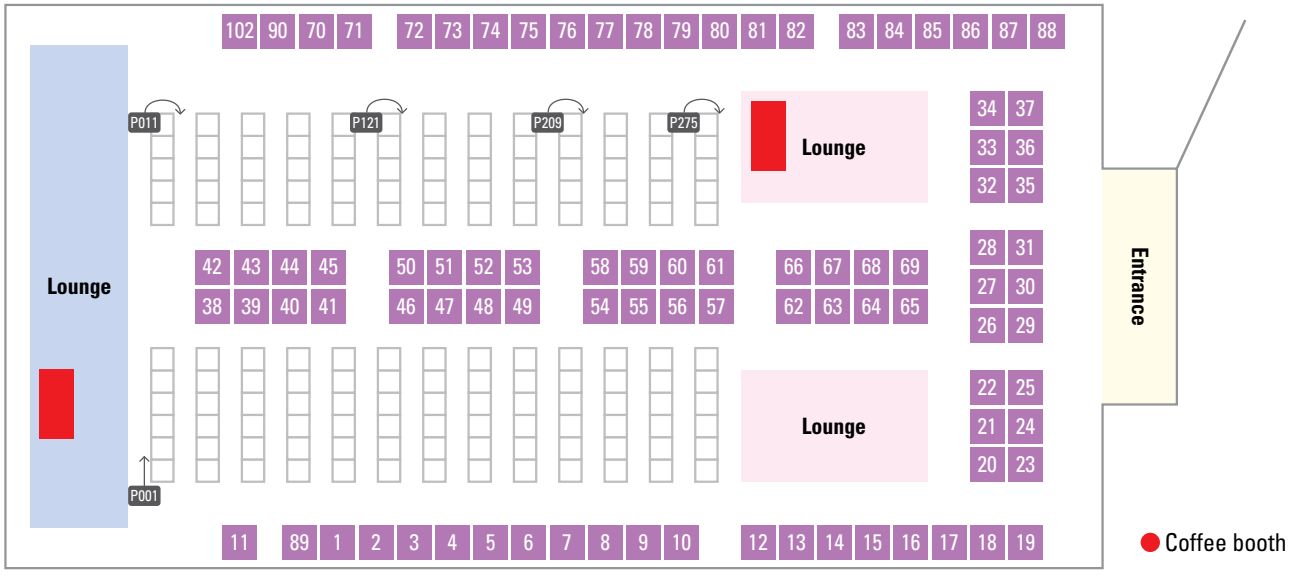
August 26

Time	Hall1	Grand Ballroom	Premier Ballroom A	Premier Ballroom B	Premier Ballroom C	Rm.113-115	Rm.116-118	Rm.204-205	Rm.206-207	Rm.104-106	Rm.107-109	Rm.110-111
8:30-10:25		**Special Session 5** Hormonal and neural control of metabolism in obesity and diabetes	**Symposium 24** Convergent mechanisms for axon regeneration and CNS repair	**Symposium 25** Decoding neuro-glial interactions: the critical role of ion channels from molecules to behaviors	**Symposium 26** Neuroscience-inspired AI: computational insights into biological and artificial intelligence	**Symposium 27** Decoding Inhibition: the interplay of GABA, chloride, and astrocytes in neural function in health and disease		**Symposium 28** Epilepsy: from gene to circuit	**Symposium 29** Decoding the neurobiology of acupuncture through modern neuroscientific approaches			Nature Masterclasses (09:00-17:00)
10:25-10:35	**Poster Session 2** (8:30-12:30)	Break								**Educ. Session 3** (10:00-12:30) Miniature brain models: from generation to application in studying brain development and function		
10:35-12:30		**Special Lecture 2** (11:35-12:35) Mickael Tanter		**Symposium 30** Precise dissection of structural and functional features in visual system	**Symposium 31** Frontiers in addiction: linking neural mechanisms to public health strategies	**Symposium 32** Connecting the Dots: illuminating the brain from connectivity to function	**Symposium 33** Neuroscience of schizophrenia: from structure to function	**Special Session 6** Spotlight on sexual dimorphism: analyzing the importance of sex and gender analysis in neuroscience research	**Symposium 34** Local mRNA translation in axon development, health and function			
12:30-13:30			Luncheon Seminar Handok (12:35-13:05)	Luncheon Seminar (12:35-13:05)	Luncheon Seminar Bruker Fluorescence Microscopy (12:35-13:05)	Luncheon Seminar Bio-Medical Science Co., Ltd. (12:35-13:05)	Luncheon Seminar Bruker Korea Co., Ltd (12:35-13:05)					
13:30-14:20		**CJK Plenary Lecture 2** Inhee Mook-Jung										
14:20-14:30		Break										
14:30-16:25	**Poster Session 3** (13:30-18:00)	**Symposium 35** Synaptic development, function, and brain disorders	**Symposium 36** Computational neuroethology of social and cognitive behaviors	**Symposium 37** Cross-regional brain circuit development: from neural differentiation to functional	**Symposium 38** Molecular probing of cognitive processes	**Symposium 39** Next-generation genetically encoded sensors and actuators for brain exploration	**Symposium 40** Basic and translational researches on myelination and demyelination		**Symposium 41** Pleiotropic roles of mitochondria in neurobiology	**Educ. Session 4** (16:00-18:00) Advancing neuroscience futures: a career development workshop		
16:25-17:40												
17:40-18:30		**KSBNS Plenary Lecture 2** Matthew Rushworth										

August 27

Time	Hall1	Grand Ballroom	Premier Ballroom A	Premier Ballroom B	Premier Ballroom C	Rm.113-115	Rm.116-118	Rm.204-205	Rm.206-207	Rm.104-106	Rm.107-109	Rm.110-111
9:00-10:55	**Poster Session 3** (9:00-12:00)	**Symposium 42** Unlocking pathophysiological and novel therapeutic mechanisms for mood disorders: insights from synapse research	**Symposium 43** Astrocyte heterogeneity from neural networks to behaviors	**Symposium 44** Audiovisual processing in rodents and marmosets	**Symposium 45** Brain cell atlas and technology		**Symposium 46** Emerging mechanisms in white matter injury: autoimmunity, vascular dysfunction, and lipid metabolism					
10:55-11:05		Break										
11:05-11:55		**CJK Plenary Lecture 3** Ikue Mori										
11:55-12:30		Break										
12:30-14:25		**Award Lecture 2** (13:00-14:25)	**Symposium 47** Recent insights into molecular orchestration of synaptic transmission and neural circuit modulation	**Symposium 48** The molecular, cellular and circuitry mechanism of pain and itch	**Symposium 49** Emergence, maintenance, and entrainment of circadian clocks: from molecules to networks	**Symposium 50** Decoding GPCR signaling: innovations in neuroscience research	**Symposium 51** Cognitive and computational neuroscience in nonhuman primate			**Educ. Session 5** How to write impactful papers?		
14:25-14:30		Break										
14:30-15:20		**Presidential Lecture 2** Peter Walter										
15:20-15:30		Break										
15:30-16:00		Closing Ceremony										

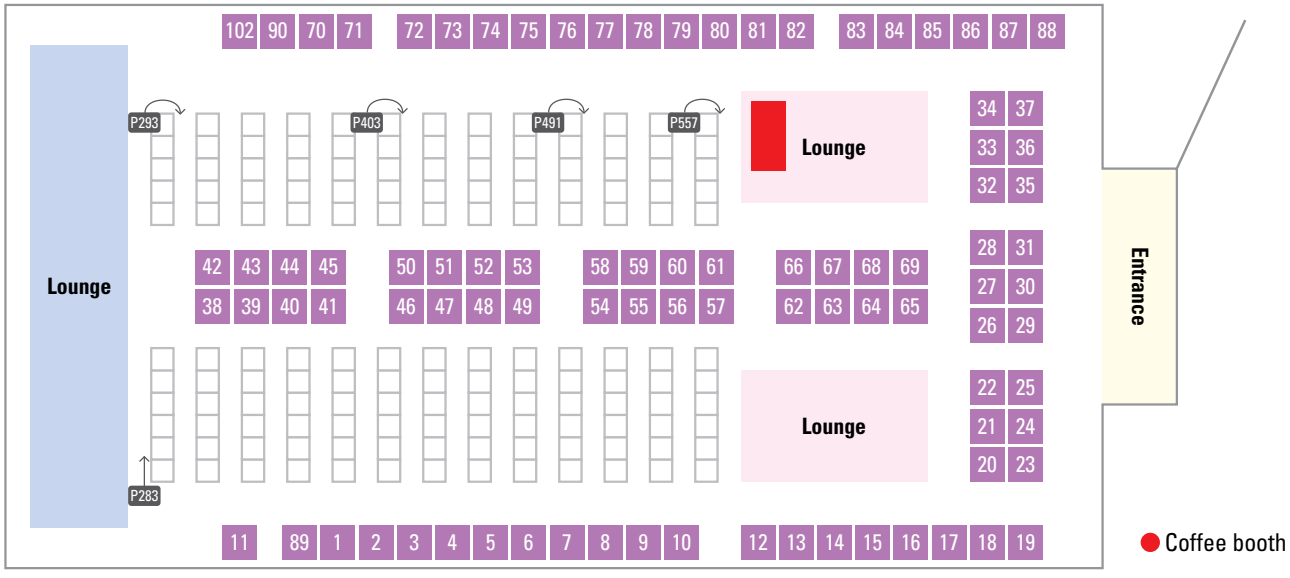
Poster Session 1



Poster No.	Session	Poster Display	Presenter Presence	Posting	Removal
P-001 ~ P-282	Poster Session 1	8.24 13:00 - 8.25 12:30 [Exhibition/Poster Hall]	8.24 15:00 - 16:35	8.24 12:00 - 13:00	8.25 12:30 - 13:00

Poster No.	Category
P-001 ~ P-059	Mechanisms of Brain Disorders
P-060 ~ P-143	Molecular and Cellular Neuroscience
P-144 ~ P-161	Neuroengineering
P-162 ~ P-188	Others
P-189 ~ P-213	Synapses and Circuits
P-214 ~ P-262	Systems and Computational Neuroscience
P-263 ~ P-282	Translational and Clinical Neuroscience

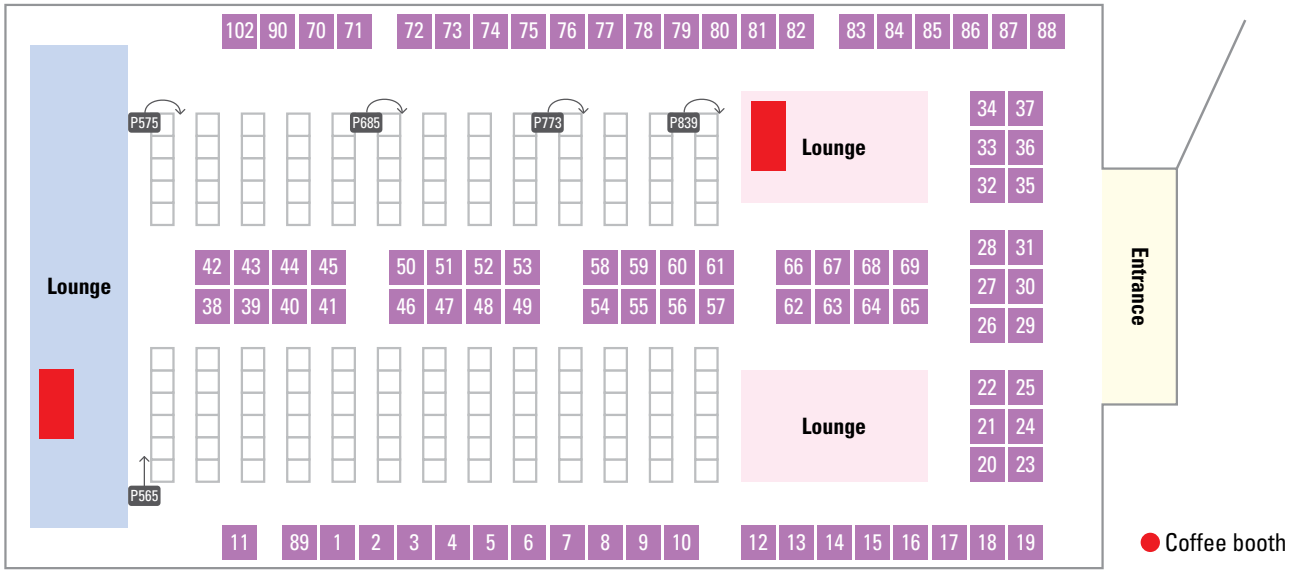
Poster Session 2



Poster No.	Session	Poster Display	Presenter Presence	Posting	Removal
P-283 ~ P-564	Poster Session 2	8.25 13:30 - 8.26 12:30 [Exhibition / Poster Hall]	8.25 16:25 - 17:40	8.25 13:00 - 13:30	8.26 12:30 - 13:00

Poster No.	Category
P-283 ~ P-341	Mechanisms of Brain Disorders
P-342 ~ P-425	Molecular and Cellular Neuroscience
P-426 ~ P-443	Neuroengineering
P-444 ~ P-471	Others
P-472 ~ P-495	Synapses and Circuits
P-496 ~ P-545	Systems and Computational Neuroscience
P-546 ~ P-564	Translational and Clinical Neuroscience

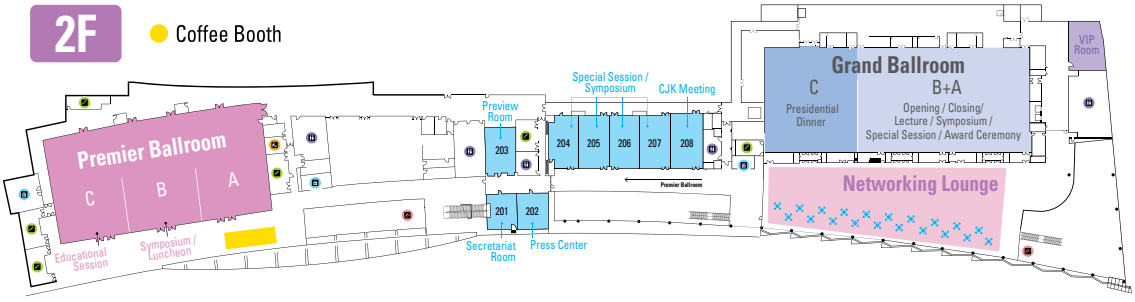
Poster Session 3



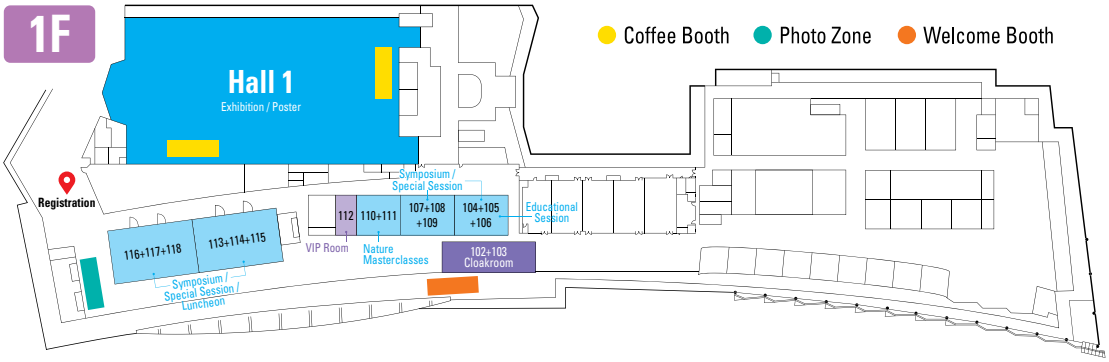
Poster No.	Session	Poster Display	Presenter Presence	Posting	Removal
P-565 ~ P-844	Poster Session 3	8.26 13:30 - 8.27 12:00 [Exhibition / Poster Hall]	8.26 16:25 - 17:40	8.26 13:00 - 13:30	8.27 12:00 - 12:30

Poster No.	Category
P-565 ~ P-621	Mechanisms of Brain Disorders
P-622 ~ P-706	Molecular and Cellular Neuroscience
P-707 ~ P-723	Neuroengineering
P-724 ~ P-751	Others
P-752 ~ P-776	Synapses and Circuits
P-777 ~ P-825	Systems and Computational Neuroscience
P-826 ~ P-844	Translational and Clinical Neuroscience

Plan



Floor	Location	Plan
2F	Grand Ballroom A+B	Opening / Closing/ Lecture / Symposium / Special Session / Award Ceremony
	Grand Ballroom C	Presidential Dinner
	Premier A	Symposium
	Premier B	Symposium / Luncheon
	Premier C	Symposium / Educational Session
	206+207	Symposium / Luncheon / Educational Session
	204+205	Symposium / Special Session
	208 (Board Room)	CJK Meeting
	203 (Board Room)	Preview Room
	201	Secretariat Room
	202	Press Center
	VIP	VIP Room



Floor	Location	Plan
1F	104+105+106	Educational Session / Symposium
	107+108+109	Symposium / Special Session
	110+111	Nature Masterclasses
	113+114+115	Symposium
	116+117+118	Symposium / Luncheon
	112	VIP Room
	102+103	Cloakroom
	Hall 1	Exhibition / Poster

Exhibition Booth Map

KSBNS 2025
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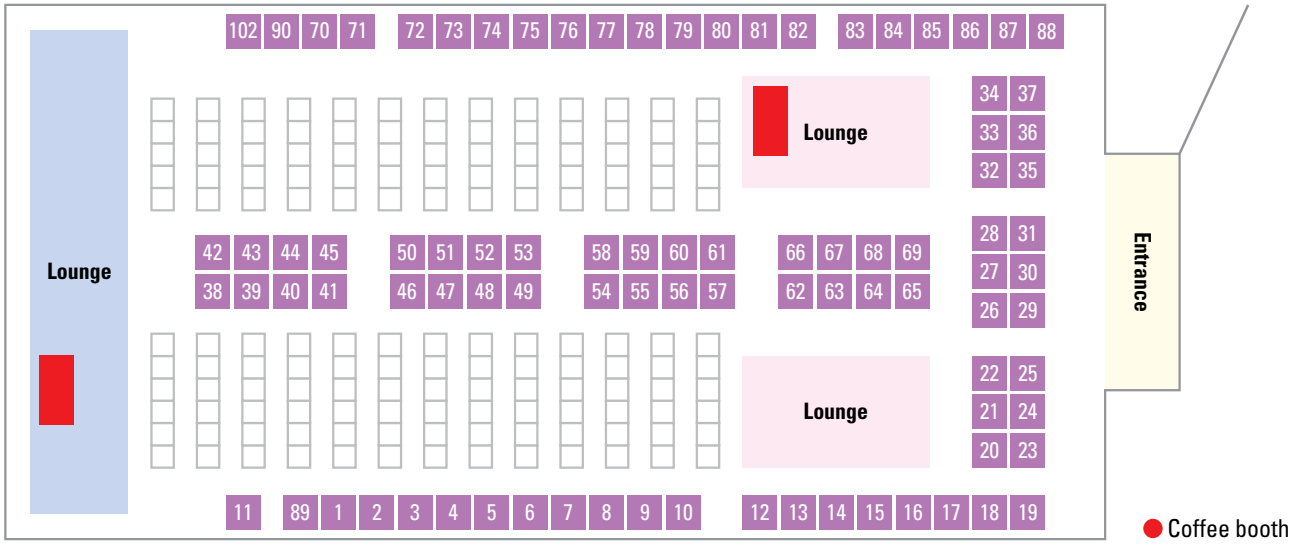


B-N.	Name of Company	B-N.	Name of Company
1, 2	Nikon Instruments Korea	54	Packgene Biotech
3	Chinese Neuroscience Society	55, 56	GaonBio
4	Hanwha Life Financial Services	57	Sang Chung Commercial Co., Ltd.
5	Cyagen	58, 59	BIOENGINE Inc.
6	VIUS Inc	60, 61	RWD Life Science Co., Ltd.
7	Nanoglia, Inc.	62, 63	IVIM Technology, Inc.
8	Bioclone Corp.	64, 65	Flashomics Corp.
9	DAWINBIO	66, 67	Bio-Medical Science Co., Ltd.
10	Neumous Inc.	68, 69	Live Cell Instrument Co. Ltd.
11	EVIDENT KOREA CO.,LTD	70	Experimental Neurobiology
12	SpikeGadgets	71	JINSUNG INSTRUMENTS, INC.
13	RAONBIO	72	Lifetech Inc.

Exhibition Booth Map

B-N.	Name of Company	B-N.	Name of Company
14	Ezdiatech Inc.	73	Bio-imaging Data Curation Center (Korea Basic Science Institute)
15	KOMABIOTECH		
16, 17	Thermo Fisher Scientific	74	MedChemExpress
18	CHAYON Loaboratories Inc.	75	New England Biolabs Korea
19	VIVO Solutions	76	LNP solution Inc.
20	Neurogrin	77	Tomocube
21, 22	Kim & Friends	78	Cell Signaling Technology
23, 24	JW Pharmaceutical	79	DAON BioSciences
25	Bruker Korea Co.,Ltd	80	Korea Institute of Science and Technology BSI
26	MAGICTREE	81	Ajou University Medical Center
27, 28, 30, 31	Scitech Korea Inc.	82	KRIBB NPRC
29	Bruker Fluorescence Microscopy	83	Daegu-Gyeongbuk Medical Innovation Foundation
32, 33	Cellution Inc.		
34	Ecocell Co., Ltd	84	Seoul National University Hospital Brain Bank
35	ZEISS	85	1st PhileKorea
36	Preclina Inc.	86	MIRAE STC
37	IBS Center for Cognition and Sociality	87	MDPI Korea
38	B2BIO,Inc.	88	ITSBIO
39	Bio-Techne Korea	89	YoungIn Scientific
40	Rhino Bio, Inc.	90	MetLife
41	MDxK	91, 92	Hanmi Pharmaceutical
42	Takara Korea Biomedical Inc.	93, 94	Korea Otsuka Pharmaceutical
43, 44	IMsystem Co., Ltd.	95	GemPharmatech
45	Optic Solution	96	NeuroLynx
46	Tecsco Korea Co.,LTD.	97	DONG-A ST
47	Signal Transduction and Targeted Therapy	98	Novonordisk
48	Woosung Cryotech Co,.LTD	99	Handok
49	Transcend Vivoscope	100	VectorBuilder Inc.
50, 51	SCIcube Co., LTD. (Leica Microsyctems)	101	Johnson&Johnson
52, 53	Gbrain Inc.	102	IWOO SCIENTIFIC CORPORATION

Presidential Lecture 1

Glial control of brain circuits and brain tumors

Benjamin Deneen (Baylor College of Medicine)

Date August 25 Time 17:40-18:30 Venue Grand Ballroom
Organizer **C. Justin Lee** (Institute for Basic Science)
Moderator **C. Justin Lee** (Institute for Basic Science)

Pioneer in Glial Biology and Cancer Neuroscience

Discovered that astrocytes regulate brain circuits governing memory, pain, emotion, and sensory processing.
Identified molecular pathways by which astrocytes interact with neurons during health and disease.
Pioneered the field of cancer neuroscience, linking glioma progression with neural circuitry.
Published 100+ papers in Nature, Science, Neuron, and other leading journals.

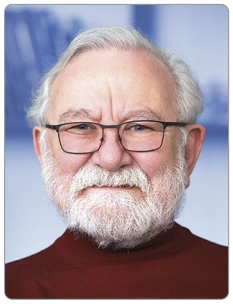
Main Publication

· Learning-Associated Astrocyte Ensembles Regulate Memory Recall – 2025, Nature
· Induction of astrocytic Slc22a3 regulates sensory processing through histone serotonylation – 2023, Science
· Inhibitory input directs astrocyte morphogenesis through glial GABABR – 2023, Nature
· PIK3CA variants selectively initiate brain hyperactivity during gliomagenesis – 2020, Nature
· Identification of diverse astrocyte populations and their malignant analogs – 2017, Nature Neuroscience

Key Publication

· **O'Donnell Award** (2024), Texas Academy of Medicine, Engineering, Science and Technology
· **NINDS Outstanding Investigator Award** (2023)
· **Sontag Foundation Distinguished Alumni Award** (2023).
· **DeBakey Excellence in Research**, Baylor College of Medicine (2015, 2021).
· Appointed **Dr. Russel J. and Marian K. Blattner Endowed Chair** at BCM (2019).
· **Scientific Research Award** (2017), National Multiple Sclerosis Society
· **Distinguished Scientist Award** (2011) Sontag Foundation
· **V Scholar Award** (2010) V Foundation for Cancer Research

Presidential Lecture 2



Targeting the Cell's Stress Pathways for Therapeutic Benefit

Peter Walter (Altos Labs)

Date August 27 Time 14:30-15:20 Venue Grand Ballroom
Organizer Bong-Kiun Kaang (Institute for Basic Science)
Moderator Bong-Kiun Kaang (Institute for Basic Science)

Supported By

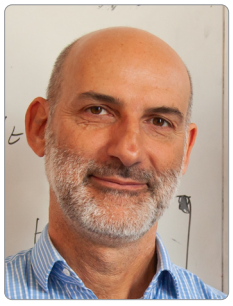
Dr. Peter Walter is a world-renowned scientist whose pioneering work on the Integrated Stress Response (ISR) has profoundly influenced our understanding of brain function and cognitive disorders. He discovered ISRIB, a small-molecule ISR inhibitor that enhances memory without toxicity, and identified its molecular target, eIF2B. His recent studies, in collaboration with Dr. Mauro Costa-Mattioli, explore the role of ISR in neurological diseases such as Down syndrome, addiction, and traumatic brain injury. Dr. Walter's research has catalyzed industry efforts to develop ISR-targeted cognitive enhancers and has earned him prestigious honors, including the Lasker Award and the Breakthrough Prize.

· 1997-2022 Howard Hughes Medical Institute (HHMI)
· 1982-1983 Assistant professor at Rockefeller University from 1982–1983
· 1983~2022 Professor at the University of California, San Francisco (UCSF)
· 2021~ Director of the Bay Area Institute of Science at Altos Lab

Main Publication

· Translation from the 5' untranslated region shapes the integrated stress response - 2016, Science
· Pharmacological brake-release of mRNA translation enhances cognitive memory - 2013, Elife
· The unfolded protein response in fission yeast modulates stability of select mRNAs to maintain protein homeostasis - 2012, Elife
· Unfolded proteins are Ire1-activating ligands that directly induce the unfolded protein response - 2011, Science
· An ER-mitochondria tethering complex revealed by a synthetic biology screen - 2009, Science

KSBNS Plenary Lecture 1



The odds of a decision

Matteo Carandini (University College London)

Date August 24 **Time** 17:40-18:30 **Venue** Grand Ballroom
Organizer Seung-Hee Lee (Korea Advanced Institute of Science and Technology)
Moderator C. Justin Lee (Institute for Basic Science)

Dr. Carandini's research focuses on understanding large-scale neural computations in the mouse brain and their impact on perception and cognition. A pioneer in neural recording technology, Dr. Carandini is the leader of the Neuropixels consortium, which has revolutionized electrophysiology by enabling the simultaneous recording of thousands of neurons. He is also a founding member of the International Brain Laboratory (IBL), a global collaboration dedicated to unraveling decision-making mechanisms across the mouse brain. Beyond his groundbreaking research, Dr. Carandini is a strong advocate for open-access publishing and scientific collaboration. His work is widely cited, and he has served as a keynote and plenary speaker at major neuroscience conferences, including SfN and FENS.

Education

· 1990, Laurea in Mathematical Physics, University of Rome
· 1995, PhD in Neural Science, New York University, "Linearity, gain control, and spike encoding in the primary visual cortex"
· 1996, Postdoctoral fellow, Northwestern University
· 1997, Research Associate, New York University
· 1998, Oberassistent, University of Zurich and ETH Zurich

Main Publication

· Peters, Fabre, Steinmetz, Harris, and Carandini, Striatal activity topographically reflects cortical activity patterns, Nature, 2021
· Bugeon, Duffield, Dipoppa, Prankerd …, Isogai, Carandini, and Harris, A transcriptomic axis predicts state modulation of cortical interneurons, Nature, 2022
· Bimbard, Sit, Lebedeva, Bai Reddy, Harris, and Carandini, Behavioral origin of sound-evoked activity in visual cortex, Nature Neuroscience, 2023
· Van Beest, Bimbard, Fabre, Dodgson, Takacs, Coen, Lebedeva, Harris, and Carandini, Tracking neurons across days with high-density probes, Nature Methods, 2024
· International Brain Laboratory et al, Reproducibility of in vivo electrophysiological measurements in mice, eLife, 2025

KSBNS Plenary Lecture 2

Building mental models for flexible behaviour in humans and macaques

Matthew F. S. Rushworth (University of Oxford)

Date August 24 **Time** 17:40-18:30 **Venue** Grand Ballroom
Organizer Min Whan Jung (Korea Advanced Institute of Science and Technology)
Moderator Min Whan Jung (Korea Advanced Institute of Science and Technology)

Conducted groundbreaking research on neural circuits involved in decision-making, learning, and social cognition.
Made significant contributions to understanding the roles of the frontal lobe and cingulate cortex.
Developed innovative research methods by integrating various techniques such as fMRI, EEG, diffusion-weighted imaging, and transcranial magnetic stimulation. Elucidated mechanisms for learning from personal experience and observing others' behavior.
His research has had a substantial impact on understanding cognitive flexibility, adaptive decision-making, and social behavior disorders. As a Fellow of the Royal Society, he continues to provide new insights into the brain's capacity for complex thought and behavior.

Main Publication

· Sallet, Jérôme, et al. "Social network size affects neural circuits in macaques." Science 334.6056 (2011): 697-700.
· Kolling, Nils, et al. "Neural mechanisms of foraging." Science336.6077 (2012): 95-98.
· Rushworth, Matthew FS, et al. "Valuation and decision-making in frontal cortex: one or many serial or parallel systems?." Current opinion in neurobiology 22.6 (2012): 946-955.
· Gould, Ian C., et al. "Effects of decision variables and intraparietal stimulation on sensorimotor oscillatory activity in the human brain." Journal of
· Neuroscience 32.40 (2012): 13805-13818.

Key Publication

· Trier, Hailey A., et al. "Emotions and individual differences shape human foraging under threat." Nature Mental Health (2025): 1-22.
· Garud, Sankalp, et al. "Friend Request Accepted: Fundamental Features of Social Environments Determine Rate of Social Affiliation." bioRxiv (2025): 2025-02.
· Trier, Hailey A., et al. "A distributed subcortical circuit linked to instrumental information-seeking about threat." Proceedings of the National Academy of Sciences 122.3 (2025): e2410955121.
· Miyamoto, Kentaro, et al. "Asymmetric projection of introspection reveals a behavioural and neural mechanism for interindividual social coordination." Nature Communications 16.1 (2025): 295.

CJK Plenary Lecture 1

Decoding the neural mechanisms of depression: insights through ketamine's pharmacological lens

Hailan Hu (Zhejiang University)

Date August 25 **Time** 13:30-14:20 **Venue** Grand Ballroom
Organizer Greg Seong-Bae Suh (Korea Advanced Institute of Science and Technology)
Moderator Greg Seong-Bae Suh (Korea Advanced Institute of Science and Technology)

Pioneer in Emotion and Social Behavior Circuitry

· Identified the neural mechanism underlying the winner effect, by which individuals increase their chance of winning after previous victories
· Discovered the neural mechanism of ketamine's rapid antidepressant effects via the lateral habenula.
· Identified how astroglial Kir4.1 channels drive bursting activity in depression models.
· Elucidated synaptic mechanisms of social dominance and hierarchy regulation in prefrontal cortex.
· Published extensively in Nature, Science, Neuron, and Nature Neuroscience.

Key Awards and Appointments

· IBRO-Kemali International Prize (2020) – for contributions to emotion circuitry and depression research.
· L'Oréal–UNESCO International Award for Women in Science (2022).
· Recognized by Cell Press as one of 50 Inspiring Scientists (2024).
· Professor and Dean at Zhejiang University School of Brain Science and Brain Medicine.
· Former faculty of Institute of Neuroscience, Chinese Academy of Sciences

Main Publication

· Ketamine blocks bursting in the lateral habenula to rapidly relieve depression – *2018, Nature*
· Astroglial Kir4.1 in the lateral habenula drives neuronal bursts in depression – *2018, Nature*
· Bidirectional control of social hierarchy by synaptic efficacy in medial prefrontal cortex – *2011, Science*
· History of winning remodels thalamo-PFC circuit to reinforce social dominance – *2017, Science*
· Circuits and functions of the lateral habenula in health and in disease – *2020, Nature Reviews Neuroscience*

CJK Plenary Lecture 2

Unlocking the gut-brain connection in Alzheimer's: vagus nerve transport of pathogenic proteins as a BBB bypass for therapeutic innovation

Inhee Mook-Jung (Seoul National University)

Date August 26 Time 13:30-14:20 Venue Grand Ballroom
Organizer Hoon Ryu (Korea Institute of Science and Technology)
Moderator Hoon Ryu (Korea Institute of Science and Technology)

Prof. Mook-Jung has been researching the pathogenesis of Alzheimer's disease (AD). She has been investigating the effects of amyloid beta and tau on the normal physiology of brain cells (astrocytes, neurons, microglia, and endothelial cells of the blood-brain barrier). Additionally, she is intrigued by the interaction between the peripheral immune system and the central nervous system in AD. Together with clinical specialists, she has also investigated therapeutic targets and blood biomarkers for the early detection of AD. She has published more than 220 SCI papers and holds 37 patents. Since 2020, Dr. Mook-Jung has been serving as the director of the Korea Dementia Research Center (KDRC).

Key Awards and Appointments

· 2023 - Order of Science and Technology Innovation Merit
· 2023 - President, The Korean Society for Neurodegenerative Disease
· 2021 - President, Women's Bioscience Forum
· 2020 - Korean Academy of Science and Technology (KAST), Physiology and Medicine Award
· 2015 - Korean L'Oréal-UNESCO For Women in Science Award
· 2014-2015 - Delegate of Korea, Session of Alzheimer's Disease, OECD

Main Publication

· Differentiating visceral sensory ganglion organoids from induced pluripotent stem cells - 2024, Nat Methods
· Microglia Gravitate toward Amyloid Plaques Surrounded by Externalized Phosphatidylserine via TREM2 - 2024, Adv Sci
· Multi-Omics-Based Autophagy-Related Untypical Subtypes in Patients with Cerebral Amyloid Pathology- 2022, Adv Sci
· Transfer of a healthy microbiota reduces amyloid and tau pathology in an Alzheimer's disease animal model- 2019, Gut
· A Breakdown in Metabolic Reprogramming Causes Microglia Dysfunction in Alzheimer's Disease - 2019, Cell Metab

CJK Plenary Lecture 3

Deciphering principles of molecular and circuit mechanisms underlying animal behavior

Ikue Mori (Nagoya University)

Date August 27 Time 11:05-11:55 Venue Grand Ballroom

Dr. Ikue Mori is a distinguished neuroscientist who has elucidated the molecular, cellular, neural, and systemic mechanisms involved in learning, memory, and decision-making using C. elegans as a model system.
She is also actively developing C. elegans-based animal models to investigate the molecular basis of human diseases and aging.
In recognition of her outstanding scientific achievements, she received the Medal of Honor with Purple Ribbon from the Emperor of Japan and the Toray Science and Technology Prize in 2023. She has published numerous papers in high-impact journals including Nature and Science.

Key Awards and Appointments

· Awarded the Toray Science and Technology Prize (a prestigious neuroscience award in Japan) in 2023
· Medal of Honor with Purple Ribbon (awarded by the Japanese government for academic excellence) in 2017
· Chunichi Cultural Award in 2016
· Kihara Prize and Tokizane Award (First female recipient; prestigious neuroscience award in Japan) in 2013
· Received Saruhashi Prize for outstanding women scientists in Japan and Inoue Prize for Science in 2006

Education

· 2004 ~ Professor in Nagoya University, Japan
· 1998-2004- Assistant Professor in Nagoya University, Japan
· 1989~1998 - Assistant Professor, Department of Biology, Kyushu University, Fukuoka, Japan
· 1988- PhD. in C. elegans Genetics Washington University of Medicine, USA
· 1983 – M.S. in Population Genetics, Ochanomizu University, Japan
· 1980 - B.S. in Biology, Ochanomizu University, Japan

Main Publication

· Context-dependent operation of neural circuits underlies a navigation behavior in Caenorhabditis elegans (2020) Proc. Natl. Acad. Sci. U. S. A. 117, 6178-6188.
· Presynaptic MAST kinase controls opposing postsynaptic responses to convey stimulus valence in Caenorhabditis elegans (2020) Proc. Natl. Acad. Sci. U. S. A. 117, 1638-1647
· Single-Cell Memory Regulates a Neural Circuit for Sensory Behavior (2016) Cell Rep. 14, 11–21.
· Regulation of behavioral plasticity by systemic temperature signaling in Caenorhabditis elegans (2011) Nat. Neurosci. 14, 984–992.
· Temperature sensing by an olfactory neuron in a circuit controlling behavior of C. elegans (2008) Science . 320: 803-7.
· Neural regulation of thermotaxis in Caenorhabditis elegans (1995) Nature , 376, 344-348.

Special Lecture 1

Lighting up, controlling, and restoring neural signaling in the living mouse brain

Won Do Heo (Korea Advanced Institute of Science and Technology)

Date August 25 Time 11:45-12:35 Venue Grand Ballroom

Organizer Eunji Cheong (Yonsei University)

Moderator Eunji Cheong (Yonsei University)

Supported By
경암교육문화재단

Professor Won contributed to the fields of bio-imaging and optogenetics by developing innovative tools and techniques
Focused on understanding cellular functions such as cell growth, migration, death, cancer metastasis, and brain functions through the lens of signaling pathways. Also, he developed and utilized a variety of optogenetic and bio-imaging technologies, including the development of tools like LARIAT and optoSTIM1and he published more than 160 papers, which are cited more than 12,000 times (H-index 54).

Key Awards

· Prize of Academic Excellence, KAIST (2022)
· Scientist of the Month, Korea Ministry of Education, Science, and Technology (2017)
· KAIST KI Excellence Research Award, KAIST Institute (2016)
· Gyeongsang PEOPLE, Gyeongsang National University (2009)
· KOSEN award, The Global Network of Korean Scientists and Engineers (2003)

Main Publication

· Programmable mRNA modification with CRISPR-Cas system - 2025, Nat Chem Biol
· Real-time visualization of structural dynamics of synapses in live cells in vivo - 2024, Nat Methods
· Label-free multiplexed microtomography of subcellular dynamics using generalizable deep learning.- 2021, Nat Cell Biol
· Opto-vTrap, an optogenetic probe for reversible inhibition of vesicular release, synaptic transmission and behavior- 2021, Neuron
· Optogenetic control of mRNA localization and translation in live cells - 2020, Nat Cell Biol

Special Lecture 2

Ultrasound in neuroscience: from functional imaging to read/write brain machine interfaces

Mickael Tanter (Institute Physics for Medicine Paris)

Date August 26 **Time** 11:35-12:35 **Venue** Grand Ballroom

Organizer Jung Ho Hyun (Daegu Gyeongbuk Institute of Science and Technology)
Alan Jung Park (Seoul National University)

Moderator Jung Ho Hyun (Daegu Gyeongbuk Institute of Science and Technology)
Alan Jung Park (Seoul National University)

Supported By

ICONEUS
REVEALING THE BRAIN

· Developed ultrafast ultrasound imaging and functional brain vascular imaging (e.g., ultrasound localization microscopy)
· Co-developed pivotal diagnostic tools (e.g., Fibroscan®)
· Published 400+ peer-reviewed articles (h-index: 106; 45,000+ citations)
· Co-inventor on 50+ biomedical engineering patents
· Active member of multiple high-profile scientific societies (French Academy of Science, European Academy of Science)

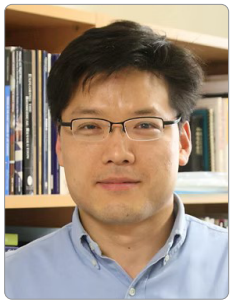
Key Awards

· Elected as a Member of the **French Academy of Science in 2025**.
· Awarded the **ERC Synergy Grant (NeuroSonoGene project)** in 2023.
· Appointed as the **Gordon Moore Professor at the California Institute of Technology (Caltech)** in 2022.
· Received numerous prestigious awards, including the IEEE Ultrasonics Society's **Carl Hellmuth Hertz Award** (2017) and the French Foundation for · Medical Research's Grand Prix (2016).
· Co-founded several medical technology companies, such as **SEISME Inc., SUPERSONIC IMAGINE Inc., CARDIAWAVE Inc., ICONEUS Inc.,** and **EMYOSOUND Inc.**.

Main Publication

· **Functional ultrasound localization microscopy reveals brain-wide neurovascular activity on a microscopic scale** - 2022, Nat Methods
· **Transcranial ultrafast ultrasound localization microscopy of brain vasculature in patients** - 2021, Nat Biomed Eng
· **Adaptive modulation of brain hemodynamics across stereotyped running episodes** - 2020, Nature Communications
· **Functional ultrasound imaging of the brain reveals propagation of task-related brain activity in behaving primates** - 2019, Nat Commun
· **Functional ultrasound imaging of intrinsic connectivity in the living rat brain with high spatiotemporal resolution** - 2014, Nat Commun

Joseph Jin Chang – GNT Pharma Research Award



Award Lecture 1
Stereociliary links: Sound mechanotransduction and control of hearing

Chul Hoon Kim (Yonsei University College of Medicine)

Date August 24 Time 16:55-17:35 Venue Grand Ballroom

Supported By

Biography & Research

Chul Hoon Kim, MD, PhD is a Professor in the Department of Pharmacology at Yonsei University College of Medicine. He specializes in neuropsychiatric disease research, with a particular focus on uncovering the underlying mechanisms. His research interests span synaptic plasticity, neurodevelopmental disorders, epilepsy, and deafness. Dr. Kim's laboratory employs genetic, organoid and molecular biology approaches to identify genes associated with brain diseases and to elucidate how these genetic factors contribute to pathogenesis.

Education & Professinal Experiences

1988-1995 Yonsei University College of Medicine, M.D.

1995-2000 Department of Pharmacology, Yonsei University College of Medicine, Ph.D.

2003-2006 NIH, Postdoc

2006-present Department of Pharmacology, Yonsei University College of Medicine, Professor

Selected Honors

2016 Research excellence award of the year 2015 from Yonsei

2015 Pfizer Medical Research Award

2011 Lecturer of the year award from Yonsei

2010 Young investigator award from Korea Institute of Medicine

2007 AstraZeneca Virtual Research Institute Program

Scitech Korea Young Scientist Award

Award Lecture 2
When the sugar code goes wrong in the brain

Boyoung Lee (Institute for Basic Science)

Date August 27 Time 13:00-14:25 Venue Grand Ballroom

Supported By
Scitech Korea

Biography & Research

Dr. Boyoung Lee is a dedicated neuroscientist whose work explores the intricate molecular processes behind neuropsychiatric disorders. She earned her Ph.D. in Neuroscience from The Ohio State University in 2007, where she investigated the role of MAPK-CREB signaling pathways in epilepsy and circadian rhythms under the mentorship of Dr. Karl Obrietan. Following her Ph.D., she pursued postdoctoral training at Yale University in the laboratory of Dr. Ronald Duman. There, her research centered on the mechanisms of depression, particularly the role of ketamine as a rapid-acting antidepressant via mTOR-dependent local protein synthesis. She also explored cell-type specific NMDA receptor modulation as a potential therapeutic target for post-traumatic stress disorder (PTSD). Dr. Lee then returned to South Korea, joining the Korea Institute of Science and Technology (KIST) as a postdoctoral researcher in Dr. Hee-Sup Shin's lab. She later moved with the lab to the Institute for Basic Science (IBS), where she served as a non-tenure track research fellow. Her research at IBS delved into the neural mechanisms of PTSD and autism. During this time, she also contributed to a project on glycosylation in the brain, which she found to be a unique and fascinating field.
Since November 2020, Dr. Lee has been an independent principal investigator at the Center for Cognition and Sociality at IBS. Her current work continues to explore the role of glycosylation, with a specific focus on its dynamic changes in neuropsychiatric disorders. Using multiomics techniques, she aims to uncover how alterations in glycosylation patterns, particularly on glycoproteins associated with the extracellular matrix, contribute to the pathology of these conditions. This research is a crucial step toward identifying novel therapeutic targets.

Education & Professinal Experiences

Education

1999 B.S. Department of Biology, College of Natural Science, Kon-Kuk University (Korea)
2001 M.S. Department of Molecular Biology, Plant Molecular Biology and Biotechnology Research Center, Gyeongsang National University (Korea)
2007 Ph.D. Department of Neuroscience, College of Medicine, The Ohio State University (USA)

Professional Experiences

07/01/2007~11/17/2008 Postdoctoral Researcher, The Ohio State University (Supervisor: Dr. Karl Obrietan)
01/01/2009~01/30/2010 Postdoctoral Associate, Yale University (Supervisor: Dr. Ronald S. Duman)
03/01/2010~02/28/2013 Postdoctoral Fellow, KIST (Supervisor: Dr. Hee-Sup Shin)
03/01/2013~02/28/2018 Research Fellow (non-tenure track), IBS (Supervisor: Dr. Hee-Sup Shin)
04/01/2018~03/31/2019 Postdoctoral Associate, Yale University (Supervisor: Dr. Ronald S. Duman)
04/01/2019~09/12/2020 Associate Research Scientist, Yale University (Supervisor: Dr. Ronald S. Duman)

Academic Appointments

11/01/2020~Present Senior Research Fellow, Center for Cognition and Sociality, IBS
03/01/2021~02/28/2024 Associate Professor, Basic Science, IBS campus, University of Science & Technology
12/01/2021~Present Adjunct Professor, Biomedical Engineering, UNIST
09/01/2023~Present Adjunct Professor, Department of Integrative Biotechnology, Sungkyunkwan University
03/01/2024~Present Adjunct Professor, Basic Science, IBS campus, University of Science & Technology

Selected Honors

12/31/2022 Scientist of the Year Award at IBS

Scitech Korea Young Scientist Award

Award Lecture 2
Microglia and Neural Organoids for Bridging Models to Mechanismsa

Jong-Chan Park, Ph.D. (Sungkyunkwan University)

Date August 27 Time 13:00-14:25 Venue Grand Ballroom

Supported By
Scitech Korea

Biography & Research

Jong-Chan Park is an Associate Professor at Sungkyunkwan University and working as a Neuroscientist for Brain Organoid-based Biometabolism Research.
He graduated Korea University (B.S.) and got Ph.D degree at Seoul National University under the supervision of Prof. Inhee Mook. He did the postdoctoral training with Prof. John Hardy at University College London in the UK.
His research focuses on developing advanced organoid-based disease models especially for the Alzheimer's disease or Parkinson's disease, and he published many high-impact journals such as Science Advances (2025), Nature Communications (2021), Brain (2019), Advanced Science (2025,2024,2022), and so on.

Education & Professional Experiences

2025- Current: Associate Professor, Department of Biophysics, Sungkyunkwan University, South Korea
2025-Current: Academic Committee Member of the Korea Society of Biomaterials (KSBM)
2023-Current: The Korean Society for Brain and Neural Sciences (KSBNS) Regular Member
2023-Current: International Society for Molecular Neurodegeneration (ISMND) Organizing Committee Member
2023-Current: The Korea Society for Neurodegenerative Disease (KSND) Organizing Board Member
2023-2025: Assistant Professor, Department of Biophysics, Sungkyunkwan University, South Korea
2020-2022: Postdoctoral Researcher, Department of Neurodegenerative diseases, University College London, United Kingdom
2013-2019: M.S-Ph.D. Seoul National University College of Medicine, South Korea
2008-2013: B.S. College of Life Science and Biotechnology, Korea University, South Korea

Selected Honors

2023-2025 Main PI for K-Brain Project, NRF, South Korea
2023 Sigma-Aldrich Award from the Organoid Society
2022-2027 Sejong Science Fellowship, NRF, South Korea
2021 Outstanding Research Award from the Association of Korean Neuroscientists (AKN)
2021 Outstanding Research Award from the Korean College of Geriatric Psychoneuropharmacology (KCGP)

KSBNS Reasearch Achievement Award

Award Lecture 2
When the sugar code goes wrong in the brain

Dr. Hyung Jin Choi (Institute for Basic Science)

Date August 27 Time 13:00-14:25 Venue Grand Ballroom

Supported By
Scitech Korea

Dr. Hyung Jin Choi's lab is dedicated to understanding the neural circuit mechanisms that govern motivated behaviors. The lab focuses on the drive to eat, a decision driven by the dual perspectives of evolutionary biology and clinical medicine. Securing energy is the most fundamental driver of survival, and as an endocrinologist, Dr. Choi witnessed how an excessive drive to eat contributes to major health challenges, including obesity, diabetes, and cardiovascular disease.
The lab's research is guided by a theoretical framework that deconstructs this complex drive into distinct psychological components. This framework is then tested using a multi-species approach that leverages the unique strengths of mice, monkeys, and humans. In animal models, the team applies cutting-edge neuroscience technologies—such as miniature microscopy, optogenetics, and AI-based behavioral analysis—to precisely map these components to their underlying neural circuits. These biological findings are then integrated with rich psychological measurements from human clinical studies, creating a powerful, translational model that links neural mechanisms to psychological interpretation.

Education & Professinal Experiences

2013	Seoul National University, PhD in Medicine (Molecular and Genomics)
2011	Seoul National University, MS in Internal Medicine
2002	Seoul National University, MD (Bachelor of Medicine, Bachelor of Surgery) Professional Experiences
2024.3.-Present	Professor, Department of Brain & Cognitive Sciences, Seoul National University College of Natural Sciences
2015.3.-Present	Assistant/Associate/Full Professor, Department of Anatomy and Cell Biology, Seoul National University College of Medicine
2012.3.-2015.2.	Clinical Assistant Professor, Chungbuk National University Hospital, Division of Endocrinology, Department of Internal Medicine, Korea
2010.5.-2012.2.	Clinical Fellow, Seoul National University Hospital, Korea
2009.5.-2010.4.	Researcher, Korea National Institute of Health, Korea
2003.3.-2007.2.	Resident, Seoul National University Hospital, Department of Internal Medicine, Korea

Selected Honors

2025 Lim Sung-ki Researcher Award Grand Prize 임성기연구자상 대상

2025 Ministry of Science and ICT's Scientist/Engineer of the Month Award 과학기술정보통신부 이달의 과학기술인상

2024 Minister's Commendation from the Government Awards for Contribution to the Promotion of Health and Medical Technology 보건의료기술진흥 유공자 정부포상 장관표창

2024 National Academy of Medicine of Korea-Pfizer Medical Award for Basic Medicine 한림원 화이자의학상 기초의학상

2023 Korean Association of Anatomists' Bitnal Award 대한해부학회 빛날상

Scientific Program

DAY 1(AUG 24, 2025)

KSBNS Plenary Lecture 1

17:40-18:30 Grand Ballroom

Symposium 1

13:00-14:55 Grand Ballroom

Molecular and circuit-level understanding of memory and memory related disorders

Organizer : Weidong Li(Shanghai Jiao Tong University), Ain Chung(Korea Advanced Institute of Science and Technology)
Moderator : Weidong Li(Shanghai Jiao Tong University)

Symposium 2

13:00-14:55 Premier Ballroom A

Mechanotransduction in the peripheral and central nerve system

Organizer : Bailong Xiao(Tsinghua University), Uhtaek Oh(Korea Institute of Science and Technology)
Moderator : Bailong Xiao(Tsinghua University), Uhtaek Oh(Korea Institute of Science and Technology)

Symposium 3

13:00-14:55 Premier Ballroom B

Supported by Life Science Institute

Neuroglia in diseases of cognition

Organizer : Chenju Yi(Sun Yat-sen University), Alexei Verkhratsky(University of Manchester)
Moderator : Chenju Yi(Sun Yat-sen University)

Symposium 4

13:00-14:55 Premier Ballroom C

Novel insights in sleep regulation and function

Organizer : Min Xu(Chinese Academy of Sciences), Thomas McHugh(RIKEN)
Moderator : Min Xu(Chinese Academy of Sciences), Thomas McHugh(RIKEN)

Symposium 5

13:00-14:55 Rm.113-115

The brainstem: a critical conduit for body-brain signaling

Organizer : Sung-Yon Kim(Seoul National University), Cheng Zhan(University of Science and Technology of China)
Moderator : Yu Fu(Agency for Science Technology and Research)

Symposium 6

13:00-14:55 Rm.116-118

Exploring the neuroscience of general anesthesia

Organizer : Soo-Jin Oh(Korea Institute of Science and Technology)
Moderator : Woosuk Chung(Chungnam National University), Soo-Jin Oh(Korea Institute of Science and Technology)"

Symposium 7

08:30-10:25 Grand Ballroom

Neuromodulation in psychiatry: from circuit to psychopharmacology

Organizer : Tifei Yuan(Shanghai Mental Health Center), Ji Hu(ShanghaiTech University)
Moderator : Tifei Yuan(Shanghai Mental Health Center)

Special Session 1

15:00-16:35 Rm.206-207

Supported by KDRC

Cutting-edge approaches to decoding dementia: from genomics to neuropathology

Organizer : Inhee Mook-Jung(Korea Dementia Research Center/Seoul National University)
Moderator : Inhee Mook-Jung(Korea Dementia Research Center/Seoul National University)

Award Lecture 1

16:55-17:45 Grand Ballroom

Supported by GNTPharma 지엔티파마

DAY 2(AUG 25, 2025)

Presidential Lecture 1

17:40-18:30 Grand Ballroom

Glial control of brain circuits and brain tumors 002
Benjamin Deneen(Baylor College of Medicine)

CJK Plenary Lecture 1

13:30-14:20 Grand Ballroom

Decoding the neural mechanisms of depression: insights through ketamine's pharmacological lens 003
Hailan Hu(Zhejiang University)

Special Lecture 1

11:45-12:35 Grand Ballroom

Supported by 경암교육문화재단

Lighting up, controlling, and restoring neural signaling in the living mouse brain 009
Won Do Heo(Korea Advanced Institute of Science and Technology)

Symposium 8

08:30-10:25 Premier Ballroom C

Gene delivery to the brain: applications in life sciences and gene therapy

Organizer : Hirokazu Hirai(Gunma University)
Moderator : Hirokazu Hirai(Gunma University)

1. Structural Analysis of Neural Networks Using High-Expression Adeno-Associated Virus Vectors. 048
   Hiroyuki Hioki(Juntendo University)
2. Micro-dissection of the connectivity of cerebellar input layer with GABRA6 promotor by exploiting dispersed developmental time of granule cells and computational modeling. 049
   Taegon Kim(Korea Institute of Science and Technology)
3. Long-term activity imaging of a neuronal population that sends input to a specific type of neurons via a low cytotoxic G-deleted rabies virus vector. 050
   Ken-ichi Inoue(Kyoto University)
4. Modulation of gene expression and signaling cascade in mice brain exposed to nano-neonicotinoid pesticides. 050
   Dhanshree Borkar(National Forensic Sciences University) IBRO AWARDEE
5. Nanoparticle-mediated gene delivery to enhance microglial phagocytosis for Alzheimer's disease therapy. 051
   Dong Woon Kim(Kyung Hee University)
6. A Compact GAD67 Promoter Enables Inhibitory Neuron-Specific Gene Modulation. 051
   Yuuki Fukai(Gunma University)

Symposium 9

08:30-10:25 Rm.116-118

Translational and clinical neuroscience: precision convergent medicine for treating intractable diseases, pain, and central nervous system trauma

Organizer : Inbo Han(CHA University), KiBum Lee(Rutgers, The State University of New Jersey)
Moderator : Inbo Han(CHA University), KiBum Lee(Rutgers, The State University of New Jersey)

1. Transforming CNS injury therapeutics using a novel nanotechnology-enabled extracellular vesicle platform. 054
   KiBum Lee(Rutgers, The State University of New Jersey)
2. Axon guidance gene-targeted siRNA delivery system improves neural stem cell transplantation therapy after spinal cord injury. 054
   Seil Sohn(CHA University)
3. Current perspectives on neuropathic pain. 055
   Junseok Hur(Korea University)
4. Advancing non-human primate disease models for superior translational research and enhanced clinical applicability. 055
   Seongjun Ryu(Eulji University)

Symposium 10

08:30-10:25 Rm.204-205

Synaptic balance in memory, homeostasis, and network stability

Organizer : Jong-Cheol Rah(Korea Brain Research Institute)
Moderator : Chul-Hoon Kim(Yonsei University)

Symposium 11

08:30-10:25 Rm.107-109

Neural codes across sensory systems: insights into perception and behavior

Organizer : Jeehyun Kwag(Seoul National University)
Moderator : Jeehyun Kwag(Seoul National University)

Symposium 12

10:35-12:30 Premier Ballroom A

Diverse aspects of social behaviors: recognition, remembering, and reacting

Organizer : Yong-Seok Lee(Seoul National University), Takashi Kitamura(University of Texas Southwestern Medical Center)
Moderator : Takashi Kitamura(University of Texas Southwestern Medical Center), Yong-Seok Lee(Seoul National University)

Symposium 13

10:35-12:30 Premier Ballroom B

Synapse function and diseases

Organizer : Jun Xia(Hong Kong University of Science and Technology)
Moderator : Jun Xia(Hong Kong University of Science and Technology)

Symposium 14

10:35-12:30 Premier Ballroom C

Decoding the cerebellum in health and disease

Organizer : Kazuo Kitamura(University of Yamanashi)
Moderator : Kazuo Kitamura(University of Yamanashi)

Symposium 15

10:35-12:30 Rm.113-115

Supported by 아주대학교 의과대학 뇌질환융합연구센터

Integrative approaches to neurodegeneration: insights from multiomics, inflammation, and cellular pathways

Organizer : Alexa Woo(Case Western Reserve University)
Moderator : David Kang(Case Western Reserve University)

Symposium 16

10:35-12:30 Rm.116-118

Recent advances in functional observation of ion channels and synaptic transmission

Organizer : Byung-Chang Suh(Daegu Gyeongbuk Institute of Science and Technology)
Moderator : Byung-Chang Suh(Daegu Gyeongbuk Institute of Science and Technology), Yasushi Okamura(Osaka University)

Symposium 17

10:35-12:30 Rm.204-205

Transforming brain networks - neuromodulation strategies for neuropsychiatric disorders

Organizer : Hyang Woon Lee(Ewha Womans University), Hao-Li Liu(National Taiwan University)
Moderator : Hao-Li Liu(National Taiwan University)

Symposium 18

14:30-16:25 Grand Ballroom

The brain-body-microbiome axis: a key to regulate ingestion and beyond

Organizer : Greg Seong-Bae Suh(Korea Advanced Institute of Science and Technology)
Moderator : Greg Seong-Bae Suh(Korea Advanced Institute of Science and Technology)

Symposium 19

14:30-16:25 Premier Ballroom A

Taste sensing from the tongue to the brain

Organizer : Myunghwan Choi(Seoul National University), Yong-taek Jeong(Korea University)
Moderator : Yong-taek Jeong(Korea University)

Symposium 20

14:30-16:25 Premier Ballroom B

Supported by

Updates on autism models and potential rescue strategies

Organizer : Xiang Yu(Peking University), Mihyun Bae(Korea Advanced Institute of Science and Technology)
Moderator : Xiang Yu(Peking University), Mihyun Bae(Korea Advanced Institute of Science and Technology)

Symposium 21

14:30-16:25 Rm.113-115

Innovations in imaging- and sequencing-based approaches in neurosciences

Organizer : Chang Ho Sohn(Korea Advanced Institute of Science and Technology)
Moderator : Chang Ho Sohn(Korea Advanced Institute of Science and Technology)

Symposium 22 14:30-16:25 Rm.204-205

Hurting inside and out: sensing pain and nausea

Organizer : Seungwon(Sebastian), Choi(University of Texas Southwestern Medical Center), Hojoon Lee(Northwestern University)
Moderator : Hojoon Lee(Northwestern University)

Symposium 23 14:30-16:25 Rm.206-207

Neuromodulation in the brain: new understanding and emerging methods

Organizer : Jung Ho Hyun(Daegu Gyeongbuk Institute of Science and Technology), Jae-Ick Kim(Ulsan National Institute of Science of Technology)
Moderator : Jung Ho Hyun(Daegu Gyeongbuk Institute of Science and Technology)

Symposium 24 08:30-10:25 Premier Ballroom A

Supported by 아주대학교 AJOU UNIVERSITY

Convergent mechanisms for axon regeneration and CNS repair

Organizer : Kevin (Kyung) Park(University of Texas Southwestern Medical Center), Byung Gon Kim(Ajou University)
Moderator : Byung Gon Kim(Ajou University)

Special Session 2 9:15-10:25 Rm.104-106

INSCOPIX 2P miniature microscope seminar

Special Session 3 14:30-16:25 Rm.116-118

Parkinson's disease: Unmet needs between clinical practice and basic research

Organizer : Jinyoung Youn(Samsung Medical Center)
Moderator : Young Eun Kim(Hallym University)

Special Session 4 13:00-17:00 Rm.107-109

Meet the Editor

Organizer : Chang Ho Sohn(Korea Advanced Institute of Science and Technology),
Moderator : Chang Ho Sohn(Korea Advanced Institute of Science and Technology), Eun Jeong Lee(Ajou University)

Educational Session 1 10:35-13:00 Rm.104-106

Supported by JS 진성인스트루먼트(주) JINSUNG INSTRUMENTS, INC

Optical techniques in neuroscience

Organizer : Hyeyoung Shin(Seoul National University), Hyung Jin Choi(Seoul National University), Min Whan Jung(Korea Advanced Institute of Science and Technology)
Moderator : Hyeyoung Shin(Seoul National University)

Educational Session 2 15:30-17:30 Premier Ballroom C

History of neuroscience

Organizer : C. Justin Lee(Institute for Basic Science), Seung-Hee Lee(Korea Advanced Institute of Science and Technology)
Moderator : C. Justin Lee(Institute for Basic Science)

Luncheon Seminar 1 12:30-13:30 Premier Ballroom A

Supported by ZEISS

Luncheon Seminar 2 12:30-13:30 Premier Ballroom B

Supported by Scitech Korea

Luncheon Seminar 3 12:30-13:30 Premier Ballroom C

Supported by CrestOptics

Luncheon Seminar 4 12:30-13:30 Rm.113-115

Supported by IVIM TECHNOLOGY

Luncheon Seminar 5 12:30-13:30 Rm.116-118

Supported by GemPharmatech

DAY 3(AUG 26, 2025)

KSBNS Plenary Lecture 2

17:40-18:30 Grand Ballroom

CJK Plenary Lecture 2

13:30-14:20 Grand Ballroom

Special Lecture 2

11:35-12:35 Grand Ballroom

Supported by ICONEUS

Organizer : Eunji Cheong(Yonsei University), Jung Ho Hyun(Daegu Gyeongbuk Institute of Science and Technology), Alan Jung Park(Seoul National University)

Moderator : Jung Ho Hyun(Daegu Gyeongbuk Institute of Science and Technology), Alan Jung Park(Seoul National University)

Symposium 25

08:30-10:25 Premier Ballroom B

Supported by NEUROBIOGEN 한국뇌연구원 Korea Brain Research Institute

Decoding neuro-glial interactions: the critical role of ion channels from molecules to behaviors

Organizer : Hyun-Ho Lim(Korea Brain Research Institute)
Moderator : C. Justin Lee(Institute for Basic Science)

Symposium 26

08:30-10:25 Premier Ballroom C

Neuroscience-inspired AI: computational insights into biological and artificial intelligence

Organizer : Sungho Hong(Institute for Basic Science) Jae Kwon(Max Planck Institute)
Moderator : Sungho Hong(Institute for Basic Science)

Symposium 27

08:30-10:25 Rm.113-115

Decoding Inhibition: the interplay of GABA, chloride, and astrocytes in neural function in health and disease

Organizer : Verena Untiet(University of Copenhagen) Heejung Chun(Yonsei University)
Moderator : Verena Untiet(University of Copenhagen) Heejung Chun(Yonsei University)

Symposium 28

08:30-10:25 Rm.204-205

Supported by KAIST GSMSE 의과학대학원 뇌 체성 돌연변이 연구단 Center for Brain Somatic Mutations

Epilepsy: from gene to circuit

Organizer : Won Seok Chang (Yonsei University) Eunee Lee(Yonsei University)
Moderator : Won Seok Chang (Yonsei University)

Symposium 29

08:30-10:25 Rm.206-207

Supported by 한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

Decoding the neurobiology of acupuncture through modern neuroscientific approaches

Organizer : Min-Ho Nam(Korea Institute of Science and Technology) Hi-Joon Park(Kyung Hee University)
Moderator : Min-Ho Nam(Korea Institute of Science and Technology) Hi-Joon Park(Kyung Hee University)

Symposium 30

10:35-12:30 Premier Ballroom B

Precise dissection of structural and functional features in visual system

Organizer : Jiayi Zhang(Fudan University) Hailan Hu(Zhejiang University)
Moderator : Wei Li(National Institutes of Health) Jiayi Zhang(Fudan University)

Symposium 31

10:35-12:30 Premier Ballroom C

Supported by 한국뇌연구원 Korea Brain Research Institute

Frontiers in addiction: linking neural mechanisms to public health strategies

Organizer : Ja Wook Koo(Korea Brain Research Institute), Heh-In Im(Korea Institute of Science and Technology)
Moderator : Ja Wook Koo(Korea Brain Research Institute)

Symposium 32

10:35-12:30 Rm.113-115

Supported by KAIST Brain Science Institute

Connecting the Dots: illuminating the brain from connectivity to function

Organizer : Jinhyun Kim(Korea Institute of Science and Technology), Jong-Hyun Park(Korea Institute of Science and Technology)
Moderator : Jinhyun Kim(Korea Institute of Science and Technology), Jong-Hyun Park(Korea Institute of Science and Technology)

Symposium 33

10:35-12:30 Rm.116-118

Neuroscience of schizophrenia: from structure to function

Organizer : Minah Kim(Seoul National University)
Moderator : Jun Soo Kwon(Hanyang University)

Symposium 34

10:35-12:30 Rm.116-118

Local mRNA translation in axon development, health and function

Organizer : Yongcheol Cho(Daegu Gyeongbuk Institute of Science and Technology)
Moderator : Yongcheol Cho(Daegu Gyeongbuk Institute of Science and Technology)

Symposium 35

14:30-16:25 Grand Ballroom

Supported by

Synaptic development, function, and brain disorders

Organizer : Eunjoon Kim(Korea Advanced Institute of Science and Technology)
Moderator : Eunjoon Kim(Korea Advanced Institute of Science and Technology)

Symposium 36

14:30-16:25 Premier Ballroom A

Computational neuroethology of social and cognitive behaviors

Organizer : Jeongjin Kim(Korea Institute of Science and Technology), Ain Chung(Korea Advanced Institute of Science and Technology)
Moderator : Jeongjin Kim(Korea Institute of Science and Technology), Ain Chung(Korea Advanced Institute of Science and Technology)

Symposium 37

14:30-16:25 Premier Ballroom B

Cross-regional brain circuit development: from neural differentiation to functional brain networks

Organizer : Keiko Tanaka-Yamamoto(Korea Institute of Science and Technology), Yoko Yazaki-Sug(Okinawa Institute of Science and Technology)
Moderator : Keiko Tanaka-Yamamoto(Korea Institute of Science and Technology), Yoko Yazaki-Sug(Okinawa Institute of Science and Technology)

Symposium 38

14:30-16:25 Premier Ballroom C

Molecular probing of cognitive processes

Organizer : Haruhiko Bito(The University of Tokyo), Xiao-Hong Xu(Fudan University)
Moderator : Haruhiko Bito(The University of Tokyo), Xiao-Hong Xu(Fudan University)

Symposium 39

14:30-16:25 Rm.113-115

Next-generation genetically encoded sensors and actuators for brain exploration

Organizer : Sangkyu Lee(Institute for Basic Science)
Moderator : Sangkyu Lee(Institute for Basic Science)

Symposium 40

14:30-16:25 Rm.116-118

Basic and translational researches on myelination and demyelination

Organizer : Hwan Tae Park(Dong-A University), Hyun-Jeong Yang(University of Brain Education)
Moderator : Hwan Tae Park(Dong-A University)

Symposium 41

14:30-16:25 Rm.206-207

Pleiotropic roles of mitochondria in neurobiology

Organizer : Seok-Kyu Kwon(Korea Institute of Science and Technology)
Moderator : Jun Young Heo(Chungnam National University), Seok-Kyu Kwon(Korea Institute of Science and Technology)

Symposium 42 09:00-10:55 Grand Ballroom

Unlocking pathophysiological and novel therapeutic mechanisms for mood disorders: insights from synapse research

Organizer : Ji-Woon Kim(Kyung Hee University)
Moderator : Ji-Woon Kim(Kyung Hee University)

Special Session 5 08:30-10:25 Grand Ballroom

Hormonal and neural control of metabolism in obesity and diabetes

Organizer : Sung Hee Choi(Seoul National University), Hyung Jin Choi(Seoul National University)
Moderator : Min-Seon Kim(Ulsan University), Hyung Jin Choi(Seoul National University)

Special Session 6 10:35-12:30 Rm.204-205

Supported by ISTeR Korea Center for Gendered Innovations for Science and Technology Research

Spotlight on sexual dimorphism: Analyzing the importance of sex and gender analysis in neuroscience research

Orgnizer : Frank Kirchhoff(University of Saarland), Heisook Lee(Korea Center for Gendered innovations for Science and Technology), Mridula Bhalla(Institute for Basic Science), Heajin Kim(Korea Center for Gendered innovations for Science and Technology)
Moderator : Frank Kirchhoff(University of Saarland)

Educational Session 3 10:00-12:30 Rm.104-106

Supported by 라이노바이오(주)

Miniature brain models: from generation to application in studying brain development and function

Organizer : Jin-A Lee(Hannam University), Ki-Jun Yoon(Korea Advanced Institute of Science and Technology), Jinju Han(Korea Advanced Institute of Science and Technology), Jinsoo Seo(Yonsei University)

Educational Session 4 15:00-17:00 Rm.104-106

Supported by IBRO

Advancing neuroscience futures: a career development workshop

Organizer : Jaekyung Kim(Korea Advanced Institute of Science and Technology), Gunsoo Kim(Korea Brain Research Institute)
Moderator : Jaekyung Kim(Korea Advanced Institute of Science and Technology)

Luncheon Seminar 6 12:30-13:30 Premier Ballroom A

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Luncheon Seminar 7-1 12:30-13:30 Premier Ballroom B

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Luncheon Seminar 7-2 12:30-13:30 Premier Ballroom B

Supported by 식품의약품안전처 식품의약품안전평가원

Luncheon Seminar 8

12:30-13:30 Premier Ballroom C

Supported by BRUKER

Luncheon Seminar 9

12:30-13:30 Rm.113-115

Supported by BMS

Luncheon Seminar 10

12:30-13:30 Rm.116-118

Supported by BRUKER

DAY 4(AUG 27, 2025)

Presidential Lecture 2

14:30-15:20 Grand Ballroom

Supported by

Targeting the cell's stress pathways for therapeutic benefit 003
Peter Walter(Altos Labs)

CJK Plenary Lecture 3

11:05-11:55 Grand Ballroom

Deciphering principles of molecular and circuit mechanisms underlying animal behavior 008
Ikue Mori(Nagoya University)

Symposium 43

09:00-10:55 Premier Ballroom A

Supported by

Advancing neuroscience futures: a career development workshop

Organizer : Ruotian Jiang(Sichuan University), Wuhyun Koh(Institute for Basic Science)
Moderator : Ruotian Jiang(Sichuan University), Kyungchul Noh(Ajou University)

1. A novel form of region-specific astrocyte morphological plasticity involved in instinct behaviors. 196
   Ruotian Jiang(Sichuan University)
2. Divergent roles of prefrontal astrocytes in social dominance behavior and victory. 196
   Kyungchul Noh(Ajou University)
3. Prefrontal cortex astrocytes modulate distinct neuronal populations to control anxiety-like behavior. 197
   Xinzhu Yu(University of Illinois)
4. An astroglial basis of major depressive disorder: molecular, cellular, and circuit heterogeneity. 198
   Xiong Cao(Southern Medical University)
5. Astrocytic phagocytosis during sleep controls systems consolidation. 198
   Won-Suk Chung(Korea Advanced Institute of Science and Technology)

Symposium 44

09:00-10:55 Premier Ballroom B

Supported by

Audiovisual processing in rodents and marmosets

Organizer : Seung-Hee Lee(Korea Advanced Institute of Science and Technology), Soo Hyun Park(Korea Advanced Institute of Science and Technology)
Moderator : Seung-Hee Lee(Korea Advanced Institute of Science and Technology), Soo Hyun Park(Korea Advanced Institute of Science and Technology)

1. Orthogonalization of spontaneous and stimulus-driven activity by hierarchical neocortical areal network in primates. 200
   Kenichi Ohki(The University of Tokyo)
2. Synaptic molecules tune neuronal feature selectivity: novel in vivo imaging techniques and gene therapy development. 200
   Ingie Hong(Johns Hopkins University)
3. Dynamic visual processing in marmoset extrastriate cortex. 201
   Soo Hyun Park(Korea Advanced Institute of Science and Technology)
4. Dendritic and circuit computation for flexible decision-making. 201
   Ninglong Xu(Chinese Academy of Sciences)
5. Balancing flexibility and stability during auditory reversal learning. 202
   Seung-Hee Lee(Korea Advanced Institute of Science and Technology)

Symposium 45

09:00-10:55 Premier Ballroom C

Brain cell atlas and technology

Organizer : Shiping Liu(BGI-Research), Ying Lei(BGI-Research)
Moderator : Linqing Feng(Zhejiang Lab)

Symposium 46

09:00-10:55 Rm.116-118

Emerging mechanisms in white matter injury: autoimmunity, vascular dysfunction, and lipid metabolism

Organizer : Sun Ah Park(Ajou University)
Moderator : Sun Ah Park(Ajou University)

Symposium 47

12:30-14:25 Premier Ballroom A

Recent insights into molecular orchestration of synaptic transmission and neural circuit modulation

Organizer : Yukiko Goda(Okinawa Institute of Science and Technology), Huang Ma(Zhejiang University)
Moderator : Yukiko Goda(Okinawa Institute of Science and Technology), Huang Ma(Zhejiang University)

Symposium 48

12:30-14:25 Premier Ballroom B

The molecular, cellular and circuitry mechanism of pain and itch

Organizer : Yongjing Gao(Nantong University), Guang-Yin Xu(Soochow University)
Moderator : Yongjing Gao(Nantong University)

Symposium 49

12:30-14:25 Premier Ballroom C

Emergence, maintenance, and entrainment of circadian clocks: from molecules to networks

Organizer : Jihwan Myung(Taipei Medical University)
Moderator : Jihwan Myung(Taipei Medical University)

Symposium 50

12:30-14:25 Rm.113-115

Supported by CUREVERSE 큐어버스

Decoding GPCR signaling: innovations in neuroscience research

Organizer : Ka Young Chung(Sungkyunkwan University)
Moderator : Jihye Seong(Seoul National University)

Symposium 51 12:30-14:25 Rm.116-118

Cognitive and computational neuroscience in nonhuman primate

Organizer : Hansem Sohn(Sungkyunkwan University), Seng Bum Michael Yoo(Sungkyunkwan University)
Moderator : Hansem Sohn(Sungkyunkwan University)

Educational Session 5 12:30-14:25 Rm.104-106

How to write impactful papers

Organizer : Seung-Hee Lee(Korea Advanced Institute of Science and Technology)
Moderator : C. Justin Lee(Institute for Basic Science)

Luncheon Seminar 11 12:00-12:30 Premier Ballroom A

Supported by Johnson&Johnson

Award Lecture 2 13:00-14:25 Grand Ballroom

Poster Session 1

Day 1(Aug 24, 2025) 13:00-17:40, Day 2(Aug 25, 2025) 8:30-12:30 [Exhibition/Poster Hall]

Mechanisms of Brain Disorders P-001~P-017

P-001 Biomarker detection with high-speed single-molecule imaging in neurodegenerative disorder
Sangjun Park

P-002 Transcriptomic evidence of hippocampal hyper-maturity and accelerated aging in mouse models of neuropsychiatric disorders with anxiety-like behavior
Hideo Hagihara, Hisatsugu Koshimizu, Satoko Hattori, Miho Tanaka, Kazutaka Ikeda, Tsuyoshi Miyakawa

P-003 Location of polyglutamine track affects pathogenic threshold of polyglutamine expansion diseases – importance of association with the proteasome
Meewhi Kim, Ilya Bezprozvanny

P-004 Dysfunctional S1P/S1PR1 signaling in the dentate gyrus drives vulnerability of chronic pain-related memory impairment
Mengqiao Cui, Jun-Li Cao

P-005 Sleep homeostasis-driving neurons from the hypothalamic paraventricular nucleus regulate glucose metabolism through adipose tissue lipolysis
Abudusalamu Awuti, Xiangtong Chen, Hong Jiang

P-006 Positive allosteric modulators of SERCA pump as potential therapeutics for Alzheimer's disease
Ilya Bezprozvanny, Russell Dahl

P-007 Antioxidant effect of Opuntia Ficus Indica cladode extract in a Wistar rat model of chronic Manganese toxicity induced Parkinson-like disease
Hala Harifi, Leila Bikjdaouene

P-008 D2R-specific deletion of NSF Induces ADHD-like behavioral phenotypes in mice
Min-Jue Xie, Koshi Murata, Hiroshi Kuniishi, Yugo Fukazawa, Hideo Matsuzaki

P-009 Restoring interbrain prefrontal theta synchronization reverses social deficits
Eunkyu Hwang, Hyoung Geun Yoon, Soogeun Shin, Anjin Lee, Woohyun Kim, Younghoon Kwon, Dongseok Seo, Eunjoon Kim, Eunee Lee

P-010 Potential of AAV-Based Gene Therapy for the Treatment of Cerebellar Ataxia
Hyemi Eo, Sehwan Kim, Un Ju Jung, Sang Ryong Kim

P-011 Neuroinflammatory and histopathological changes in the human olfactory system across the Alzheimer's disease continuum
Da Hae Jung, Eunji Park, Hyeon Chang Ju, Ali Jahanshahi, Cheil Moon

P-012 Isopropylphenidate exhibits addictive-like properties via the dopaminergic pathway in mice
Seong-Gon Lee, Youyoung Lee, Wun-A Kook, Choon-Gon Jang

P-013 Black Ginseng mitigates Alzheimer's cognitive decline by activating Nrf2/HO-1 and inhibiting p38 MAPK/NF-κB/STAT3 and NLRP3 via TLR2/4 modulation.
Yujeong Ha, Hyo-Sung Jo, Tae Woo Kwon, Seung Ho Jeon, Sang-Kwan Moon, Ji Hoon Jung, Min Soo Kim, seung-Yeol Nah, Jong Kil Lee, Ik-Hyun Cho

P-014 Febrile seizures induce hippocampal Nav1.1 downregulation and deficits in fear-related cognitive function in a rat model
Yeon Hee Yu, Yujeong Song, Beomjong Song, Dae-Kyoon Park, Duk-Soo Kim

P-015 Abnormal O-glycan Sialylation in Depression induced by Chronic Variable Stress
Youngsuk Seo, Inwoong Song, Boyoung Lee

P-016 AAV-mediated SCA3 Primate Model Reveals Early Cerebellar Neurochemical and Histopathological Changes
Keonwoo Kim, Aryun Kim, Jinyoung Won, Junghyng Park, Kyung Seob Lim, Chang-Yeop Jeon, Jee-Hyun Cho, Youngkyu Song, Dong-Seok Lee, Youngjeon Lee

P-017 Sex-Specific Salivary Proteomic Profiles as Biomarkers for Suicidal Ideation in Adolescents: A Novel Approach for Early Detection
Carlos Spuch, María Sánchez-Luaces, Tania Rivera-Baltanás, Beatriz Gómez-Gómez, Icía Nistal-Franco, Antía Branas-Gonzalez, Mario Manso-Vázquez, José Ramírez-Sánchez, Laura Docío-Fernandez, Carmen García-Mateo, Manuel José Fernández-Iglesias, Jose Olivares-Diez, Alejandro García-Caballero

Molecular and Cellular Neuroscience P-018~P-059

P-018 Cancer-associated metabolic reprogramming facilitated by astrocyte glycogenolysis mediates neuropathic pain chronification
Junseo Park, Kwanghwan Kim, Hyewon Jun, Sungjoong Lee

P-019 Korean Red Ginseng Marc-Derived Gintonin Improves Alzheimer's Cognitive Dysfunction by Upregulating LPAR1
Yujeong Ha, Rami Lee, Seung Ho Jeon, Ji-Hun Kim, Hyo-Sung Jo, Tae Woo Kwon, Sung-Hee Hwang, Jong Kil Lee, Seung-Yeol Nah, Ik Hyun Cho

P-020 Initiation of neuronal degeneration by secretory lysosome in Alzheimer's disease
Hyun Jin Jung, Soonbong Baek, Jaemyung Jang, Seungeun Yeo, Youngshik Choe

P-021 Single-cell Multiomics Integration of Microglia Across Alzheimer's Disease Continuum
Jaemyung Jang, Seungeun Yeo, Soonbong Baek, Hyun Jin Jung, Youngshik Choe

P-022 Asymmetric α-synuclein accumulation and neurodegeneration in a hemiparkinsonian primate model induced by unilateral intracarotid MPTP
Jincheol Seo, Chang-Yeop Jeon, Thi Hai Thanh Nguyen, Seung Ho Baek, Gahye Moon, Sojeong Lee, Jae-Won Huh, Youngjeon Lee, Kyung Seob Lim

P-023 Hippo signaling pathway is implicated in TSC-associated Intellectual Disability
Jahong Koo, Subin Park, Kyoung-Shim Kim, Da Yong Lee

P-024 Medial amygdala's role in abnormal social behavior in Shank2 haploinsufficiency
HYOUNG GEUN YOON, EUNKYU HWANG, YOUNGHOON KWON, EUNEE LEE

P-025 Non-saponin experimental autoimmune encephalomyelitis by maintaining blood-brain barrier integrity via NF-κB and p38 MAPK signaling pathway in
Yujeong Ha, Jinhee Oh, Tae Woo Kwon, Hyo-sung Jo, Da Yeon Park, Ik-Hyun Cho

P-026 Loss of Cyclin Y modulates autistic-like behaviors in Shank3InsG3680 mice
Jiyeon Seo, Mikyoung Park

P-027 Dysregulation of the FGFR1 signaling in hippocampus facilitates depressive disorder
Jongpil Shin, Hyeonsik Oh, Ji Hye Park, Hyunsik Bae, Chan Mo Yang, Minju Lee, Seokhwi Kim, Won Do Heo

P-028 Anxiolytic Effects of Gami-Guibitang in Autism Spectrum Disorder Mouse Model
Ji Hye Yoon, Duk Jin Jung, Junhyuk Choi, Jinyoung Maeng, Yujin Kim, Sungho Maeng

P-029 Exacerbation of Alzheimer's Disease Pathology by Brain Insulin Resistance in the 5xFAD Mouse Model
Jinyoung Maeng, Ji Hye Yoon, Junhyuk Choi, Yujin Kim, Sungho Maeng

P-030 Effect of chronic corticosterone administration on acute stress-mediated gene expression in the cortex and hippocampus
Kanzo Suzuki, Hirono Shiraki, Eri Segi-Nishida

P-031 Interoceptive sensing process against chronic colitis present to anxiety and depressive-like behavior
Jaehyun Jeong, Hyun Joo Choi, Sangyun Kim, So Yeon Park, Min Joung Lee, Jong Hun An, Chang Hee Pyo, Young Eun Kim, Taewan Kim, Dayoung Kang, Min-Kyung Yeo, Woosuk Chung, Jun Young Heo

P-032 Astrocytic O-GlcNAcylation modulates Social and Affective Behaviors in Mice
Prajitha Pradeep, Sehoon Keum, C Justin Lee, Boyoung Lee

P-033 Effect of environmental enrichment on chronic unpredictable mild stress - Focused on microbiota-gut-brain axis
Seung Ju Kang, Sae Yeon Son, Hyeong Ju Nam, Min Kyung Song

P-034 Dopaminergic regulation in the synaptic transmission of developing prefrontal cortex and cortisol-mediated disruption.
Hee-Young Kim, Khulan Amarsanaa, Eun-Bok Baek, Eun-A Ko, Oh-Bin Kwon, Sung-Cherl Jung

P-035 Transcriptomic analysis of senescence induced in AD patient-derived fibroblasts reveals AD-specific aging signatures
Young Joon Cho, Sunwoo Yoon, Yeojin Kim, Homin Song, Hyun Woong Roh, Sang Joon Son, Chang Hyung Hong

P-036 Dynamic interaction between interneuron and GPR56 expressing cells during the tangential migration of cortical formation
Hyeryun Shin, Byung-Geun Ha, Tae-Shin Park, Yu-Jin Jang, Sung-Jin Jeong

P-037 Translating schizophrenia pathology: The MAM model as a preclinical mirror of human disease
Jin Ju Kim, Eun Kyeoung Kim, Byung Soo Kim, Tae Young Lee, Jung Ho Hyun

P-038 Elucidating the protective mechanisms of the APOE Christchurch variant (R136S) against Alzheimer's disease via LRP1 interaction
Juyeong Jeon, Hyein Lee, Beom Soo Kim, Simsung Bae, Juwon Lee, Fan Gao, Jong Hyuk Yoon, Wookyung Yu, Sung Bae Lee, Jinsoo Seo

P-039 KINE-PD-28, a cytokine-derived small peptide, improves motor dysfunction through anti-inflammatory-related neuroprotection in PD animal models.
Ki Bum Um, Inhyun Ryu, Siyeon Park, Daeho Cho, Changkyu Gu

P-040 Alcohol Addiction-like Behaviors in Operant Ethanol Self-Administration Mediated by the mPFC Reward Circuit
Jiyun Lee, Sumin Kang, Eum-Ji Kim, Shijie Xu, Ja Wook Koo

P-041 Inflamed Lung Signals Alert to the brain that present to anxiety like behavior
Sang Yun Kim, Jong Hun An, Hyun Joo Choi, Chang Hee Pyo, Tae Wan Kim, Jae Hyun Jeong, Da Young Kang, So Yeon Park, Young Eun Kim, Min Joung Lee, Woosuk Chung, Jun Young Heo

P-042 Mitochondrial Complex I Deficiency Modulates Motor Behavior and Anxiety: Insights into Neurodegenerative Disorders
Su Been Park, Won-Seok Choi

P-043 GSK3b activation was modulated the pathology of Alzheimer's disease.
Yeon-Ji Seo, Won-Seok Choi

P-044 The Impact of Chronic Social Isolation on Memory Decline: The Role of Inflammation and Myeloid Receptor Dysregulation in Aging
Bo-Ram Mun, Won-Seok Choi

P-045 Investigation of Electrophysiological Abnormalities in Local Circuits of Brain Tissue from Drug-Resistant Epileptic Patients
Dongseok Seo, Wonseok Chang, Wonkyung Ho, Eunee Lee

P-046 Ursolic acid ameliorates LPS-induced cognitive impairment by modulating microglial activation and neurotrophic signaling in mice
Ga-Young Choi, Seohyeong Lee, Eunyoung Moon, Hyosung Choi, Hee-Seok Kweon

P-047 Exploring FK506 Derivatives as Potential Therapeutic Agents for Alzheimer's Disease.
Jaeho Yoon, Go Eun Ha, HeeJung You, Yeleen Lee, Denise Lee, Yeonju Lee, MyoungChong Song, Young Ji Yoo, Hunsang Lee, Yeo Joon Yoon, Eunji Cheong

P-048 Electrophysiological effect of FK506 derivates in Alzheimer's disease mouse model.
Yeleen Lee, Go Eun Ha, HeeJung You, Jaeho Yoon, Denise Lee, Yong Ji Yoo, Hunsang Lee, Yeo Joon Yoon, Eunji Cheong

P-049 Thalamic cell-specific Alterations in an Alzheimer's Disease Mouse Model
Go Eun Ha, Han-Eol Park, Denise Lee, Yeleen Lee, Jaeho Yoon, Yu Tak Lee, Chang Ho Sohn, Eunji Cheong

P-050 Ablation of microglial Connexin43 promotes short term and long term recovery from traumatic brain injury.
Yixun Su, Chenju Yi

P-051 STIM1-dependent calcium signaling in astrocytes controls glutamate accumulation and ischemic brain injury during acute stroke in mice
Seunghwan Choi, Geehoon Chung, Sun Kwang Kim

P-052 Cerebellar gliosis and motor impairments in autism-like phenotypes induced by maternal cadmium exposure
Junseok Oh, Joo-Ok Min, Juwon Choi, Won-seok Lee, Mi-Hye Kim, Hee Jung Kim, Bo-Eun Yoon

P-053 Prasugrel attenuates dopaminergic neuronal loss in an MPTP-induced model of Parkinson's disease
Seulah Lee, Jaehoon Kim, Eunji Cho, Hae-Un Jung, Ye-Jin Kim, Hagyeong Lee, Hyang-Sook Hoe, Dayea Kim, Jong Hyuk Yoon

P-054 Cerebrovascular dysfunction may contribute to cognitive impairment in Down syndrome
Joonhong Kwon, Joonhee Lee, Sihwan Seol, Hyo Jung Kang

P-055 GATA1-mediated brain-immune interactions in major depressive disorder: a comprehensive analysis of neuroimmune crosstalk in mice
Songah Shin, Joonhee Lee, Joonhong Kwon, Koeul Choi, Hyo Jung Kang

P-056 Pharmacological blockade of TRPA1 modulates morphine withdrawal syndrome and emotion-like behaviors in male and female mice
Audrey Lynn Donio, Choon-Gon Jang

P-057 A RAS family GTPase Rit1 regulates synaptic plasticity and memory in mice
Min-Gyun Kim, Sun Yong Kim, Sang Jeong Kim, Pau Castel, Yong-Seok Lee

P-058 Neuroprotective Effects of Astragalus mongholicus via Antioxidant and Anti-Inflammatory Mechanisms in Ischemic Stroke
Yongjae Hong, Geon Ko, Yeong-Jae Jeon, Hyeon-man Baek, Juni Lee, Donghun Lee, Jieun Park, Jaehong Kim, Keun-A Chang

P-059 Cerebellar Glial Alterations and Impaired Motor Coordination in a VPA-Induced Mouse Model of Autism Spectrum Disorder
Tae-Woo Ha, Jinhui Chao, Won-Seok Lee, Bo-Eun Yoon

Molecular and Cellular Neuroscience P-060~P-143

P-060 Inositol 1,4,5-Trisphosphate Receptor 1 Mediated Intracellular Calcium Dyshomeostasis Facilitates Trigeminal Neuropathic Pain
Meng-Xuan Huang, Ning-Yi Ren, Yi-Fan Wang, Yong-Jing Gao, Huan-Jun Lu

P-061 Distinct Roles of Somatostatin and Parvalbumin Interneurons in tec LEARNING
Qian-Quan Sun, jiaman dai, Chunzhao Zhang

P-062 A specific association of presynaptic K+ channels with Ca2+ channels underlies K+ channel-mediated regulation of glutamate release
Byoung Ju Lee, Young-Eun Han, Seungbok Lee, Suk-Ho Lee, Won-Kyung Ho

P-063 Protective effects of polyphenols against oxidative stress and inflammation caused by intracellular zinc deficiency in microglial cells
Masato Inazu, Ayumi Matsushita, Maki Kimura, Naoko Tajima, Tsuyoshi Yamanaka

P-064 MDGA2 constrains NMDAR functions by targeting EphB2-Ephrin signaling pathway
Hyeonho Kim, Younghyeon Jeon, Seunghye Kim, Yuxuan Guo, Dongwook Kim, Gyubin Jang, Julia Brasch, Ji Won Um, Jaewon Ko

P-065 Peripheral Neuronal NPTX2 Exacerbates Chronic Itch in an Atopic Dermatitis Model via Enhancing IL-31/IL-31R Signal Axis
Xue-Qiang Bai, Yu-Qi Zhang, Zhi-Jun Zhang

P-066 Astragaloside IV improves Muscle Atrophy by modulating UPS and ALP via suppressing Oxidative Stress and Inflammation in denervated mice
YaNan Ji, HuaLin Sun

P-067 The identification of a distinct astrocyte subtype that diminishes in Alzheimer's disease
Jiaqian Wu

P-068 Celecoxib alleviates denervation-induced muscle atrophy by suppressing inflammation and oxidative stress and improving microcirculation
tongxin shang, hualin sun

P-069 Prion protein-mediated inflammatory responses attenuated by melatonin through calcineurin signal
Jeong-Min Hong, Sang-Youel Park

P-070 Presynaptic CASKIN2 controls postsynaptic NMDA receptor functions via transsynaptic mechanism
Kyung Ah Han, Gyubin Jang, Hee-Yoon Lee, Byeongchan Kim, Xinran Liu, Se-Young Choi, Ji Won Um, Jaewon Ko

P-071 Guanine and isoguanine promote axon regeneration of dorsal root ganglion neurons and survival of retinal ganglion cells after injury
Hui Li, Bin Yu

P-072 H2O2-induced astrocytic collagen triggers neuronal death via fucosylation-dependent glial barrier formation upon ischemic stroke
Jae-Hun Lee, Hyun Jun Jang, In-Young Hwang, Jiwoon Lim, Jiwoong Jung, Myungju Kim, Eunji Lee, Woojin Won, Elijah Hwejin Lee, Ki Jung Kim, Ki Duk Park, Woonggyu Jung, Boyoung Lee, Seungjun Ryu, C. Justin Lee

P-073 Mitochondria-associated ER membranes (MAMs) mediate depressive-like behavior and neuronal stress responses via NR3C1 and its proximal protein
Jin Yeong Yoo, Cheolhun Park, Truong Thi My Nhung, Dong Jin Mun, Youngsik Woo, Ju Hee Park, Yeongjun Suh, Tran Diem Nghi, Eun Jin Jang, Bon Seong Goo, Seunghyun Kim, Gyuwon Lee, Seong-Guk Bae, Jisoo Lee, Seungha Shin, Jong-Seo Kim, Hyun-Woo Rhee, Sang Ki Park

P-074 Heterodimerization and Interaction of the Serotonin-Receptors 5-HT1A and 5-HT2C
Imandra Kempe, Michael Koch, Olivia Masseck

P-075 Microglial NLRP3 dysregulation augments repetitive behavior of mice via IL-1R-NMDAR interplay
Hyeji Jung, Byeongchan Kim, Gyubin Jang, Hyeonho Kim, Ae-Ree Lee, Sung-Hyun Yoon, Kyung-Seo Lee, Gaeun Hyun, Younghye Kim, Jaewon Ko, Je-Wook Yu, Ji Won Um

P-076 Intrahippocampal delivery of hyperphosphorylated human tau oligomers induces neurodegeneration in non-transgenic wild-type mice
Hong-Ru Chen, Hsiao-Tien Hagar, Kuan-Wei Wang, Stacy Hovde, Hsiang-Ying Lin, Min-Hsuan Lin, Cheng-Chun Chang, Ching-Yung Wang, Chia-Yen Chen, Emily Bian, Melissa Kinkaid, Min-Hao Kuo, Chia-Yi Kuan

P-077 The overexpression of TIAM2S alters the macrostructure of the mouse embryonic brain.
Chun-Hsien Chu

P-078 A high-performance fluorescent sensor spatiotemporally reveals cell-type specific regulation of intracellular adenosine in vivo
Qingpeng Wei, Zexiao Bai, Lei Wang, Chun Li, Yulong Li, Zhaofa Wu, Jing Wang

P-079 Properties of tonic inhibition change in age-dependent manner within auditory thalamus
Yujin Cho, Sunghyun Kang, Gunsoo Kim, Eunji Cheong

P-080 Ligand-independent EPHA2 signaling preserves neocortical progenitor identity by sustaining mitochondrial Complex I
Tran Diem Nghi, Jonghyeok Yun, Jin Yeong Yoo, Sung Ryong Shin, Eun Jin Jang, HyeonAh Gi, Wonhyeok Lee, Sang Ki Park

P-081 Research about the cerebrovasculature & BBB distribution and glymphatic system of olfactory bulb as a CSF drainage hub.
Oh-Hoon Kwon, Cheil Moon

P-082 The antipsychotic chlorpromazine reduces neuroinflammation by inhibiting microglial voltage-gated potassium channels
Hee-Yoon Lee, Young Lee, Chaelin Chung, Su-Hyun Jo, Se-Young Choi

P-083 Astrocytic ET-1 System Determines Microglia Phenotype Following Spinal Cord Injury
ZhiLong Cao, YongJun Wang

P-084 GIRK channel activation modulates circadian membrane excitability in SCN Prokineticin 2 neurons via G protein signaling
Jaehun JUNG, Michihiro MIEDA, Takashi MAEJIMA

P-085 TRPA1 mediates dimethyl fumarate - induced allergic contact dermatitis and pruritus in mice
Shiyu Sun, Guokun Zhou, Tong Liu

P-086 Histo-fMOST: 3D architectonic mapping of intact organs at the mesoscopic scale across diverse animal species/models
Jingyi Che, Jiajia Wang, Xinle Zhang, Xiaoyan Li, Xiaojun Wang, Qingming Luo

P-087 Autophagy activation ameliorates SARM1-dependent axon degeneration in CMT2B sensory neuropathy
Hye Ran Kim, Jin Young Lee, Hwan Tea Park

P-088 Activation of GLP-1R alleviates macrophage senescence-induced efferocytosis dysfunction via the AMPK/Gas6/Axl pathway following spinal cord injury
Mingjie Xia, Zhanyang Qian, Zhiming Cui

P-089 Application and evaluation of DREADD-mediated neuronal activity suppression in songbirds
Chenyi Song, Mizuki Fujibayashi, Kentaro Abe

P-090 Microglial O-GlcNAcylation regulates inhibitory tone in the hippocampus
Yeonjoo Kim, Jieun Lee, Ha-Eun Lee, Kyungjae Myung, Jae-Ick Kim

P-091 GelMA hydrogel loaded with MenSCs-derived exosomes shapes the ecological niche for functional recovery after spinal cord injury
Longju Qi, Bin Yu

P-092 NAD+ supplementation enhances mitochondrial respiration and protects blood-brain barrier integrity in endothelial cells and hemorrhagic stroke model
Min Joung Lee, Jong Hun An, Hyun Joo Choi, Chang Hee Pyo, Taewan Kim, Sangyun Kim, Jaehyun Jeong, Da Young Kang, So Yeon Park, Young Eun Kim, Jun Young Heo

P-093 Compartment-specific mitochondrial Ca2+ dynamics and molecular composition in neurons
Su Yeon Kim, Dong Cheol Jang, Won Seok Kim, Hyunsu Jung, Yongcheol Cho, Kihoon Han, Seok-Kyu Kwon

P-094 Neuron-derived alpha-synuclein triggers aberrant cholesterol accumulation in glial cells
Joo-Ok Min, Bo-Eun Yoon

P-095 Investigate the underlying mechanism of dendrite degeneration of adult Drosophila peripheral sensory neurons during aging
Shiang-Chi Lin, Min-Hsien Wang, Han-Hsuan Liu

P-096 Motivational Neural Circuitry and Epigenetic Regulation in a VR-Based Decision-Making Task
Dae-Si Kang, A-Hyeon Lee, Joon Ho Choi, kipom Kim, Ja Wook Koo

P-097 mScarlet Based Calcium and Serotonin Indicators for Improved Compatibility with Optogenetics and Multiplex Imaging
Ryan Fink, Shosei Imai, Mason Thom, Nala Gockel, German Lauer, Kim Renken, Jonas Wietek, Paul J. Lamothe-Molina, Falko Fuhrrmann, Tim Ziebarth, Martin Kubitschke, Vivien Kistmacher, Takuya Terai, Jan Gründemann, Sami Hassan, Tommaso Patriarchi, Andreas Reiner, Martin Fuhrmann, Robert E. Campbell, Olivia Andrea Masseck

P-098 Microglial Spatial Proteomics: Unraveling Function in Alzheimer's Disease and the Aging Brain
In Soo Kim, JinKyu Kang, A-Reum Park, Dong Woon Kim, Hyo Jung Shin

P-099 Perineural nets in anterior cingulate cortex involves sensitive period for social abnormality induced by social isolation
Riku Adachi, Hiroshi Kuniishi, Hideo Matsuzaki

P-100 Neurodevelopmental function of Zfp536
Chaeyoung Ahn, Ki Hurn So, Hee-Eun Lee, Eun-jeong Kim, Eun-Jin Yun, Cheol-Hee Kim, Seung Tae Baek

P-101 Advancing holotomography for multi-dimensional, high-resolution imaging of mouse brain tissue and organoid structures
Haesoo Kim, Hayoung Kang, Junhyung Park, Genehong Park, Hyejin Kim, Sumin Lee, YongKeun Park

P-102 Follistatin regulates voltage-gated sodium channels and potassium channels contributing to neuropathic pain
Yue-Juan Ling, Bing Zhu, Zuo-Hao Yao, Jun-You Wu, Yong-Jing Gao

P-103 Establishment of an Optimized Protocol for Isolation of Exosomes from Mouse Brain Microvessels
Jonghun An, Hyun Joo Choi, Chang Hee Pyo, Sang Yun Kim, Tae Wan Kim, Jae Hyun Jeong, Da Young Kang, So Yeon Park, Young Eun Kim, Min Joung Lee, Woosuk Chung, Jun Young Heo

P-104 In vitro modeling of the crosstalk between neurons and breast cancer cells
Eloise Happernegg, Julien Cicero, Loris Delfly, Nathan Laneret, Fabien Gosselet, Xuefen Le Bourhis, Caroline Mysiorek, Yoshiho Ikeuchi, Robert-Alain Toillon

P-105 Presynaptic APP–Contactin complex regulates GABAergic inhibition in hippocampal circuits
GYUBIN JANG, Hyeonho Kim, Seungjoon Kim, Byeongchan Kim, Jinhu Kim, Kisang Eom, Jung Ho Hyun, Ji Won Um, Jaewon Ko

P-106 Slitrk3 differentially regulates inhibitory synaptic properties of distinct GABAergic inhibitory neural circuits of medial prefrontal cortex in mice
Dongwook Kim, Byeongchan Kim, Hyeonho Kim, Jaewon Ko, Ji Won Um

P-107 Compound A attenuates non-cell-autonomous neurotoxicity in multiple preclinical ALS/FTD models
Myungjin Jo, Seyeon Kim, Shinrye Lee, Hyung-Jun Kim

P-108 Alleviation of Neuropathic Pain via Intrathecal Administration of ZEB1 siRNA-Loaded PLGA Nanoparticles in a Rat Spinal Nerve Ligation Model
Sujeong Choi, Jiyong Lee, Zhihuan Tian, Juhee Shin, Tae-Kyeong Lee, Sun Yeoul Lee, Dong Woon Kim

P-109 Therapeutic Effects of PLGA-Melatonin Nanoparticles in a Murine Model of Ischemic Stroke via Enhanced Microglial Phagocytosis
Tae-Kyeong Lee, Sujeong Choi, Seung Gyu Choi, Hyewon Park, Zhihuan Tian, Dong Woon Kim

P-110 Morphological plasticity of astrocytes in the SCN
Bin Zhou, Mengchan Su, Qingran Li, Ping Liao, Qin Hou, Ruotian Jiang

P-111 Gabapentin Attenuates Oxidative Stress–Related Cognitive Dysfunction via Sirt3/MnSOD Signaling in a Tibial Fracture Model
Hyojin Park, Inja Cho, Bon-Nyeo Koo

P-112 Co-culture of skeletal muscle cells with motor neurons, both differentiated from human iPS cells, leads to NMJ formation and muscle cell maturation
Moe Yamashita, Masayoshi Kamon, Shuji Wakatsuki, Toshiyuki Araki

P-113 Porphyromonas Gingivalis Infection induces the cognitive dysfunction via gut microbiota dysbiosis and IGFBP2 regulation
Inja Cho, A Young Sim, Jiwon Kim, Hyojin Park, Jong Eun Lee, Jong Youl Kim, Bon-Nyeo Koo

P-114 Temporal Dynamics of Microglial and Macrophage Responses in the MCAO Stroke Model: A single cell RNA sequencing analysis
Hyoin Hwang, Ji-Hye Han, Hyekyoung Shin, Dong-jae Yu, Sung-Tae Yang, Moon-Chang Choi, Jisoo Yun, Younghyun Jun, Junghee Park

P-115 UCN1 contributes to the maintenance of trigeminal neuropathic pain in the trigeminal ganglion of mice
Lin-Peng Zhu, Ling-Jie Ma, Fei-Fei Xu, Yong-Jing Gao

P-116 Hypothalamic microglial IL-4 signaling mediates cancer-associated cachexia
Sooyeon Jang, Saeha Kim, Subin Moon, Yejin Park, Dan-Gyeong Song, Daechul Shin, Songyi Park, Min-Seon Kim, Chanhee Lee

P-117 Dynamics of hippocampal synaptic landscape underlying associative memory formation
Yongmin Sung, Chaery Lee, Hyunsu Jung, Hyunmin Park, Bong-Kiun Kaang

P-118 Fine tuning gustatory acuity by glia-like type I cells
Gha Yeon Park, Nico Buerger, Myunghwan Choi

P-119 Cytokine-Mediated Restoration of Social Deficits in Shank2-deficient mice, an animal model of autism
Yu Kyeong Lee, Juli Choi, Jae Jin Shin, Gi Cheon Kim, Eunjoon Kim, Hokeun Kwon, Eunee Lee

P-120 Morphological characteristics of Layer 6b neurons in the mouse cortex
Juhyun Lee, Su-Jeong Kim, Jeong Eun Lim, Solange P. Brown, Juhyun Kim

P-121 Cereblon deficiency sensitizes neuroimmune responses and induces affective disturbances
Young lee, Chaelin chung, Hee-yoon lee, Se-young choi

P-122 Channel-mediated astrocytic volume transient is required for synaptic plasticity and spatial memory
Victor Drew, Junsung Woo, Jungmoo Lee, Wuhyun Koh, Joungha Won, C. Justin Lee

P-123 Effect of maternal probiotics supplementation on fetal neural development and cognition
Ying-Hang Wang, Yu-Hsin Chen, Jia-Yun Wu, Sabrina Wang

P-124 KCC-07, MBD2 inhibitor, expands the therapeutic window of DNA damage inducing reagents in neural tumor cells.
Junyoung Kim, Darom Lee, Keeeun Kim, Youngsoo Lee

P-125 Mitochondrial stress protein induced by pancreatic dysfunction mediates increase of anxiety-like behavior
Hyun Joo Choi, Jong Hun An, Chang Hee Pyo, Sang Yun Kim, Tae Wan Kim, Jae Hyun Jeong, Da Young Kang, So Yeon Park, Young Eun Kim, Min Joung Lee, Woo Suk Chung, Jun Young Heo

P-126 RESTORING AIBP EXPRESSION IN THE RETINA PROVIDES NEUROPROTECTION IN GLAUCOMA
Wonkyu Ju, Keunyoung Kim

P-127 Screening of novel asymmetric pyridinium-based fluorescent probes with large stokes shifts for imaging live neural stem/progenitor cells
Ye Ri Han, Dongwan Ko, Yeongran Hwang, Myeong A Choi, Do-Geun Kim, Jung Yeol Lee, Beomsue Kim

P-128 Divergent Roles of Macrophages and Microglia in Ischemic Stroke: Insight from Multi-omics Analysis
Ji-Hye Han, Yejin Bae, Hyoin Hwang, Hyekyoung Shin, Dong-Jae Yu, Sung-Tae Yang, Moon-Chang Choi, Jisoo Yun, Yonghyun Jun, Youngae Jung, Junghee Park

P-129 Neuroprotective effects of adenosine in models of vincristine-induced peripheral neuropathy
Hwigyeong Kim, Jung Eun Shin

P-130 The mechanism of oxaliplatin-induced peripheral neuropathy : sensory neuron degeneration and neuronal death
Yoon Kyung Shin, SeRi Kim, Yun Young Choi, Min Kyeong Kim, Jung Eun Shin

P-131 The transcriptome analysis for SARM1-dependent axon degeneration-regeneration coupling mechanism.
Minjae Kang, So Young Jang, Hwan Tae Park, Jung Eun Shin

P-132 Mitochondrial Metabolic Reprogramming in Cortical Neurons by Prenatal Corticosterone : A Shift from ATP Synthesis to Membrane Potential Maintenance
Khulan Amarsanaa, Hee-Young Kim, Eun-Bok Baek, Eun-A Ko, Oh-Bin Kwon, Sung-Cherl Jung

P-133 Western diet-induced visceral adipose tissue inflammation promotes Alzheimer's disease pathology via microglial activation in a mouse m
Soyoung Kwak, Ye Jin Kwon, Ji Sun Lim, Mi-Hee Yu, Mee-Ma Park, Hye Suk Baek, Junho Kang, Jeong-Ho Hong, Jin Kyung Kim, Hye Won Lee, Kyoung Sook Won, Bong-Il Song, Shin Kim, Hae Won Kim

P-134 Identification and functional characterization of Layer 6b neurons in the neocortex
kiwoong Lee, Su-Jeong Kim, Solange Brown, Juhyun Kim

P-135 Algorithm-Based Identification of Subtype-Specific Therapeutic Targets in the Nervous System
Miri Kim, Songhyeon Kim, Yebeen Kim, Chaeeun Kim, Minseok Kim, Ji Yeon Lim, Minji Jeon, Sun Wook Hwang

P-136 Intracellular cleavage domain of PROM1 modulates RNA regulatory networks via post-translational control
Hoyong Jin, Jinyoung Lee, Yongcheol Cho

P-137 Neural progenitor cell-like cells in the lateral ventricle of embryonic mouse forebrain
Suk Hyung Kim, Yu-Jin Jang, Jung Yoon Heo, Byung Geun Ha, Sung-Jin Jeong

P-138 HDAC6 Inhibition by Tubastatin A and Vagus Nerve Stimulation Promote Epigenetic Activation of Schwann Cells and Modulate Inflammation
YUNHA HAN, KI JOONG KIM, UK NAMGUNG

P-139 Spatiotemporal control of synapse pruning via enhanced synthetic trogocytosis
Seungkyu Son, Dong Yeop Kang, Shin Heun Kim, Gyu Hyun Kim, Kea Joo Lee, Sangkyu Lee

P-140 Optogenetic inhibition of inflammasome in microglia to relieve neuropathic pain
Juhee Shin, Daeun Lee, Dong Yeop Kang, Yeon Hee Kook, Seungkyu Son, Dong Woon Kim, Sangkyu Lee

P-141 Effects of psilocybin on immediate early gene expression and electrophysiological properties in the mouse somatosensory cortex
Minji Kang, Juhyun Lee, Juhyun Kim

P-142 A K+ channel in oligodendrocyte precursor cells regulating chronic pain
Jianing Wang, Shen Yu, Rong Luo, Ruotian Jiang

P-143 Selective roles of astrocytes in the acquisition of spatial representation of place cells in the hippocampus
Myeongjong Yoo, Seung-Woo Jin, Sang Jeong Kim, Inah Lee, Yong-Seok Lee

Neuroengineering P-144~P-161

P-144 Improvements in primary visual functions in photoreceptor-degenerated mice and macaque monkeys using retinal prosthesis
Biao Yan, Ruyi Yang, Peng Zhao, Chunhui Jiang, Yuanzhi Yuan, Jiayi Zhang

P-145 Bioresorbable, Self-Deploying Electronics for Minimally Invasive Brain Interfaces
Jae-Young Bae, Jun-Seok Shim, Seung-Kyun Kang

P-146 An ECoG integrated platform for real-time Electrophysiology and Fluorescence imaging
Jonghee Eun, Jeongseop Kim, Tae-Eun Kim, Ja Wook Koo, Namsun Chou

P-147 Hour-long voltage imaging in behaving mice using a set of photostable genetically encoded indicators
Kiryl Piatkevich

P-148 MEG-Based Affective BCI for Emotion Recognition and Dynamic Tracking
Moon-A Yoo, Dong-Uk Kim, Soo-In Choi, Min-Young Kim, Sung-Phil Kim

P-149 Inferring Time Information of Imagined Speech from Human ECoG
Dojin Heo, Jii Kwon, Chun Kee Chung, Sung-Phil Kim

P-150 Numerical Study on the Effects of Transducer Design on Trans-Spinal Focused Ultrasound Stimulation
Koharu Isomura, Wenwei Yu, Gomez-Tames Jose

P-151 The Role of Mental Fatigue in Modulating Behavioral Responses
Issei Kato, Kazuya Oshima, Yu Mikami, Rieko Osu, Atsuya Kimura, Kazuhiro Katagiri

P-152 Shape Memory Polymer based Cuff Electrode for Chronic Peripheral Nerve Interfacing
Seungjun Lee, Jonghee Eun, Namsun Chou

P-153 A screw-mounted modular optical window system for long-term, device-compatible optical neurophysiology in non-human primates
Wonjoon Jeong, Dongsu Kim, Jaehyun Kim, Seong Hwan Hwang, Myeonghwan Choi, Hyoung F. Kim

P-154 Implementation of an Eye-Gaze Input System and Evaluation of Physical and Mental Fatigue
JIHOON WOO, Issei Kato, Riku Nakazato, Rieko Osu, Chiaki Tomita, Kazuhiro Katagiri

P-155 Is Modeling of Temporal Interference Valid for Predicting Stimulation?
Kanata Yatsuda, Wenwei Yu, Gomez-Tames Jose

P-156 A 3D-Printed Microfluidic Platform for Aligned Sensory Neurite Extension and Functional Myelination
Sang Wook Shim, Ailian Jin, Mikang Shim, Yoon Lee, Jongho Hong, Dahee Roh, Sujin Hyung, Noo Li Jeon, Seog Bae Oh

P-157 High-frequency focused ultrasound neuromodulation with sonosensitive ion channels in behaving mice
Eungyeong Cho, Hyeongyu Park, Jungho Hyun

P-158 A novel biocompatible brain-interfaced electrode using laser-assisted structuring of Graphene film
Chin Su Koh, Dong Hyeon Lee, Tae Jun Kim, Joonsoo Jeong, Hyun Ho Jung

P-159 InGEL Platform for Neural Organoid Culture with Porous Hydrogels Enabling Controlled Network Formation and Cellular Complexity
Seo Kyung Kong, Aeri Shin, Woong Sun

P-160 A new optokinetic response gain analysis based on mean squared error for accurate and universal visual function assessment in animal study
Yusol Lee, Chaeyeon Lee, Minju Kim, Chaesung Kim, Dae yang Oh, Hyeonhee Roh, Subeen Park, Jae Hun Kim, Maesoon Im

P-161 Fully Transparent Neural Interfaces for Simultaneous Recording of Electrophysiology and Cell Photon Imaging
Hyun Woo Kim, Ki Jun Yu

Others : (Behavioral neuroscience)

P-162 A marker-based behavioral analysis system allows for in-depth analysis of the behavior and cognition of songbird
Mizuki Fujibayashi, Kentaro Abe

Others : (Astrocyte-Neuron Interaction)

P-163 Serotonin1A-Receptor-mediated signaling in Astrocytes and its influence on Major Depressive Disorder
Svenja Bremshey, Maja Neubauer, Anastasia Strietzel, Michael Koch, Olivia Masseck

Others : (Neurophysiology)

P-164 Identifying neural circuitry for exercise-induced growth hormone secretion
Michelle Sung, Yunseok Choi, Jong-Woo Sohn

Others : (Molecular Calcium-Neuronal Imaging)

P-165 Intravital Microscopy Enables Real-Time Visualization of PTZ-Induced Epileptic Calcium Dynamics in Thy1-GCaMP Mice
Sowon Lee, Hyunseok Kim

Others : (Brain drug delivery)

P-166 Intracalvariosseous administration readily delivers molecular to colloidal drugs to the brain via skull-to-brain route
Ji Hee Kang, O Hyun Lee, Da Hee Oh, Min Suk Shim, Sehoon Kim, Dongyun Shin, Young Tag Ko

Others : (Proteome analysis)

P-167 Proteomic Characterization of Human Meningeal Fibroblasts Across Neurological Diseases
Byung Geun Ha, Jung Yoon Heo, Yu-Jin Jang, Byung-Gyu Kim, Kyungjae Myung, Ji Yeon Lee, Sung-Jin Jeong

Others : (Integrative Physiology)

P-168 Orexin activates a distinct subpopulation of arcuate pro-opiomelanocortin neurons to promote food intake
Jeewon Choi, Seyoung Jin, Eun-Seon Yoo, Daesoo Kim, Pann-Ghill Suh, Inkyung Jung, Jong-Woo Sohn

Others : (Neuroimmunology)

P-169 Early-life regulatory T cells orchestrate brain immunity to establish proper brain function
Leechung Chang, Juli Choi, Eunkyu Hwang, Yeo-Jin Jeong, Seoyeong Kim, Sungji Ha, Keun-Ah Cheon, Eunee Lee, Xia Cao, Ho-Keun Kwon

Others : (Alzheimer's disease, Tau)

P-170 HYP-101, inhibited OGA, attenuated tauopathy, and improved memory deficits in an acute tauopathy model.
Heejeong KIM, Soojeong Baek, Jin-mi Kang, Yongseok Kim, Kang Kim, Gwangjeong Seok, Jeongtae Kim, Yong-su Han, Jaehong Im

Others : (Neuroinflammation, Microglia)

P-171 HYP-102 regulates NLRP3 inflammasome activity in BV-2 cells to confer neuroprotection.
Soojeong Baek, Heejeong Kim, Jin-mi Kang, Yongseok Kim, Kang Kim, Gwang Yeong Seok, Yong-su Han, Jeongtae Kim, Jae Hong Im

Others : (Acupuncture related therapies for Drug addiction)

P-172 Acupuncture related therapies for Drug addiction: A systematic review and network meta-analysis
HuiYan Zhao, Chang-Hyun Han, Yeon-Hee Ryu

Others : (Oral-Gut Axis Research)

P-173 Oral mucosal alterations reflect intestinal barrier dysfunction in a DSS-induced colitis model
Sangeun Han, Young Ju Do, Mudan Cai, Sangehun Lee, Su Yeon Seo

Others : (Integrative physiology)

P-174 Metabolic Function of Leucine-Rich Repeat Transmembrane Neuronal 4 Expressed by Arcuate AgRP Neurons
Seungjik Kim, Yurim Shin, Jaewon Ko, Jong-Woo Sohn

Others : (Integrative physiology)

P-175 Role of dorsal raphe serotonergic neurons in the regulation of sodium appetite
Yurim Shin, Seungjik Kim, Jong-Woo Sohn

Others : (Traditional and alternative medicine)

P-176 Moxibustion reduces DSS-induced brain stress via gut-brain axis inflammation
Su Yeon Seo, Sangeun Han, Mudan Cai, Young Ju Do

Others : (Cognition and Behavior)

P-177 Odor descriptor profile is influenced by association between color and odor
Yu yeon Lee, Kiwon Choi, Cheil Moon

Others : (Cognition and Behavior)

P-178 Associations Between Categorized Odors and Color Stimuli: Behavioral and EEG Experiment
Yujin Ahn, Seongwon Yoon, Cheil Moon

Others : (Cognitive Neuroscience)

P-179 The effects of Repetitive Transcranial Magnetic Stimulation (rTMS) over the left DLPFC on working memory in young adults
Shueh-Ni Chang, Yuju Sally Chou

Others : (Drug delivery)

P-180 Intraventricular Baclofen infusion via Implantable Osmotic Pump for Mouse Model of Traumatic Brain Injury.
Hyeon-Ju Lee, Junwon Park, Sooyoung Lim, Chaewon Song, Young Goo Kim, Won Seok Chang

Others : (social neuroscience)

P-181 PLCb1 regulates observational fear via mediating myelination in ACC-BLA circuits
sangyeong lee, jonghyun kim, bomi chang, eunjin shin, boyoung lee, C.Justin lee, Hee-sup shin

Others : (Aging Neuroscience)

P-182 Age-related muscle loss: Tracing its origins to the brain
Sehwan Kim, Youngpyo Nam, Un Ju Jung, Sang Ryong Kim

Others : (alternative medicine/ behavior)

P-183 Stress-induced preference for antioxidant by Drosophila
Gayoung Hwang*, Dae-Wook Yang*, Terezia Klaudia Geisseova, Hae A Kim, Yangkyun Oh, Greg S. B. Suh

Others : (Neuroimaging)

P-184 Comparative Analysis and Applications of High-Resolution Multimodal Imaging Techniques Using Correlative Light and Electron Microscopy (CLEM)
MinKyo Jung, Seulgi Noh, Jiyoung Mun

Others : (Neural mechanisms of mood disorder)

P-185 Context-Dependent Engagement of mPFC Neurons During Active and Passive Coping in a Sex-Dependent Manner
SeoYeon Yoon, Woonhee Kim, ChiHye Chung

Others : (Behavior)

P-186 Gut-brain axis for the maintenance of sodium homeostasis
Haeun Kang, Seongju Lee, Greg Seong-Bae Suh

Others : (cognitive science)

P-187 EEG alpha phase synchronization correlates with reaction times during inhibitory control
SANGBIN YUN, JAEWON YANG, BYOUNG-KYONG MIN

Others : (Decision Neuroscience)

P-188 Neural mechanisms of uncertainty in intertemporal decision-making: examining the impact of risk and ambiguity on time preferences
Iuliia Kleimenova, Jiho Kim, Wooree Shin, Jeongbin Kim, Jaeseung Jeong

Synapses and Circuits P-189~P-195

P-189 Specific and plastic: axo-axonic innervation of pyramidal neurons by GABAergic chandelier cells
Yilin Tai, Yang Li, Jifeng Tian

P-190 Optogenetic modulation of orbitofrontal cortex astrocytes alleviates trigeminal neuropathic pain via restoration of descending pain circuits
Jaisan Islam, Md Taufiqur Rahman, Muhammad Ali, Young Seok Park

P-191 Sleep oscillations induce systems consolidation through astrocytic synapse phagocytosis
Chi Hong Shin, Jeonghyun Park, Sungbin Kim, Jisu Lee, Eunjoon Kim, Jaekyung Kim, Won-Suk Chung

P-192 Magnetothermal brain stimulation enhances tactile discrimination by modulating synaptic plasticity in the adult mouse barrel cortex
Minhee Jeong, Hohyeon Kim, Ji-Hyun Jeong, Ji-Woong Ahn, Soonyong Kwon, YoungJi Kown, Seungjun Oh, Jungwon Yoon, Seungsoo Chung

P-193 Distinct modes of dopamine modulation on striatopallidal synaptic transmission
Youngeun Lee, Maria Reva, Ki Jung Kim, Yemin Kim, Eunjeong Cho, Hyun-Jin Kim, Minseok Jeong, Kyungjae Myung, Yulong Li, Seung Eun Lee, C. Justin Lee, Christian Lüscher, Jae-Ick Kim

P-194 Flexible fiber–based CaMKIIα-NpHR-mediated optogenetic silencing of dorsal root ganglion glutamatergic neurons attenuates chronic neuropathic pain
Muhammad Ali, Jaisan Islam, Md Taufiqur Rahman, Young Seok Park

P-195 Thalamic reticular circuit refinement via LRRTM3 shapes post-critical period sensory tuning
Dongsu Lee, Kyung Ah Han, Hyeonyeong Jeong, Go Eun Ha, Hyeongjin Lee, Beom Soo Kim, Chanmi Park, Yao Piao, Taek Han Yoon, Seungjoon Kim, Byeongchan Kim, Jungsu Shin, Yujin Cho, Sunghyun Kang, Han-Eol Park, Ji Won Um, Chang Ho Sohn, John R. Huguenard, Jaewon Ko, Eunji Cheong

Molecular and Cellular Neuroscience P-196

P-196 Slitrk paralogs configure excitatory synaptic specificity via different extracellular and intracellular mechanisms
Byeongchan Kim, Dongwook Kim, Jinhu Kim, Ji Won Um, Jaewon Ko

Synapses and Circuits P-197~P-213

P-197 Astrocytic MDGA proteins orchestrate synapse formation and function
Khai Huynh Ngoc, Younghyeon Jeon, Gyubin Jang, Byeongchan Kim, Woochan Jeong, Hyeonho Kim, Jiwon Um, Jaewon Ko

P-198 A top-down insular cortex-parabrachial circuit is crucial for non-nociceptive fear learning
Junho Han, Boin Suh, Jin-Hee Han

P-199 Synaptic plasticity in mice treated with single-dose psilocybin
Ziming Li, Francesca Pia Sellitti, Crystal Weber, Linda Simmler

P-200 Social motivation for effortful reward is reinforced by mesolimbic dopamine via D1R-mediated epigenetic regulation
Tae-Eun Kim, Jeongseop Kim, Ja Wook Koo

P-201 Rapid systems consolidation and reshuffling of engram cells in the hippocampal-cortical network by repeated learning
Boin Suh, Mujun Kim, Yire Jeong, Sunhoi So, Jaemin Hwang, Juhee Park, Jin-Hee Han

P-202 Sleep-dependent Memory Consolidation of Reward Locations Under Landmark-Based and Path Integration-Assisted Strategies
Abolfazl Badripour, Dahee Jung, Sebastien Royer

P-203 Septo-entorhinal GABAergic neurons switch memories to enable update
Mujun Kim, Boin Suh, Sunhoi So, Jung Wook Choi, Jaemin Hwang, Juhee Park, Jin-Hee Han

P-204 Two-photon optogenetic microcircuit mapping: Insights from V1, M1, and beyond
Elia Painchaud-Lakatos, Shawniya Alageswaran, Haley N. Renault, Meghan Appleby, Christina Y.C. Chou, Aparna Suvrathan, P. Jesper Sjöström

P-205 Optogenetic dissection of serotonergic modulation in dCA1: Electrophysiological validation and behavioral correlates
Juliana Gross, Jill Gerdey, Olivia Andrea Masseck

P-206 A non-hallucinogenic psychedelic reprograms stress resilience
Jeongseop Kim, Tae-Eun Kim, Yeo-Jin Ko, Jessica L Ables, Ja Wook Koo

P-207 Dorsomedial hypothalamic circuit mediates anxiety-induced arousal following psychosocial stress
Ho-Yong Choi, Jeong-Tae Kwon

P-208 Raphe-driven glutamate co-transmission shapes hippocampal function via modulation of cholecystokinin-expressing inhibitory neurons
Ha-Eun Lee, Minseok Jeong, Seung Eun Lee, Jae-Ick Kim

P-209 Top-down and reciprocal synaptic organization between the medial prefrontal cortex, claustrum, sensory cortices, and amygdala
Jeong Eun Lim, Juhyun Kim

P-210 Stress engages the noradrenergic brainstem-to-hypothalamus circuit to suppress appetite.
Myungmo An, Junkoo Park, Sumin Lee, Se-Young Choi, Sung-Yon Kim

P-212 Effect of social relationships during adolescence on the development of vHPC-mPFC pathway
Juyong Lee, Ain Chung

P-213 Prefrontal inputs to the basolateral amygdala differentially regulate context-dependent fear renewal
Jieun Lee, Eum-Ji Kim, Seunghwan Choi, Jungeun Ji, Joon-Yong An, Ja Wook Koo

Systems and Computational Neuroscience P-214~P-262

P-214 Neural mechanisms for regulating impulsive choice via directional visual stimuli in time perception
Wi Hoon Jung, Euitae Kim

P-215 Testosterone Administration Slows Prosocial Learning to Avoid Harm in Healthy Men
Yin Wu

P-216 An open-source system designed for synchronised neural and behavioural data acquisition
Maja Neubauer, Anastasia Strietzel, Joscha Schmiedt, Olivia Masseck, Sami Hassan

P-217 In-depth analysis of interbrain correlation with machine learning models
Anjin Lee, Eunkyu Hwang, Eunee Lee

P-218 Closed-loop disruption of cortico-cortical communication in NREM impairs skill refinement
Jaekyung Kim, Linmeng He, Karunesh Ganguly

P-219 Distinct roles of regional proximal and distal synaptic weights in neurodevelopmental and neurodegenerative disorders
Yeongjun Park, Bo-yong Park

P-220 Neural mechanisms of acupuncture stimulation in autism spectrum disorders: Protocol for a randomized, placebo-controlled, fNIRS-EEG neuroimaging study
Dong Hyuk Lee

P-221 Blocking D1 receptors in entorhinal cortex disrupts value-dependent conditioned responses
Jaehun Kim, Minyeong Seo, Min Whan Jung

P-222 High-Precision and Efficient Suppression of Pathological Brain Activity in Parkinsonian Rats via a Closed-Loop Deep Brain Stimulation Approach
Jenq-Wei Yang, Ramesh Perumal, Yu-Hsiu Kuo, Hsin Chen

P-223 Cortical-amygdalar neural dynamics during grooming behavior in rodents
Ye-Ri Choi, Tae Ho Park, Woo Sung Joo, Jee Hyun Choi, Hio-Been Han

P-224 Container-based high-performance computing for modeling large-scale biological neural networks
Oliver James, Sungho Hong

P-225 Place cells in CA3 require more complex visual scenes for spatial firing than in CA1 in VR environment
Eun-Ho Lee, Inah Lee

P-226 Differential encoding of value-based contextual behavior in the intermediate and dorsal regions of the hippocampus
Su-Bin Chung, Inah Lee

P-227 A pharynx-to-forebrain circuit for rapid thirst quenching
Gilju Han, Minyoo Kim, Dong-Jun Koo, Hyeongujun Cho, Sung-Yon Kim

P-228 Dynamic encoding of numbers in the hippocampus
Chuljung Kwak, Hyung-Bae Kwon, Bong-Kiun Kaang

P-229 A custom imaging-guided intranasal system for brain delivery in a cynomolgus monkey (Macaca fascicularis)
Hyeon-Gu Yeo, Chang-Yeop Jeon, Jinyoung Won, Kyung Seob Lim, Junghyung Park, Jae-Won Huh, Youngjeon Lee

P-230 Altered spine architecture and epileptogenesis : A simulation study in human dysplastic neocortex
Jawon Gim, Na Young Seo, Gyu Hyun Kim, Kea Joo Lee, Joon Ho Choi

P-231 Regularization of High-Dimensional Cerebellar Representations by Sparse Parallel Fiber Inputs: A Virtual Sample-based L2 Regularization Perspective
Taerim Yun, Jundong Kim, Chang-Eop Kim

P-232 Move All Together (MovAI): A New Framework for Multi-Animal Identity Tracking and Pose Estimation
Sunjin Kim, Yejin Jeong, Haeri Choi, Sunwoo Park, Ain Chung

P-233 Distinct neural coding of sensory and mnemonic representations in the human early visual cortex
Sungje Kim, Joonwon Lee, Hyunwoo Gu, Heeseung Lee, Jaeseob Lim, Minjin Choe, Hyang-Jung Lee, Dong-Gyu Yoo, Sang-Hun Lee

P-234 Temporally dynamic prefrontal processing during goal-dependent memory retrieval
Jisu Park, Sue-Hyun Lee

P-235 Ventral medial prefrontal and motor cortex interaction mediates cost-benefit tradeoffs
Yonil Jung, Daigo Okada, Hidehiko Inagaki

P-236 Common neural processes engaged during memory retrieval under self-distancing
Inho Shin, Sue-Hyun Lee

P-237 Disruption of Social Experience During Early Adolescence Induces Long-term Behavioral and Neural Alterations
Haeri Choi, Yeon Lee, Sooyoun Bae, Sunjin Kim, Ain Chung

P-238 Exploring More Efficient Methods for Habit Formation Through Count Based and Time Based Learning
Yujin Kim, Jinyoung Maeng, Ji Hye Yoon, Junhyuk Choi, Sungho Maeng

P-239 Harmonizing Cerebellar Uniformity and Diversity: A Transformer-Inspired Hierarchical Algorithm Perspective for Neuroscience and Machine Intelligence
Bongsu Kang, Chang-Eop Kim

P-240 Dopamine Signaling in the Retrosplenial Cortex During Goal-Directed Navigation
Wooyoung Na, Jeehyun Kwag

P-241 Intralayer Disinhibitory Circuit Regulates Feedforward Circuit of Somatosensory Cortex
With Drawn
Kyeong Seok Kim, Bo Gyeom Park, Seungjoo Chung

P-242 Prefrontal representational changes during learning predict long-term associative memory
Subin Cho, Minjae Kwon, Sue-Hyun Lee

P-243 Auditory Alarm Modulates Hippocampal Theta Phase Resetting and Hippocampal Theta-Cortical Gamma Coupling to Enhance Associative Memory Encoding
Seongjin Lee, Chun Kee Chung

P-244 Phonetic vs. Phonemic Representation in Neural Activity During Speech Production: Evidence from Denasalized [n] Sounds Resembling [t] in Ko
Yong Hyeon Gwon, Chun Kee Chung

P-245 Neural Representations of the Clarity of Subjective Emotion
Jaewon Han, Wonjun Kang, Doyoung Park, Jisu Park, Sue-Hyun Lee

P-246 Differential Integration of Visual Value and Feature Information in Basal Ganglia regions
Seong-Hwan Hwang, Masaharu Yasuda, Hyoung.f Kim

P-247 Differences in modality-selective value neurons of the primate striatum underlie functional dissociation of tactile and visual value-guided behavior
Ji-Woo Lee, Min Seo Kim, Seong-Hwan Hwang, Hyoung F. Kim

P-248 Parallel processing of tactile and visual value information in the globus pallidus externa
Min Seo Kim, Ji-Woo Lee, Hyoung F. Kim

P-249 The role of the primate caudal subthalamic nucleus in processing long-term value memory for habitual behavior
Keonwoo Lee, Myong Lee, Hyoung F. Kim

P-250 Learned value and spatial preference, but not visual salience, shape value-based habitual hand choice in primates
Yun-Hyuk Kim, Jun Park, Yu Gyeong Kim, Youngjeon Lee, Hyoung F. Kim

P-251 Comparison of advanced augmentation methods for predicting postoperative delirium in older adults undergoing spine surgery
Jungmin You, Jeongeun Choi, Jeongmin Kim, Bon-Nyeo Koo

P-252 Topographic cortico-basal ganglia computational model reveals motor and non-motor symptom comorbidity in Parkinson's disease
Jieun Kim, Taegon Kim

P-253 A computational modeling approach to the role of Serotonin in cued fear learning and extinction
Afarin Badripour, Taegon Kim

P-254 Memory trace of a virtual butterfly encounter
Dahee Jung, Sebastien Royer

P-255 The role of retrosplenial cortex input to nucleus accumbens in modulating behavior
Shinyoung Kim, Jeehyun Kwag

P-256 Structured semantic information is reflected in cerebral cortical activity during single-word production
Sinhwa Roh, Chun Kee Chung

P-257 Multidimensional dynamics of the cerebellar output neurons encoding saccadic eye movement
Jisub Bae, Zongpeng Sun, Peter Thier, Sungho Hong

P-258 Higher-order connectivity, jointly determined by distance, net synaptic inputs and outputs, influences recurrent dynamics in mouse V1 layer 2/3
Dongho Kang, Hyeyoung Shin

P-259 Value-Related Activity of Interneuron Subtypes in Hippocampus
Jaesong Ju, Minwhan Jung

P-260 Dissecting Temporal Dynamics and Cross-Area Information Integration During Online Goal Correction
Min-Ki Kim, Sang-Hoon Kim, Jeong-Woo Sohn

P-261 Thalamocortical Circuit Mapping in Macaque Monkeys Using Combined Stimulation-fMRI
Jimin Lee, Min-Jun Han, Seong-Gi Kim, Hansem Sohn

P-262 Place fields as probabilistic cognitive maps induced by predictive learning
Yeowon Kim, Yul Kang

Translational and Clinical Neuroscience P-263~P-282

P-263 A novel therapeutic strategy and drug candidate for treating Spinal Cord Injury
Vance P. Lemmon, Abdiel Badillo-Martinez, Indigo P. Williams, Omar S. Elwardany, Bassel Awada, Sierra J. Bagwell, Aya Hanna, Jae K. Lee, John L. Bixby, Hassan A. Ali

P-264 Cross-species transcriptome profiling of mesial temporal lobe epilepsy and corresponding rodent models
Joonho Kim, Sangbo Lee, Won-Joo Kim, Sangwoo Kim

P-265 Development of a Serum-based miRNA Panel for Alzheimer's Disease Diagnosis
Qi Qin

P-266 Early activity rhythm disruption and behavioral changes in a long-term non-human primate model of Alzheimer's disease
Yu Gyeong Kim, Junghyung Park, Jinyoung Won, Chang-Yeop Jeon, Kyung Seob Lim, Gyu-Seo Bae, Eunsu Jeon, Youngjeon Lee

P-267 Cerebellum and Self-esteem in Children and Adolescents: The Moderating Effect of Depression
Haemi Choi, Jeongeun Lee, Jeongeun Cho, Yeeun Kim, Bumhee Park, Min-Hyeon Park

P-268 Novel microRNA biomarker in human blood and convergence diagnostic medical device for early Alzheimer's disease
Min Hwa Kang, Jun Sung Park, Kyonghwan Choe, Heeyoung Kang, Snag Bae Ma, Myeong Ok Kim

P-269 Sustainability of the effect of taste recall training on taste sensitivity in healthy adults
Uijin Park, Satoru Ebihara

P-270 Leveraging Inflammatory Plasma Protein Ratios for Enhanced Parkinson's Disease Diagnosis
Youngtae Choi, Shinrye Lee, Gyuri Park, Jisu Jeong, Do-Geun Kim, Hyung-Jun Kim, Mookyung Cheon

P-271 Risk factors for postoperative cognitive dysfunction in older adults undergoing elective spine surgery: a prospective cohort study
Jeongeun Choi, Jeongmin Kim, Bon-Nyeo Koo

P-272 A Synthetic RNA Enhances Functional Restoration Following CNS Injury Through Neuroepigenetic Modulation
Youwon Lee, Eunsu Jang, Yongcheol Cho

P-273 Chlorpromazine increases the frequency of EPSC by non-canonical Ca2+ elevation of astrocytes
Hye-Won Lim, Kyung-Seok Han, Dong Ho Woo

P-274 Cell-Type specific contributions of PRX isoforms to Alzheimer's pathology and their therapeutic implications With PRX mimetic
Hojin Lee, Sun-Young Kook, Soohyun Hong, Jiran Kim, Dong Hoon Kang, Sang Won Kang

P-275 Electrophysiological Signatures of Network Remodeling in the Retinal Detachment Mouse Model
Daejin Park, Sumin Jo, So Jeong Kim, Eoi Jong Seo, Yong Sook Goo

P-276 Dynamic Patterns of Relative Phase in ADHD Brain Activity: A Resting-State EEG Study
Jiwon Kim, Seoyeon Kim, Younghwa Cha, Joon-Young Moon

P-277 Altered muscle synergies during gait in posterior cord syndrome
Da Yeon Lee, Nackhwan Kim, Min Hee Kim, Yu Ho Jeon, Hyeong-Dong Kim

P-278 Generating 3D whole-brain neurovascular coupling maps using resting-state fMRI and ASL: a preliminary study
Yechan Kim, Jonghun Lee, Junbeom Lee, Cheol-Woon Kim, Junghoon J. Kim, Joon Yul Choi

P-279 Prediction of acute postoperative pain intensity using EEG phase characteristics in patients under propofol anesthesia
Yeji Lee, Joon-Young Moon, Hyoungkyu Kim, Jaegeum Shim

P-280 Enhancing the Efficacy of Low-Dose Doxorubicin Using Focused Ultrasound: A Strategy to Reduce Toxicity
Chaewon Song, Junwon Park, Wonseok Chang

P-281 Developed a novel peptide targeting the high-affinity EPOR site activated in ischemic stroke and verified receptor-level changes in silico.
Oh-Hoon Kwon, Jinsik Bae, Seung-Jun Yoo

P-282 Effects of a biofeedback-based sleep aid smartphone application on post-stroke sleep disorders: Case report
Aiden Lee, Jisoo Park, Jiyeon Ha, Jonghwa Park, Sun Im

Poster Session 2

Day 2(Aug 25, 2025) 13:30-18:00, Day 3(Aug 26, 2025) 8:30-12:30 [Exhibition/Poster Hall]

Mechanisms of Brain Disorders P-283~P-341

P-283 Neurodevelopmental disease-associated WWP1 gain-of-function drives developmental anoikis through TGFβ pathway
Ki Hurn So, Jiayi Wong, Hyunsik Lee, Eun-Jin Yun, Hee-Jung Choi, Jong-Hee Chae, Seung Tae Baek

P-284 Neuregulin-1 Mitigates Autism-like Behaviors in Adolescent Rats Prenatally Exposed to Valproic Acid
Yu Jin Kim, Han Byeol Kim, Hyo Min Lim, Yoori Choi, Ran Sook Woo

P-285 Effect of Transcutaneous Vagus Nerve Stimulation on Ketamine Reinstatement
Minjin Oh, Sejin Jeong, Suchan Chang, Ja Wook Koo

P-286 Cognitive reserve and its genetic basis modulate transsynaptic tau propagation in Alzheimer's disease
Hyewon Shin, Yong Jeong

P-287 Astrocyte priming enhances microglial Aβ clearance and is compromised by APOE4
Jichang Yu, Se-In Lee, Hyein Lee, Buyun Kim, Min Jun Jang, Hyeonbin Jo, Na Yeon Kim, Malk Eun Park, Jae Kwang Kim, Sukhee Cho, Hong-Hee Won, Min Soo Kim, Fan Gao, Sung Bae Lee, Younghoon Go, Jinsoo Seo

P-288 Longitudinal characterization of seizure evolution in CYFIP2 p.Arg87Cys mouse model of West syndrome
RUIYING MA, Muwon Kang, Gyu Hyun Kim, Hyojin Kang, Sunho Lee, Yeji Yang, Hae Ji Lee, Seungji Choi, Seungsoo Kim, Seoyeong Kim, Yukyung Jun, Hyewon Kim, Yinhua Zhang, Geum-Sook Hwang, Jungmin Choi, Youngae Jung, Jin Young Kim, Eunjoon Kim, Kea Joo Lee, Kihoon Han

P-289 Investigating the Effects of Thalamic Reactive Astrocytes on Alzheimer's Disease Progression
Denise Lee, Go Eun Ha, Jaeho Yoon, Yeleen Lee, Beomsoo Kim, Dongsu Lee, Chanmi Park, Jooyoung Kim, Yujin Cho, Piao Yao, Hyunkeong Lim, Mijin Yun, Eunji Cheong

P-290 Discriminative Stimulus Properties of Psilocybin and Substituted Tryptamines on Mesolimbic Area
Su min Kang, Dae Si Kang, Min Jin Oh, Sejin Jeong, Eum Ji Kim, Jieun Lee, Suchan Jang, Ja Wook Koo

P-291 Neurovascular Restoration through Treadmill Exercise Mitigates Age-related Cognitive Impairment
Jae Min Lee, Da-Eun Sung, You Jung Choi, Jong ho Lee, Seung Geun Yeo, Youn-Jung Kim

P-292 Adenine Base Editing of BEST1 for Modeling Best Disease
Na-Yoon Lee, Dong Ho Woo

P-293 SGLT2 inhibition by Enavogliflozin significantly reduces Aβ pathology and restores cognitive function via upregulation of microglial AMPK signaling
Jihui Han, Jaehoon Song, Eun Sun Jung, Ji Won Choi, Hye Young Ji, Inhee Mook-Jung

P-294 Neuroprotective effect of pimobendan in amyloid-beta treated primary neurons and 5xFAD Alzheimer's disease mice model
Ye-Jin Kim, Seulah Lee, Jaehoon Kim, Eunji Cho, Hae-Un Jung, Jong Hyuk Yoon

P-295 Impact of SSRI Exposure during Development on Autism Spectrum Disorder (ASD)
Haeun Noh, Jeong Hyun Jeong, Eunseo Park, Jinhyeok Kim, Hyunah Choo

P-296 Effects of Humulus japonicus Water Extract on the Cholinergic System and Neuroplasticity in Age-Related Cognitive Decline
JU-EUN KIM, KYEONG-SEON MIN, JUN GO, HYE-YEON PARK, YOUNG-KEUN CHOI, IN-BOK LEE, JAEWON SHIN, H YUN-JU CHO, HONG-SIK KIM, DAE YOUN HJWANG, WON-KEUN OH, KYOUNG-SHIM KIM, CHUL-HO LEE

P-297 Optogenetic induction of TDP-43 proteinopathy drives neuronal vulnerability and behavioral deficits in C. elegans.
Kyung Hwan Park, Kyung Won Kim

P-298 Synergistic enhancement of structural plasticity and functional recovery via combined PTEN deletion and activity modulation after ischemic stroke
Hyung Soon Kim, Seung Ah Jee, Hyo Gyeong Seo, Seung-Hyun Yoon, Bumhee Park, Hyang Woon Lee, Byung Gon Kim

P-299 Role of DRG2 in the regulation of dopamine release and changes in energy metabolism
Sung Rae Kim, Chang Man Ha

P-300 Nonlinear dynamics of microRNAs in alzheimer's disease: biomarker mining and clinical validation
Seong-Hun Lee, Seung-Bo Lee, Shin Kim

P-301 Nanoplastics-induce NLRP-3 activation via labile iron in proteinopathy and neurodegeneration
Ariunzaya Jamsranjav, Khanh Van Do, Minh Tran Thi, Min Woo Kim, Min Joon An, You Jung Kang, Hansang Cho

P-302 Spatial and Temporal Dynamics of Progenitor Cell Activation in the Neonatal Brain After Ischemic Stroke
Indra Gendenpeljee, Sung Jin Jeong, Byung Geun Ha, Hyeryun Shin

P-303 Social defeat stress induces alterations in the glutamatergic system during adolescence
Bo Hyun Kim, Jong Hee Choi, Kyung Rok Nam, Kyung Jun Kang, Sang Jin Han, Jae Yong Choi

P-304 Electroacupuncture at GB34 and BL60 enhances subventricular zone neurogenesis via BDNF-ERK signaling in a mouse model of Parkinson's disease&
Ji Eun Seo, Wenqiang Xu, Yukyoung Lee, Hee-Young Kim, Seungtae Kim

P-305 Modulation of creatine energy metabolism mediates mitochondrial hormesis enhancement in intracerebral hemorrhage
Chang Hee Pyo, Jong Hun An, Hyun Joo Choi, Sang Yun Kim, Tae Wan Kim, Jae Hyun Jeong, Da Young Kang, So Yeon Park, Young Eun Kim, Min Joung Lee, Woosuk Chung, Jun Young Heo

P-306 Vitamin D Improves Cognitive Function through Neurovascular remodeling in an Aging Mouse Model
Youjung Choi, Da-Eun Sung, Jae Min Lee, Jong Ho Lee, Youn-Jung Kim

P-307 The Role of Sleep Stages and Cyclic Rhythms in Seizure Dynamics of Temporal Lobe Epilepsy Rat Model
Seoyeong Yun, Yunseo Choi, YuJaung Kim, Sol ah Kim, Hyangwoon Lee

P-308 Neuroprotective effect of Korean red ginseng extract in the hippocampus of mice acutely exposed to polystyrene nanoparticles
Hyo Sung Jo, Tae Woo Kwon, Won Myoung Lee, Ik Hyun Cho

P-309 CHO001 inhibits experimental autoimmune encephalomyelitis by downregulating microglial NF-κB/NLRP3 inflammasome signaling pathways
Tae Woo Kwon, Da Yeon Park, Seikwan Oh, Ik Hyun Cho

P-310 Populus tomentiglandulosa Exerts Neuroprotective Effects in an MPTP-Induced Parkinson's Disease Model by Growing Antioxidant and Inh<
Won Myoung Lee, Tae Woo Kwon, Hyo-Sung Jo, Yu-jeong Ha, Sanghyun Lee, Ik-Hyun Cho

P-311 Overexpressing TFEB in microglia attenuates Aβ pathology by enhancing the autophagy lysosomal pathway
Yeji Kim, Tae-Young Ha, Myung-Shik Lee, Keun-A Chang

P-312 Bestrophin1 drives glioblastoma progression and suppresses apoptosis via Ca^{2+}-dependent glutamate release
Jae Hong Yoo, Joon Ho Kwon, Hee Jung Park, Yongmin Mason Park, Woo-Suk Roh, Myunghoon Lee, Jae-Hun Lee, Hyeonseon Park, Tai Young Kim, Jiwoong Jung, In-Young Hwang, Donghwan Shim, Mijin Yun, C. Justin Lee, Kyung-Seok Han

P-313 Cooperative Regulation of Compulsive-like Eating Behavior by Dopamine D2 and Insulin Receptors
Bokyeong Kim, Minji Kim, Hyun-Yong Lee, Jung Hyun Pyo, Jihee Seo, Yoon Jeon, Ho Lee, Joung-Hun Kim, Seung Hyun Ahn, Sung Wook Chi, Je Kyung Seong, Ja-Hyun Baik

P-314 ORP1L deficiency disrupts endolysosomal function in neurons and exacerbates amyloid pathology in a mouse model of Alzheimer's disease
Eunjeong Cho, Soyeon Lee, Soyeong An, Youngeun Lee, Yeonjoo Kim, Seong Eun Lee, Ja Yil Lee, Jae-Ick Kim

P-315 The circuit and molecular mechanisms underlying hypothalamic and oxytocin neuronal abnormalities in 15q11-13 duplication mice
Yuyang Guo, Chuan Xing, Xiang Yu

P-316 Identifying disease-associated neuronal differences using neurons directly converted from Alzheimer's disease patient-derived fibroblasts
Sunwoo Yoon, Yeojin Kim, Young Joon Cho, Homin Song, You Jin Nam, Sang Hyuk Lee, Sehee Lee, Sang Joon Son, Chang Hyung Hong, Hyun Woong Roh

P-317 Orally Active Tau-ATTEC Demonstrates In Vivo Efficacy in P301S Tauopathy Model: Novel Breakthrough Therapeutic Modality for Tauopathies
Chaemi Lee, Jiin Kim, Hye Yeon Cho, Jin Sook Song, Kwan Young Jeong, Seong Hwan Kim

P-318 Gut-derived pathologic α-synuclein and its transmission through neural circuits
Byung-Kwon Jung, MinKyung Song, DongWoo Kim, Yoon-seong Kim, Greg Seong-Bae Suh

P-319 Effects of sitagliptin on L-dopa induced dyskinesia in 6-OHDA-induced mouse model of Parkinson's disease
Hye-yeon park, Young-Kyoung Ryu, Ga Seul Lee, Jun Go, Ju-Eun Kim, Kyeong-Seon Min, Chul-Ho Lee, Jeong Hee Moon, Kyoung-Shim Kim

P-320 From Acupoint to Biomarker: Metabolomic Insights into the Therapeutic Effects of Invasive Laser Acupuncture in Parkinson's Disease
Halin Jeon, Ju-young Oh, Sora Ahn, Mijung Yeom, In Jin Ha, Hong-Seok Son, Seong-Eun Park, Juhan Park, Eugene Huh, In-Yeop Baek, Min-Ho Nam, Changsu Na, Myung Sook Oh, Hi-Joon Park

P-321 Synergistic effects of Environmental Enrichment and Aptamin C on Amyloid-beta Clearance via Enhanced Autophagy in the 5xFAD Mice
Da-Eun Sung, Jae Min Lee, You Jung Choi, Jong Ho Lee, Youn-Jung Kim

P-322 Regional Tau Resistance Mediates Genetic Contributions to Cognitive Reserve in Alzheimer's Disease
Seoyeon Kim, Yong Jeong

P-323 DTI-ALPS Reveals Glymphatic Mediation of Choroid Plexus and Ventricular Enlargement in MCI patients
Giho Jeon, Jake Jeong, Young Min Lee, Kwangyeol Baek

P-324 Ultrastructural analysis of scar-forming PDGFR-β+ fibroblasts after photothrombotic stroke
Ji-Won Hwang, Hong Lim Kim, Yuna Oh, Soon-Young Jung, Mun-Yong Lee, Tae-Ryong Riew

P-325 Antioxidant Microglial Subtypes Mitigate Ischemic Injury in a Photothrombotic Stroke Model via Prdx1-Dependent Mechanisms
Hyemin Park, Huiju Jo, Goo Taeg Oh

P-326 Patient-Derived iPSC-Based Modeling of Microglial Function in Alzheimer's Disease
Homin Song, Yeojin Kim, Sunwoo Yoon, Youngjoon Cho, Hyunwoong Roh, Changhyung Hong, Sangjoon Son

P-327 Acute stress impairs subregion-specific dopamine signaling in the nucleus accumbens shell
Minsung Sim, Gihun Nam, Hoyong Park, ChiHye Chung

P-328 Age-Dependent Behavioral and Synaptic Changes in 3xTg-AD Mice: Insights into Alzheimer's Disease Progression
Jin Ho Baek, Won-Seok Choi

P-329 NRA-specific role for autophagy disruption-based pathogenesis of Alzheimer's disease
Ji-Young Choi, Jung Hyun Park, Young Ho Koh

P-330 Distinct Behavioral Phenotypes in Multi-Gene Transgenic Mouse Models of Alzheimer's Disease
Ga Young Park, Won-Seok Choi

P-331 Focused ultrasound stimulation recovers abnormal ciliary defects by enhancing mitochondrial respiration.
Tae Wan Kim, Min Joung Lee, Jong Hun An, Hyun Joo Choi, Chang Hee Pyo, Sang Yun Kim, Jae Hyun Jeong, Da Young Kang, So Yeon Park, Young Eun Kim, Woo Suk Chung, Jun Young Heo

P-332 Human-like Glycosylation in Mice Alters Neurobehavioral Phenotypes
Minji Son, Jae Ho Kim, Bomi Chang, Inwoong Song, Jeong-Heon Ko, Hyun Joo An, Jeong-Gu Kang, Boyoung Le

P-333 Therapeutic Effects of Transcranial Direct Current Stimulation in an Alzheimer's Disease Mouse Model via a Glial Mechanism
Seungyeong Yu, Mahnoor Zaheer, Mincheol Park, Tae Kim

P-334 Sleep deprivation in adolescent mice impairs long- term memory till early adulthood via suppression of hippocampal astrocytes
Ji-Yun Kang, Chang-Gue Son

P-335 GAT-3 Inhibition Restores Gait and Behavioral Transition Deficits via Tonic Inhibition in an ADHD Mouse Model
Jong Min Kim, Moonsun Sa, C. Justin Lee, Bo-Eun Yoon

P-336 The astrocytic MAOB-GABA axis suppresses spinal cord regeneration by downregulating BDNF-TrkB signaling
Hye Yeong Lee, Hye-Lan Lee, Jung Moo Lee, Jiyeon Park, Sang Wook Kim, Ki Duk Park, SeungHwan Lee, C. Justin Lee, Yoon Ha

P-337 Enhanced Homeostatic Sleep Response and Decreased Neurodegenerative Proteins in Cereblon Knock-out mice
Jinhong Kim, Jun-hyung Jung, Chul-seung Park, Tae Kim

P-338 Sleep Deprivation Triggers Neuroinflammation and Memory Decline
WonA Kim, Won-Seok Choi

P-339 NF-κB Dysregulation Impairs Microglial Polarization and Morphology.
Min Seok Jang, Won-Seok Choi

P-340 Disrupted Amygdala–Frontal Connectivity Drives Psychopathy-like Antisocial Behavior Following Early Life Stress
Jiye Choi, Hyoin Lee, Seungmoon Jung, Dahm So, Sehoon Keum, Yong Jeong

P-341 Comprehensive Behavioral Characterization and Latent Trait Mapping in SHR Rats: A Validated Model for ADHD
Han-Byeol Kim, Yu-Jin Kim, Hyo-Min Lim, Yoori Choi, Ran-Sook Woo

Molecular and Cellular Neuroscience P-342~P-425

P-342 N-Acetylcysteine Alleviates Depressive-Like Behaviors in Adolescent EAAC1-/- Mice and Early Life Stress Model Rats
Han-Byeol Kim, Yu-Jin Kim, Ye-Ji Lee, Ji-Young Yoo, Yoori Choi, Eun-Mee Kim, Sang Won Suh, Ran-Sook Woo

P-343 KCTD3 mutations cause neurodevelopmental disorder through DAAM1-mediated axon initial segment disruption
Yeonsoo Oh, Murim Choi, Yongcheol Cho

P-344 Chronic Stress-Induced Alterations in Feeding Behavior and Emotional Phenotypes via Glp1R and MC4R Downregulation in the Nucleus Accumbens
Yeo Jin Ko, Jeongseop Kim, Ja Wook Koo

P-345 Autophagic regulation of myelin protein zero during myelination in Schwann cells
Da Jeong Jeoung, So Young Jang, Hye Ran Kim, Young Hee Kim, Jin Young Lee, Su Yeon Jo, Hwan Tae Park

P-346 Interleukin-2 improves insulin sensitivity through hypothalamic sympathetic activation in obese mice
Subin Moon, Yejin Park, Sooyeon Jang, Saeha Kim, Dan-Gyeong Song, Dae-Chul Shin, Chan Hee Lee

P-347 Neurotoxic effects of carbon black on amyloid pathology and behavior in transgenic Alzheimer's model mice.
Dabin Song, Hyunjeong Kim, Eosu Kim

P-348 Could Arginine-driven polyamine synthesis explain CA2's resistance to excitotoxicity?
Aleksandra Skweres, Małgorzata Beręsewicz-Haller, Aleksandra Duchnowska, Martyna Nalepa, Francesco Bellomi, Claudia Caturano, Barbara Zabłocka, Giorgio Vivacqua, Michał Węgrzynowicz

P-349 MICU1 perturbation impairs mitochondrial Ca^{2+} uptake and suppresses intrinsic excitability in cortical neurons
Dong Cheol Jang, Su Yeon Kim, Seok-Kyu Kwon

P-350 Trehalose-mediated neuroprotection in acute brain injury via lysosomal and zinc homeostasis
Jin Yeon Lee, Yang Hee Kim

P-351 A Novel Aβ B-Cell Epitope Vaccine, Aβ-10 with Carrier Protein OVA and KLH reduce Aβ-induced Neuroinflammation in Alzheimer's Disease
Jun Sung Park, Kyonghwan Choe, Riaz Ahmad, Hyun Young Park, Min Hwa Kang, Tae Ju Park, Myeong Ok Kim

P-352 Circadian clocks are modulated by compartmentalized oscillating translation
Yi Lin

P-353 Dab1 expression controls Reelin-induced PI3K-Akt activation in early GABAergic neurons
Kavitha Sajukumar, Gum Hwa Lee

P-354 Molecular alterations induced by fear conditioning in the cerebellum
Jinhee Baek, Jungeun Ji, Kyoung-doo Hwang, Seunghwan Choi, Junko Kasuya, Sang Jeong Kim, Ted Abel, Joon-Yong An, Yong-Seok Lee

P-355 Identification of Drugs That Suppress Cyclin Y Expression to Enhance AMPA Receptor Trafficking During Long-Term Potentiation
Kijin Kim, Ja-Hyun Baik, Mikyoung Park

P-356 Long-term Suppression of Glutamate Decarboxylases After Glutamate Excitotoxicity in Primary GABAergic Neurons
Prabhakar Yadav, Gum Hwa Lee

P-357 Decoding hippocampal subfield and glial responses in ischemia using single-cell transcriptomics
Donghee Kwak, Ji Hyun Park, Yun Hak Kim, Deok-Ho Kim, Hong Il Yoo

P-358 ZCC1 attenuates ischemic stroke damage by selectively inhibiting MMP-9 and suppressing zinc toxicity
Yeabin Kwon, Jin Yeon Lee, Yang-Hee Kim

P-359 Phoenix dactylifera extract mitigates D-galactose-induced oxidative stress and neurodegeneration in the mouse hippocampus.
Young Mi Youk, Mun Gyu Song, Sang Hyeon Kim, Hyeong Ju Seo, Hyo Young Jung

P-360 Functional and distinct roles of Piezo2-mediated mechanotransduction in dental primary afferent neurons
Kihwan Lee, Pa Reum Lee, Ji Min Park, Shinae Kim, Jung Hoon Jung, Seog Bae Oh

P-361 TARP γ-8 orchestrates AMPA receptor stability in the hippocampus
Jae-man Song, Young Ho Suh

P-362 Regulation of BAT Thermogenesis via TRPA1-Expressing Hypothalamic POMC Neurons
Arbi Bahtiar Boedi Iman Halanobis, Ju Hwan Yang, Eun Hye Byeon, Dong Kun Lee, Dawon Kang, Bo Hyun Lee, Min Seok Song

P-363 Identification and characterization of intestinal cells that detect each essential amino acid
JONG HOON WON, Jinhyeong Lee, Boram Kim, Greg S. B. Suh

P-364 Disrupted Zinc Homeostasis and MMP-9 Activation in L-BMAA-Induced ALS Models: Therapeutic Potential of ZCS1
Song Hee Kim, Hyun Seung Lee, Yang Hee Kim

P-365 Astrocyte-specific regulation of clock proteins by Tmem44 in cultured mouse cortical astrocyte
Ji Eun Ryu, Minsung Park, Hyun Woong Roh, Eun Jeong Lee, Jaerak Chang, Eun Young Kim

P-366 Sonically enhanced adult-born neurogenesis represents a novel paradigm for improving cognitive function
Nishani Jayanika Jayathilake, Sangyep Shin, Kyu Pil Lee, Joo Min Park

P-367 Aberrant MAOB-dependent H2O2 cause neuropathic pain and exacerbates nocturnal pain via REVERBα-dependent MAOB disinhibi
Song-I Kim, Sun Yeul Lee, Dong Woon Kim, C. Justin Lee

P-368 Dual CRBN-dependent and -independent neuroprotective actions of the thalidomide analog in a mild traumatic brain injury model
SooJin Kim, Hannah Joo, Hajin Jeong, Hyunjeong Kim, Eosu Kim

P-369 Regulation of cyclin Y and CYBP3 interaction with an in silico-in vitro integrated approach
Jonghee Kim, Jiyeon Seo, Hark Kyun Kim, Bong-June Yoon, Dong-Gyu Jo, Mikyoung Park

P-370 Remaining Nav1.8-positive nociceptors drive persistent tactile hypersensitivity after partial sciatic nerve crush injury in mice
Yoon Kyung Lee, Sang Wook Shim, Dahee Roh, Kihwan Lee, Hyoung Woo Kim, Seog Bae Oh

P-371 Advancing AAV Capsid Engineering for Targeted Gene Therapy Using PackGene's π-Icosa Platform
Ye Bu, Daniel Mchugh, Amos Gutnick, Xin Swanson, Changsong Heo, Paul Li

P-372 Region-Specific Epigenetic Regulation of Cerebellar Astrocytes by NFIB in Motor Circuits
Ukbong Kwon, Benjamin Deneen

P-373 Glio-vascular contributions to oxidative stress and neurodegeneration in chronic cerebral hypoperfusion mouse model
Benedict Delmo, Yong Jeong, C. Justin Lee

P-374 Therapeutic potential of mesenchymal stem cells in cerebellar ataxia
Sehwan Kim, Gi Beom Lee, Se Min Park, Un Ju Jung, Sang Ryong Kim

P-375 Integrative proteomic approach to reveal altered signaling modules during Alzheimer's disease progression in Tau P30
Eunji Cho, Seulah Lee, Hagyeong Lee, Jaehoon Kim, Yang Woo Kwon, Dayea Kim, Hyang-Sook Hoe, Jong Hyuk Yoon

P-376 Molecular basis for pore blockade of Tentonin 3, a mechanosensitive channel by a conopeptide, NMB-1
Sujin Lim, Sungmin Pak, Pareum Lee, Jiwon Lee, Gyu-Sang Hong, Uhtaek Oh

P-377 Downregulation of GCH1 significantly alleviates hypersensitivity in neuropathic pain models
Heesue Chang, Minkyung Park, Kyungjin Lee, Ha-Na Woo, Ji Hyun Kim, Im Kyung Kang, Heuiran Lee, Hyun Ho Jung

P-378 Fine-Tuning of Dopaminergic Synapse by Microglial Engulfment
Yemin Kim, Yeonjoo Kim, Jaewook Jeong, Young-Jin Choi, Won-Suk Chung, Jae-Ick Kim

P-379 An efficient strategy for developing a human brain cell-type-specific fluorescent probe with a molecular target
Minji Kim, Dongwan Ko, Jung Yeol Lee, Young-Tae Chang, Beomsue Kim

P-380 hDPSC secretome alleviates hypoxic injury in hippocampal neurons by modulating mitochondrial function and preventing mitophagy
Kyung-Joo Seong, Su-Bin Seong, Hyo-Seon Park, Sam-Young Park, Ji-Yeon Jung, Won-Jae Kim

P-381 Maternal transcutaneous auricular vagus nerve stimulation prevents maternal immune activation-induced behavioral deficits in offspring mice
Hiroshi Kuniishi, Min-Jue Xie, Hideo Matsuzaki

P-382 Astrocytic AQP4/TRPA1/BEST1/D-serine Signaling Modulates Brain Hemodynamics and Sensory Perception through NMDA Receptors
Myeongju Joy Kim, C. Justin Lee, Minah Suh

P-383 Bisphenol A upregulates CHMP2B to promote neuron-to-glia mitochondrial transfer, accelerating neurodegeneration via exosome
Ba Le Duy Vu, Gee Euhn Choi

P-384 Ovariectomy Alters Bone-Marrow-Associated Immune and Cardiovascular Gene Networks in the Amygdala of Spontaneously Hypertensive Rat
Thuy Linh Pham, Jimmy Kim, Ko Yamanaka, Hidefumi Waki, Sabine Gouraud

P-385 Visualization of the existence of LEAP2 in the nucleus accumbens and its role in amphetamine-induced locomotor activity
Seohyeon Lee, Ga Young Yoo, Hyung Shin Yoon, Jeong-Hoon Kim

P-386 Real-Time Imaging and Optimization of Cortical Neuron Morphology Analysis Using High-Content Screening Systems
Hye Ryeong Lim, Kunhyung Kim, Myungjin Kim, Yoonju Kim, Taekwan Lee

P-387 Identification of Aurora Kinase as a pivotal regulator of the pro-neurodegenerative phenotype in macrophages
Yeojin Seo, Seung Ah Jee, Hyungsoon Kim Kim, Byung Gon Kim

P-388 Astrocytic Ankyrin2 Enables Memory Persistence
Hayoung Kim, Jiwoon Lim, Jooyoung Kim, Erva Ozkan, Hyojin Park, Mingu Gordon Park, Sangkyu Lee, Bong-kiun Kaang, C. Justin Lee, Wuhyun Koh

P-389 Association of altered αCaMKII phosphorylation with male-specific sensorimotor gating impairments in a mouse model of Noonan syndrome
Soobin Kim, Sohyeon Park, Hung M. Vu, Yujin Kim, In Gyeong Koh, Gaeun Park, Minkyung Kang, Sang Jeong Kim, Joon Yong An, Min-Sik Kim, Moo Kyun Park, Yong-Seok Lee

P-390 Therapeutic potential of KBN-2202 in alzheimer's disease through modulation of microglial phagocytosis
Moonhang Kim, Sun-Young Lee, Mi Ran Choi, Sang-Rae Lee

P-391 Exposure to air pollutants disrupts the spontaneous activity of inner support cells in the developing cochlea
Kwon Woo Kang, Eunyoung Yi

P-392 Astrocyte-mediated synaptic trogocytosis via engineered ligand-receptor system: impact on memory in aged mice
Songhee Choi, Shin Heun Kim, Sangkyu Lee, Yong Jeong

P-393 Spatial Alterations of N-Glycans and Amino Acids in Photothrombosis-Induced Ischemic Stroke Models Revealed by Mass Spectrometry Imaging
Hyun Jun Jang, Jae-Hun Lee, Boyoung Lee, C. Justin Lee

P-394 NCF1–Moesin Binding Controls $CD8^+$ T Cell Fate in Neuroinflammatory Conditions after Ischemic Stroke
Jiwon Kim, Jong Youl Kim, Ho-Keun Kwon, Jong Eun Lee

P-395 Neurensin1 Regulates Social Memory Engram Formation in the Ventral Hippocampus
Mei Zhuang, An Liu

P-396 PFOA induces cell cycle arrest mediated by ER stress in neural stem cells and impairs hippocampal neurogenesis.
Chang Yup Kim, Sunguk Yang, Duwon Jung, Seonghyun Cho, Jeon Yoon Kim, Seonghoo Lee, Jaewon Lee

P-397 GPR40 Activation Attenuates Neurodegeneration in Alzheimer's Disease
Tae-Young Ha, Yeji Kim, Keun-A Chang

P-398 Inhibition of LRRK2 kinase promotes axon regeneration after peripheral nerve injury
Eun Mo Yang, Eun-Hae Jang, Gil Song, Harryn Choi, Jaeyong Kim, Yunho Gim, Yewon Cho, Eun-Mi Hur

P-399 Piezo1 activation promotes glial anti-inflammation and tau dephosphorylation in human Alzheimer's disease model
Xiaohui Zhu, Yen N. Diep, Van Thi Ai Tran, You Jung Kang, Hansang Cho

P-400 Immune-Neural Crosstalk and Divergent Cell-Specific Immune Programs Are Modulated by Diet in Drosophila Melanogaster Ischemic Stroke.
Subin Choi, Yangkyun Oh

P-401 Identification of a neuroprotective compound for the treatment of ischemic stroke through drug repurposing
Jieun Park, Hee jeong Jang, Sang soo Park, Jaehong Kim, Dong-eog Kim

P-402 Down-regulation of glucocorticid receptor modulates glial cell inflammatory response and neural stem cell proliferation
Duwon Jung, Sung Min Moon, Chang Yup Kim, Seonghoo Lee, Jeongyoon Kim, Seonghyun Cho, Da Seul Choi, Jaewon Lee

P-403 The role of dopamine receptors on microglial functions and motor-related behaviors
Jieun Lee, Hansol Oh, Yeonjoo Kim, Sung Ho Park, Jae-Ick Kim

P-404 Pulsatile GnRH Signaling in the Hippocampus Promotes Neurotrophic Effects
Yumi Son, Hyunjeong Kim, Eosu Kim

P-405 TWIK-1 regulates mitochondrial homeostasis and protects against acoustic stress
Hojin Lee, Jonghoon Jung, Teayeon Kim, Jea-Yong Park, Jeakwang Lee

P-406 Optimal Low-Dose Pregabalin Enhances Functional Recovery After Spinal Cord Injury
Da Bin Kim, Lina Liu, Jung Keun Hyun

P-407 Gap junction-mediated modulation of neural circuit function in the thalamus
Chanmi Park, Yao Piao, Yumin Cho, Eunji Cheong

P-408 Microplastics promote extracellular vesicle-mediated Amyloid-beta release
Ju Hui Choi, Seoeun Lee, Gee Euhn Choi

P-409 GenX exposure alters cortical organization and synaptic function in cerebral organoids.
Eui Jun Min, Moon Yi Ko, Min Jeong Kim, Byoung-seok Lee, Sung-Ae Hyun, Minhan Ka

P-410 VPS26B enhances motor learning ability via glutamate receptor recycling in the primary motor cortex in a parkinsonian mouse model
Thi Hai Thanh Nguyen, Jung Bae Seong, Jincheol Seo, Jinyoung Won, Se-Hee Choe, Hae Rim Kim, Young-Hyun Kim, Ki-Hoan Nam, Youngjeon Lee

P-411 Acetate-induced Cathepsin B expression in reactive astrocytes of GBM patients
Jin Ho Nam, Suhyun Kim, HeeJung Park, Dongwoo Kim, Min-Jung You, Hee Yeon Kim, UiYeol Park, Hoon Ryu, Mijin Yun

P-412 Griseofulvin Attenuates Rotenone-Induced Dopaminergic Cell Toxicity by Modulating Microtubule Dynamics and Autophagy
Jin Ho Lee, Won-Seok Choi

P-413 PAD4-mediated NEMO (IKKγ) citrullination in microglia promotes neuroinflammation in the post-ischemic brain
Sang-A Oh, Il-Doo Kim, Ja-Kyeong Lee

P-414 Mass screening of FDA-approved compounds identifies neuroprotective and neuroregenerative agents for treatment of spinal cord injury
Eun Jae Do, Bong Geun Choi, Soo Bin Choi, Da Un Jang, Ji Hyun Lee, Song Kyu Woo, Jung Keun Hyun

P-415 ATP acts as a neurotransmitter for Type III cells in the fungiform papillae taste buds
MinJae Kim, Eunju Sung, Sungho Lee, Myunghwan Choi

P-416 Agbl4 knockout mice display autistic-like behaviors and prefrontal dysfunction.
Eum-Ji Kim, Jiyun Lee, Dae-Si Kang, Soo Min Kang, Yeo Jin Ko, Cheol-Hee Kim, Ja Wook Koo, Tae-Yong Choi

P-417 Two distinct RhoGTPase pathways regulating post-tetanic potentiation
Yeongjin David Kim, Seungbok Lee

P-418 Therapeutic Effects of Ifenprodil on Pain and Neuroinflammation in a Rat Model of Chronic Polyarthritis
Ain' Sabreena Mohd Noh, Che Aishah Nazariah Ismail, Anani Aila Mat Zin, Idris Long

P-419 The role of LRRK2 in stress granules formation
HO JIN JANG, Byoung Dae Lee

P-420 Synaptoporin is essential for the structural integrity and functional plasticity of hippocampal mossy fiber synapses
Gyu Hyun Kim, Na-young Seo, Hyeyeon Kim, hyungju park, Kea Joo Lee

P-421 Minimally invasive chemogenetic modulation of the Dorsal Motor Nucleus of the Vagus
Yeongho Ji, Hye Yeong Lee, C. Justin Lee, Moon sun Sa, Wuhyun Koh, Seung Jun Ryu

P-422 Age-dependent alterations of SELENBP1 in microglia of 5XFAD mice
Su-Yeon Sim, Jung-Soo Han, Soojin Kim, Yeon-Soo Kim

P-423 TMEM43 tunes hippocampal networks via an astrocytic gap junction
Ki Jung Kim, Minwoo Wendy Jang, Jiwoon Lim, Woo Suk Roh, Yongmin Park, Tai Young Kim, Young-Eun Han, Jae-Hun Lee, Eunjin Shin, Kyung-Seok Han, C. Justin Lee

P-424 c-Kit signaling confers damage-resistance to sweet taste cells upon nerve injury
Su Young Ki, Yong Taek Jeong

P-425 Investigating cortical adenosine dynamics during the sleep-wake cycle of the mouse
Joohyeon Hong, Hankyul Kwak, Jungryun Lee, Dongsu Lee, Beomsoo Kim, Hyeonyeong Jeong, Chanmi Park, Yujin Cho, Go Eun Ha, Seonghyeon Kang, Jisoo Park, Eunji Cheong

Neuroengineering P-426~P-443

P-426 Locomotor kinematics shapes spatial patterns of cortical activity and connectivity
Minyong Lee, Changhak Lee, Hyowon Kim, Kwang Lee

P-427 A wireless autonomous soft optogenetic stimulator with neural signal monitoring for freely behaving animals under indoor ambient light
Chanwoo Lee, Ki Jun Yu

P-428 Flexible high-definition active neural interface for single spike neural recording
Shinil Cho, Ki Jun Yu

P-429 Miniaturized implantable stimulator using liquid crystal polymer for deep brain stimulation targeting the ventral posterolateral nucleus (VPL)
Wonki Mun, Chin Su Koh, Seung-Hee Ahn, Joonsoo Jeong, Hyun Ho Jung

P-430 An AAV Toolset for Microglia-Specific Transgene Targeting across Species
Fengting Yu, Minmin Luo

P-431 Disentangling Attention Dynamics through EEG-Based Relative Phase Analysis
Jehyeop Lee, Joon-Young Moon

P-432 Electrochemical Impedance Sensing of Dopamine for Real-Time Neurochemical Monitoring in Neuroengineering
Daerl Park, Jungsik Choi, Heon-Jin Choi

P-433 Development of TMP-tag based chemigenetic neuromodulator sensors for multiplex imaging
En Ji, Shengwei Fu, Zizhe Zhou, Yuqi Zhang, Sunlei Pan, Yaohan Huang, Yu Zheng, Xiaoyan Cui, Ting Wang, Junwei Zhang, Zhixing Chen, Yulong Li

P-434 Proprioception can be recalibrated by sensory deception in arm matching task
Youngdeok Kim, Seunghyeon Han, Jong Weon Lee, Deog Young Kim, Hangue Park

P-435 Microcoil-based magnetic stimulation in a Parkinson's disease mouse model
Seonghyun Park, Si-jeong Lee, Minseo Bang, Ye Eun Seo, Hyun Ji Yoo, Tae-in Kam, Seungwoo Lee

P-436 Theoretical approach to High-Frequency Magnetothermal Dissipation in Ferrofluids for Wireless Deep Brain Stimulation
Mingu Song, Jeonghyun Choi, Haesung Kim, Hyungeun Kim, Hyunjae Lee, Jeiwon Cho, Yeowool Huh, Sanggeon Park, Jinho Jeong, Heon-jin Choi

P-437 Correlation between number of stimulation channel and therapeutic effects of transcutaneous nerve stimula
Yunbeom Lee, Hyunjong Moon, Sangmin Song, Jaejun Park

P-438 Modeling motor learning as hysteresis: a quantitative approach to assess aftereffects of sensory modulation
Myounghyun Kim, Hangue Park

P-439 Enhanced tool end-effector control accuracy and retention through multi-modal augmented feedback in virtual reality environments
Chanyang Park, Hangue Park

P-440 Microchannel-structured nerve conduits enhance functional recovery following peripheral nerve injury in rats
Soo Bin Choi, Bong Geun Choi, Jung Keun Hyun

P-441 Multi-BRET Biosensors For Resolving Biased Gα Coupling Dynamics in GPCRs
Duwan Kwon, Hyunbin KIm, Hyunah Choo, Jihye Seong

P-442 Reliable Cortical Mapping Using Randomized I/O Curve in Transcranial Magnetic Stimulation
Rintaro Aoki, Wenwei Yu, Gomez-Tames Jose

P-443 Therapeutic effects of low-intensity focused ultrasound neuromodulation in a mouse model of tic-like behavior using clinically relevant parameters
Subeen Kim, Miseon Kang, Myunghyun J. Jeong, Yehhyun Jo, Jeongyeon Kim, Hyunjoo J. Lee

Others : (Computational Neuroscience)

P-444 Visual reconstruction based on temporal encoding information of visual cortex neurons
Qingyuan Chen, Jiayi Zhang

Others : (Research on Drug Development for Neurodegenerative Diseases)

P-445 Discovery and Optimization of a Series of Vinyl Sulfoximine-Based Analogues as Potent Nrf2 Activators for the Treatment of Multiple Sclerosis
Jaehwan Kim, Yoowon Kim, Byungeun Kim, Rium Kim, Yong-Sun Bahn, Ji Won Choi, Jong-Hyun Park, Ki Duk Park

Others : (integrative physiology)

P-446 Serotonin 2C Receptors Expressed by CRH and TRH Neurons Regulate Metabolism
Jieun Yu, Jong-Woo Sohn

Others : (Social behaviors and Circuits)

P-447 Drawn to delight: A vicarious reward paradigm unveils neural circuits of positive empathy
Junweon Byun, Jong-Hyun Kim, Sang-Yeong Lee, Da-Eun Choi, Hee-Sup Shin

Others : (Behavior)

P-448 Postprandial sodium sensing by enteric neurons in Drosophila
Byoungsoo Kim, Gayoung Hwang, Sung-Eun Yoon, Meihua Kuang, Jing Wang, Young-Joon Kim, Greg Suh

Others : (Sarcopenia and Neuromuscular junction)

P-449 Organoid modeling of functional neuromuscular junctions and therapeutic screening of natural extracts for sarcopenia
So Young Eun, Heeju Kim, Seong-Kyu Choe, Chae-Seok Lim

Others : (Network meta analysis)

P-450 Network Meta-Analysis Identifies Epigenetic Mechanisms Supporting Functional Recovery After Spinal Cord Injury
Yoon Koo Han, Lina Liu, Sung Ryul Shim, Jung Keun Hyun

Others : (Brain tumor)

P-451 Dual Delivery of Light/Prodrug Nanoparticles using tumor-implantable micro light-emitting diode on a optofluidic system for combinational glioma tr
Junwon Park, Jakyeong Koo, Jun Seo Lee, Seong Ik Jeon, Jeongrae Kim, Tae-il Kim, Kwangmeyung Kim, Won Seok Chang

Others : (Neuro imaging technique)

P-452 Enhanced optical clearing for efficient imaging of genetically encoded fluorescence and multicolor staining in mouse brain tissue&
Youngjae Ryu, Sung Rae Kim, Chang Man Ha

Others : (Cognition and Behavior)

P-453 The role of the prefrontal cortex in the emotional evaluation of ambivalent stimuli
Jaewoong Hwang, Minsoo Kim, ChiHye Chung

Others : (Cancer neuroscience)

P-454 Area postrema detects circulating tumor-derived soluble factors at the earliest stage of cancer associated cachexia
Jaehun Kim, SangHyeon Ju, HyunJung Hong, Sihyeon Kim, Seohyun Choi, Minho Shong

Others : (Human Learning)

P-455 Frequency-Based Imitation as an Independent Learning Heuristic
Aner Zheng, Seungdae Baek, Hyeonsu Lee, Jaeson Jang, Se-Bum Paik

Others : (Cognitive neuroscience)

P-456 Unfairness affects the perception of pain and altruistic behavior
Da-Eun Yoon, Heeyoung Moon, Min-Jung Kwon, Dong-Ju Lim, In-Seon Lee, Younbyoung Chae

Others : (Neuroimaging)

P-457 Fluorinated THK-5320 Derivatives for In Vivo PET Imaging of ApoE-Binding Amyloid Plaques
Ryuichi Harada, Hendris Wongso, Rumi Nakayama-Naono, Takayuki Sakai, Shozo Furumoto, Nobuyuki Okamura

Others : (Neuroaesthetics)

P-458 The Neural Signature of Music Preference: Musical Complexity, Ratings, and Relative Phase
Sunhyun Min, Younghwa Cha, Marcus Pearce, Joon-Young Moon

P-459 Neurobehavioral and Histopathological Assessment of 3-Fluorophenmetrazine Neurotoxicity in Mice
CheLynn Jeon, Nayoung Gong, Mingyeong Kim, Nayoung Lim, Sujeong Park, Kikyung Jung

Others : (Ecotoxicology)

P-460 Suppression of BDNF-CREB Signaling by Prenatal RF Exposure in Wild-Type Mice: Insights into Developmental Sensitivity versus AD Pathology
Yeonghoon Son, Yoonsoo Choi, Ye Ji Jeong, Hyung-Do Choi, Hae-June Lee

Others : (Ecotoxicology)

P-461 Effects of RF-EMF Exposure on Impulsive Behavior and Immediate-Early Gene Expression in the Striatum
Yeonghoon Son, Yoonsoo Choi, Suyeon Lee, Hyung-Do Choi, Hae-June Lee

Others : (Materials Engineering)

P-462 Liquid metal based Flexible Electrodes for Neural Stimulation and Recording
TAE JUN KIM, Chin Su Koh, Won Ki Mun, Yong Won Kwon, Young-Geun Park, Jang-Ung Park, Hyun Ho Jung

Others : (Cognitive Neuroscience (eg behavioural fMRI study))

P-463 REWARD-RELATED FUNCTIONAL CONNECTIVITY: COMPARING SELF-REWARDS AND FILIAL MOTIVATION IN ADOLESCENTS
Siti Hajar Zabri, Aini Ismafairus Abd Hamid, Asma Hayati Ahmad, Siti Mariam Roslan, Muhammad Riddha Abdul Rahman

Others : (Social and Cognitive Neuroscience)

P-464 Theory of mind mediates adolescents' age-related increase in interest-based gossip sharing
SeungYoon Oh, Youngjo Song, Yueun Jung, Jaeseung Jeong

Others : (Brain/Cognitive Aging)

P-465 Sex differences in modifiable risk factors influencing cognitive decline
Maithreyee Devi, Aram Cho, Soriul Kim, Seung Ku Lee, Hyeon-Jin Kim, Chol Shin, Hyang Woon Lee

Others : (Muscular dystrophy, myogenesis)

P-466 Inactivation of Protein X by HDAC8 represses myogenic differentiation via miR-18b/CTGF/TrkA/Erk1,2 signaling pathway in Duchenne muscular dystrophy
Kyung Won Choi, Ki Yoon Kim, Jung Joon Sung

Others : (Computational Modeling)

P-467 A Naturalistic Decision-Making Task Revealing Differences in Explore–Exploit Trade-Offs in Addiction
Hyeonmin Lee, Jaeyoung Jeon, Juha Lee, Won Mok Shim, Woo-Young Ahn

Others : (behavior and neurophysiology)

P-468 Astrocytic Calcium Mirrors Neuromodulator Release in the Hippocampus During Anxiogenic Contexts
Unjin Lee, Kwang Hwan Kim, Sung Joong Lee

Others : (Cognitive Neuroscience)

P-469 Deterioration and Compensation of Episodic Memory in Aging
Maria Jieun Hwang, Sang-Eon Park, Sang Ah Lee

P-470 Glial scar formation in the peritumoral reactive astrocytes via the TGF-β2 signaling pathway regulates glioblastoma progression
Hyein Yu, Hansol Choi, Sunhwa Lim, Soo-Jin Oh

Others : (Methods Development)

P-471 Fixative-eXchange (FX)-seq: a platform for transcriptomics analysis of PFA-Fixed and FFPE Samples
Han-Eol Park, Yu Tak Lee, Jaewon Lee, Chae Young Byun, Junsuk Lee, Hyelin Ji, Young-Lan Song, Sung-Yon Kim, Junho K. Hur, Eunha Kim, Chung Whan Lee, Yoon Dae Han, Hyunki Kim, Chang Ho Sohn

P-472 Investigation of synaptic connectivity between CA1 and ACC during systems consolidation
Hyunmin Park, Chaery Lee, Jooyoung Kim, Hyunsu Jung, Yongmin Sung, Bong-Kiun Kaang

P-473 Astrocytic Slitrk2 competitively constrains neuronal Slitrk2-mediated excitatory synaptic functions
Younghyeon Jeon, Byeongchan Kim, Khai Huynh Ngoc, Jaewon Ko, Ji Won Um

P-474 Anatomical and Functional Evidence for Vestibular-Auditory Integration via the LVN-IC Pathway
Sunghee Kang, Jisoo Han, Young Rae Ji, Gunsoo Kim

P-475 Parafascicular Thalamic Glutamatergic Activity Encodes the Transition from Alcohol Consumption to Motivational Engagement
Hyein Song, Jiyong Lee, Jongseo Lee, Yunseo Baek, Shinwoo Kang

P-476 Activation of Pallidal Prototypic Neurons Regulates Behavioral Flexibility
Shinwoo Kang, Minsu Yang, Jiyong Lee, Hyein Song, Aubrey Bennett, Seungwoo Kang, Sang Wan Lee, Doo-Sup Choi

P-477 In Vitro electrophysiological Analysis of Taurine Function and Receptor Expression in rat primary cultured neurons and astrocytes
Da-Eun KIM, Dong Ho WOO

P-478 Lateral hypothalamus directs stress-induced modulation of acute and psoriatic itch
Arnab Barik

P-479 Analgesic effects of 10 kHz low-intensity DBS in Agranular Insular Cortex for Neuropathic Pain Rat Model
Seung Hyun Min, Chin Su Koh, Heesue Chang, Tae Jun Kim, Won Ki Mun, Hyun Ho Jung

P-480 Behavioral benefits of prolonged exercise rely on plasticity in cerebellar granule cell networks
Heeyoun Park, Taehyeong Kim, Yukio Yamamoto, Keiko Tanaka-Yamamoto

P-481 Hindbrain cold-sensitive neurons orchestrate integrated homeostatic responses
Sieun Jung, Myungsun Lee, Anna Kondaurova, JiSoo Kwon, Hyeyoung Shin, Sung-Yon Kim

P-482 Sexual dimorphism in social recognition following resocialization after social isolation in mice
Taewoo Kim, Gaeun Park, Yong-Seok Lee

P-483 The role of Myosin V in synaptic plasticity
Yufang Zhong, Xiaomin Zhang, Boxing Li, Lianyan Huang

P-484 Role of hypothalamic circuitry for social interaction under threatening conditions
Yoonjeong Cho, Yujin Jang, Soonil Pyo, Thomas McHugh, Jahyun Baik, Jeongjin Kim

P-485 Recalled NR2D- NMDARs in the hippocampal GABAergic interneurons regulate E/I balance during epileptogenesis
Ramesh Sharma, Nahyeon Park, Chaerin Yoon, Min-Ho Nam, Jin Bong Park

P-486 Bergmann glia activation induces Purkinje cell suppression via interneurons
Jaegeon Lee, Seung Ha Kim, Mirae Jang, Yong-Seok Lee, Sang Jeong Kim

P-487 Neuromodulator Effects on ARC Neurons: Unraveling Mechanisms of Feeding Regulation in the CNS
Donghee Rhee, Se-Young Choi

P-488 Pathway-specific chemogenetic modulation of BLA projections to PrL and NAc subregions controls amphetamine-induced conditioned place preference
Joonyeup Han, Haeun Rim, Hanbyual Jang, Wen Ting Cai, Wha Young Kim, Jeong-Hoon Kim

P-489 The influence of internal state changes on social behavior
Subeen Shin, Hyoin Lee, Yong Jeong

P-490 The vDB-vHPC cholinergic projection mediates long-term social memory deficits
Meng Li, An Liu

P-491 Brainstem enkephalinergic neural circuit underlying cold-induced pain relief in mice
Hayun Kim, Yoonkyung Lee, Seog Bae Oh

P-492 Mapping of the Gut-Brain Axis Induced by PINK1 Deficiency Using Viral Tracing
Yiseul Bae, Eunhye Joe, Eun Jeong Lee

P-493 The role of SST interneuron in early life adversity-induced deficits in empathic freezing
Dahm So, Sua Lee, Sowon Kim, Jiye Choi, Sehoon Keum

P-494 A GFRAL–Spinal Circuit Links Mitochondrial Stress to Sympathetic Thermogenesis and Adipose Remodeling
Sang-Hyeon Ju, Ji Eun Kim, Min Hee Lee, Hyun Jung Hong, Uzma Yaseen, Jung Tae Kim, Benyuan Zhang, Hyon-Seung Yi, Seong Eun Lee, Yea Eun Kang, Minsung Park, Jinkuk Kim, Jong-Woo Sohn, Minho Shong, Ju Hee Lee

P-495 Infantile silent engram cells modulate memory formation during adulthood
Joo Hee Yang, Sunhoi So, Jin-Hee Han

Systems and Computational Neuroscience P-496~P-545

P-496 Phase preservation of EEG reflects distraction control of visual working memory
Hansol Lee, Yelyn Lee, Jinseo Park, Min-Suk Kang

P-497 Comparative Analysis of Spike-Timing Correlation in Wild-Type and Optogenetically-Treated Degenerate Retinas
Yeonsu Kim, Sein Kim, Da Eun Kim, Hyeonhee Roh, Maesoon Im,

P-498 A neural circuit integrating sensory and memory signals underlying social novelty preference
Seong-Rae Kim, Jinseong Kim, Sung-Yon Kim

P-499 Spatial context and past experiences build spatial memory
Minjae Jo, Sunyoung Park, Min-Suk Kang

P-500 Systematic proteogenomic analysis identifies causal plasma proteins and subtype-specific biomarkers for Alzheimer's disease&
Hae-un Jung, Seulha Lee, Ye-Jin Kim, Eunji Cho, Jong Hyuk Yoon

P-501 A noradrenergic brainstem-to-hypothalamus circuit for sustained appetite suppression following stress
Myungmo An, Junkoo Park, Sumin Lee, Se-Young Choi, Sung-Yon Kim

P-502 EEG Analysis of Hierarchical Processing in Deviant Auditory Stimuli: Oddball Paradigm
Seoyeon Kim, Jehyeop Lee, Joon-Young Moon

P-503 Human Analogical Reasoning Violates Geometric Assumptions of Vector-Based Model
Selin Samra, Seng Bum Michael Yoo

P-504 Metabolically-Informed Dynamic Causal Modeling of Ketogenic Therapy in Childhood Epilepsy
Jiyoung Kang, Euisun Kim, Hae-Jeong Park

P-505 Insights in rats: Behavioral investigation in Tolman's Maze
Teoman Dayı, Seungmin Yu, Jaekyung Kim

P-506 Effect of motion speed expectation on visually guided oculomotor behavior
Jaeseong Yoon, Joonyeol Lee

P-507 Movement shapes decisions via multiplexing neurons in the mesencephalic locomotor region
Wooyeon Shin, Juri Kim, Dajung Jung, Se-Bum Paik, Jeongjin Kim

P-508 Psychobehavioral analysis and neural decoding of food addiction in non-human primates: From model development to pharmacological intervention
Yunkyo Jung, Hanseob Kim, HyeonGu Yeo, Hyerin Jang, Jisun Min, Wonseok Choi, Sunghyun Park, Eunsu Jeon, Gyuseo Bae, Kangjin Jeong, Yeonghyun Kim, Jaewon Huh, Seungho Baek, Yeongjeon Lee, Hyungjin Choi

P-509 Forelimb trajectory stability in reach-to-grasp task reflects long-term motor learning progression
Haeun Yeo, Hyoseok Jang

P-510 Neural basis of approximate object counting in human single-neuron activity
Shin-young An, Sameer Sheth, Benjamin Hayden, Seng Bum Michael Yoo, Hansem Sohn

P-511 Explainable machine learning EEG data analysis framework for predicting vagus nerve stimulation effects in epilepsy patients
Donghwan Lim, Joonho Lee, Euisun Kim, Jinseok Eo, Jiyoung Park, Sangbo Lee, Ara Ko, Joonsoo Lee, Hae-Jeong Park

P-512 Latent Attractor Dynamics in OFC and RSC During Naturalistic Foraging
Seunghan Lee, Maya Zhe Wang, Benjamin Yost Hayden, Seng Bum Michael Yoo, Sung-Phil Kim

P-513 Comprehensive analysis of naturalistic behaviors enables tailored diagnosis of depressive disorder in mice
Hyeonsik Oh, Sang Kun Choi, Jinsu Lee, Heeyoung Lee, Jongpil Shin, Seungkyu Son, Bobae Hyeon, Won Do Heo

P-514 Frequency-Selective Sound Localization Mechanism in Drosophila Mediated by WV-WV Interneurons
Seongyeon Kim

P-515 Dopamine neurons flexibly compute reward proximity during foraging competition
Rin Wang, Seungyub Lee, Hyunggoo Kim

P-516 Acetylcholine enhances deviance detection in Hodgkin-Huxley neuronal networks
Fei Fang, Zi-Gang Huang, Zenas C. Chao

P-517 Neural geometry of relational representation in the monkey posterior parietal cortex
Somang Paeng, Su-Jin An, Hansem Sohn, Mehrdad Jazayeri

P-518 Inferring Temporally Resolved Directionality Transition Dynamics in fMRI via Phase Analysis
Eunhee Ji, Jehyeop Lee, Joon-Young Moon

P-519 Establishing Awake Monkey fMRI Platform for Whole-Brain Imaging and Perturbation
Su-Jin An, Somang Paeng, Hansem Sohn

P-520 Connectome-based Cognitive Prediction Models: Integrating Functional and Structural Brain Networks
Eunku Bae, Kwangsun Yoo, Chang-hyun Park, Hyang Woon Lee

P-521 Context-dependent reward processing reflected in central positivity
Jiyeon Jeong, Hyunhoe An, Suxian Li, Seok-Jun Hong, Min-Suk Kang

P-522 Rhythmic but fading: damped oscillation reveals the temporal dynamics of retroperception
Sugeun Yun, Younglae Kim, Jaeseung Jeong, Yee Joon Kim

P-523 Comparison of BGRU, EEGNet, and EEG Conformer from the Perspectives of Performance and Design Principles in EEG-Based Emotion Recognition
Ye-Ji Yoo, Kyu-Hyeok Lee, Hyoung-Gook Kim, Jörn Fischer

P-524 Dynamic Control of Neural Activity via Real-Time Brain-Machine Interface Across Brain Regions
Nahyun Kim, Taegyun Jin, Dohoung Kim

P-525 Neural Circuit Dynamics During the Acute Phase of Stroke Recovery
Dokyeong Kim, Yena Hyun, Dohoung Kim

P-526 Weighted Maximum Likelihood Estimation: Explanation of biased visual-proprioceptive integration
June Seung Lee, Hangue Park

P-527 Emergence of aesthetic preference from hierarchical neural circuits
Aysenur Deniz Song, Minjun Kang, Se-Bum Paik

P-528 Real-Time Individual Sleep Prediction Enabled by Probabilistic Modeling of Wearable Data and Functional Brain Activity Analysis
Jisoo Yang, Jihoo Park, Chul-Hyun Cho, Yul HR Kang

P-529 Spontaneous social change driven by Stochastic Individual Behavior
Hyeonsu Lee, Seungdae Baek, Jaeson Jang, Se-Bum Paik

P-530 Population-level encoding of mixed tones from the auditory neural assemblies
Gyumin Park, Jeehyun Kwag

P-531 One-Shot Preconditioning for Robust and Efficient Neural Learning
Jeonghwan Cheon, Jaehyuk Bae, Se-Bum Paik

P-532 Oxytocin dynamically gate prefrontal-amygdala-auditory networks to enable selective processing of socially salient cues in awake mice
DaYoung Jung, Hio-Been Han, Jungyoung Kim, Robert Froemke, Jee Hyun Choi

P-533 Reconstructing latent neural attractors during motor learning with false-nearest-neighbor-regularized autoencoders
With Drawn
Junyoung Maa, Jaekyung Kim

P-534 Neural correlates of interleaved practice explaining superior motor learning
JoonHyun Ko, Alyssa Han, Taewon Kim

P-535 A hypothalamus-to-dorsal pons circuit for palatability-guided consummatory behaviors
Myungsun Lee, Sieun Jung, Jisoo Jennifer Kwon, Myungsun Nam, Sung-Yon Kim

P-536 Brain's dynamic functional connectivity predicts general attention
Yongkak Kwon, Kwangsun Yoo

P-537 Selective attention in spiking neural network
Yelim Lee, Dongmyeong Lee, Hae-Jeong Park

P-538 Long-Tail Structure Enables Functional Flexibility in Brain Networks
Dongmyeong Lee, Yelim Lee, Hae-Jeong Park

P-539 Differential Value Coding in CA1 and Medial Entorhinal Cortex
Minyeong Seo, Jaehun Kim, Min Whan Jung

P-540 Encoding of vocal communicative contexts by marmoset prefrontal neurons
Yukai Xu, Joji Tsunada

P-541 Neuromodulation supports projection-specific roles of the anterior cingulate cortex in visuomotor transformation
Dong-Hyun Ma, Hae-Yong Park, Ilayda Demir, Bo-Kyung Park, Isaac Kim, Yulong Li, Hanseul Yang, Seung-Hee Lee

P-542 Who do you want to team up with? How reward probability and partner support guide decision-making
With Drawn
Seyedeh Hasti Jalali[1], Maria Sanz Bernal[1], Seng Bum Michael Yoo[1]

P-543 Number concepts and Bayesian inference in Large Language Models and Humans
Arghavan Bazigaran, Hansem Sohn

P-544 Disrupted Synchrony of Egocentric Spatial Cells in 5XFAD Mouse Model of Alzheimer's disease
Yoonsoo Yeo, Jeehyun Kwag

P-545 Neural and behavioral correlation of mating decision-making in female mice
Mingyeong Seo, Jungyoung Kim, Jeyoon Lee, Yuvin Kim, Demian Battaglia, Jee Hyun Choi

Translational and Clinical Neuroscience P-546~P-564

P-546 Grabody B, an IGF1R-Targeting Molecular Shuttle, Enhances Brain Penetration via Multiple Novel Transcytosis Pathways
Miran Yoo, Sungwon An, Dongin Kim, Sumin Hyeon, Seung-Hwan Kwon, Dongwhan Kim, Dongwhan Bruce Kim Kim, Hakju Kwon, Do-Geun Kim, Sang Hoon Lee

P-547 The development of new dopamine with less toxicity and less autoxidation
Ye-Ji Kim, Dong Ho Woo

P-548 Regional transcriptomic differences of cortical dyslamination in human focal cortical dysplasia.
Younghoon Kwon, Joonho Kim, Yubin Ohn, Wonseok Chang, Sangwoo Kim, Eunee Lee

P-549 Manipulating autophagy pathways strengthens the tumor-killing capabilities of photodynamic therapy for glioblastoma
Sangheon Han, Junwon Park, Chanho Kong, Won Seok Chang

P-550 Standardization of brain lesioning in real time thermal monitoring radiofrequency ablation by sEEG electrodes
Sooyoung Lim, Junwon Park, Seoung Bo Shim, Kyo Jin Kang, Kyumin Yoo, Jiwoong Ahn, Soo Jeong Oh, Hosung Han, Yong Sup Hwang, Junhyung Kim, Won Seok Chang

P-551 AI-powered 3D pathology provides novel visualizations and quantifications with clinical diagnostic value
Young Hyun Yun, Kee Young Chung, Yunjoo Lee, Tae Sik Sung, Dayoung Ko, Seung-Bum Ryoo, Hyun-Young Kim, Kyu Joo Park,

Jong Pil Im, Byeong Gwan Kim, Joo Sung Kim, Seong-Joon Koh, Hyung Jin Choi

P-552 Suppression of Astrogliosis and Significant Functional Recovery in Traumatic Spinal Cord Injury via Combined Pharmacotherapy and Rehabilitation
SunYeong Choi, Woonggyu Jung, C. Justin Lee

P-553 Functional network alterations among tau-based alzheimer's subtypes and their association with cognitive decline
Gaeun Ryu, Jaeseung Jeong

P-554 GLP-1 modulates cognitive satiation via dopaminergic and hypothalamic pathways in mice and humans
Joon Seok Park, Hyung Jin Choi

P-555 Potential effects of ambroxol-modified new drug in α-synuclein(A53T)-upregulated animal model of Parkinson's disease
Hyemi Eo, Semin Park, Gibeom Lee, Su-kyeong Hwang, Jungwan Hong, Sang Ryong Kim

P-556 Optimized imaging protocols for visualization of human dura mater
Min-Jin Park, Min Jee Seo, Do-Gyun Kim, Youngseo Cho, Jihyoung Chang, Seoyoung Kim, In-Beom Kim, Mun-Yong Lee, Tae-Ryong Riew

P-557 Effects of the use of mindfulness-based mobile application on sleep in nocturnal phone users
Wing Kei LAM, Chuan LI

P-558 Slice Based High Density Micro Electrode Array Assay for Circuit Level Evaluation in Painful Diabetic Neuropathy
Akm Ashiquzzaman, Eunbin Lee, Hyuk-Sang Kwon, Sang Seong Kim, Euiheon Chung

P-559 Repurposing procaine and valproic acid to enhance motor recovery after spinal cord injury in rats
Lina Liu, Jung Keun Hyun

P-560 Optimized Fixation and Autofluorescence Reduction Methods for Correlative Light and Electron Microscopy in Postmortem Human Brain Tissue
Ha-Eon Lee, Hong Lim Kim, Ara Cho, Do-Gyun Kim, Yuna Oh, Rafael T. Han, Mun-Yong Lee, In-Beom Kim, Tae Ryong Riew

P-561 Injection of an engineered hydrogel promotes structural tissue repair in a rat model of intracerebral hemorrhage
Ariandokht Einisadr, Byung Gon Kim

P-562 Personalized SEEG Stimulation Framework for Epileptogenic Zone Targeting Using FEM and Reciprocity Principle
Joonho Lee, Donghwan Lim, WooYong Lee, Euisun Kim, Jiyoung Park, Dongmyeong Lee, Sora An, Hae-Jeong Park

P-563 Increased Sensitivity to Loss during Reversal Learning in Individuals with Food addiction and Bulimia nervosa
Jake Jeong, Jungwon Jang, Kwangyeol Baek

P-564 Therapeutic index of acupoints based on effective and hazardous depth measurement
Minjae Lee, Beomku Kang, Da-Eun Yoon, Younbyoung Chae

Poster Session 3

Day 3(Aug 26, 2025) 13:30-18:00, Day 4(Aug 27, 2025) 9:00-12:30 [Exhibition/Poster Hall]

Mechanisms of Brain Disorders P-565~P-621

P-565 Top-down modulation of acupuncture in Parkinson's disease: Enhancing gut function via MCH neurons
Ju-Young Oh, Hyowon Lee, Mijung Yeom, Su-Yang Park, Sun-Young Jang, Min-Ho Nam, Hi-Joon Park

P-566 Abnormal N-Glycosylation in the mPFC Contributes to Cognitive Impairment in Schizophrenia
Bomi Chang, Myung Jin Oh, Eunjin Shin, Jua Lee, Jae Ho Kim, Dongtan Yin, Juhee Shin, Prajitha Pradeep, Inwoong Song, Seung Eun Lee, Inyoung Hwang, Sangkyu Lee, C Justin Lee, Hee-Sup Shin, Hyun Joo An, Boyoung Lee

P-567 Microglial HIF-1α–CCL2 axis mediates radiation-induced cognitive impairment: evidence from single-cell transcriptomics
Yoonsoo Choi, Joong-Sun Kim, Changjong Moon, Ja-Hyun Baik, Hae-June Lee, Yeonghoon Son

P-568 Activation of perineural microglial cells supports functional axon regeneration following Facial Nerve Injury
Hyo Gyeong Seo, Hyung Soon Kim, Yeo Jin Seo, Ji Su Yoon, Seung Ah Jee, Byeong Seong Jang, Ariandokht Einisadr, Shivani Singh, Byung Gon Kim

P-569 Astrocytic putrescine degradation by polyamine acetyltransferase mediates astrocytic GABA synthesis and memory impairment in Alzheimer's disease.
Jiwoon Lim, Kijung Kim, Taehee Lee, Jinhyeong Joo, Mridula Bhalla, Mingu Gordon Park, Myeong-Ju Joy Kim, Victor J. Drew, Wuhyun Koh, C. Justin Lee

P-570 Functional and Regional Validation of an AAV-delivered Human DRD1 Promoter for Targeted Genetic Manipulation in the Mouse Brain
Dong-Chan Seo, Sung Min Ahn, Soo-Jin Oh, Min-Ho Nam, Seung Eun Lee

P-571 Hippocampal SARS-CoV-2 Spike Protein accumulation Induces Cognitive Decline via Pyroptosis and Neuroinflammation with Glial Reactivation
Dong-Chan Seo, Soo-jin Oh, Min-Ho Nam, Eun Mi Hwang, Jaeyong Park, Seung Eun Lee

P-572 Hippocampal Progranulin Alleviates Mood Disorders via Autophagy in Estrogen Withdrawal Mice
Liang-Yu Ni, Ting-Hui Chen, Si-Qi Jia, Yun Wang

P-573 Reactive astrogliosis drives neuronal hypometabolism and tau hyperphosphorylation via acetate-induced, MAOB-dependent oxidative stress in GBM
Yongmin Mason Park, Hee Jung Park, Dongwoo Kim, Hae Young Ko, Wongu Yun, Ki Duk Park, Seok-Gu Kang, C. Justin Lee, Mijin Yun

P-574 Sleep Loss Impairs Neuropathic Pain Modulation through Homer1a-Dependent Synaptic Remodelling
Anh Ho, MinCheol Park, Tae Kim

P-575 Hypothalamic circuit plasticity drives pain sensitization and anxiety in neuropathic pain
Yifei Yu, Yuran Song, Yiwei Hu, Lan Bao, Yan Chen, Xu Zhang

P-576 Neuroprotective Effect and Mechanism of Transcutaneous Auricular Vagus Nerve Stimulation in a Parkinson's disease model
Jae-Nam Park, Ju-Young Oh, Sora Ahn, Se Hoon Jang, Su-Yang Park, Hi-Joon Park

P-577 Microstate-specific functional connectivity in Alcohol Use Disorder using resting-state EEG
Hanjin Park, Jung-Seok Choi, Dongil Chung

P-578 Stress responsiveness shapes neuronal dynamics in the lateral habenula
Hoyong Park, ChiHye Chung

P-579 Linking VWA7-Associated ECM Dysregulation to Cerebellar Dysfunction in Schizophrenia
Woo Suk Roh, Ki Jung Kim, Jae-Hun Lee, Sun-Yeong Choi, Cheol-Hee Kim, Kyung-Seok Han, C. Justin Lee

P-580 Histological and Behavioral Characterization of TDP-43A315T Mice
Soomin Um, Seong-Ryeong Lim, Sehyun Chae, Miseon Kang, Sukwoon Song, Jeongyeon Kim

P-581 Protein denitration by tyrosine-containing peptides is a new strategy to treat intractable diseases.
Eun Bin Hong, Jae Soon Kang, Hwa Jin Kim, Ji Hyeong Baek, Dong Kun Lee, Hye Jin Chung, Sang Won Park, Hyun Joon Kim

P-582 Screening of bioactive flavonoids with anti-Alzheimer's potential from Cirsium japonicum
Byeong Wook Noh, Hyun Young Kim, Sanghyun Lee, Eun Ju Cho, Ji Myung Choi

P-583 Neuroprotective effects of Cirsium japonicum var. maackii flower in oxidative and cognitive impairment models
Su Young Kim, Hyun Young Kim, Sanghyun Lee, Eun Ju Cho, Ji Myung Choi

P-584 The minimum effective dose of LYQ as an antidepressant and a new antidepressive effect of D-tyrosine (DY), an enantiomer of LY
Hyeongchan Park, Jae soon Kang, Miyoung Song, Wonjune Jeong, Eunbin Hong, Soomin Han, Hyun Joon Kim

P-585 Tonic GABA and H2O2 production via the astrocytic glucocorticoid receptor activation pathway causes memory deficits in the Cushing's disease model.
Jinhyeong Joo, Junsung Woo, Minho Nam, Wuhyun Koh, C. Justin Lee

P-586 Early Olfactory Dysfunction and Immune Alterations in the Olfactory Epithelium of 5xFAD Mice
Eun Hwa Jo, Hye-Sun Kim, Hongyoon Choi, Yoori Choi

P-587 Posterior parietal cortex dysfunction underlies sensory deficits in the Shank3Δ14–16 mice
Seung-Mi Oh, Hae-Yong Park, Yi-Seon Jeon, You-Hyang Song, Jun-Ho Song, Se-Bum Paik, Eunjoon Kim, Seung-Hee Lee

P-588 BNIP3L/NIX-Mitophagy Sustains Astrocytic Neuroprotection Against Chronic Glucocorticoid-Induced Aging
Khanh Do, Minh tran, You Jung Kang, Won Jong Yu, Jong-Chan Park, Hansang Cho

P-589 Integrative single-cell multi-omics analysis of epigenetic markers during the transition from impulsive to compulsive use of drug
Chang Hyeon Kong, Hyunjeong Jin, Jinhee Bae, Heh-In Im

P-590 Biobehavioral sequelae of an animal model of cannabinoid oral self-administration
Jeeyoung Seo, Baeksun Kim, Heh-In Im

P-591 Cell type specific striatal neuronal ensemble dynamic alteration in Parkinsonian state
Hyun Kyung Chung, Horim Shin, Jinkyu Lee, Chanhee Jeong, Jun Ho Park, Jung Hwan Shin

P-592 Modulation of Insular Cortex Neurons Alleviates Motor Symptoms and Gut Dysfunction in Parkinson's Disease
Sun-Young Jang, Su-Yang Park, Hyowon Lee, Ju-Young Oh, Min-Ho Nam, Hi-Joon Park

P-593 Cerebellar Activation Differences in Major Depressive Disorder and Controls During Emotional Music and Non-Music Stimuli: An fMRI Study
Yashu Shukla, June Kang

P-594 Slc45a1-Htr2a axis as a regulator of female-biased neurodevelopmental disorder
Hyunjin Kim, Hyowon Lee, Yeon Ha Ju, Sharon Jiyoon Jung, Seung Jae Hyeon, HaeNim Lee, Hoon Ryu, Jihye Seong, Minji Go, Kayeong Lim, Bum-Ho Bin, Min-Ho Nam

P-595 MLC1 deficiency alters microglial phenotype and disrupts homeostasis of adult neural stem cells
Yubin Park, Jeong-Sun Choi, Kyung-Ok Cho

P-596 Astrocyte-derived extracellular vesicles induced by glutamate suppress glioblastoma growth
Joon-Ho Kwon, Yoon-Kyoung Cho, C. Justin Lee

P-597 Dose-Dependent Inversion of LSD-Induced Behavior Suggests β-arrestin2-Mediated Addiction Potential at Ultra-Low Concentrations
Hyunjeong Jin, Heh-In Im

P-598 PLXDC2 fine-tunes microglial inflammatory and phagocytic responses in Alzheimer's disease
Yoonah Oh, Minkyoo Shin

P-599 MICROGLIAL EXTRACELLULAR VESICLE BIOMOLECULE TRACKING SYSTEM (micEV-BTS) FOR PREDICTION OF MICROGLIA-NEURON INTERCELLULAR COMMUNICATIONS
Won Jong YU, Dang Du Nguyen, Aleksandr Barulin, Inki Kim, Jong-Chan Park

P-600 Primary visual cortex dysfunction underlies visual learning deficits in a Grin2bC456Y/+ mouse model of ASD
Jong-Yeon Yoo, Eunji Yoon, Eunjoon Kim, Seung-Hee Lee

P-601 Female-specific role of basolateral amygdala endocannabinoid signaling in an animal model of depression
Jimin Nam, Seungjae Zhang, ChiHye Chung

P-602 A homozygous missense of TTYH3, a volume-regulated anion channel(VRAC), links lysosomal dysregulation to Autism spectrum disorder
Taehee Lee, Hyunji Kang, Jinhyeong Joo, C. Justin Lee

P-603 Subunit-selective BK channel modulation rescues behavioral and electrophysiological deficits in Angelman syndrome.
Catherine Yen Li Kok, Weonjin Yu, Fionicca Teo, Seoyoon Kim, Duyoung Min, Jackie Ang, Hsiang Ling Teo, Chenxi Cui, Ji Sun, Hyunsoo Shawn Je

P-604 Comparative Analysis of Subcortical Diffusion Metrics in 3T and 7T MRI: Implications for Parkinson's Disease Imaging Using Lead-DBS and HCP D
Kyoung Jin Roh, Ji-Yeon Suh, Hyeon-Man Baek

P-605 Scn2a-linked myelination deficits and synaptic plasticity alterations drive auditory processing disorders in an ASD mouse model
Han-Gyu Bae, Wan-Chen Wu, Kaila Nip, Elizabeth Gould, Jun Hee Kim

P-606 Endothelial DR6 Mediates Blood-Brain Barrier Dysfunction in Alzheimer's Disease
Xiaomin Huang, Chenju Yi

P-607 Chemical A ameliorates cognitive impairment and neuroinflammation in a mouse model of Alzheimer's Disease
Jeong Seok So, Jae Gwang Song, Dae-Sung Kim, Hyung-Wook Kim

P-608 Tiny monkey astronauts: A Feasibility validation of Marmoset-based realtime monitoring technology for space station brain networks
Zhen Xu, Weidong Li

P-609 Acupuncture modulates the expression of circadian clock genes in a Parkinson's disease mouse model
Ju-Young Oh, Su-Yang Park, Halin Jeon, Jae-Nam Park, Hi-Joon Park

P-610 Glial-Mediated Neuroinflammation in Chronic Stress: A Molecular Link to Brain Disorders
Catharine Basty

P-611 Hippo kinases MST1/2 (STK4/3) regulate microglial homeostasis and inflammation in the CNS
Jae Lee, Suhyun Yoon, Jimin Baik, Charles W. Pfeifer, Andrea Santeford, Tae Jun Lee, Rajendra S. Apte, Jongshin Kim

P-612 Novel Intranasal Delivery of Sihosogansan Demonstrates Rapid Antidepressant Activity via GABAergic and BDNF/TrkB Pathways
Khoa Nguyen Tran, Yeasmin Akter Munni, Gia Linh Mac, Sarmin Ummey Habiba, Tae Woo Oh, Ho Jin Choi, Il Soo Moon, In-Jun Yang

P-613 CREB2 as a Key Mediator of Oxidative Glutamate Toxicity in Neurons: Implications for Microglia-Induced Neuroinflammation
HYE JOUNG CHOI, Uk Yeol Moon, Bao-Ting Zhu, Sukjun Song, Dong Gyun Ko, Young Eun Kim

P-614 Neural precursor cells restore cognition and attenuate neuroinflammation by modulating autophagic mechanisms in Alzheimer's disease models
CHAEWON BAEK, KYUHO SHIM, JEEIN CHOI, MINYOUG KIM

P-615 Synaptic ultrastructural alterations in human focal cortical dysplasia: insights from volume electron microscopy
Gyu Hyun Kim, Na-young Seo, Yang Hoon Huh, Ji Yeoun Lee, Kea Joo Lee

P-616 Distribution of ChAT-Positive Neurons in the DMV of a Primate Parkinsonism Model
Gahye Moon, Sojeong Lee, Thanh Thi Hai Nguyen, Chang-Yeop Jeon, Jincheol Seo, Youngjeon Lee, Kyung Seob Lim

P-617 Exploring Brain-Heart Interaction in Cognitive Function: The Roles of Heart Rate Variability and Sex Differences
So Yi Yoon, Hee Sang Yang, Hyang Woon Lee

P-618 Hippocampal Microstructural and Proteomic Changes in Pilocarpine-induced Temporal Lobe Epilepsy Model
Sol Ah Kim, Eun-Hwa Lee, YuJaung Kim, Yun Seo Choi, Kea Joo Lee, Sehyun Chae, Hyungju Park, Hyang Woon Lee

P-619 Estrogen deficiency induces anxiety and depression-like behaviors via caspase-1-mediated neuroinflammation
Dong Cheol Baek

P-620 Protective effects of Dioscorea bulbifera and Zingiber officinale mixed extracts against glutam
Seung Woo Im, Younghoon Go, Tae Woo Oh

P-621 Time-dependent mitochondrial fission through Calpain-2/CDK5/p25 and Drp1 signal pathway in MPTP-induced cynomolgus monkey model of Parkinson's disease
Junghyung Park, Jincheol Seo, Jinyoung Won, Youngjeon Lee

Molecular and Cellular Neuroscience P-622~P-706

P-622 Paradoxical Modulation of cAMP level by hM4Di
In-Yeop Baek, Hyunbin Kim, Hyowon Lee, Duwan Kwon, Sharon Jiyoon Jung, Soo-Jin Oh, Hi-Joon Park, Jihye Seong, Min-Ho Nam

P-623 Astragalus mongholicus and Scutellaria baicalensis Extracts Mixture as a potential therapeutic against inflammation and Pyroptosis in ischemic stroke
GEON KO, JINHO KIM, YONG-JAE HONG, YEONG-JAE JEON, HYUN-MAN BAEK, DONGHUN LEE, KEUN-A CHANG

P-624 Ginsenoside Rk1 Induces ER Stress–Mediated Apoptosis via Caspase-12 Activation in Human Brain Cancer Cells
Jung-Mi Oh, sungkun Chun

P-625 Neuropathic Pain from Corneal Nerve Damage: Ultrastructural and Histological Characterization of the Trigeminal Ganglion and Brain
Mohd. Afzal Khan, Gehan Fatima, Euiheon Chung, Young Ro Kim

P-626 Molecular basis of PIP2 regulation in L-type 1.2 Ca2+ channel
Soohyeon Bae, Byung-Chang Suh

P-627 Characterization of TRPA and TRPV orthologs in the gastropod mollusk Pacific abalone
Mi Ae Kim, Shubhash Chandra Chaudhary, Gyu Ri Min, Young Chang Sohn

P-628 The Role of ITPKB in Regulating Calcium Homeostasis in Dopaminergic Neurons and Astrocytes in Parkinson's Disease
Eun-Bin Hong, Young-Jung Kim, Seulkee Yang, Seung Eun Lee, Eunji Cheong, Min-Ho Nam

P-629 Dopamine D2 receptor antagonists promotes primary cilia elongation and induce ER-stress mediated apoptosis in brain cancer cells
Jung-Mi Oh, Young-Bae Kwon, Sungkun Chun

P-631 Functional specialization of border-associated macrophages is defined by niche-specific transcriptomic and ultrastructural profiles in mouse and human
Dogyun Kim, Youngseo Cho, Seoyoung Kim, Yuna Oh, Hong Lim Kim, Rafael T. Han, Tae-Ryong Riew

P-632 Harnessing theta-gamma coupled brainwaves using ultrasound for spinal astrocyte revitalization and sustained neuropathic pain relief
Tien Thuy Phan, Sangyep Shin, Ho Jeong Kim, Keunhyung Lee, Tai-Young Kim, Jae Hoon Lee, Dong-Wook Kang, Hyunjin Shin, Hye Eun Lee, Nishani Jayanika Jayathilake, Minseok Koo, Hyungju Park, Hyun-Woo Kim, Yee Joon Kim, Ji Young Mun, Jinhyoung Park, Kyu Pil Lee, C. Justin Lee, Joo Min Park

P-633 Structure Studies of the Neuroinflammatory Lcn2–Slc22a17 Complex
Jina Kim, Junmo Hwang, Hyun-Ho Lim

P-634 A Journey Structural Determination of Human MLC1
Sujin Shin, Junmo Hwang, Hyun-Ho Lim

P-635 Structural and functional modulation of human BEST1 channel by an amino acid metabolic enzyme
Euna Lee, Junmo Hwang, Min-Sik Kim, Hyun-Ho Lim

P-636 Structural studies on the microglia TREM2-DAP12 complex
Eunbi Kim, Kunwoong Park, Byungwon Kim, Hyun-Ho Lim

P-637 Hypoxia induces immediate awakenings in Drosophila melanogaster
Nguyen Minh Anh Hoang, Hyeyoon Lee, Yangkyun Oh

P-638 Impact of dysregulated miR-204 on NPTX1 expression and neurodegeneration in Alzheimer's disease
Seung Min Lim, Tae-Young Ha, Keun-A Chang

P-639 Non-invasive ultrasound treatment induces neuroprotective astrocytes
Seong-Ryeong Lim, Sukwoon Song, Heeyoung An, Miseon Kang, Kyu-Sung Kim, Yehhyun Jo, Jonghee Eun, Namsun Chou, Do-Geun Kim, Hyunjoo J. Lee, Jeongyeon Kim

P-640 Discovery of TRPV1-selective inhibitory peptides via phage display screening for non-opioid pain modulation
Seung Hoon Yum, Eun Jin Go, Sung-Min Hwang, Yong Ho Kim, Chul-Kyu Park

P-641 Neuroprotective and anti-depressant effects of Tenebrio Molitor hydrolysate in LPS-induced neuroinflammation models.
Younsoo Byun, Jiaxiang Zheng, Yoonhwa Jeong, Jihyun Noh

P-642 Short-chain fatty acids-induced cholecystokinin secretion leading to neuroprotective anti-inflammation in gut–blood–brain model
Chaeyeon Been, Tran Minh, Hansang Cho

P-643 Human iPSC-derived microglia provide a platform for neuroimmunology research
Jae-Hwan Hyeon, Jeongwoo Kwon, Yujin Jo, Seung-Bin Yoon, Hyoyun Cho, Seokho Kim, Ji-su Kim

P-644 Diosgenin alleviates pain by preserving mitochondrial and endoplasmic reticulum function in a sciatic nerve injury model
Tae Su Yoon, Md. Mahbubur Rahman, Eun Jin Go, Sung Min Hwang, Chul Kyu Park, Yong Ho Kim

P-645 Analysis of Cardiac Changes Under Diverse Physiological Conditions in Drosophila melanogaster Using High-Frequency Ultrasound Imaging
KyeHyun Hong, Yangkyun Oh

P-646 A cardiac steroid digoxin induces pro-regenerative macrophages to promote axon growth
Jee Seung Ah, Seo Yeo Jin, Lee Hae Seung, Kim Byung Gon

P-647 Role of Shank2 in human neuron development and function
Xin Yi Yeo, Suji Hong, Han-Gyu Bae, Sejin Lee, Junho Park, Jeongeun Lee, MinYoung Kim, Dong-Gyu Jo, Weiping Han, Jiong Tang, Sangyong Jung

P-648 Translatome Profiling of Perisynaptic Astrocytic Processes in the Spinal Cord After Nerve Injury
Sung Joong Lee, Hye Won Jun

P-649 Astrocytic OAT Tunes Tonic E/I Balance to regulate synaptic plasticity and Hippocampal Memory
Heesu Na, Yeon Ha Ju, Mridula Bhalla, Seulkee Yang, Hyunbeom Lee, Mijin Yun, C. Justin Lee, Min-Ho Nam

P-650 New small molecule probe for visualizing choroid plexus
Wonju Kim, Naoki Miyamoto, Do young Na, Dongwan Ko, Youngran Hwang, Young-Tae Chang, Beomsue Kim

P-651 Profiling diuretic hormone 44 (DH44) neurons as internal nutrient sensors in the Drosophila brain
Gahbien Lee, Greg S.B. Suh, Yangkyun Oh

P-652 State-Dependent Retrieval of Sodium-Associated Flavor Memory in Mice
Hyunji Kim, Yong Taek Jeong

P-653 Tweety-homolog (TTYH) family is stretch-sensitive anion channel regulating astrocytic volume
Young-Eun Han, Hyunji Kang, Tai-Young Kim, Mishra Ankitendaran, Andrew Choi, Jun Ho Kang, Eui-Sung Yoon, C. Justin Lee, Soo-Jin Oh

P-654 Astrocyte-specific deletion of TTYH1 enhances neuronal excitability and long-term memory persistence
Young-Eun Han, Jae-Jun Heo, Myung-jin Kwak, C. Justin Lee, Soo-Jin Oh

P-655 Microbial conversion of MSG to GABA enhances sleep via gut-brain signaling in Drosophila
Ji-Hyeon Park, Yangkyun Oh

P-656 Reactive astrocytes exacerbate tau pathology via impaired autophagy and elevated MAO-B under neuroinflammatory conditions
Jiyoung Yoon, Heejung Chun

P-657 Physiopathological role of astrocytic DNAJC6 in Parkinson's disease
Wahyu Handoko Wibowo Darsono, Yeong Ran Hwang, Erica Valencia, Leonardo Tejo Gunawan, Seung Jae Hyeon, Hoon Ryu, Mi Yoon Chang, Noviana Wulansari, Sang Hun Lee

P-658 Lysophosphatidylcholine-induced mitochondrial stress and MAO-B–driven oligodendrocyte inflammation promote demyelination in Multiple Sclerosis
Niloofar Etemadi, Minh Tran, Hansang Cho

P-659 MSG's Effects on Neural Stem Cells and Hippocampal Neurogenesis
Seonghoo Lee, Jeong Yoon Kim, Seonghyun Cho, Sung Min Moon, Chang Yup Kim, Duwon Jung, Jaewon Lee

P-660 Generation of Neurosupportive Active Astrocytes Induced by Single-Cell Nanoencapsulation
Wongu Youn, Jiwoon Lim, Sunghoon Joo, Seoin Yang, Beom Jin Kim, Hojae Lee, In Young Hwang, Insung S Choi, C Justin Lee

P-661 PLCγ1 dependent neural plasticity is required for dynamic hippocampal CA2 network processing social memory in mice
Sukwoon Song, Jeongyeon Kim

P-662 Human brain and organoid transcriptomes reveal key receptor tyrosine kinase pathways and genetic signatures in Alzheimer's disease
Saewoon Shin, Xiaohui Zhu, Sarnai Amartumur, Taehoon Lee, Won Jong Yu, Soomin Park, Niloofar Etemadi, Ariunzaya Jamsranjav, Rian Kang, Gyusoo Bak, Dongjoon Lee, Jieun Kim, Jong Won Han, Chaejeong Heo, Hansang Cho, Sunghoe Chang, Inhee Mook-Jung, Sang-Eun Lee, Jong-Chan Park

P-663 Single nucleotide differences in Gpr151 functional RNA 5'UTR sequence changes axon regenerative potential in CAST/EiJ mice
Eunsu Jang, Yongcheol Cho

P-664 Modulation of gating kinetics by β subunits in N-type calcium channel
Jin-Nyeong Woo, Byung-Chang Suh

P-665 NS1 Binding Protein Regulates Stress Granules via p62 Ubiquitination and GABARAP Recruitment in ALS
Pureum Jeon, Hyun-Ji Ham, Haneul Choi, Semin Park, Jae-Woo Jang, Sang-Won Park, Dong-Hyung Cho, Hyun-Jeong Lee, Hyun Kyu Song, Masaaki Komatsu, Dohyun Han, Deok-Jin Jang, Jin-A Lee

P-666 Activating Odorant Receptors in Hypothalamic Astrocytes Sex-differentially Regulates High-fat-diet induced Obesity
Younghyun Lee, Jiwoon Lim, Nahye Lee, Moonsun Sa, Jaehyung Koo, C. Justine Lee

P-667 PDGF-BB Treatment Activating pCREB to Restore Gliovascular Unit in a Parkinson's Disease Model
Minjoon An, Minh Tran, Hansang Cho

P-668 Temporal Remodeling of Collagen fibers After Spinal Cord and Peripheral Nerve Injuries
Seo Hyeon Jang, Ahyeon Song, Young-Jin Son, Jung Keun Hyun

P-669 Age-dependent effects of HDAC4 haploinsufficiency on sleep and cognitive function
Hyunmin Lee, Staci J. Kim

P-670 Polarization of microglia on nanopatterned titanium
Jeong Woo Park, Byeng Gyu Song, Jung-Hwan Lee, Bo-Eun Yoon

P-671 Depth of anesthesia alters surgery-induced neuroinflammation and microglia activity in young mice
Yulim Lee, Xianshu Ju, Tao Zhang, Jiho Park, SEUNG GWAN KANG, Jun Young Heo, Woosuk Chung

P-672 Examination of the contribution of Nodal Modulator 1 (Nomo1) in neuronal function and the development of autism spectrum disorder
With Drawn
Yunseon Choi, Xin Yi Yeo, Sangyong Jung

P-673 The effects and mechanism of virgin coconut oil on learning and memory impairment and amyloid precursor protein processing pathway in aging mice
Huiling Jin, Yiru Dong, Chenyu Liu, Yinglin Liu, Yanji Xu

P-674 ATP-sensitive potassium channel–dependent inhibition of hypothalamic MC4R neurons underlies atypical antipsychotic–induced hyperphagia
Hyeonju Yun, Jinyong Kim, Jong-Woo Sohn

P-675 In Vivo CRISPR/Cas9 Screening Identifies Subunit-Specific Roles of proprioceptor ENaC in gait behavior
Yurim Seong, Han Kyoung Choe

P-676 BMDA prevents dopaminergic neuron loss by attenuation of astrocyte-mediated neuroinflammation in Parkinson's Disease.
Jeong Yoon Kim, Sung Min Moon, Duwon Jung, Chang Yup Kim, Seonghyun Cho, Seonghoo Lee, Da Seul Choi, Jaewon Lee

P-677 Dysregulation of MeCP2 contributes to cognitive impairment in noise induced hearing loss models
Eunjin Choi, Kwangil Jeong, So Young Kim, Sangjoon Lee, Heh-In Im

P-678 Prion Infection in a 3D Spheroid Culture System for Antiprion Drug Screening
HyeRi Kim, YoonJeong Lee, HyunJung Park

P-679 A Transcriptomic analysis of gyrencephalic cortex development in the miniature pig
Kyung-Tai Kim, Jeong Ho Hwang, Su-Cheol Han

P-680 Correlation between anesthesia-induced tonic inhibition mediated by astrocytic γ-aminobutyric acid and cognitive dysfunction
Elliot Hwejoon Lee, Dongwook Won, Jee-Eun Chang, Min-Ho Nam, Ki Duk Park, Eunji Cheong, Jinyoung Hwang, Soo-Jin Oh

P-681 Microglial Apolipoprotein E Genotype Regulates PI3K-Akt Signaling Pathway in Brain Assembloids
Rian Kang, Jiyu Na, Sang-Eun Lee, Jong-Chan Park

P-682 Novel neuroprotective drug development strategy targeting tau hyperphosphorylation in AD
Seonghyun Cho, Sung Min Moon, Duwon Jung, Chang Yup Kim, Jeong Yoon Kim, Seonghoo Lee, Jaewon Lee

P-683 Multiplex Imaging of ATP and Ado Dynamics in vivo with an Expanded Toolbox of GRAB Sensors
Peiyao He, Bohan Li, Yumo Li, Zexiao Bai, Jing Wang, Zhixiong Ma, Yulong Li, Zhaofa Wu

P-684 Functional Role of EBP1 in MFN2-Mediated Mitochondrial Fusion and Mitophagy under Aβ-Induced Stress
Youngkwan Kim, Jee-Yin Ahn

P-685 A NanoLuciferase-based reporter system for screening GCase-enhancing CPPs in Parkinson's disease
Hyerynn Kim, Sangjune Kim

P-687 Effects of co-administration of aripiprazole and fluoxetine on mossy and granule cell activity in a mouse model of depression
Hyunsung Kang, Dahyeon Jeong

P-688 Monitoring the Dynamics of Alzheimer's Disease Biomarkers and the APOE–Tau Axis via Human Cerebral Organoids with Immuno-SERS
Yongjae Jo, Youngjun Kim, Rian Kang, Luke P. Lee, Jong-Chan Park, Inki Kim

P-689 Deficiency of Chi3L1 promotes schizophrenia-like phenotypes by lowering BDNF levels
In Jun Yeo, Ji Eun Yu, Jun Sang Yu, Hanyang Liu, Min Ji Kim, Seong Hee Jeon, Jaesuk Yun, Dong Ju Son, Sanghyeon Kim, Sang-Bae Han, Jin Tae Hong

P-690 Desensitization of TRPA1 by dimethyl itaconate attenuates acute and chronic pain in mice
Sen Xu, Junyi Ma, Tong Liu

P-691 Cell-type-resolved mosaicism decodes clonal architectures of the human forebrain
Changuk Chung, Xiaoxu Yang, Joseph Gleeson

P-692 Taurine inhibited astrocyte-mediated neuroinflammation and dopaminergic neuron loss in the PD mouse model
Sung Min Moon, Duwon Jung, Chang Yup Kim, Jeong Yoon Kim, Seonghoo Lee, Seonghyun Cho, Jaewon Lee

P-693 Host longevity promoting bacterial genes protect dopaminergic neurons in Caenorhabditis elegans
Suyeon Kim, Min-Gi Shin, Eun Jeong Lee

P-694 Argonaute-mediated small RNA Pathways Mediate Maternal Age-Dependent Behavioral Plasticity in C. elegans
Taehyun Kim, Hyeonjeong Hwang, Rinho Kim, Kyuhyung Kim

P-695 Targeting Lipocalin-2 with a Small-Molecule Inhibitor to Suppress Neuroinflammation
Jiwon Kwon, Jong-Heon Kim, Jae-Hong Kim, Jieon Lee, Minsoo Song, Kyoungho Suk

P-696 The mRNA Translation Initiation Factor eIF4G1 Controls Mitochondrial Oxidative Phosphorylation, Axonal Morphogenesis, and Memory
Hyunji Seo, Sung-Hoon Kim

P-697 2′-Fucosyllactose Mitigates Cognitive Deficits in Alzheimer Models: Targeting Amyloid Pathology, Oxidative Stress, and Synaptic Plasticity
Yeasmin Akter Munni, Khoa Nguyen Tran, Tae Woo Oh, Sarmin Ummey Habiba, Gia Linh Mac, In-Jun Yang

P-698 Mechanisms underlying the segregation and intracellular sorting of synaptic vesicles and ATG9 vesicles
Ji Young Choi, Yumei Wu, Daehun Park

P-699 Age-dependent brain change depending on ApoE genotype
Kyeong Jae Lee, Yeon Hee Kim, Jeong Hyun Lee, Sun Ah Park

P-700 Central Amygdala Pathway Mediates GLP-1-Induced Aversion
Yu-Been Kim, Nayoung Lee, Se Eun Park, Jinew Seo, Deok-Hyeon Cheon, Hyung Jin Choi

P-701 Confirmation of Curcumin-Mediated Inhibition of Tau Aggregation Using a Tau-NanoLuc Assay System
Min kyoung Kam, Ji-Young Choi, Young Ho Koh, Chulman Jo

P-702 Investigation of the Microenvironmental Influence on Glycoprotein Secretion in Blood–Brain Barrier Protection
Young Eun Kim, Min Joung Lee, Jong Hun An, Hyun Joo Choi, Chang Hee Pyo, Sangyun Kim, Taewan Kim, jaehyun Jeong, Da Young Kang, So Yeon Park, Woosuk Chung, Jun Young Heo

P-703 A distinct isoform of the mechanosensitive channel PIEZO mediates mating behavior in C. elegans
Jihye Cho, Sujin Jo, Taehyun Kim, Hyun-Ho Lim, Kyuhyung Kim

P-704 CNMa Shapes the Behavioral and Survival Response Pattern to Macronutrient Environments
Ji-Hyeon Lee, Boram Kim, Greg Suh

P-705 Sigma-1 receptors increase spinal peroxynitrite production after spinal cord injury in mice
Sheu-Ran Choi, Nam Hyun Kim, Cil-Han Lee, Jang-Hern Lee

P-706 Structural and Functional Investigations on the Voltage-Dependent Mechanism of a Hyperpolarization-activated Cl- Channel, CLC-2<
Hyeon Seong Jeong, Kunwoong Park, Kwonwoo Kim, Hyun-Ho Lim

Neuroengineering P-707~P-723

P-707 Engineering a Light-Activated Dopamine Receptor for Precise Control of GPCR Signaling
Hyunbin Kim, Geunhong Park, Duwan Kwon, Chanyoung Choi, Jeongjin Kim, Jihye Seong

P-708 Discovering GPCR Heterodimerization: functional dynamics and therapeutic Implications
Huimin Lee, Hyunbin Kim, Jihye Seong

P-709 Timed electrical stimulation training to change tingling to a natural-like pressure
Hamdi Qraiqea, MINJU OH, Hangue Park

P-710 Neural recording device capable of neurotransmitter monitoring according to deep brain stimulation in mouse brain model
Seonghoon Park, Jungsik Choi, Daerl Park, Mingu Song, Inwoo Park, Heonjin Choi

P-711 A miniaturized ultrasound stimulation system for wireless neuromodulation in freely moving mice
Jihong Lim, Chaerin Oh, Xiaojia Liang, Yehhyun Jo, Hyunjoo Lee

P-712 Tactile encoding in S1 and exploration of information expansion via patterned ICMS in monkeys
Sang-Hoon Kim, Min-Ki Kim, Gyeong-Ha Ahn, Hyejin Park, Jeong-Woo Sohn

P-713 Performance and Safety Evaluation of Ultrasound Device for Blood-Brain Barrier Opening in Non-Human Primates
Hee Gyu Baek, Chan Yuk Park, Juyoung Park

P-714 Temperature-dependent modulation of visual behaviors in Drosophila Melanogaster
Jehyoung Lee, Jonathan Edward Madar, Anmo J Kim

P-715 Temporal modulation of early-stage organoid differentiation using precision ultrasound stimulation
Jinseong Jeong, Yehhyun Jo, Youngsun Lee, Mi-Ok Lee, Hyunjoo Jenny Lee

P-716 Patternable luminescent patch for selective, wide-field cortical stimulation
Minji Choi, Yehhyun Jo, Xiaojia Liang, Jiwan Woo, Yakodl Cho, Hyunjoo Jenny Lee

P-717 A single, versatile algorithm for segmenting cells immunolabeled with diverse cell-type marker proteins from whole-brain images
Daye Kim, Jounghyo Lee, Jimin Kim, Young-Gyun Park

P-718 Combined 3D-CNN and 4D-Swin Transformer on Resting-State fMRI Using Multi-stage Classification for Cognitive Dysfunction
Suji Lee, Chang-hyun Park, Hyang Woon Lee

P-719 Improving B1 Homogeneity in 7T MRI Using High-Dielectric Pad: Effects on T1 Imaging, Brain Segmentation, and Diffusion Tensor Metrics
Yun-Ju Lee, Ji-Yeon Suh, Hyeon-Man Baek

P-720 3D bioprinted GelMA/TMP scaffold incorporating neural stem cell-derived EVs and NPCs for enhanced spinal cord injury repair
Gyubin Kim, Inbo Han

P-721 Effects of Chemogenetic Virus Injection and Clozapine Administration in Spinal Cord Injury
JIHYEON KIM, SAE YEON HWANG, HYE-LAN LEE, SOL LIP YOON, YOON HA, HYE YEONG LEE, SEUNG JUN RYU

P-722 Real-Time Induction of K-Complexes by Non-Invasive DBS
KwangWoo Kim

P-723 Effects of Long-Term High-Fat Diet Intake on Inflammatory Mediators and Dopamine-Related Genes in the Striatum
Jimmy Kim, Thuy Pham Linh, SeungAh Han, Yamanaka Ko, Hedefumi Waki

Others : (Ion Channel Modulation)

P-724 Screening of novel TMEM16C activators
Eunyoung Kim, Byoung-Cheol Lee

Others : (Neurotoxicity)

P-725 Standardizing C. elegans as a NAMs Platform to Advance Alternative Neurotoxicity Testing
Sooji Choi, Seonyu Lim, Chanmi Jang, Kyung Won Kim

Others : (Taste)

P-726 Establishment of Taste Bud Organoids from Anterior Lingual Mucosa
Min Gyeong Lee, Yong Taek Jeong

Others : (Safety Pharmacology Assessment)

P-727 Evaluation of QT/QTc interval changes and proarrhythmic risk of five drugs of abuse using in vitro and in vivo approaches
Hanbi Kim, Seunghye Kim, Daehun Kim, Tae Woong Na, Sujeong Park, Kikyung Jung

Others : (others)

P-728 Discovery of a Potential Neuroprotective Agent Against Cerebral Ischemia/Reperfusion through Inhibiting CaMKIIα Autophosphorylation Overactivation
Qifan Yang, Ting Wu, Yun Wang

Others : (Glia)

P-729 The effects of Glucagon-like peptide-1 receptor agonist in senescent microglia
Yu-lim Seo, Gyun Jee Song, Young-Sun Lee

Others : (Neurophysiology)

P-730 The Body-Brain axis mediating the responses to protein deprivation
Boram Kim, Seongju Lee, Hyeyeon Bae, Jong Hoon Won, Dongwoo Kim, Byungkwon Jung, Makoto Kanai, Gahbien Lee, Yangkyun Oh, Won-Jae Lee, Greg S. B. Suh

Others : (Aging Glioscience)

P-731 Geroprotection in female mouse brains by long-term MAOB inhibition
Mridula Bhalla, Jiwoon Lim, Kiduk Park, C Justin Lee

Others : (Cardiovascular sensor)

P-732 Glucose Sensor and Cholesterol Sensor for Diabetes Monitoring and Cardiovascular Disease Prevention
Do Youn Kim, Su-Eun Choi, Hyo-Ryoung Lim

Others : (Behavioral science)

P-733 Reproductive Experience Shapes Distinct Behavioral Profiles in Female Mice
Jeongha Kim, Hyunwoo Kim, Jeong Hun Kim, Jinseop Kim, Suyeon Lim, Seon-Ju Jeong, Sukwon Lee

Others : (Imaging Technique)

P-734 A Multiplexed Imaging Workflow for Spatial Proteomic Analysis of the Mouse Brain
Chan E Park, In Cho

Others : (Cognitive Neuroscience)

P-735 Age- and Disease-Related Dysfunction and Compensation of Neural Oscillations During Episodic Memory Retrieval
Jeonghyun Lee, Sang-Eon Park, Jieun Maria Hwang, So Yeon Jeon, Sang Ah Lee

Others : (Depression caused by environmental pollutant)

P-736 Long-term bis (2-ethylhexyl) phthalate exposure changes subthreshold stress to be severe stress, evoking depressive behaviors
Wonjune Jeong, Hyeongchan Park, Miyoung Song, Eunbin Hong, Soomin Han, Hyejin Chung, Dong Kun Lee, Jae Soon Kang, Hyun Joon Kim

Others : (cognitive neuroscience)

P-737 Effects of pulsed transcranial photobiomodulation of the prefrontal cortex on temporal credit assignment
Jiwon Park, Minjae Kim, Junghoon Ahn, Minho Hwang, Sunmin Kim, Hanjin Park, Jaemin Park, HeeYoung Seon, Dongil Chung

Others : (systems neuroscience)

P-738 Behavioral and neural signatures during discriminating emotional valence in mice
Gyeongmee Kim, Doyeon Ham, ChiHye Chung

Others : (Neuromodulation)

P-739 Low-Intensity Ultrasound (LIUS) Relives Bladder Dysfunction and Pain in Cyclophosphamide-Induced Cystitis Mice models
Jeongsook Kim, Kyungmi Kim, Nishani Jayanika Jayathilake, Beno Ramesh Nirujan, Kyu Pil Lee

Others : (Multisensory cognition in VR)

P-740 Immersive visual-thermal stimulation applied to a third person virtual avatar modulates upper limb skin temperature
Eunji Yoo, Seong geon Pyo, Hyuk-June Moon

Others : (Neurophysiology)

P-741 TRPV1 Expressed by Melanocortin-4 Receptor Neurons Regulate Body Weight
Youngjun Kim, Jong-Woo Sohn

Others : (Training)

P-742 Establishment of a treadmill-based training protocol for gait assessment in mini-pigs
Sojeong Lee, Jincheol Seo, Gahye Moon, Philyong Kang, Heechang Son, Junghyung Park, Sun-Uk Kim, Youngjeon Lee, Kyung Seob Lim

Others : (Neurogenetics)

P-743 Identification and characterization of GAL4 drivers that mark distinct cell types and regions in the Drosophila adult gut
Jinhyeong Lee, Seung Yeon Lim, Hyejin You, Jaejin Lee, Sung-Eun Yoon, Jae Young Kwon, Won-Jae Lee, Young-Joon Kim, Greg S.B. Suh

Others : (Computational Modeling)

P-744 Real-Time Decision Making under Uncertainty: An IRL-Based Analysis of Naturalistic Driving Task
Chae-Youn Chung, Sang Ho Lee, Jinwoo Jeong, Min-hwan Oh, Woo-Young Ahn

Others : (Multisensory integration)

P-745 Motion Cues Delivered via Somatosensory inputs can Increase or Decrease the Level of Motion Sickness caused by Virtual-Reality Experience
Minju Oh, Byounghyun Yoo, Hangue Park

Others : (Drug deliver system)

P-746 Brain-Targeted Delivery of Fluoxetine via Red Blood Cell Membrane Biomimetic Nanocarriers with Stiffness Optimization to Reverse Depressive Behavio
Zhaohui Lan, Qian Zhao, Qiushi Ju, Chunxi Qian, Xiangzhao Ai, Weidong Li

Others : (memory)

P-747 Study on the Effects of Alcohol Exposure on Learning and Memory in Mice and Its Underlying Mechanisms
Qian Zhao, Huaiyu Chen, Weidong Li

Others : (Neuroscience)

P-748 A neuropeptide signaling pathway mediates pheromone avoidance behavior in C. elegans
Eujeong Oh, Hyeonjeong Hwang, Kyuhyung Kim

Others : (Behavior)

P-749 Predictive coordinated eye and tail movements in response to periodic visual motion in goldfish
Ryujiro Tanahashi, Toshimi Yamanaka, Hirata Yutaka

Others : (Neuromodulation in the brain: new understanding and emerging methods)

P-750 Self-powered neural modulation via cervical motion-induced bioelectrical harvesting in an implantable system
Hyunwoo Cho, Jonghyeon Yun, Geunchul Kim, Daewon Kim

Others : (Sleep)

P-751 Regulation Mechanisms and Functions of Fast Adenosine Release in Dorsal Striatum
Luyan HUANG, Wanling PENG, Min XU

Synapses and Circuits P-752~P-776

P-752 Gene Therapy Targeting Synapses Through AAV9 Delivery Boosts Functional Recovery Following Spinal Cord Injury
Ahyeon Song, You Jang Noh, Bong Geun Choi, Jung Keun Hyun

P-753 Encoding the Glucose Identity by Discrete Hypothalamic Neurons via the Gut-Brain Axis
Jineun Kim, Shinhye Kim, Wongyo Jung, Yujin Kim, Seongju Lee, Sehun Kim, Hae-Yong Park, Dae Young Yoo, In Koo Hwang, Robert C. Froemke, Seung-Hee Lee, Young-Gyun Park, Gary J. Schwartz, Greg S. B. Suh

P-754 Frontoparietal as well as cholinergic inputs are necessary for the activity of the posterior parietal cortex during short-term memory
soyoun park, yoon sil yang, joonho Choi, Jong-cheol Rah

P-755 Persistence of CTA Memory in PBN Ensembles Following Extinction
Jiarun Yang, Xu Zhang, Weidong Li

P-756 Inhibitory Interneurons in the Mediodorsal Nucleus of the Thalamus and their Modulation and Termination of Short-Term Memory
ChaeWon Kang, Yena Kim, Joon Ho Choi, Jong-Cheol Rah

P-757 Role of Basal Ganglia Network Regulation in ADHD-like phenotypes in mice
Ahrim Lee, Young Lee, Hee-yoon Lee, Se-young Choi, Bong-June Yoon

P-758 Mitochondrial calcium modulates odor-mediated behavioral plasticity in C. elegans
Hee Kyung Lee, Abe Gayle Santos, Kyu Sang Park, Kyoung-hye Yoon

P-759 Acetylcholine switches the frequency-dependent activity filtering of thalamofrontal synapses and activity loop in short-term memory
Yeri Kim, Jinmo Kim, Jungmin Lee, In-Sun Choi, Ji-Woong Choi, Joon Ho Choi, Jong-Cheol Rah

P-760 Asymmetric co-transmission by VGluT3+ neurons in the anterior bed nucleus of the stria terminalis
Hyogyun Kim, Minsung Sim, ChiHye Chung

P-761 Thalamic Spike Frequency Adaptation Enhance Feature Selectivity via Intrinsic and Synaptic Modulation
Hyeonyeong Jeong, Eunji Cheong

P-762 Synapse-specific N-glycosylation by B3gnt2 is critical for synaptic function and learning and memory behavior.
Ji Woong Bae, Ji yoon Baik, Woo Suk Roh, Myung Jin Oh, Dongtan Yin, Hyun Joo An, Kyung-Seok Han

P-763 Analysis of AMPA receptor GluA1 subunit distribution at excitatory synapses of mouse auditory cortex upon acute nicotine exposure.
Toma Kojima, Takahiro Nagayama, Anna Suzuki, Kenichi Yamasaki, Hideki Kawai

P-764 Adolescent social isolation alters social novelty preference and synaptic transmission in the lateral septum
Se-Young Choi, Seon-Yong Kim

P-765 Synaptic correlates of operant learning and memory encoding
Yeojin Jung, HyoJin Park, Bong-Kiun Kaang

P-766 Chemogenetic activation at LI11 mitigates atopic dermatitis via the vagus nerve–spleen axis
Se Hoon Jang, Mijung Yeom, Sora Ahn, Jaenam Park, Su-Yang Park, Min-Ho Nam, Hi-Joon Park

P-767 Hippocampal encoding of a sequence of reward journeys
Junho Son, Dahee Jung, Sebastien Royer

P-768 Stimulation of the STING–GATs signaling pathway improves the cognitive dysfunction in APP-PS1 mice
Nahyeon Park, Ramesh Sharma, Chaerin Yoon, Jin Bong Park

P-769 Nicotinic regulation of thalamocortical inputs to fast-spiking interneurons in mouse primary auditory cortex
Makoto Nakanishi, Hideki Kawai

P-770 Effects of Gamma-Ray Irradiation-Induced Neurogenesis Reduction on Cognitive Function in Monkeys
Minji Kim, ChangYeop Jeon, Yeonghoon Son, Youngjeon Lee, Ain Chung

P-771 Long-Range Brain Network Modulation via Functionally Targeted Ultrasound Stimulation
Ho-Jeong Kim, Joo Min Park, Sung-Phil Kim

P-772 CXCL5-CXCR2 constitutively maintains GABAAR tonic inhibition restraining seizure-prone changes in the hippocampus
Chaerin Yoon, Sunjung Yang, Ramesh Sharma, Nahyeon Park, Jin Bong Park

P-773 Each component of glutamate-glutamine cycle within the medial prefrontal cortex works differently to keep homeostasis and normal emotional behavior
Soomin HAN, Jae Soon Kang, Ji Hyeong Beak, Hyeongchan Park, Naveed Ur Rehman, Hye Jin Chung, Dong Kun Lee, Sekyung Oh, Hyun Joon Kim

P-774 Pre-Cerebellar Brainstem Nucleus as a Source of Internal Timing Signals for Predictive Eye Movements
Toshimi Yamanaka, Yutaka Hirata

P-775 Analgesic Effect of Human Placenta hydrolysate on CFA-Induced Inflammatory Pain in Mice
DongWoo Kang, HeeJoon Jo, KeunTae Park, WooJin Kim

P-776 Low frequency Electro-acupuncture Treatment alleviates STZ induced diabetic neuropathic pain through noradrenaline system modulation
Heejoon Jo, Hyojin Kim, Dongwoo Kang, Inseon Lee, Woojin Kim

Systems and Computational Neuroscience P-777~P-825

P-777 EEG decoding study on model-based transfer learning
Jungryul Ahn, Hyeokjin Park, Sanghum Woo, Joonyeol Lee

P-778 Inhibitory threshold modulation in visual cortex explains expectation-driven enhancement of sensorimotor behavior
Jungryul Ahn, Seolmin Kim, Sanghum Woo, Joonyeol Lee

P-779 Unbiased Imitation Optimizes Group Behavior
Seungdae Baek, Hyeonsu Lee, Aner Zheng, Jaeson Jang, Se-Bum Paik

P-780 Conjunctive Representation of Value and Space in the retrosplenial cortex
Daeul Kong, Eun Ju Shin, Min Whan Jung

P-781 Neural dynamics of emergent social roles in collective foraging by mice
Jaehyun Lee, Gyu-Hwan Lee, Seo Young Kim, DaYoung Jung, Jaehoon Kim, Jee Hyun Choi

P-782 Temporal Expectation Modulates Directional Expectation Through Alpha Oscillations during Sensorymotor Processing
Sanghum Woo, Joonyeol Lee

P-783 The Role of Hippocampal Backprojections to the Medial Entorhinal Cortex in Spatial Cognition
Hong Jin, Chenglin Miao, Qichen Cao

P-784 Inter-individual entrainment of respiratory rhythm induced by huddling during sleep in mice
With Drawn
Jeyoon Lee, Byoung-Kyoung Min, Jee Hyun Choi

P-785 Modeling human elbow joint operation under proprioceptive error: a comparison between reinforcement learning and inverse kinematics
Eunsoo Yoo, Hangue Park

P-786 Spectral TRF(sTRF) – Linear Regression model using spectral information of EEG
Donghoon Ko, Jonghwa Park, Yoonseob Lim

P-787 Versatile visual stimulation for awake mice in ultra-high field fMRI reveals diverse patterns in visual cortex
SeungYub Lee, GeunHo Im, Sanghan Choi, Seong-Gi Kim, HyungGoo Kim

P-788 Projection-specific diversity of dopaminergic activity under aversive situations
Mijoo Park, Jongwon Yun, Jihye Yang, HyungGoo Kim

P-789 Behavioral Identification of Loss Perception
Jinhwan Jung, Jung Ho Hyun

P-790 Intermittent social isolation enhances social investigation but impairs social memory in adult mice
Shuyan Geng, Zixu Zhang, Xing Liu, Haoyu Sun, Tianxiang Xu, Chuanyao Sun, Shengru Hu, Zixuan Lei, An Liu, Zhiyuan Yang, Wei Xie, Mingdao Mu

P-791 Two-Stage Learning Framework for Cross-Subject and Real-Time Seizure Detection Using Domain Generalization and Source-Free Adaptation
Seoyoung Lee, Sol Ah Kim, Yunseo Choi, Hyang Woon Lee

P-792 Stochastic Innovation and Imitation Enhance Coordination in Multi-Agent Systems
Youngil Seo, Seungdae Baek, Se-Bum Paik

P-793 Hierarchical dynamics of information processing during auditory reversal learning
Jong-Hoon Lee, Eunji Jung, Geonhui Ryu, Seung-Hee Lee

P-794 Coordinated multi-frequency oscillatory bursts enable time-structured dynamic information transfer
Jungyoung Kim, Jee Hyun Choi, Demian Battaglia

P-795 Real-time and periodic individual identification in freely moving mice using a bit-based LED tagging system
With Drawn
Sehyeon Jang, Sangyun Lee, Deokha Woo, Sung Chan Jun, Jee Hyun Choi

P-796 Serial Dependence in Categorical Decision-Making on Human Faces and Biological Motion
Minsu Yeo, Sang-Hun Lee

P-797 Music Genre Similarity in Human Brain: Investigation of Genre Classification Regions Using fMRI Data and Comparison with Actual Classificat
Baekho Jang, June Kang

P-798 Roles of entorhinal cortex and anterior thalamic inputs in population-level representation of egocentric geometry in the retrosplenial cortex
Daehyun Oh, Jeehyun Kwag

P-799 Distributed neural dynamics underlying sensory-to-motor transformation during olfactory decision making
Jongrok Do, Doyun Lee

P-800 Natural image training enables robust generalization in visual number sense of deep neural networks
Joohyun Lee, Joonkoo Park, Hansem Sohn

P-801 Dopaminergic activities in the striatal subregions show distinct representations but common learning mechanisms
Jihye Yang, Mijoo Park, HyungGoo Kim

P-802 Multiple visual features in naturalistic environments shape steering responses in flying Drosophila
Kyungjun Kim, Minkyung Jo, Sangbin Jeong, Anmo Kim

P-803 Dopamine activity in the tail of striatum predicts avoidance behaviors in complex threatening situations
Nawoon Kwon, HyungGoo Kim

P-804 Neurodevelopment-inspired learning of abstract and compositional representations
Jeonghwan Cheon, Se-Bum Paik

P-805 Cerebellar Cortical Initial Learning: A Strategy for Adaptation in Non-stationary Environments
Jundong Kim, Hyojin Bae, Chang-Eop Kim

P-806 Accumbal Neuropeptide Y Neurons Promote Reward Learning through Value Updating for Palatable Food
Yu-Been Kim, Deok-Hyeon Cheon, Sang-Ho Jung, Leslie Jaesun Ha, Jeewon Choi, Solin Baek, Jong-Woo Sohn, Hyung Jin Choi

P-807 Connectome-GAN: A Generative Model for Transforming Resting-state Brain Networks to Task-specific States
Donggyu Kim, Kwangsun Yoo

P-808 Molecular and Functional Heterogeneity of CaMKIIα+ Neurons in the Lateral Hypothalamus: Encoding Appetitive Motivation Over Food Consumption&
SheeJune Park, HanGyeol Bae, MinSeo Koo, DongHoon Lee, Young Hee Lee, Hyung Jin Choi

P-809 Multi-modal gating of visual input tunes the Drosophila heading compass
Geonil Kim, Seongyeon Kim, Anmo Kim

P-810 Parallel top-down projections from the posterior parietal cortex facilitate behavioral flexibility in auditory reversal learning</
Eunji Jung, Jong-Hoon Lee, Geonhui Ryu, Gil-Hyun Kim, Seung-Hee Lee

P-811 Axially multifocal metalens for 3D volumetric photoacoustic imaging of neuromelanin in live brain organoid
Gyusoo Bak, Aleksandr Barulin, Elena Barulina, Dong Kyo Oh, Yongjae Jo, Hyemi Park, Soomin Park, Hyunjun Kye, Jeesu Kim, Jinhee Yoo, Junhyung Kim, Yangkyu Kim, Hyunjung Kang, Yujin Park, Junsuk Rho, Byullee Park, Inki Kim, Jong-Chan Park

P-812 Thalamocortical Neuropharmacology in Absence Epilepsy: A Computational Model of T-type Ca^{2+} and Na^{+} Channel Dynamics
Euisun Kim, Jiyoung Kang, Jinseok Eo, Ara Ko, Joon Soo Lee, Sangbo Lee, Hae-Jeong Park

P-813 Dopaminergic regulation of reward-associated social memory in the hippocampal CA1
Subeen Park, Doyun Lee, Jung-Hoon Park

P-814 A sleep-active hippocampal interneuron for memory consolidation
Yili Feng, Wanling Peng, Min Xu

P-815 Map-like Representations of Interpersonal Relationships in the Human Hippocampus
Wonjun Kang, Minjae Kwon, Sue-Hyun Lee

P-816 Development of an auditory feedback experiment for rats and its application for measuring vocalization-induced suppression.
Amarbayasgalant Badarch, Chinzorig Choijiljav, Tsuyoshi Setogawa, Hisao Nishijo, Hiroshi Nishimaru, Jumpei Matsumoto

P-817 Flexible sensorimotor associative learning in frontal motor cortical circuits
Jianxiang Zhou, Ninglong Xu

P-818 Category-based generalization and underlying circuit mechanism
Ruoqing Wang, Ninglong Xu

P-819 The Cerebellar Variance Paradox: A Formal Proof for Why a Complex System Must Be Low-Variance
Chang-Eop Kim

P-820 Somatostatin-expressing interneurons encode a negative reward prediction error in the mouse primary visual cortex
Jiwon Yoon, Sangwoo Kim, Dong-Hyun Ma, Ilsong Choi, Seung-Hee Lee

P-821 Closed-Form Brain–Plasma PK Solutions Coupled with an Optimization Algorithm for CNS Drug Regimens
Yena Lee

P-822 Towards a Novel Encoding Model of Striatal Medium Spiny Neurons: Multiplex and Heterogeneous Value Encoding Patterns
Junseok Kim, Hyunkyung Jung, Chanhee Jeong, Seungmin Baek, Junghwan Shin

P-823 Dopaminergic signaling underlies reward devaluation by repetitive consumption
Yunjin Lee, Yu-been Kim, Hyung Jin Choi

P-824 The Cortical Mechanism of Cooperative Choices in Social Decision-Making

P-825 Layer-specific and temporally organized neural dynamics supporting working memory in the prefrontal cortex
Seok Woo Ko, Jung Won Bae, Min Whan Jung

Translational and Clinical Neuroscience P-826~P-844

P-826 Gait analysis using supervised deep learning to evaluate chemogenetic neuromodulation in non-human primate stroke models
Jisun Min, Hyeon-Gu Yeo, Jinyoung Won, Junghyung Park, Kyung Seob Lim, Chang-Yeop Jeon, Hyerin Jang, Jongwook Cho, Ji-Young Park, Hyoung-Ihl Kim, Youngjeon Lee

P-827 Therapeutic Effects of Transcranial Ultrasound Pulsed at 40 Hz in Alzheimer's Disease Mouse Model: Focusing on Changes in Glial Cells
Mincheol Park, Hoang Gia Minh, Yumi Lee, Junghye Park, Jaegwan Kim, Tae Kim

P-828 REM sleep suppression during diazoxide-induced acute hyperglycemia in a non-diabetic mouse model
Prabesh Baniya, Chanyoung Cheong, Euisuk Yoon, Tae Kim

P-829 Structural Brain Volume Alterations Associated with Sleep Disturbance and Cognitive Impairment in Depression
Jihye Lee, Soo In Kim, Ga Eun Kim, Hee Youn Won, Hyang Woon Lee

P-830 Enhanced Neurogenesis and Therapeutic Effects of Aducanumab by Focused Ultrasound in Alzheimer's Disease
Jaewoo Shin, Chanho Kong, Eun-Jeong Yang, Junwon Park, Won Seok Chang, Changhan Lee, Bo Young Choi, Hyunju Kim, Hye-Sun Kim, Jin Woo Chang

P-831 High-beta band EEG network connectivity as a potential biomarker for differentiating PTSD from other anxiety disorders: a preliminary study
Minhee Kim, Hyunjo Ji, Ajin Yun, Jaehui Kim, Yelin Park, Deung Hyun Kang, Soo-Hee Choi

P-832 Modulatory effects of transcranial photobiomodulation and vagus nerve stimulation on alcohol dependence and craving
Minjae Kim, Manjae Kwon, Jungyoon Kang, Minkyung Park, Ara Cho, Minho Hwang, Sunmin Kim, Sanyeowool Oh, Jiwon Park, Goeun Seong, Woo-Young Ahn, Jung-Seok Choi, Young-Chul Jung, Seung Wan Kang, Daekeun Kim, Dongil Chung

P-833 Single-Cell Transcriptomics Reveals CCL7+ Microglia as Mediators of White Matter Damage in Renovascular Hypertensive Brain
Shivani Singh, Hyo Gyeong Seo, Xuelian Jin, Han Ki Kim, Eun Jeong Lee, Byung Gon Kim

P-834 KBN2201 ameliorates amyloid pathology, neuroinflammation, neuronal degeneration, and neurogenesis deficits in 9-month-old 5xFAD mice
Sun-Young Lee, Moon Hang Kim, Mi Ran Choi, Sang-Rae Lee

P-835 A drug discrimination test of four stimulants in rats trained with methamphetamine and cocaine
Su-Nyeong Jang, Hyun Kyu Min, Tae Woong Na, Su-Jeong Park, Chan Hyeok Kwon, Kikyung Jung

P-836 The effects of Heart-tonification acupuncture on a Chronic Stress-induced Mouse model of Depression
Ji-Hye Song, Geun Hyang Eom, Seul-Ki Won, Yun-Ji Kang, Ji-Yeun Park

P-837 Crosstalk between sleep homeostasis and circadian rhythm: the implications of photobiomodulation
Jiwon Baek, Jieun Jung, Mincheol Park, Yoonho Oh, Jinhong Kim, Tae Kim

P-838 Neural Markers of Listening Effort: An EEG Framework for Clinical Assessment of Auditory Disorders
Jaewon Lee, Jonghwa Park, Yoonseob Lim

P-839 Development of a rapid response platform integrating AI-based CBRN detection and regenerative medicine technologies
Keunhong Jeong, Dong-Myung Shin, Gyeong Joon Moon

P-840 Neuroimaging, psychopathology and cognitive features of impulsivity subtypes in adolescents: implications for transdiagnostic psychiatry
Hang Wu, Xiongying Chen, Bofan Zhang, Caiying Luo, Xinyue Zhang, Jing Shi, Jun Li

P-841 East Asian Traditional Medicine for attention-deficit hyperactivity disorder in children and adolescents: A scoping review
Jihong Lee, Hyun-Kyung Sung

P-842 Sex differences in the effects of sleep efficiency on brain structure and cognitive aging: Literature review
Hee Sang Yang, So Yi Yoon, Jihye Lee, Maithreyee Devi, Aram Cho, Hyang Woon Lee

P-843 Evaluating Cognitive and Neural Changes in Mild Cognitive Impairment with Portable Prefrontal EEG
Joel Eyamu, Wuon-Shik Kim, Kahye Kim, Kun Ho Lee, Jaeuk U. Kim

P-844 An insight into aging breakpoints through multisystem biomarkers in the Korean population
Sakinah Hilya Abida, Sanghun Lee, Dieu Ni Thi Doan, Jaeuk Kim,

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Lecture

Day (August 24~27) **11:05 -18:30** **Grand Ballroom**

Presidential Lecture 1
Glial control of brain circuits and brain tumors / Benjamin Deneen

Presidential Lecture 2
Targeting the Cell's Stress Pathways for Therapeutic Benefit / Peter Walter, PhD

KSBNS Plenary Lecture 1
The odds of a decision / Matteo Carandini

KSBNS Plenary Lecture 2
Building mental models for exible behaviour in humans and macaques / Matthew Rushworth

CJK Plenary Lecture 1
Decoding the neural mechanisms of depression: insights through ketamine's pharmacological lens / Hailan Hu

CJK Plenary Lecture 2
Unlocking the gut-brain connection in Alzheimer's: vagus nerve transport of pathogenic proteins as a BBB bypass for therapeutic innovation / Inhee Mook-Jung

CJK Plenary Lecture 3
Deciphering principles of molecular and circuit mechanisms underlying animal behavior / Ikue Mori

Special Lecture 1
Lighting up, controlling, and restoring neural signaling in the living mouse brain / Won Do Heo

Special Lecture 2
Ultrasound in neuroscience: from functional imaging to read/write brain machine interfaces / Mickael Tanter

Presidential Lecture 1

Glial control of brain circuits and brain tumors

Benjamin Deneen

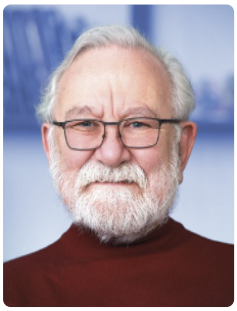
Department of Neurosurgery, Center for Cancer Neuroscience, Center for Cell and Gene Therapy, Baylor College of Medicine

Astrocytes are the predominant glial cell in the adult central nervous system and play essential roles in neural circuit function. Accordingly, astrocytes respond- and adapt- to a range of experiences, exhibiting experience dependent plasticity. In the first part of my seminar, I will describe astrocyte plasticity and discuss recent work from my lab that focuses on transcriptional responses in astrocytes resulting from olfactory experience and memory events. I will discuss new work that highlights astrocytes as active participants in memory engrams and their role and associated molecular mechanisms in memory recall. In the second part of my seminar, I will shift gears and discuss the burgeoning field of cancer neuroscience, with an emphasis on adult- and pediatric- glioma. Malignant glioma is universally lethal disease for which standard of care and survival rates have not improved over several decades, highlighting the need for new perspectives and approaches. Here I will describe how glioma tumors interact with resident neurons and discuss paracrine signaling events between tumors and a host of neural circuits. I will discuss work from lab that has defined the lines of communication between tumors and neurons, while also exposing the audience to new models of glioma and functional genomics screening approaches. Overall, this seminar will provide the audience with a new perspective and insight into how astrocytes and glioma tumor cells communicate with neurons and how these lines of communication are essential for brain function.

Keywords:

· Astrocyte, Experience Dependent Plasticity, Engram, Cancer Neuroscience, Brain Tumors

Presidential Lecture 2



Targeting the Cell's Stress Pathways for Therapeutic Benefit

Peter Walter (Altos Labs)

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From its birth in the cradle of the ribosome to its demise in the fangs of proteolytic enzymes, a protein continuously explores different folding states. In most cell compartments, molecular sensors carefully monitor protein folding and instruct downstream effectors to take corrective actions as needed. In response, cells can make adjustments to their protein folding and degradation machineries to stay in a healthy state of homeostasis. If protein folding defects occur and cannot be corrected in a sufficient and timely manner, cells induce suicide programs. Programmed cell death is thought to protect an organism from malfunctioning rogue cells that result from an accumulation of defective protein. In various pathologies, the life/death balance can inappropriately err on either side: killing cells that would be beneficial if kept alive or, alternatively, inappropriately protecting dangerous, disease-propagating cells. Studies of the regulation of proteostasis now emerge as focal points of foundational basic research that powerfully connects to a broad spectrum of unmet clinical needs.

I will discuss advances in our lab's efforts to understand the molecular details of the unfolded protein response (UPR), a conserved signaling network that surveys the protein folding status in the endoplasmic reticulum. The UPR signals through three molecularly distinct branches. The development of small, drug-like molecules that selectively target each of the UPR's signaling branches has opened promising new therapeutic opportunities in areas as divergent as cancer, neurodegeneration, diabetes, inflammation, aging, and cognition. As such, the UPR emerges as a prime example of the power of fundamental cell biological discoveries to address problems of immense societal impact.

Keywords:

· protein folding, unfolded protein response, proteostasis

KSBNS Plenary Lecture 1

The odds of a decision

Matteo Carandini

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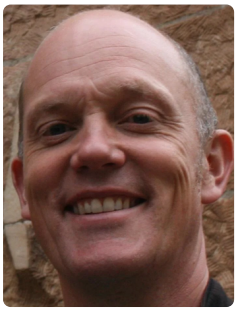
To make a decision, we must often combine diverse factors such as sensory inputs, past actions, and estimates of value. There is increasing evidence that the brain does this via a simple operation involving sums and multiplications. This operation is common in machine learning and economics, and has close cousins in psychology. Its neural correlates can now be identified in mice thanks to large-scale neural recordings and to localized optogenetic inactivations. These methods reveal how the components of an audiovisual choice are progressively computed at key stages in visual cortex, auditory cortex, prefrontal cortex, and superior colliculus. The results point to a single view of how the brain makes a variety of decisions.

Keywords:

· Decision making, Optogenetics, Vision, Audition, Neuropixels recordings

KSBNS Plenary Lecture 2



Building mental models for flexible behaviour in humans and macaques

Matthew Rushworth

Department of Experimental Psychology, University of Oxford, Oxford, United Kingdom

In order to thrive in a changing environment it is necessary for animals to be flexible. Humans and other animals should change the way in which they behave depending on the context that they find themselves in. It is widely agreed that prefrontal cortex is central to behavioural flexibility but there have been different views of the nature of its contribution. In recent experiments we have re-examined how macaques perform well known tests of behavioural flexibility such as reversal tasks. Rather than simply inhibiting inappropriate behaviour in the wrong setting, macaques identify and track states that are latent in the task and the ability to do this depends on interactions between dorsomedial prefrontal cortex (dmPFC) and hippocampus. Transient disruption of either dmPFC or hippocampus can change the way that macaques navigate through latent task states. In humans, hippocampus and prefrontal cortex activity maps out the graph of connections between latent task states and, using new techniques for transiently disrupting human hippocampus, it is possible to show that the ability to make inferences that depend on such graphs can be transiently compromised. Hippocampal activity allows humans to navigate through a range of arbitrary task spaces in much the same way that hippocampus activity has long been thought to allow animals to navigate through physical space. The latent stages identified in the hippocampus are then used during learning by dmPFC.

Keywords:

· prefrontal cortex, hippocampus, decision making

CJK Plenary Lecture 1

Decoding the neural mechanisms of depression: insights through ketamine's pharmacological lens

Hailan Hu

Zhejiang University, China

Depression, a highly polygenic and heterogeneous disorder, has long eluded mechanistic understanding due to the limitations of traditional forward genetic approaches. Here, we propose a complementary strategy: leveraging the rapid, targeted action of ketamine—a potent NMDA receptor (NMDAR) antagonist with robust antidepressant effects—to reverse-engineer the primary neural mechanisms underlying depression.

Over the past decade, we have elucidated the mechanisms behind ketamine's rapid, sustained, and brain-region-specific action. By uncovering how ketamine works, we identified increased neuronal burst firing in the lateral habenula (LHb), the brain's "anti-reward hub, as a core driver of depression etiology. Expanding this framework, our recent work extends beyond NMDARs, identifying two additional ion channels as critical mediators of LHb bursts and antidepressant efficacy. Through the characterization of one of these channels, the glia-specific potassium channel Kir4.1, we discovered a novel form of neuron-glia interaction, where astrocytic processes tightly envelop neuronal soma to regulate burst firing. I will present our ongoing work exploring how neurons and astrocytes dynamically interact in the LHb to modulate stress responses and depressive-like behaviors.

Keywords:

· Ketamine, glia, lateral habenula, depression, psychedelic

CJK Plenary Lecture 2

Unlocking the gut-brain connection in Alzheimer's: vagus nerve transport of pathogenic proteins as a BBB bypass for therapeutic innovation

Inhee Mook-Jung

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Recent research on Alzheimer's disease (AD) has increasingly focused on the gut–brain axis as a key contributor to disease pathogenesis. While much attention has been given to the gut–blood–brain axis, in the early stages of AD its impact may be limited due to the presence of an intact blood–brain barrier (BBB). In contrast, the vagus nerve provides a direct neural communication route between the gut and the brain, effectively bypassing the BBB. This bidirectional conduit comprises visceral sensory neurons (VSNs), which transmit signals and molecular cargo from the gut to the brain, and visceral motor neurons (VMNs), which carry efferent signals from the brain to the gut.We propose that in early AD, VSNs play a crucial role in mediating the transport of pathogenic molecules—including amyloid-beta (Aβ), tau, and lipopolysaccharides (LPS)—from the gut to the brain, while VMNs may facilitate the propagation of brain-derived pathological proteins to the gut. This bidirectional exchange could create a pathological feedback loop, exacerbating disease progression through sustained peripheral and central inflammation, metabolic dysregulation, and amyloid/tau pathology.

Keywords:

· Gut-brain axis, Vagus nerve, Alzheimer's disease, Pahtologic proteins, BBB

CJK Plenary Lecture 3

Deciphering principles of molecular and circuit mechanisms underlying animal behavior

Ikue Mori

Chinese Institute for Brain Research

How neural circuits encode learning, memory and decision-making is an important question to understand animal behaviors. To reveal molecular and circuit mechanisms underlying animal behaviors, we focus on thermotaxis in the nematode C. elegans as a behavioral paradigm. Thermotaxis in C. elegans reflects thermal memories toward animals' previous cultivation temperatures, which involves association of food signals with cultivation temperatures. By changing the feeding status or the cultivation temperatures under C. elegans' physiological range, we can monitor animals' ability to learn and recall the memory for cultivation environments. From behavioral and neural computational perspectives, it is important to understand how the nervous systems bias animals' behaviors toward a neutral stimulus after learning and revise this bias after new experiences. We have been conducting comprehensive and interdisciplinary approaches on thermotaxis, by identifying genes and neurons involved in thermotaxis, developing several custom-made microscopic devises to auto-tracking and detailed analysis of animal movements during thermotaxis, and conducting optogenetic manipulation of neurons. Our recent studies also clarified the importance of non-neuronal cells that affect neural cell functions. We are currently dissecting interactions between different types of cells or tissues in order to understand how a behavior is generated.

Keywords:
Animal behavior, Learning and memory, Decision-making, Thermotaxis, C. elegans

Special Lecture 1

Lighting up, controlling, and restoring neural signaling in the living mouse brain

Won Do Heo

Department of Biological Sciences Korea Advanced Institute for Science and Technology

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Understanding how neuronal signaling molecules operate in space and time, and how their dysregulation leads to brain disorders, requires technologies that can both reveal and precisely manipulate their activity in living systems. While traditional genetic approaches have been foundational for dissecting molecular function, they generally lack reversible, time locked control in awake brains. Molecular optogenetics provides spatiotemporally precise, reversible control that enables causal interrogation and active reprogramming of signaling in the brains of awake mice. Our research integrates synthetic biology with neuroscience to achieve this molecular level control in vivo. At the core of our work are molecular optogenetic systems that precisely and reversibly regulate diverse pathways—including calcium dynamics, receptor tyrosine kinase (RTK) activation, and RNA processes such as mRNA localization and translation—from live cells to awake, behaving mice. These actuators allow direct, time locked tests of how specific molecular events shape neuronal signaling and function. In parallel, we develop advanced biosensors such as SynapShot, which offers reversible, dual color visualization of structural and functional synapse dynamics in awake animals, providing a real time readout of the changes induced by optogenetic modulation. By combining molecular optogenetics with advanced sensing technologies, we have restored normal signaling in multiple disease models. In neurodegeneration, targeted activation of growth factor pathways has promoted axonal remodeling and functional recovery; and in Parkinson's disease and depression models, reprogramming RTK pathways has normalized aberrant signaling and alleviated behavioral symptoms. This talk will highlight how molecular optogenetics can illuminate the brain's signaling networks, control them with spatiotemporal precision, and restore healthy function in disease states—paving the way for next generation molecular therapies in neuroscience.

Keywords:

Biosensors, Optogenetics, Calcium optogenetics, mRNA optogenetics, Mouse behavior

Special Lecture 2

Deciphering principles of molecular and circuit mechanisms underlying animal behavior

Mickael Tanter

Institute of Physics for Medicine, ESPCI PSL Paris, Inserm, CNRS

Biomedical ultrasound has undergone a true revolution over the past two decades. In the field of imaging, three fundamental barriers have been surpassed—temporal resolution, sensitivity to blood flow, and spatial resolution—by several orders of magnitude. These conceptual changes have a major impact in the field of radiology, particularly in brain imaging, for both fundamental neuroscience research and clinical applications in neuroimaging.

Firstly, leveraging the concept of acoustic holography, ultra-fast ultrasound imaging at thousands of frames per second has made it possible to detect very subtle variations in blood flow in small cerebral vessels during neuronal activity. This has introduced functional ultrasound (fUS) imaging as a full-fledged modality for brain imaging. Its portability, cost, and sensitivity make it particularly suitable for brain imaging during behavior, learning, or cognitive studies in awake and freely moving animals, for functional brain connectomics in small animal models, and for systemic neuroscience. Clinical applications are already under study for functional brain imaging in human newborns, intraoperative functional imaging, and future contactless brain-machine interfaces.

Secondly, when combined with intravenously injected contrast agents, ultra-fast imaging enables non-invasive, in vivo imaging of cerebral hemodynamics at the microscopic scale throughout the entire brain. Such Ultrasound Localization Microscopy (ULM) of the cerebrovascular system is achieved by locating and tracking the exact position of millions of microbubbles, ranging from 1 to 3 µm in diameter, moving within the cerebral vascular network. Finally, by tracking the dynamics of these microbubbles during neuronal activity, it is now possible, for the first time, to perform functional brain imaging of the entire brain at the microscopic scale in rodents. With growing evidence of early vascular or neurovascular dysfunction in neurodevelopmental and neurodegenerative diseases, such functional Ultrasound Localization Microscopy could enhance fundamental understanding, early detection, and monitoring of alterations in the developing and aging brain. Ultrasound is thus the first medical modality capable of completely non-invasively visualizing an entire organ at the microscopic scale.

Beyond ultrasound applications enabling the "reading" of brain activity, our recent work demonstrates that it is also possible to "write" in the brain using ultrasound, thanks to the recent concept of sonogenetics. The initial proof-of-concept shows that it should soon be possible to restore vision in blind patients by directly imprinting images of the surrounding world into the visual cortex.

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Award Lecture

Day 1 (August 24) **16:55-17:35** **Grand Ballroom**

Award Lecture 2 Organizer : Donghyun Kim (ZEISS Korea)

Stereociliary links: Sound mechanotransduction and control of hearing
Chul Hoon Kim(Yonsei University College of Medicine)

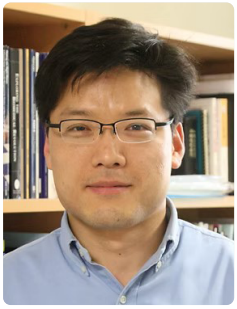
When the sugar code goes wrong in the brain
Boyoung Lee(Center for Cognition and Sociality)

Day 4 (August 27) **13:00-14:25** **Grand Ballroom**

Award Lecture 2 Organizer : Donghyun Kim (ZEISS Korea)

Microglia and Neural Organoids for Bridging Models to Mechanisms
Jong-Chan Park(Sungkyunkwan University)

Award Lecture 1



Stereociliary links: Sound mechanotransduction and control of hearing

Chul Hoon Kim

Yonsei University College of Medicine

Supported By
GNTPharma 지엔티파마

Hair bundles, consisting of a precisely regulated number of stereocilia, are deflected thousands of times per second in response to sound vibrations. These deflections trigger the mechanoelectrical transduction (MET) process, which is essential for hearing. Due to their mechanical sensitivity, hair bundles are among the most vulnerable structures within the organ of Corti. Stereocilia are interconnected by several specialized nanostructures: A) Tectorial membrane-attachment crowns (TM-ACs), which anchor the tallest stereocilia of outer hair cells (OHCs) to the overlying tectorial membrane; B) Tip links, which connect taller stereocilia to shorter ones and transmit mechanical force to MET channels; and C) Horizontal top connectors (HTCs), which link adjacent stereocilia, ensuring the cohesive structure and mechanical stiffness required for effective transduction. We have identified several key proteins critical for the assembly and maintenance of these nanostructures. In this presentation, I will discuss how these cochlear nanostructures contribute to normal hair cell physiology, as well as how their dysfunction leads to auditory pathology.

Keywords:
Stereocilia, nanostructure, outer hair cells, hair-bundle links

Award Lecture 2

When the sugar code goes wrong in the brain

Boyoung Lee

Institute for Basic Science

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Glycosylation is one of the most complex post-translational modifications (PTMs). Recent research highlights its importance in various brain disorders, including Alzheimer's disease and schizophrenia, as well as in the process of aging. As a key modification on membrane and secreted proteins, glycosylation acts as a frontline responder to environmental stimuli. Despite its significance, its study has been underexplored due to technical challenges. My interest in this field began when I found distinct glycan expression patterns across different brain regions, suggesting that these "sugar codes" may contribute to unique regional functions and overall brain health. In this talk, I will focus on our recent study of O-glycosylation in depression. We discovered that sialylated O-glycans were significantly reduced in the prefrontal cortex (PFC) of stressed animals. We identified a unique enzyme, St3gal1, which was significantly decreased in our model and has been linked to mental components in human psychiatric disorders. To investigate its role, we reduced St3gal1 expression in the medial PFC of adult wild-type mice, which was sufficient to induce depressive-like behaviors without stress. Conversely, overexpression of this gene in stressed mice significantly attenuated their depressive-like symptoms as well as the electrophysiological phenotypes associated with GABAergic neurotransmission. We were also able to suggest specific downstream glycoprotein targets and their glycosylation sites. This study is the first to examine the dynamics of O-glycan profiles across multiple brain regions in a depression model. Furthermore, it is the first to show that modulating glycosylation can reverse depressive-like symptoms. Collectively, our findings demonstrate that ST3GAL1-mediated O-sialylation is a critical component of stress-mediated depression and represents a promising new therapeutic target.

Keywords:

Depression, Prefrontal cortex, Glycosylation, ST3GAL1

Award Lecture 2

Microglia and Neural Organoids for Bridging Models to Mechanisms

Jong-Chan Park, Ph.D.

Sungkyunkwan University

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Our laboratory is dedicated to advancing organoid-based precision medicine by visualizing complex biological mechanisms and constructing integrated biological and mathematical models of disease. Through these efforts, we aim to bridge fundamental discoveries with clinically relevant applications.

In particular, we are actively developing novel and diverse neural organoid platforms that incorporate iPSC-derived microglia. These platforms provide a powerful means to investigate microglia–neuron (or other glial cells) interactions and can be applied to a wide range of neurodegenerative diseases, including Alzheimer's disease and related disorders. By using such models, we hope to reveal disease-specific mechanisms, identify therapeutic targets, and ultimately accelerate translational research.

In this presentation, I will introduce the diverse neural organoid platforms established in our lab and highlight our most recent findings from iPSC-derived microglia research, which is currently one of our most active areas of investigation. Through this, we aim not only to share our progress but also to foster enthusiastic collaboration with other researchers working across related fields.

Keywords:
Neural Organoid, Microglia, iPSC, Disease modeling, Precision medicine

Award Lecture 2

Anatomy of motivated behavior: mapping the neurons that drive us to eat

Hyung Jin Choi, MD, PhD

Seoul National University

The evolutionary pressure to secure adequate energy has shaped the brain to orchestrate complex eating behaviors for survival. We propose a theoretical framework and present experimental evidence that distinct and dissociable neural components orchestrate eating: need, motivation, pleasure, and prediction. Using a multi-species approach in mice, monkeys, and humans, we have mapped these components to specific, dissociable neural circuits. Our results show that the motivation to eat is encoded by leptin receptor neurons in the lateral hypothalamus. This drive is gated by homeostatic need, which originates from AgRP/NPY neurons in the arcuate hypothalamus. Critically, a prediction signal, mediated by GLP-1R neurons in the dorsomedial hypothalamus, anticipates future caloric intake and preemptively inhibits the need circuit upon food detection, thus reducing the need and the motivation before consumption. Finally, food preference is shaped by pleasure, a signal encoded by NPY neurons in the nucleus accumbens. By mapping fundamental psychological concepts to specific cell types, these works provide a foundational model for understanding the principles that govern all motivated behaviors.

Keywords:

Motivation, Need, Pleasure, Prediction, Eat

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 1

Day 1 (August 24) **13:00-14:55** **Grand Ballroom**

Molecular and circuit-level understanding of memory and memory related disorders

Organizer : Weidong Li (Shanghai Jiao Tong University)
Ain Chung (Korea Advanced Institute of Science and Technology)
Moderator : Weidong Li (Shanghai Jiao Tong University)

Epigenetic and engram mechanisms in remote memory dysfunction
Weidong Li (Shanghai Jiao Tong University)

Hippocampal cellular and molecular representations of fear memory reconsolidation and extinction
Satoshi Kida (The University of Tokyo)

Two orthogonal ensembles encoding of engram in the dentate gyrus
Yi Zhong (Tsinghua University)

Septal GABAergic neurons switch memories to enable update
Jin-Hee Han (Korea Advanced Institute of Science and Technology)

Exploring the impact of cognitive training on hippocampal synaptic circuit function
Ain Chung (Korea Advanced Institute of Science and Technology)

Serpina1e mediates the exercise-induced enhancement of hippocampal memory
Hyunyoung Kim (Korea Brain Research Institute) Scitech Korea AWARDEE

S1-1

Epigenetic and engram mechanisms in remote memory dysfunction

Weidong Li

Shanghai Jiao Tong University

Kabuki syndrome (KS), a rare developmental disorder, causes congenital anomalies and intellectual disability. UTX, a histone demethylase gene, is a key risk factor for KS, with no targeted therapies currently available. We created UTX conditional knockout mice to study its role. UTX deletion reduced calmodulin transcription by impairing H3K27me3 demethylation, decreasing calcium/calmodulin-dependent protein kinase II phosphorylation, and disrupting long-term potentiation and remote contextual fear memory. These deficits were reversed by desipramine, an FDA-approved drug.

Further research revealed UTX regulates synaptic remodeling during late memory consolidation. Knockout mice showed impaired remote memory, reduced neural projections, and disrupted engram subtype integration, affecting transcriptomic identity, synaptic gene expression, and engram cell numbers. These findings highlight UTX's critical role in synaptic plasticity and cognitive function, suggesting potential therapeutic targets for KS-related memory dysfunction.

S1-2

Hippocampal cellular and molecular representations of fear memory reconsolidation and extinction

Satoshi Kida

Graduate School of Agriculture and Life Sciences, The University of Tokyo, Tokyo, Japan

Memory retrieval is not a passive phenomenon. Previous studies have presented evidence that memory retrieval is a dynamic process during which memories can be made stronger, weakened, or their content can be altered. Recent studies have shown that reactivated memory becomes labile after retrieval and is re-stabilized through a gene expression-dependent process known as memory reconsolidation. Memory reconsolidation after retrieval may be used to maintain or update long-term memories, reinforcing or integrating new information into them. In classical Pavlovian fear conditioning paradigms, the reactivation of conditioned fear memory by re-exposure to the conditioned stimulus (CS) in the absence of the unconditioned stimulus (US) also initiates extinction as a form of new learning that weakens fear memory expression (i.e., a new CS-no US inhibitory memory that competes with the original CS-US memory trace). Thus, in the fear conditioning paradigms, memory retrieval also includes extinction learning. Therefore, when fear memory is retrieved, the dominance of the original (fear) or new (extinction) memory traces is thought to determine the fate of memory through their competition. We have tried to understand the mechanisms by which the fate of retrieved fear memory is determined. We compared cellular and molecular signatures of reconsolidation and extinction of contextual fear memory and found that the hippocampus shows contrasting molecular representations of reconsolidation and extinction of contextual fear memory. These changes of hippocampal molecular and cellular representations must be important for the transition of memory phases from reconsolidation to extinction.

Keywords : Reconsolidation, Extinction, Retrieval, Fear memory, Hippocampus

S1-3

Two orthogonal ensembles encoding of engram in the dentate gyrus

Yi Zhong

Tsinghua University

S1-4

Septal GABAergic neurons switch memories to enable update

Jin-Hee Han

Department of Biological Sciences, KAIST, Daejeon, Republic of Korea

New experiences are integrated with existing knowledge to continually update memory, a process essential for organisms' survival in a dynamic environment. While updating memory, the brain can still access previous memories spontaneously or willingly as needed to guide behaviors. However, how the brain organizes the retrieval of old and new experiences remains unknown. In this study, we discovered a neural switch mechanism mediated by the septo-entorhinal GABAergic circuit that contributes to the control of memory retrieval. This circuit was required for retrieving updated memories. Strikingly, when this circuit was inactivated, the retrieval switched back to previous memories. At the cell population level, we observed similar switching in temporal activity patterns in the hippocampal CA1 by the same optogenetic circuit manipulation, suggesting a potential mechanism. This study provides a novel framework for understanding the mechanism of memory updating and gives insights into how episodic memories are temporally organized within brain networks.

Keywords : Memory, Update, Medial Septum, GABAergic neurons, Hippocampus

Acknowledgements : This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MIST) (RS-2023-NR077269), and partly by Samsung Science and Technology Foundation Project SSTF-BA1801-10.

S1-5

Exploring the impact of cognitive training on hippocampal synaptic circuit function

Ain Chung

Department of Bio and Brain Engineering, KAIST

Learning and memory are fundamental cognitive processes that enable animals to store information persistently and stably, while flexibly adapting to dynamic environments. My research investigates how persistent changes in neural circuit function allow the brain to acquire long-lasting memories and achieve sustained cognitive enhancement in new learning contexts. I examined how cognitive control training induces broad cognitive improvements by altering hippocampal circuit function beyond the formation of specific, explicit memories. I found that cognitive control facilitates the acquisition of new tasks and rapidly modifies medial entorhinal cortex (MEC) to dentate gyrus (DG) synaptic function, producing an excitatory–inhibitory subcircuit reorganization that persists for months. Specifically, cognitive control training increases inhibition, which attenuates DG responses to MEC input, and through disinhibition, enhances responses to strong inputs; resulting in an overall improvement in signal-to-noise ratio. I next tested whether genetically increasing inhibitory interneuron activity in the hippocampus could improve cognitive function. I found that augmented parvalbumin (PV) inhibitory contacts in CA2/3 and strengthened inhibitory synaptic inputs onto CA2/3 neurons were associated with enhanced contextual and social discrimination in mice. Furthermore, chemogenetic activation of inhibitory interneurons was sufficient to reduce social interference. Together, these findings suggest that enhancing inhibitory circuit function can optimize information processing and improve cognition.

Keywords : Cognitive control training, Inhibitory interneuron, Hippocampus, Synaptic plasticity, Cognitive enhancement

S1-6

Serpina1e mediates the exercise-induced enhancement of hippocampal memory

Hyunyoung Kim[1,2], Sanghee Shin[3,4], Jeongho Han[1], Jong-Seo Kim[3,4], Hyungju Park[1]

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[2]Department of Brain Science, Daegu-Gyeongbuk Institute of Science and Technology, Daegu, Republic of Korea
[3]Center for RNA Research, Seoul National University, Seoul, Republic of Korea
[4]School of Biological Sciences, Seoul National University, Seoul, Republic of Korea

The exercise-induced enhancement of learning and memory is thought to be regulated by body–brain interactions via secretory proteins in the blood plasma. Given the prominent role that skeletal muscle plays during exercise, the beneficial effects of exercise on cognitive functions appear to be mediated by muscle-derived secretory factors, including myokines. However, the specific myokines that exert beneficial effects on cognitive functions remain to be elucidated. Here, we reveal that a novel myokine, Serpina1e, acts as a molecular mediator that directly supports long-term memory formation in the hippocampus. Using an *in vivo* myokine-labeling mouse model, proteomic analysis revealed that the Serpina1 family of proteins is the myokine whose levels increased the most in plasma after chronic aerobic exercise for 4 weeks. Systemic delivery of recombinant Serpina1e into sedentary mice was sufficient to reproduce the beneficial effect of exercise on hippocampus-associated cognitive functions. Moreover, plasma Serpina1e can cross the blood–cerebrospinal fluid (CSF) barrier and blood–brain barrier to reach the brain, thereby influencing hippocampal function. Indeed, an increase in the plasma level of Serpina1e promoted hippocampal neurogenesis, increased the levels of brain-derived neurotrophic factor (BDNF), and induced neurite growth. Our findings reveal that Serpina1e is a myokine that migrates to the brain and mediates exercise-induced memory enhancement by triggering neurotrophic growth signaling in the hippocampus. This discovery elucidates the molecular mechanisms underlying the beneficial effects of exercise on cognitive function and may have implications for the development of novel therapeutic interventions for alleviating cognitive disorders.

Keywords : exercise, myokine, muscle-brain interaction, hippocampal memory, Serpina1e

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 2

Day 1 (August 24) **13:00-14:55** **Premier Ballroom A**

Mechanotransduction in the peripheral and central nerve system

Organizer : Bailong Xiao (Tsinghua University)
Uhtaek Oh (Korea Institute of Science and Technology)
Moderator : Bailong Xiao (Tsinghua University)
Uhtaek Oh (Korea Institute of Science and Technology)

Molecular and physiological functions of a mechanically activated ion channel, Tentonin 3.
Uhtaek Oh (Korea Institute of Science and Technology)

Structure-function and physiological roles of mechanically activated PIEZO channels
Bailong Xiao (Tsinghua University)

ATP release in physiology and pathology: A mechanobiological perspective
Masahiro Sokabe (Kanazawa Institute of Technology)

Identification of the brain-to-spinal opioidergic circuits driving tactile pain
Longzhen Cheng (Southern University of Science and Technology)

Mechanically evoked ATP release from Merkel cells mediates non-neuronal paracrine signaling
Young Min Bae (Konkuk University)

S2-1

Molecular and physiological functions of a mechanically activated ion channel, Tentonin 3.

Uhtaek Oh

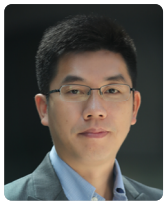
Brain Science Institute, KIST, Seoul, Republic of Korea

Mechanosensation is essential for the survival of animals. Numerous physiological functions such as tactile sensation, proprioception, hearing, baroreceptor reflex, and mechanical pain require mechanotransduction processes. Mechanosensation begins with mechanotransduction channels in nerve terminals or receptor cells. Many genes were reported for mechanosensitive (MS) channels. Using bioinformatics, we identified that Tentonin 3 (TTN3/TMEM150C) confers slowly-adapting (SA)-type MS currents in DRG neurons. In HEK cells, TTN3 is activated by mechanical stimuli with distinct SA inactivation kinetics. TTN3 is a cation channel with higher Ca2+ permeability over Cs+. TTN3 is a tetramer and pore-forming subunit of MS channel because spontaneous single-channel currents are observed in lipid bilayer incorporated with purified TTN3 proteins. We recently identified its specific blocker, NMB-1, a conopeptide known to block SA-type MS currents in DRG neurons. However, NMB-1 did not block Piezo channels. TTN3 orthologs of many phyla of vertebrates also show SA-type MS currents, suggesting that the unique kinetics of TTN3 is conserved throughout the vertebrate phyla. TTN3 requires much greater mechanical stimuli for its activation than Piezo1. In addition, TTN3 also requires relatively strong cytoskeleton integrity for its mechanosensitivity. In summary, TTN3 is a bona fide mechanically activated channel with unique inactivation kinetics.

Keywords : Tentonin 3, Tmem150c, Mechanosensitive, Channel, NMB-1
Acknowledgements : Supported by National Research Foundation of Korea (RS-2023-00254795)

S2-2

Structure-function and physiological roles of mechanically activated PIEZO channels



Bailong Xiao[1,2,3,4]

[1]Tsinghua University, School of Pharmaceutical Sciences, Beijing, China
[2]Tsinghua University, Beijing Advanced Innovation Center for Structural Biology, Beijing, China
[3]Tsinghua University, IDG/McGovern Institute for Brain Research, Beijing, China
[4]Tsinghua University, Tsinghua-Peking Center for Life Sciences, Beijing, China

PIEZO1 and PIEZO2 have been identified by Patapoutian and colleagues as bona fide mechanoreceptors, which mediate the sense of gentle touch, proprioception, blood pressure, tactile pain and regulate the development and functions of cardiovascular, bone and brain. For the landmark discovery of PIEZO2 as touch receptor in mammals, Ardem Patapoutan has shared the 2021 Nobel Prize in Physiology or Medicine with David Julius, who discovered the first temperature receptor TRPV1. Combining cryo-EM structure determination, mutagenesis, electrophysiology, mouse genetics and pharmacology, we have aimed to systematically understand how PIEZOs function as mechanically activated cation channels to effectively convert piconewton-scale forces into selective cation permeation. In this talk, I will present our current understanding of PIEZOs with a particular focus on their unique structural designs, physical principles and gating dynamics that might enable them to serve as versatile and professional mechanosensors not only in primary somatosensory neurons, but also in various cell types in the central nervous system.

Keywords : PIEZOs, Mechanosensors, Ion Channel, Mechanotransduction

S2-3

ATP release in physiology and pathology: A mechanobiological perspective

Masahiro Sokabe

Human Information Systems Lab, Kanazawa Institute of Technology, Hakusan, Ishikawa, Japan

Mechanical forces play a pivotal role in coordinating collective cell behaviors such as embryogenesis and wound healing. A growing body of research highlights mechanically induced ATP release as a key mechanism translating physical stimuli into multicellular responses. This presentation examines two systems- milk ejection and skin wound healing- where ATP orchestrates spatial and temporal cell dynamics. During lactation, suckling-induced mechanical stimulation activates sensory nerves in the nipple, which relay signals to the posterior pituitary via the thalamus, triggering release of oxytocin (OXT). OXT travels through the bloodstream to the mammary alveolus, which consists of secretory epithelial (SE) cells surrounded by contractile myoepithelial (ME) cells, binding to receptors on ME cells. As milk fully accumulates, SE cells stretch and release ATP that lowers the OXT activation threshold of ME cells by ~10 times. Thus, OXT levels during suckling (~50 pM) are below the normal activation threshold; only alveoli with filled milk can contract, ensuring physiologically reasonable milk ejection.

In a skin wound healing model, transient stretching of a HaCaT keratinocyte monolayer accelerates repair via an intercellular Ca^{2+} wave initiated at the wound edge. This wave is triggered by ATP release through mechanosensitive pannexin hemichannels expressed at the wound margin. Released ATP propagates outward, activating P2Y receptors and subsequently TRPC6 channels in neighboring cells, leading to Ca^{2+} influx and wave propagation. The Ca^{2+} wave promotes sequential formation of cryptic lamellipodia, facilitating smooth, coordinated cell migration necessary for re-epithelialization.

These findings suggest that mechanically triggered ATP release is a general mechanism converting physical cues into spatiotemporally coordinated multicellular activities, where ATP functions as a force-sensitive extracellular messenger beyond its metabolic role.

Keywords : Mechanosensitive ATP release, Purinergic signaling, Milk ejection, Wound healing, Calcium wave propagation

Acknowledgements : I want to express sincere thanks to Drs. Kisho Furuya (Nagoya Univ) and Hiroya Takada (Nippon Medical School) for their significant contributions to this work. Supported by a grant for collaborative research between Nagoya University and R-Pharm (2614Dj-02b).

S2-4

Identification of the brain-to-spinal opioidergic circuits driving tactile pain

Jiantao Huo, Chao Guo, Dong Dong, Xi Liu, Changyi Zhang, Guangjuan Yin, Kaifang Duan, Longzhen Cheng

Department of Neuroscience, Southern University of Science and Technology, Shenzhen, Guangdong, China

Mechanical allodynia (MA) is a common and debilitating symptom of inflammatory and neuropathic pain. How can non-painful mechanical stimuli like light pressure or gentle brush evoke painful perception? Our previous study identified the brain-to-spinal circuits that control the laterality and duration of mechanical allodynia; however, the brain-to-spinal circuits that control the initiation of MA remain unsolved. Here we show that the contralateral (but not ipsilateral) brain-to-spinal opioidergic circuits, from proenkephalin (Penk) neurons in the parabrachial nucleus (PBN^{Penk}), via μ-opioid receptor (MOR)-expressing neurons in the lateral hypothalamus (LH^{MOR}), to the spinal dorsal horn (SDH), control the initiation of peripheral inflammation and nerve injury-induced MA via the "Enk–MOR" endogenous opioidergic system in mice. We found that peripheral inflammation or nerve injury caused hyper-activity of the LH-projecting PBN^{Penk} neurons, but hypo-activity of the SDH-projecting LH^{MOR} neurons. Conditional deletion of Penk from PBN→LH neurons, or MORs from LH→SDH neurons, or chemogenetic silencing $Penk^{PBN→LH}$ neurons, or chemogenetic activating $MOR^{LH→SDH}$ neurons, all completely prevented the induction of peripheral inflammation- (hindpaw capsaicin-, formalin- or CFA- injection) or spared nerve injury (SNI)-induced MA. Conversely, chemogenetic activating $Penk^{PBN→LH}$ neurons, or silencing $MOR^{LH→SDH}$ neurons, could mimic peripheral inflammation and nerve injury in uncovering the normally gated MA in naive mice. Targeting the above brain to-spinal opioidergic system could provide preclinical studies and/or clinical trials a central mechanisms-based, modality-specific strategy to resolve peripheral inflammation and nerve injury-induced mechanical pain hypersensitivity.

Keywords : Mechanical pain, Mechanical allodynia, Descending control, Parabrachial nucleus, hypothalamus

S2-5

Mechanically evoked ATP release from Merkel cells mediates non-neuronal paracrine signaling

Mi Seon Seo[1,2], Sang Woong Park[3], Young Min Bae[1]

[1]Department of Physiology, Konkuk University School of Medicine, Chungju-si, Chungcheongbuk-do, Republic of Korea
[2]Department of Physiology, Dongguk University College of Medicine, Gyeongju, Gyeongsangbuk-do, Republic of Korea
[3]Department of Emergency Medical Services, Eulji University, Seongnam, Gyeonggi-do, Republic of Korea

Merkel cells are mechanosensitive epithelial cells residing at the base of touch domes, classically known for their synaptic-like interactions with afferent sensory neurons. While their role in neuron-mediated light-touch sensation is well established, it remains unclear whether Merkel cells also engage in local intercellular communication independent of neural pathways. Using a human Merkel cell line (MCC13), we applied localized mechanical stimulation via a precision piezoelectric actuator system and monitored intracellular Ca^{2+} dynamics through real-time fluorescence imaging. Mechanical poking elicited Ca^{2+} transients not only in the stimulated cell but also in neighboring Merkel cells. These secondary responses were abolished by P2X purinergic receptor antagonists, indicating a role for ATP-mediated paracrine signaling. ATP release was visualized directly using a fluorescent ATP-binding dye and was blocked by vesicular exocytosis inhibition. Interestingly, serotonin and norepinephrine were also co-released upon mechanical stimulation, but their lack of effect on adjacent cells—along with the absence of corresponding receptor expression—suggests a minimal role in local signaling. These findings support a novel model in which Merkel cells, beyond their neural interface, actively shape cutaneous mechanosensitivity through non-neuronal ATP-based communication within the skin microenvironment. This mechanism may enhance signal amplification in response to fine tactile stimuli and provides new insight into the epithelial component of mechanotransduction.

Keywords : Merkel cells, ATP release, Paracrine signaling, Tactile mechanosensation, P2X receptor
Acknowledgements : This research was supported by Eulji University in 2022 and by the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIT) (NRF-2021R1A6A3A01086791 and RS-2023-00278350).

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Symposium 3

Supported By IBS Life Science Institute

Day 1 (August 24) **13:00-14:55** **Premier Ballroom B**

Neuroglia in diseases of cognition

Organizer : Chenju Yi (Sun Yat-sen University)
Alexei Verkhratsky (University of Manchester)
Moderator : Chenju Yi (Sun Yat-sen University)

Astrocyte atrophy and asthenia lead pathophysiology of cognitive disorders
Alexej Verkhratsky (University of Manchester)

Turning microglia neuroprotective: towards connexin43-specific therapy of Alzheimer's disease
Chenju Yi (Sun Yat-sen University)

Dysfunctional astrocyte signaling in cognitive inflexibility
Jun Nagai (RIKEN)

Suppression of microglial Cx43 hemichannel promotes short-term and long-term recovery from traumatic brain injury
Yixun Su (Sun Yat-sen University)

Ependymoglial CSF-periphery gate in health and disease
Baoman Li (China Medical University)

Excitatory Neuronal ERBB4 Drives Early Pathophysiology of Alzheimer's Disease
Se Young Lee (Korea Advanced Institute of Science and Technology) Scitech Korea AWARDEE

S3-1

Astrocyte atrophy and asthenia lead pathophysiology of cognitive disorders

Alexei Verkhratsky

Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, United Kingdom

Astroglial atrophy and functional asthenia is widely present across neurological disorders. Asthenic and atrophic changes are accumulating with ageing thus reducing neuroprotection and lowering brain resilience, therefore increasing the susceptibility to age-dependent neurodegenerative disorders. Morphological atrophy of astrocytes leads to a decrease in synaptic coverage and synaptic maintenance thus affecting both excitatory-inhibitory balance and synaptic plasticity. Deficient glutamate clearance drives neuronal damage in neurotoxic disorders such as Wernicke-Korsakoff encephalopathy or hepatic encephalopathy, whereas diminished K^+ buffering together with insufficient glutamate clearance leads to spreading depression, migraine, and epilepsy. Morphological atrophy of astrocytes is a common sign of stress-induced depression, while manipulation with plasmalemmal linker ezrin that controls extension of peripheral astrocytic leaflets alleviates depressive-like behaviours. Functional deficiency of astrocytic glutamate clearance and K^+ buffering is a the primary cause of neuronal damage in neurodegenerative diseases, most notably in amyotrophic lateral sclerosis and Huntington disease; whereas functional asthenia of astrocytes may exacerbate b-amyloid pathology in the context of AD. Fundamentally, the loss of astrocytic support and neuroprotection rather than emergence of 'toxic' phenotypes take a leading role in mediating neuronal damage and death across all type of neuropathology.

Keywords : Astrocyte, Depression, Neurodegenration, Atrophy, Asthenia

S3-2

Turning microglia neuroprotective: Towards connexin43-specific therapy of Alzheimer's disease

Yixun Su, Chenju Yi

The Seventh Affiliated Hospital of Sun Yat-sen University

Alzheimer's disease (AD), the leading cause of senile dementia, lacks effective therapies. While microglia are central to AD pathology, key therapeutic targets remain unclear. Here we identify microglial connexin43 (Cx43) hemichannels as a regulator of microglial reactivity in AD, positioning them as a promising therapeutic target. Post-mortem AD patient tissue showed elevated Cx43 levels in periplaque microglia. In the APPswe/PS1dE9 (APP/PS1) mouse model of amyloidosis, we demonstrated that microglial Cx43 hemichannels correlated with microglial malfunction, which in turn exacerbated β-amyloid pathology. Ablation of microglial Cx43 hemichannels by genetic knockout shifts microglia to a neuroprotective phenotype, enhancing the microglia-plaque interaction while suppressing neurotoxicity, thereby mitigating the progression of AD-like pathology. We developed TAT-Cx43@LNPs, a Cx43 hemichannel-targeting peptide delivered by a lipid nanoparticle system, which effectively delayed and rescued β-amyloid-related neuropathology and cognitive impairment in APP/ PS1 mice. This study provides evidence for advancing Cx43 hemichannel targeting therapy into clinical trials.

Keywords : Microglia; Connexin; hemichannel; Alzheimer's disease

S3-3

Dysfunctional astrocyte signaling in cognitive inflexibility

Jun Nagai

Laboratory for Glia-Neuron Circuit Dynamics, RIKEN Center for Brain Science, Saitama, Japan

The brain depends on precisely regulated energy metabolism to sustain neural activity and guide behavior. Astrocytes play a key role in this process by mediating the transfer of metabolic substrates between blood vessels and neurons, thereby supporting the energy needs of local circuits. In this study, we demonstrate that behavioral stimuli in mice evoke astrocyte-driven metabolic signals that facilitates both local and distributed neuronal ensemble formation and contributes to memory processes. Through a combination of in vivo cell-type-specific lactate imaging, circuit-targeted astrocyte pharmacogenetic manipulation, omics profiling, and brain-wide functional imaging, we found that external stimuli elevate lactate levels in the prefrontal cortex, a hub region for behavioral flexibility and memory updating, via activation of astrocytic Gq-coupled alpha1a-adrenoceptors. Disrupting this pathway impaired astrocytic metabolic flux, dampened neuronal responsiveness, and hindered ensemble formation and memory modulation. These results position astrocytes as key mediators linking local metabolic dynamics to large-scale circuit reorganization essential for flexible learning.

Keywords : Glia, Astrocyte, Memory, Flexibility, Prefrontal

S3-4

Suppression of microglial Cx43 hemichannel promotes short-term and long-term recovery from traumatic brain injury.

Yixun Su, Chenju Yi

Research Centre, Seventh Affiliated Hospital of Sun Yat-sen University, Shenzhen, 518107, China

Traumatic brain injury (TBI) triggers neuroinflammation and secondary neurodegeneration, with microglia playing dual roles in exacerbating damage and facilitating repair. We have previously shown that Connexin43 (Cx43), a gap junction protein highly expressed in reactive microglia, regulates neuroinflammatory responses in the context of Alzheimer's disease, a chronic neurodegenerative disease. However, the role of microglial Cx43 in acute nervous system insult such as TBI remain unclear. This study investigates how microglial Cx43 influences acute and chronic outcomes after TBI. We found an upregulation of microglial Cx43 hemichannel at the acute phase in the controlled cortical impact (CCI) model of TBI. Using a tamoxifen-inducible, microglia-specific Cx43 knockout mouse model (Cx43flox/flox::CX3CR1-CreERT2), we subjected mice to CCI and assessed recovery at short-term (1–7 days) and long-term (30 days) timepoints. Longitudinal behavioral assessments demonstrated accelerated motor recovery (Catwalk, beam walk) by day 2~7 and sustained cognitive improvement (Novel object recognition) on 30 days post-injury ($p<0.05$). Acute-phase analysis revealed that Cx43 ablation attenuated microglial hyperactivation and peripheral immune cell infiltration compared to controls, and may thereby mitigates neuroinflammatory cascades, promotes tissue repair, and drives functional recovery post-TBI. Targeting Cx43 in microglia presents a promising therapeutic strategy to improve both short- and long-term outcomes after brain trauma.

Keywords : Microglia, Connexin, Traumatic brain injury.

S3-5

Ependymoglial CSF-periphery gate in health and disease

Baoman Li

China Medical University

S3-6 Scitech Korea AWARDEE

Excitatory Neuronal ERBB4 Drives Early Pathophysiology of Alzheimer's Disease

Se Young Lee[1,3], Eunseok Park[1,3], Juwon Park[1], Young-Jin Choi[1,3], Seongbin Kim[2], Yeji Yeo[1,2], Kiheon Lee[1], Ki-Jun Yoon[1], Eunjoon Kim[1,2], Won-Suk Chung[1,3]

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Neuroinflammation and synapse loss synergistically contribute to cognitive decline in Alzheimer's disease (AD). Although microglial hyper-phagocytic activity has been shown to mediate synapse loss, the exact mechanisms underlying these pathologies remain obscure. Here, we first demonstrate that astrocytes and microglia increase the phagocytic elimination of excitatory synapses, but significantly decrease their elimination of inhibitory synapses during AD progression, suggesting neuroinflammation may be dispensable for early AD synapse loss. Instead, through single-nucleus RNA sequencing (snRNAseq), we identified the emergence of Disease-Initiating Excitatory Neurons (DIENs), characterized by ectopic *Erbb4* expression, as the earliest major alteration in an AD mouse model. Notably, specific deletion of *Erbb4* in 5XFAD excitatory neurons abrogated abnormal neuronal network activities and synapse loss, as well as reactive gliosis, amyloid plaque deposition, and cognitive deficits. Conversely, overexpression of *Erbb4* in wild-type (WT) excitatory neurons recapitulated these key AD phenotypes in the absence of amyloid plaques. Subsequent snRNAseqs following *Erbb4* deletion and overexpression confirm that excitatory neuronal *Erbb4* is both sufficient and necessary to induce DIEN and reactive gliosis. Together, these findings reveal that the early pathophysiology of AD arises largely due to aberrant *Erbb4* expression in excitatory neurons, and that targeting excitatory neuronal *Erbb4* may thus represent a novel therapeutic strategy for mitigating multiple neurodegenerative diseases.

Keywords : Alzheimer's Disease, Synapse elimination, Excitatory Neurons, ERBB4, Glia

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 4

Day 1 (August 24) **13:00-14:55** **Premier Ballroom C**

Novel insights in sleep regulation and function

Organizer : Min Xu (Chinese Academy of Sciences)
Thomas McHugh (RIKEN)
Moderator : Min Xu (Chinese Academy of Sciences)
Thomas McHugh (RIKEN)

Learning during sleep
Thomas McHugh (RIKEN)

Neuromodulator control of hippocampal-dependent memory processing during sleep
Min Xu (Chinese Academy of Sciences)

Indigenous herb TCU410 mitigates memory impairment in sleep-deprived and triple transgenic Alzheimer's disease mice
Peeraporn Varinthra (Tzu Chi University) IBRO AWARDEE

Mechanisms underlying the regulation of sleep homeostasis: exploring key signaling pathways
Staci Jakyong Kim (Korea Advanced Institute of Science and Technology)

Synaptic regulation in sleep homeostasis
Shoi Shi (University of Tsukuba)

Memory editing during sleep: mechanisms, clinical applications, and technological innovations
XiaoQing Hu (The University of Hong Kong)

S4-1

Learning during sleep

McHugh Thomas[1,2]

[1]Center for Brain Science, RIKEN, Wako-shi, Saitama, Japan
[2]Brain Science Institute, KIST, Seoul, Republic of Korea

During slow-wave sleep the hippocampus exhibits sharp-wave ripples (SWRs), short high-frequency, high-amplitude oscillations, that organize the reactivation of neurons in an experience dependent manner. Interventions that disrupt SWRs can impair learning and while the canonical model of SWRs generation have emphasized CA3 input to CA1 as the source of excitatory drive, recent work suggests there are multiple circuits, including in the CA1 and CA2 regions, that can generate, shape and organize SWRs. Thus, despite tremendous progress in characterizing these events and their role in memory, a detailed understanding of the circuitry and mechanisms that control their content, properties and timing remains elusive. Here I will present our recent work examining neural circuits, both within and outside the hippocampus, that influence SWR occurrence, replay precision and memory during sleep.

Keywords : memory, social memory, sleep, ripples, hippocampus

S4-2

Neuromodulator control of hippocampal-dependent memory processing during sleep

Min Xu

InInsInstitute of Neuroscience, AS Center for Excellence in Brain Science and Intelligence Technology, Shanghai, China

Neuromodulators play a pivotal role in memory formation, yet most research has focused on their functions during wakefulness. Recent advances using GRAB sensors have uncovered intricate neuromodulator dynamics during NREM sleep, suggesting their active involvement in offline memory processing. In my presentation, I will explore how two key neuromodulators—norepinephrine and acetylcholine—orchestrate hippocampal-dependent memory consolidation during sleep.

Keywords : Memory, Sleep, Hippocampus

S4-3 IBRO AWARDEE

Indigenous Herb TCU410 Mitigates Memory Impairment in Sleep-Deprived and Triple Transgenic Alzheimer's Disease Mice

Peeraporn Varinthra[1], Mubashir Raza[2], Shu-Ching Shih[2], Li-Jen Chen[3], Ingrid Y Liu[1]

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Up to 30 percent of middle-aged and older adults who experience sleep deprivation (SD) develop Alzheimer's disease (AD), linked to synaptic disruption and impaired GABAergic signaling. Currently, available therapies have restricted efficacy and significant adverse effects. We investigate the effect of the indigenous herb TCU410, which has been demonstrated to promote sleep, in treating SD-induced memory impairment and triple transgenic AD (3xTg-AD) mice. The results revealed that SD mice exhibited working and spatial reversal memory impairments resembling the pathology of 3xTg-AD mice. TCU410 extracts and its fractions reversed these memory deficits measured by the T-maze and Morris water maze. In SD mice, TCU 410 water extract decreased hippocampal $GABA_BR1$ overexpression and increased PSD95-TrkB complexes. In 3xTg-AD mice, TCU410 ethanol extract upregulated the TrkB/BDNF pathway, enhanced synaptic plasticity, and reduced hippocampal amyloid-beta oligomers. These results indicate that TCU410 may be a promising natural remedy for preventing memory deficits in SD and AD.

Keywords : Sleep Deprivation, Alzheimer's Disease, Indigenous Herb, GABAergic Signaling, TrkB/BDNF pathway
Acknowledgements : This study was supported by the Buddhist Tzu Chi Medical Foundation (Grant #: TCMF-SP 112-02) and the National Science and Technology Council (NSTC), Taiwan (Grant #: NSTC 113-2410-H-320 -004 -MY2). We are grateful for the support from the Core Facility Center, Tzu Chi University.

S4-4

Mechanisms underlying the regulation of sleep homeostasis: exploring the key signaling pathways

Staci J. Kim[1,2]

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[2]International Institute for Integrative Sleep Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan

Sleep is a fundamental behavior across species, regulated by complex molecular and cellular processes. In a forward genetics study using mice, salt-inducible kinase 3 (SIK3) and histone deacetylase 4 (HDAC4) have emerged as key regulators of sleep homeostasis. Our study explored the intracellular signaling pathways essential in both sleep and circadian rhythm regulation, emphasizing the pivotal role of SIK3-HDAC4 interaction in the cerebral cortex and hypothalamus. Specifically, SIK3 in cortical excitatory neurons modulates non-rapid eye movement sleep (NREMS) delta power, reflecting sleep depth, while SIK3 in hypothalamic neurons controls NREMS duration. HDAC4 plays a dual role in regulating sleep and synaptic plasticity. A key mechanism involves SIK3-mediated phosphorylation of HDAC4, which promotes HDAC4's cytoplasmic localization. In the nucleus, HDAC4 interacts with transcription factors like MEF2, deacetylating histones to suppress genes essential for synaptic remodeling and activity-dependent plasticity. Neuronal activity promotes HDAC4 phosphorylation and nuclear export, relieving transcriptional repression and facilitating the expression of genes required for synaptic signaling. While these findings underscore the critical role of the SIK3-HDAC4 axis in sleep and synaptic regulation, the exact molecular mechanisms linking these pathways to the dynamic changes in brain state during wake and sleep remain incompletely understood. Further investigation into the precise intracellular signaling networks and their functional consequences on synaptic transmission across sleep-wake states is essential to fully elucidate these complex processes.

Keywords : Sleep, Gene transcription, Forward genetics, Kinase, HDAC

S4-5

Synaptic Regulation in Sleep Homeostasis

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[2]Tsukuba Institute for Advanced Research (TIAR), University of Tsukuba, Tsukuba, 305-8575, Japan.

Sleep is regulated by homeostatic processes, yet the biological basis of the “sleep pressure” that accumulates during wakefulness remains elusive. Our recent work revealed a causal link between synaptic strength and EEG delta power. A mathematical model and in vitro primary neuron experiments showed that increased synaptic strength promotes neuronal down states and raises delta power. Additionally, using a molecular tool (SYNCit-K) to enhance synaptic strength of prefrontal cortex excitatory neurons, we found a corresponding increase in both NREM sleep duration and delta power. To further probe these mechanisms, we utilized an in vitro multi-electrode array to investigate the functional and structural dynamics of neurons in wake-like or stress-like states. In this talk, I will present our latest findings suggesting that synaptic strength may encode sleep homeostasis and will discuss the underlying mechanisms involved.

Keywords : Sleep, Synapse, Molecular Tool, mathematical modeling, MEA

S4-6

Memory editing during sleep: mechanisms, clinical applications, and technological innovations

Xiaoqing Hu

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Not all memories are welcome by the mind. Over-consolidation of aversive or traumatic memories poses significant threats to our emotional well-being. Can we edit unwanted memories during sleep, bypassing our conscious awareness? Our recent work suggests that the sleep-mediated memory reactivation processes can be leveraged to foster positive memories and to weaken aversive memories. Via unobtrusively delivering auditory cues during non-rapid-eye-movement sleep (targeted memory reactivation), we found that both affect tones and memory contents of aversive memories can be modified. Cueing benefits are associated with cue-elicited delta/theta/sigma power, and with the coupling between slow oscillations and external emotional stimuli. These results suggest that sleep-mediated memory reactivations play adaptive roles in memory editing and even forgetting. Clinical translations will then be discussed.

Keywords : Memory editing, sleep, targeted memory reactivation

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 5

Day 1 (August 24) **13:00-14:55** **Rm.113-115**

The brainstem: a critical conduit for body-brain signaling

Organizer : Sung-Yon Kim (Seoul National University)
Cheng Zhan (University of Science and Technology of China)
Moderator : Yu Fu (Agency for Science Technology and Research)

A pharynx-to-forebrain circuit for rapid thirst quenching
Sung-Yon Kim (Seoul National University)

Brainstem catecholaminergic/NPY neurons: pivotal players in orchestrating energy intake and expenditure
Cheng Zhan (University of Science and Technology of China)

Parallel Gut-to-Brain Pathways Orchestrate Feeding Behaviors
Ling Bai (Chinese Institute for Brain Research)

NTS catecholamine neurons mediate hypoglycemic hunger via medial hypothalamic feeding pathways
Deniz Atasoy (University of Iowa)

Brainstem opioid peptidergic neurons regulate cough reflexes in mice
Peng Cao (National Institute of Biological Sciences)

Hypothalamic endothelial Notch suppression drives obesity-associated impairment of glucose uptake and insulin signaling
Yiyi Zhu (Sun Yat-sen University) IBRO AWARDEE

S5-1

A pharynx-to-forebrain circuit for rapid thirst quenching

Sung-Yon Kim

Department of Chemistry, Seoul National University, Seoul, Republic of Korea

Drinking fluids rapidly quenches thirst within seconds, well before fluids are absorbed in the gut and restore homeostatic balance. However, the sensory origin and neural mechanisms underlying this rapid satiation remain elusive. Here, in mice, we identify pharyngeal mucosal mechanosensation that occurs during swallowing reflex as the sensory origin for rapid thirst quenching. Using an integrated approach combining anatomical tracing, nerve transection, neural activity recording and manipulation, we delineate an ascending sensory pathway from the pharynx to the forebrain thirst center. Strikingly, this circuit functions as a high-pass filter, selectively transmitting signals from closely-paced swallows characteristic of fluid intake, while excluding those associated with solid food consumption. Disrupting this signaling prolongs ongoing drinking, establishing its causal role in thirst satiation. Our findings pinpoint the long-sought sensory origin of rapid thirst satiation and demonstrate the comprehensive characterization of the pharynx-to-forebrain circuit, which transforms pharyngeal mechanosensory signals into drinking-specific thirst-quenching signals.

Keywords : Pharynx, swallowing reflex, thirst satiation, interoception, brain-body interaction
Acknowledgements : We are grateful to members of the S.-Y.K. laboratory for helpful discussions. This work was supported by Samsung Science and Technology Foundation under Project Number SSTF-BA2001-09.

S5-2

Brainstem catecholaminergic/NPY neurons: pivotal players in orchestrating energy intake and energy expenditure

Jing Chen, Yan Zhang, Cheng Zhan

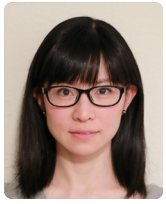
Division of Life Sciences and Medicine, University of Science of Technology of China, HeFei, 230001, China

The brain regulates energy intake and energy expenditure in response to changes in internal and external environment, as well as varying energy demands. For decades, extensive research has underscored the importance of the hypothalamus in maintaining energy homeostasis. In recent years, however, the brainstem has emerged as another key region in energy regulation, gradually capturing the scientific community's attention. Despite this growing interest, our understanding of the brainstem's functions in energy balance remains relatively limited. Questions abound: Which neuronal populations within the brainstem are involved? Does the brainstem merely modulate short-term food intake, or does it also contribute to the long-term regulation of energy balance, similar to hypothalamic neurons? I have dedicated over ten years to researching the brainstem, with a specific focus on catecholaminergic and neuropeptide Y (NPY) neurons located in the nucleus of the solitary tract (NTS) and the ventrolateral medulla (VLM). In this presentation, I will share our recent findings on the multifaceted and interconnected roles of these brainstem catecholaminergic/NPY neurons in the control of energy intake and energy expenditure.

Keywords : Nucleus of the solitary tract, Catecholaminergic neurons, NPY, Energy intake, Energy expenditure

S5-3

Parallel Gut-to-Brain Pathways Orchestrate Feeding Behaviors



Ling Bai[1], Hongyun Wang[1,2], Runxiang Lou[1], Yunfeng Wang[1], Liufang Hao[1], Qiushi Wang[1], Rui Li[1,3], Jiayi Su[1], Shuhan Liu[1,3], Xiangyu Zhou[1,6], Xinwei Gao[1,5], Qianxi Hao[1], Zihe Chen[1], Yibo Xu[1], Chongwei Wu[1], Yang Zheng[1], Qingchun Guo[1,4]

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Animal behaviors are tightly regulated by internal signals. The brainstem serves as a central hub for integrating interoceptive cues from diverse visceral sensory pathways. However, how brainstem neurons transform these signals into specific behavioral outputs remains poorly understood. In this talk, I will discuss our recent work identifying key brainstem cell types that process visceral signals to orchestrate feeding behaviors. Using fiber photometry and targeted sensory pathway manipulations, we uncovered the sensory coding properties of these neurons and their underlying mechanisms. I will also discuss how distinct interoceptive signals, characterized by different temporal dynamics and sensory modalities, are selectively transformed into specific behavioral functions that regulate food intake. Together, our findings reveal fundamental principles by which the brainstem integrates internal signals to control feeding, shedding light on the neural basis of interoceptive regulation of behavior.

Keywords : Interoception, Feeding, Nutrient, Distension

S5-4

Integration of appetite and stress by ascending adrenergic pathways

Deniz Atasoy

University of Iowa

Stress is thought to be an important contributing factor for eating disorders; however, neural substrates underlying the complex relationship between stress and appetite are not fully understood. Using in vivo recordings from awake behaving mice, we show that various acute stressors activate catecholaminergic nucleus tractus solitarius (NTS^{TH}) projections in the paraventricular hypothalamus (PVH). Remarkably, the resulting adrenergic tone inhibits MC4R-expressing neurons (PVH^{MC4R}), which are known for their role in feeding suppression. We found that PVH^{MC4R} silencing encodes negative valence in sated mice and is required for avoidance induced by visceral malaise. Collectively, these findings establish PVH^{MC4R} neurons as an effector of stress-activated brainstem adrenergic input in addition to the well-established hypothalamic-pituitary-adrenal axis. Convergent modulation of stress and feeding by PVH^{MC4R} neurons implicates $NTS^{TH} \rightarrow PVH^{MC4R}$ input in stress-associated appetite disorders.

Keywords : Stress, appetite, norepinephrine, melanocortin

S5-5

Brainstem opioid peptidergic neurons regulate cough reflexes in mice

Peng Cao, Haicheng Lu

National Institute of Biological Sciences, Beijing, China

Cough is a vital defensive reflex for expelling harmful substances from the airway. The sensory afferents for the cough reflex have been intensively studied. However, the brain mechanisms underlying the cough reflex remain poorly understood. Here, we developed a paradigm to quantitatively measure cough-like reflexes in mice. Using this paradigm, we found that prodynorphin-expressing (Pdyn+) neurons in the nucleus of the solitary tract (NTS) are critical for capsaicin-induced cough-like reflexes. These neurons receive cough-related neural signals from Trpv1+ vagal sensory neurons. The activation of Pdyn+ NTS neurons triggered respiratory responses resembling cough-like reflexes. Among the divergent projections of Pdyn+ NTS neurons, a glutamatergic pathway projecting to the caudal ventral respiratory group (cVRG), the canonical cough center, was necessary and sufficient for capsaicin-induced cough-like reflexes. These results reveal that Pdyn+ NTS neurons, as a key neuronal population at the entry point of the vagus nerve to the brainstem, initiate cough-like reflexes in mice.

Keywords : cough, airway, vagus nerve, nucleus of solitary tract, dynorphin

S5-6 IBRO AWARDEE

Hypothalamic endothelial Notch suppression drives obesity-associated impairment of glucose uptake and insulin signaling

Yiyi Zhu[1,2], Jens Bruening[2]

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Short-term high-fat diet (HFD) feeding rapidly alters the molecular architecture of the blood-brain barrier (BBB), increases its permeability, and impairs brain glucose uptake; however, the underlying mechanisms remain poorly understood. In this study, we identify a swift downregulation of Notch signaling following short-term HFD exposure. Notably, activation of the Notch pathway restores Glut1 expression and glycolytic activity in cultured brain microvascular endothelial cells (BMECs) treated with serum from HFD-fed mice. In vivo, selective and inducible expression of the Notch intracellular domain (NotchIC) in BMECs preserves Glut1 levels and maintains hypothalamic glucose uptake under short-term HFD conditions. Concurrently, short-term HFD feeding increases Cav-1 expression in BMECs, enhancing caveola formation and BBB permeability. However, NotchIC^{BMECs} mice exhibit reduced caveolae density and decreased BBB permeability. These changes ultimately lead to improved hypothalamic insulin transport and signaling, as well as enhanced systemic insulin sensitivity. Together, our findings demonstrate a pivotal role of endothelial Notch signaling in mediating the rapid BBB dysfunction and metabolic impairments induced by dietary fat overload.

Keywords : High-fat diet, Blood-brain barrier, Notch signaling, Insulin sensitivity

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 6

Day 1 (August 24) **13:00-14:55** **Rm.116-118**

Exploring the neuroscience of general anesthesia

Organizer : Soo-Jin Oh (Korea Institute of Science and Technology)
Moderator : Woosuk Chung (Chungnam National University)
Soo-Jin Oh (Korea Institute of Science and Technology)

Brain Network Mechanisms of Consciousness Loss and Recovery in General Anesthesia
UnCheol Lee (University of Michigan)

Anesthesia-induced neuroprotection against perioperative stroke, is it possible?
Woosuk Chung (Chungnam National University)

predictive biomarker for postoperative delirium status after spinal surgery
Bon-Nyeo Koo (Yonsei University)

Postoperative Neurocognitive Disorder (postoperative NCD) in Clinical Practice
Jin-Young Hwang (SMG-SNU Boramae Medical Center)

Role of astrocytes in general anesthesia and postoperative cognitive dysfunction
Soo-Jin Oh (Korea Institute of Science and Technology)

S6-1

Brain Network Mechanisms of Consciousness Loss and Recovery in General Anesthesia

UnCheol Lee

Department of Anesthesiology, University of Michigan Medical School, Center for Consciousness Science, Center for the Study of Complex Systems, Neuroscience Graduate Program, University of Michigan, Ann Arbor, Michigan 48109, United States.

Understanding why some patients recover quickly from pharmacologically or pathologically induced unconsciousness, while others take longer, is crucial for improving patient outcomes. Recent empirical and computational studies suggest that brain criticality—a balanced state at the edge of chaos—is a necessary condition for the emergence of consciousness, and that deviations from criticality correlate with consciousness levels. Yet, if brain criticality is the “sweet spot” for consciousness, it remains unclear why some brains lose and regain criticality, and thus consciousness, more rapidly or slowly under anesthesia.

In physics, state transitions are broadly categorized into two types: first-order transitions (abrupt, such as water freezing into ice) and second-order transitions (continuous, such as the ferromagnetic transition from a magnet to a metal). We propose that individual brains can similarly be characterized by their phase transition type, which is determined by brain network configurations. In this talk, we show that brain networks closer to a first-order transition are more vulnerable to loss of consciousness and exhibit slower recovery due to higher instability of brain criticality. Moreover, we demonstrate that the trajectories of consciousness loss and recovery can be systematically predicted and even modulated by shifting a brain network’s phase transition type between first- and second-order.

These findings provide a framework for understanding diverse recovery trajectories and suggest effective brain modulation strategies for more resilient brain networks that withstand perturbations and recover efficiently, with potential applications in sleep, delirium, and coma.

Keywords: Consciousness, Anesthesia, Brain Dynamics, Criticality, EEG

S6-2

Anesthesia-induced neuroprotection against perioperative stroke, is it possible?

Xianshu Ju[1,2,3], Tao Zhang[1,2,3], Jianchen Cui[4], Yulim Lee[1,2,3], Suho Lee[5], Ho Min Kim[6], Boohwi Hong[7], Jiho Park[7], Chul Hee Choi[1,3,8], Hyon-Seung Yi[1,9], Jun Young Heo[1,2,3], Woosuk Chung[1,3,7]

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The growing number of older adults undergoing surgery necessitates that we address the adverse effects of overt and covert perioperative stroke. Preclinical studies have suggested that anesthesia-induced preconditioning may provide neuroprotection by preserving mitochondrial function, activating cytosolic signaling pathways, and reducing neuroinflammation. However, these promising findings from animal studies have not yet translated into improved clinical outcomes. We demonstrate that sevoflurane-induced neuroprotection is associated with the upregulation of genes involved in the mitochondrial unfolded protein response (UPRmt) and mitochondrial bioenergetic metabolism. Our findings emphasize the critical role of ATF5, a key transcription factor, in mediating these protective effects. Sevoflurane preconditioning markedly increases ATF5 expression and its downstream target GDF15, a key regulator of mitochondrial homeostasis, in the cerebral cortex. However, this protective mechanism is not activated in the aged brain, suggesting that aging impairs the ability to mount a mitochondrial stress response. Our results imply the need for age-specific strategies to reduce perioperative stroke risk, including approaches that target mitochondrial function in elderly patients.

Keywords : Anesthesia, ATF5, GDF15, Preconditioning, Stroke

S6-3

predictive biomarker for postoperative delirium status after spinal surgery

Bon-Nyeo Koo

Anesthesiology and Pain Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

Postoperative delirium (POD) is a common neurocognitive complication in older adults undergoing surgery, particularly spinal procedures. Despite previous research exploring neurodegenerative markers and systemic cytokines as predictive tools, these biomarkers have shown limited utility in distinguishing patients who will develop POD. In this prospective study of 128 patients aged 70 years or older undergoing elective spine surgery, we evaluated multiple preoperative variables including neurocognitive scores, systemic cytokines, neurodegeneration-related markers, gut microbiota composition, and systemic bacterial extracellular vesicles (BEVs). While conventional biomarkers such as IL-6, TNF-α, and neuronal injury markers failed to show significant differences between POD and non-POD groups, systemic BEV profiles demonstrated distinct taxonomic and diversity differences. Notably, BEV α- and β-diversity indices were significantly reduced in POD patients. Specific taxa such as *Acinetobacter* and *Moraxellaceae* were overrepresented in the POD group, while *Sphingomonas* and *Bacilli* were enriched in non-POD cases. A machine learning model using BEV features outperformed models using clinical or gut microbiota data, achieving superior predictive power in both discovery and validation cohorts. These findings suggest that preoperative systemic BEV profiling may serve as a novel, non-invasive biomarker strategy for POD risk stratification, especially when traditional markers fail to differentiate high-risk individuals.

Keywords : Bacterial extracellular vesicle, postoperative delirium, random forest, prognostic factor, metabolite

S6-4

Postoperative Neurocognitive Disorder (postoperative NCD) in Clinical Practice

Jin-Young Hwang

Department of Anesthesiology and Pain Medicine, SMG-SNU Boramae Medical Center College of Medicine, Seoul National University

Postoperative Neurocognitive Disorder (postoperative NCD) is a neurologic complication that occurs after anesthesia and surgery, and characterized by impairments in memory, learning, executive function, language, and social integration. It leads to prolonged hospital stay, reduced quality of life, social dependence, and increased mortality. As the elderly surgical patients have grown, postoperative NCD has been the major concern of perioperative care.
The mechanism of postoperative NCD is considered to be multifactorial and complicated. Surgery-induced neuroinflammation, neurotoxicity of anesthetics, and patient factors such as age, vulnerable brain, or underlying diseases contribute to the development of postoperative neurocognitive disorders. Astrocytes and microglia may be involved in the development of postoperative NCD. There are no standard diagnostic criteria for postoperative NCD. It can be only detected with neurocognitive testing before and after surgery, but it takes time and cost; therefore, neurocognitive testing is not a routine part of clinical care, and detection of postoperative NCD is difficult. Non-pharmacological preventive strategies against postoperative NCD are as follows; preoperatively comprehensive geriatric assessment, and pre-habilitation and patient education; intraoperatively, maintenance of adequate depth of anesthesia, and application of minimally invasive surgical techniques; and postoperatively, early mobilization and rehabilitation, and effective pain management and delirium prevention. Currently, there is no definite pharmacological preventive strategy against postoperative NCD.
As the aging population grows, the number of elderly patients undergoing surgery continues to increase. Future researches on this topic, including diagnosis, mechanism, and prevention and treatment of postoperative NCD are required.

Keywords : Postoperative neurocognitive disorder, anesthesia, surgery, mechanism, prevention

S6-5

Role of astrocytes in general anesthesia and postoperative cognitive dysfunction

Elliot H Lee[1,3], Jin-Young Hwang[2] and Soo-Jin Oh[1]

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Postoperative cognitive decline (POCD) is a frequent complication after anesthesia and surgery, with some anesthetics targeting inhibitory extrasynaptic GABAA receptors mediated by astrocytic GABA. However, the contribution of tonic inhibition from astrocytic GABA to POCD remains unclear. Our previous work showed that monoamine oxidase B (MAO-B), a key enzyme for astrocytic GABA synthesis, partially mediates the immobility and hypnosis effects of inhaled anesthetics. Building on this, we examined whether astrocytic GABA-mediated tonic inhibition contributes to POCD. In 8-week-old C57BL/6 mice, isoflurane and sevoflurane, but not desflurane, significantly enhanced hippocampal tonic GABA currents, astrocytic GABA levels, and α5 GABAA receptor activity during anesthesia, persisting for 24 h but not 1 week. These changes coincided with transient trends of increased MAO-B expression in multiple brain regions. In aged mice, sevoflurane induced cognitive deficits lasting 1 month post-anesthesia, resembling POCD. These findings suggest that astrocytic GABA plays a key role in hippocampal dysfunction and POCD induced by certain inhaled anesthetics in aged mice.

Keywords : Anesthesia, Postoperative cognitive decline, GABA, Monoamine oxidase B, Astrocyte

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 7

Day 2 (August 25) **08:30-10:25** **Grand Ballroom**

Neuromodulation in psychiatry: from circuit to psychopharmacology

Organizer : Tifei Yuan (Shanghai Mental Health Center)
Ji Hu (ShanghaiTech University)
Moderator : Tifei Yuan (Shanghai Mental Health Center)

Maintenance repetitive transcranial magnetic stimulation for depression: A randomized clinical trial
Yoshihiro Noda (Keio University)

Transcranial Pulse Stimulation for depression – a new kid on the block
Georg Kranz (Hong Kong Polytechnic University)

Brain Mechanisms of Excitatory Transcranial Magnetic Stimulation for Treatment-Resistant Depression
Cheng-Ta Li (National Yang-Ming Chiao-Tung University)

Investigation of the D5DR-PMCA Complex as a Potential Therapeutic Target for Hypertension
Fang Liu (University of Toronto)

Neural-immune communication
Ji Hu (ShanghaiTech University)

Rethinking depression: cannabinoid-inspired targets without the legal baggage
Elisha Ab Rashid (Monash University Malaysia) IBRO AWARDEE

S7-1

Maintenance repetitive transcranial magnetic stimulation for depression: A randomized clinical trial

Yoshihiro Noda

Psychiatry, International University of Health and Welfare, Tokyo, Japan

Depression relapse poses significant medical and economic challenges. Repetitive transcranial magnetic stimulation (rTMS) treatment may prevent relapse of treatment-resistant depression (TRD). To compare the effectiveness between rTMS and lithium in preventing TRD relapse. Participants with TRD aged ≥18 years with moderate-to-severe depressive symptoms despite at least two adequate antidepressant treatments who subsequently responded to an acute course of bilateral rTMS. Participants were randomly assigned at a 1:1 ratio to receive right prefrontal 1Hz-rTMS (24 weekly sessions; 120% resting motor threshold, 900 pulses in 15 min) or 24-week maintenance treatment with lithium pharmacotherapy. Participants were maintained on the same venlafaxine dose (150–225 mg/day) as the acute-phase dose. The primary outcome was the between-group difference in baseline-adjusted Montgomery-Åsberg Depression Rating Scale (MADRS) scores at week 24, which was analyzed using a linear mixed-effect model for repeated measures in an intention-to-treat sample. The secondary outcome was the time to relapse (defined as a MADRS >22), which was analyzed using Kaplan–Meier survival curves. Additionally, we compared adverse events in both groups. Among 75 participants, 38 and 37 were assigned to the rTMS and lithium groups, respectively (baseline MADRS scores: 8.9 [4.7] and 7.9 [4.5], respectively). There was no significant between-group difference in the primary outcome at week 24 (95% confidence interval [CI]: -2.67 to 3.26, p=0.844). Survival analysis showed no meaningful between-group difference in relapse rates (p=0.92). During the 24-week maintenance phase, there were seven relapse cases in each group. Low-frequency rTMS of the right prefrontal cortex as maintenance treatment had comparable efficacy, as well as better safety and tolerance, compared with lithium. This suggests that low-frequency rTMS could be a promising relapse prevention strategy for TRD.

Keywords : Treatment-resistant depression, Relapse prevention strategy, Maintenance treatment, Repetitive transcranial magnetic stimulation
Acknowledgements : We would first like to thank all the participants in this study. We would also like to express our appreciation to the Research Assistants in the Multidisciplinary Research Lab, Department of Neuropsychiatry, Keio University School of Medicine for their assistance with this research.

S7-2

Transcranial Pulse Stimulation for depression – a new kid on the block

Georg Kranz

Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, SAR, Hong Kong, China

Transcranial pulse stimulation (TPS) is a non-invasive brain stimulation technique that utilizes shockwaves to modulate brain function. Preliminary evidence suggests that TPS has a potential therapeutic effect on depressive symptoms in patients with Alzheimer's disease and major depressive disorder (MDD).
In this talk, I will present several trials that investigate the effects of TPS on human behavior and its underlying neural correlates. In one study, we targeted the primary motor cortex aiming to examine TPS effects on motor performance using the Nine-hole peg test (NHPT), a standard test for measuring manual dexterity. The study was designed as a randomized, double-blind, sham-controlled, crossover trial, applying a single session of 1000 TPS pulses to the primary motor cortex.
I will then go on to present results from a randomized, double-blind, sham-controlled TPS trial in MDD. We targeted the left dorsolateral prefrontal cortex (MNI coordinates x=-38, y=+44, z=+26 mm, defined on individual T1-weighted MRIs). TPS treatment involved 3 TPS sessions per week for 4 weeks, with 1000 pulses per session. Depressive symptom reduction, as well as response and remission rates were assessed using the Montgomery-Asberg Depression Rating Scale.
In the last part of my talk, I will outline a recently commenced RCT that aims to examine the behavioral effects of stimulating deeper cortical regions such as bilateral anterior insular cortex and bilateral dorsal anterior cingulate cortex. This research aims to unveil the utility of alternative treatment targets for depression and other psychiatric disorders.

Keywords : transcranial pulse stimulation, shock wave, depression

S7-3

Brain Mechanisms of Excitatory Transcranial Magnetic Stimulation for Treatment-Resistant Depression

Cheng-Ta Li[1,2]

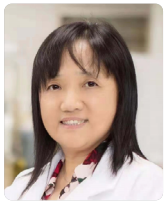
[1]Psychiatry, Taipei Veterans General Hospital, Taipei, Taiwan
[2]School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan

A significant proportion of individuals with major depressive disorder (MDD) do not improve significantly following several adequate trials of antidepressant medications. Treatment-resistant depression (TRD) refers to patients who are highly resistant to medications. TRD is linked to the prefrontal cortex (PFC)[1] and related brain pathways. Theta-burst stimulation (TBS) is a modified version of repetitive transcranial magnetic stimulation (rTMS) which could be used to treat TRD. In this talk, I will discuss the antidepressant effects of intermittent TBS (iTBS) in a prolonged manner (1800 pulses; 80% active motor threshold)[2,3] and the brain mechanisms involved [4,5]. We reported that iTBS is not inferior to 10Hz rTMS in treating depression[3,6]. I will also demonstrate the brain mechanisms and molecular underpinnings of iTBS for treating depression. We discovered that the applied rhythm is crucial to the antidepressant effects of non-invasive brain stimulation, whereas glutamate and GABA all play roles in the antidepressant processes of prefrontal iTBS. I will use resting state functional MRI (rsfMRI) to illustrate the distinct antidepressant effects of excitatory 10-Hz rTMS and iTBS on cortico-striatal functional connectivity. In this talk, I will also present the AI findings of using EEG and 18F-FDG PET to predict TRD and antidepressant responses to rTMS and iTBS in our recently established depression treatment center, "Precision Depression Intervention Center (PreDIC)".

Keywords : Depression, Treatment resistant depression, Theta burst stimulation, Resting state functional MRI, Repetitive transcranial magnetic stimulation

S7-4

Targeting protein complexes as therapeutic targets for the treatment of neuropsychiatric diseases



Shuxin Yan[1,2], Le Wang[1], Zeyue Mu[1], James N Samsom[2], Anlong Jiang[2], Bin Zhang[1], Houlin Chen[1], Buxun Sun[1], Yunqi Yan,[1] Emily M. Wiljer[3,4], Mengchu Zhu[5,6], Sheng Chen[2], Ping Su[2], Daniel Felsky[3,4,7,8], Albert HC Wong[2,3,7,9], Fang Yuan[5,6] and Fang Liu[1,2,3,4,7,9,10,11,12]

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[12]Department of Physiology, University of Toronto, Toronto, ON, Canada

Although major psychiatric diseases such as mood disorders and schizophrenia are among the most common and destructive of all human illnesses, the molecular and cellular mechanisms underlying their complex pathophysiology remains to be fully elucidated. Efforts to understand the biochemical foundations of these disorders commenced in earnest with the introduction of clinically effective psychotropic medications in the late 1950s and early 1960s. However, progress in deciphering the neurobiological aspects of these complex disorders has been limited when relying solely on these strategies. In recent years, there has been a comprehensive expansion in the understanding of neural circuits and the diverse mechanisms of synaptic transmission, alongside an enhanced elucidation of the molecular mechanisms underlying receptor and post-receptor signaling in psychiatry, facilitated by current rapid advancements of genetics and molecular technologies. The translation of these findings into clinical applications for psychiatric disorders has not advanced at a corresponding rate. This slow progression can be attributed to the inherent complexity of the central nervous system (CNS) and the multifaceted nature of psychiatric disorders. The challenges in elucidating the etiology and pathophysiology of these disorders are further compounded by several factors, including the absence of a clearly defined pathology, limited accessibility to relevant tissues. Despite this, significant progress has been achieved in elucidating the role of neurotransmitter receptor complexes, particularly G protein-coupled receptors (GPCRs), in the pathophysiology and treatment of major psychiatric disorders. In the reports presented within this perspective, we critically review and synthesize the available data, and examine their implications for the strategic development of enhanced therapeutic interventions.

Keywords: G protein-coupled receptors (GPCRs), protein-protein interaction, interfering peptide

S7-5

Neural-immune communication

Ji Hu

ShanghaiTech University, Shanghai1, 201210, China

The nervous and immune systems jointly monitor internal state and external threats to preserve homeostasis. Using viral tracing, optogenetics, chemogenetics, and single-cell transcriptomics, we have delineated a brain-spleen axis in which paraventricular CRH neurons project polysynaptically to splenic sympathetic fibers. Optogenetic stimulation of this pathway acutely increases plasma cell output after T-dependent immunization, whereas CRH neuron ablation or splenic denervation abolishes the humoral response. Mild environmental stress engages the same circuit, elevating antigen-specific IgG and providing a mechanistic explanation for stress-induced immunopotentiation. Conversely, the immune system feeds information back to the brain: anti-NMDAR antibodies from patients with autoimmune encephalitis accumulate in medial prefrontal PV interneurons, dampen gamma oscillations, and produce reversible cognitive deficits that can be rescued by optogenetic activation of the affected cells. These findings establish bidirectional, neurotransmitter- and neuropeptide-defined channels through which brain states sculpt adaptive immunity and immune molecules modulate cognition.

Keywords : neuro-immune axis; CRH neurons; stress; anti-NMDAR encephalitis; optogenetics

S7-6 IBRO AWARDEE

Rethinking Depression: Cannabinoid-Inspired Targets Without the Legal Baggage

Elisha Ab Rashid, Satoshi Ogawa

School of Medicine, Monash University Malaysia, Bandar Sunway, Selangor, Malaysia

Depression remains the most prevalent global mental health disorder, with current antidepressants often limited by delayed onset, treatment resistance, and side effects. Cannabidiol (CBD), a non-intoxicating cannabinoid, has shown promising antidepressant-like effects by modulating serotonergic transmission, neuroinflammation, and the endocannabinoid system. However, its widespread use is hindered by legal restrictions and variability in purity and supply. This study investigates GPR55 antagonists as an alternative therapeutic approach. GPR55 is a cannabinoid like receptor implicated in pain, inflammation, and emotional regulation, and may mimic some of CBD's antidepressant effects without cannabis-related legal challenges. Using zebrafish, we evaluate the behavioural and neuroendocrine effects of a GPR55 antagonist (CID16020046) in comparison to CBD. Following acute toxicity testing, depressive-like behaviours are induced using the zebrafish tail immobilisation paradigm, followed by drug exposure and behavioural assays. This research aims to identify novel, accessible treatments for depression by targeting the endocannabinoid system through both plant-based and synthetic approaches.

Keywords : depression, CBD, GPR55, mental health, zebrafish
Acknowledgements : I would like to acknowledge Yayasan Penyelidikan Otak, Minda dan Neurosains (YPOMNM) for the support for me to conduct this project.

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

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Symposium 8

Day 2 (August 25) **08:30-10:25** **Premier Ballroom C**

Gene delivery to the brain: applications in life sciences and gene therapy

Organizer : Hirokazu Hirai (Gunma University)
Moderator : Hirokazu Hirai (Gunma University)

Structural Analysis of Neural Networks Using High-Expression Adeno-Associated Virus Vectors
Hiroyuki Hioki (Juntendo University)

Micro-dissection of the connectivity of cerebellar input layer with GABRA6 promotor by exploiting dispersed developmental time of granule cells and computational modeling
Taegon Kim (Korea Institute of Science and Technology)

Long-term activity imaging of a neuronal population that sends input to a specific type of neurons via a low cytotoxic G-deleted rabies virus vector
Ken-ichi Inoue (Kyoto University)

Modulation of gene expression and signaling cascade in mice brain exposed to nano-neonicotinoid pesticides
Dhanshree Borkar (National Forensic Sciences University) IBRO AWARDEE

Nanoparticle-mediated gene delivery to enhance microglial phagocytosis for Alzheimer's disease therapy
Dong Woon Kim (Kyung Hee University)

A Compact GAD67 Promoter Enables Inhibitory Neuron-Specific Gene Modulation
Yuuki Fukai (Gunma University)

S8-1

Structural Analysis of Neural Networks Using High-Expression Adeno-Associated Virus Vectors

Hiroyuki Hioki

Department of Neuroanatomy, Juntendo University Graduate School of Medicine, Tokyo, Japan

Adeno-associated virus (AAV) vectors are one of the most versatile tools for in vivo gene delivery in neuroscience research. They have greatly contributed to the advancement of our understanding of neural circuits and functions by enabling efficient and long-lasting gene delivery into neurons and glial cells without inducing pathological changes. To further improve gene delivery to neurons, we developed the SynTetOff platform (Sohn et al., 2017), a TetOff-based expression system that achieves neuron-specific expression levels approximately 40-fold higher than those of conventional vectors. Building on this platform, we established a multicolor signal amplification strategy based on the tyramide signal amplification method (Yamauchi et al., 2022, 2025), which significantly enhances the detection sensitivity of reporter proteins expressed via AAV vectors. This substantially improves both imaging sensitivity and acquisition speed, allowing efficient observation of neural structures. Furthermore, we developed a tissue-clearing protocol compatible with both light microscopy and electron microscopy (Furuta et al., 2022). This approach enables direct three-dimensional imaging of thick tissue samples and volumetric data acquisition without sectioning, providing a powerful means for multi-scale structural analysis. By integrating these technologies, we have established a robust pipeline for efficient and high-resolution analysis of neural circuit structures. In this presentation, I will introduce each of these technologies and demonstrate their application to morphological analysis of inhibitory neurons in the claustrum (Takahashi et al., 2023). I will conclude by discussing the potential of these methods for advancing whole-brain structural analysis.

Keywords : adeno-associated virus, central nervous system, mouse, neuron, tissue-clearing
Acknowledgements : This work was supported by KAKENHI (JP23K20044 and JP25K02371) from JSPS, Brain/MINDS (JP21dm0207112) and Brain/MINDS 2.0 (JP24wm0625103) from AMED, and Moonshot R&D (JPMJMS2024) and FOREST (JPMJFR204D) from JST.

S8-2

Micro-dissection of the connectivity of cerebellar input layer with GABRA6 promotor by exploiting dispersed developmental time of granule cells and computational modeling

Taegon Kim, Heeyoun Park, Keiko Tanaka-Yamamoto, Yukio Yamamoto

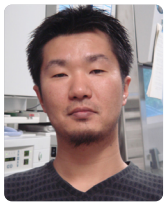
Brain Science Institute, Korea Institute of Science and Technology, Seoul, Republic of Korea

The cerebellum is a densely packed structure made of an extremely large number of neurons, and a major contribution to this crowdedness comes from its input layer, the cerebellar granule cell layer (GCL). In the GCL, granule cells (GrCs) receive inputs from mossy fibers (MFs) originating in the brainstem and other brain regions, relaying information to Purkinje cells via GrC axons, the parallel fibers (PFs). Considering the extreme numerosity of GrCs, which are generally assumed to be identical, subgroup labeling of GrCs is a crucial strategy for investigating the principle of MF–GrC connectivity. We utilized the fact that GrCs mature through postnatal developmental processes consisting of proliferation in the external GCL, migration, and differentiation and settlement in the internal GCL. An adeno-associated viral (AAV) vector containing the GABRA6 promoter triggers selective molecular expression in GrCs at specific developmental stages. Thus, to exploit the asynchrony among GrC developmental timelines, we injected AAV-GABRA6 at different times. A day gap between injections successfully segregated labeling into subgroups of GrCs. However, because GrCs have only 3–5 short dendrites and each synapse between an MF terminal and dendrites of GCs forms a complex entanglement called a glomerulus, detailed connectivity is largely inaccessible through simple quantification of confocal images of labeled tissue. Thus, we performed computational modeling of the MF–GrC network, simulating various mechanisms of network formation; this revealed a mild preferential connection from an MF to GrCs that developed at similar times. In addition, we found that this biased connectivity correlates with MF input origin. These findings imply that MF–GrC connectivity is not homogeneous but can be interpreted as highly overlapping modules relaying distinct inputs, indicating that the expansion and mixing of inputs in the GCL are orchestrated in an organized manner.

Keywords : cerebellar granule cell layer development, adeno-associated virus, GABRA6, biased connectivity, computational model of network formation
Acknowledgements : This was supported by KIST Intramural Program (2E33701) and K-brain Project (RS-2023-00262880) of National Research Foundation funded by the Ministry of Science and ICT.

S8-3

Long-term activity imaging of a neuronal population that sends input to a specific type of neurons via a low cytotoxic G-deleted rabies virus vector



Ken-ichi Inoue

Center for the Evolutionary Origins of Human Behavior, Kyoto University, Aichi, Japan

Investigating the input to a specific neuronal population within a given neural circuit is critical for understanding the information-processing algorithms of the brain. The G-deleted rabies virus vector (ΔG-RV) pseudotyped with envelope protein from avian sarcoma leukosis virus (Env) can selectively infect a target neuronal population expressing its receptor (TVX) via recombination. The expression of rabies virus glycoprotein in this population leads to monosynaptic propagation of ΔG-RV, thus allowing visualization of the input to this population. However, since the conventional ΔG-RV is highly cytotoxic because it expresses the viral gene as well as the inserted gene, neuronal activity can only be measured for a very short period, resulting in the restriction of its application to chronic functional experiments. Here, we developed a novel low-cytotoxic ΔG-RV that maintains the ability to express a foreign gene. First, we created a modified full-length vector with a super-slow growth rate, but with a high level of foreign gene expression (ssRV) by inserting a foreign gene into the tip of the viral genome and modifying the genome sequence. Then, we confirmed that the ΔG-ssRV reduced its cytotoxicity, and that the ΔG-ssRV expressing GCaMP achieved stable measurement of cortical neuron activity for several months after its injection into the mouse striatum. Furthermore, using the ΔG-ssRV-GCaMP pseudotyped with Env, we successfully and continuously performed calcium imaging of mouse cortical neurons sending input to striatal dopamine D1 receptor-expressing neurons that constitute the direct pathway of the basal ganglia. The ΔG-ssRV we developed in the present study enables us to explore the information about the input to a specific neuronal population in relation to a behavioral task, and will greatly be useful for evaluating the mechanism underlying information processing in the brain.

Keywords : Rabies Virus, Tracing, Calcium Imaging, Viral Vector
Acknowledgements : KAKENHI JP22H05157 and JP23K27472 AMED 24wm0625103s0301

S8-4 IBRO AWARDEE

Modulation of gene expression and signaling cascade in mice brain exposed to nano-neonicotinoid pesticides

Dhanshree Borkar[1], Dnyaneshwari Pande[1], Shivendra Chaurasiya[2], Rajesh Yadav[1]

[1]School of Forensic Science, National Forensic Sciences University, Bhopal, Madhya Pradesh, India, India
[2]Department of Biological Sciences & Engineering, Maulana Azad National Institute of Technology, Bhopal, Madhya Pradesh, India, India

Background: The use of nano-formulations of pesticides has recently increased in agriculture. Their non-targeted toxicity has not yet been reported due to a lack of studies. There is a strong need to assess the neurotoxic effects of nano-pesticides to explore their toxicity pattern and mechanism of action. Objective: The present study investigates the neurotoxicity linked with gene modulation induced by nano-imidacloprid and nano-acetamiprid in the frontal cortex of mice. Methods: Male mice weighing 30 ± 2 g were divided into four groups. They received nano-formulations of neonicotinoids: nano-imidacloprid (T1 = 25 mg/kg body weight, p.o.), nano-acetamiprid (T2 = 25 mg/kg body weight, p.o.), and a mixture of both formulations (T3 = half of the dose of both formulations) for 28 days, with the control group receiving normal saline. Mice were sacrificed, and the frontal cortex was dissected. TBP and HPRT were used as the housekeeping genes. Results: Alterations in the expression of genes involved in brain functioning were observed in the frontal cortex of mice brains. Genes related to neurotransmission showed that AChE was upregulated in all the groups, GABA was upregulated in the T1 group and downregulated in the T2 and T3 groups, while HTR1B was upregulated in the T1 group and downregulated in the T3 group. Genes associated with apoptosis, including Bax, Bcl2, Caspase-3, and Caspase-9, were upregulated in all three groups. Genes linked with molecular signaling, such as MAO-A, Nrf-2, and COMT, were also upregulated in all three groups. FKBP5 was upregulated in the T1 group and downregulated in the T2 and T3 groups. Conclusion: The results of the present study indicate that nano-formulations of acetamiprid and imidacloprid influence the expression of various genes in the frontal cortex. Disruptions in gene function in this area can lead to behavioural and cognitive impairments and impair neuronal transmission and functioning, highlighting their possible neurotoxic effects.

Keywords : Neurotoxicity, Nanopesticides, Gene Expression, Acetamiprid, Imidacloprid
Acknowledgements : The authors are thankful to the National Forensic Sciences University (An Institution of National Importance), Bhopal (MP), India, for providing the opportunity to work and their support and interest. Ms. Dhanshree Sayangrushi Borkar is thankful to the UGC, New Delhi, India, for providing the research fellowship.

S8-5

Nanoparticle-mediated gene delivery to enhance microglial phagocytosis for Alzheimer's disease therapy

Dong Woon Kim

Kyung Hee University

Age-dependent accumulation of amyloid plaques in patients with sporadic Alzheimer's disease (AD) is associated with reduced amyloid clearance. Older microglia have a reduced ability to phagocytose amyloid, so phagocytosis of amyloid plaques by microglia could be regulated to prevent amyloid accumulation. Furthermore, considering the aging-related disruption of cell cycle machinery in old microglia, we hypothesize that regulating their cell cycle could rejuvenate them and enhance their ability to promote more efficient amyloid clearance. First, we used gene ontology analysis of microglia from young and old mice to identify differential expression of cyclin-dependent kinase inhibitor 2A (p16ink4a), a cell cycle factor related to aging. We found that p16ink4a expression was increased in microglia near amyloid plaques in brain tissue from patients with AD and 5XFAD mice, a model of AD. To regulate microglial phagocytosis by gene transduction, we used poly (D,L-lactic-co-glycolic acid) (PLGA) nanoparticles, which predominantly target microglia, to deliver the siRNA and to control microglial reactivity. Nanoparticle-based delivery of p16ink4a siRNA reduced amyloid plaque formation and the number of aged microglia surrounding the plaque and reversed learning deterioration and spatial memory deficits. Additionally, we will show the results of phagocytosis through trem2 expression using the iba1 promoter. We propose that the enhancement of phagocytic activity in microglia is a promising strategy for the treatment of Alzheimer's disease.

Keywords : Nanomedicine, Nanoparticle, Microglia, Senescence, Cell cycle, Alzheimer’s disease

S8-6

A Compact GAD67 Promoter Enables Inhibitory Neuron-Specific Gene Modulation

Yuuki Fukai[1,2], Ayumu Konno[1,2], Yasunori Matsuzaki[1,2], Nobutake Hosoi[2], Hirokazu Hirai[1,2]

[1]Viral Vector Core, Gunma University Initiative for Advanced Research (GIAR), Maebashi, Gunma, Japan
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Approximately 85% of neurons in the cerebral cortex are excitatory, relaying signals to other brain and spinal cord regions. The remaining 15% are inhibitory neurons that modulate local excitation and network activity by suppressing excitatory (and some inhibitory) neurons. Dysfunction in inhibitory neurons can lead to epilepsy, autism spectrum disorder, and schizophrenia. Gene therapy targeting inhibitory neurons holds promise for effective treatment of these disorders. Cell type-specific promoters are typically large in size and weak in activity, often making them incompatible with AAV vectors or ineffective upon delivery. We developed the cmGAD67 promoter, a compact 410 bp element with strong activity specific to inhibitory neurons. We investigated whether modulating inhibitory neuron function using cmGAD67-driven AAVs could influence seizure susceptibility. Expression of the inhibitory designer receptor hM4Di in hippocampal inhibitory neurons followed by systemic administration of its ligand DCZ triggered seizures. Conversely, intravenous delivery of an AAV expressing the GABA-synthesizing enzyme GAD65 under the control of the cmGAD67 promoter significantly suppressed seizures and seizure-induced mortality triggered by intraperitoneal injection of the GABAA receptor antagonist pentylenetetrazole (PTZ). Our compact and potent cmGAD67 promoter enables both suppression and enhancement of inhibitory neuron function via AAV, making it a valuable tool for both basic research and gene therapy targeting neuropsychiatric disorders involving inhibitory neuron dysfunction.

Keywords : AAV, Inhibitory neuron, cmGAD67 promoter, DREADD, Epilepsy
Acknowledgements : This work was supported by grants from the Program for Brain Mapping by Integrated Neurotechnologies for Disease Studies (Brain/MINDS; JP20dm0207057/JP21dm0207111), Multidisciplinary Frontier Brain and Neuroscience Discoveries (Brain/MINDS 2.0; JP24wm0625103) from AMED, MEXT/JSPS KAKENHI (20K06906/24K10022, 22K06454/24H01221 and 23H02791) and Next-GIP (JPMJSP2146).

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Songdo Convensia, Incheon, Korea

KSBNS 2025

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Symposium 9

Day 2 (August 25) **08:30-10:25** **Rm.116-118**

Translational and clinical neuroscience: precision convergent medicine for treating intractable diseases, pain, and central nervous system trauma

Organizer : Inbo Han (CHA University)
KiBum Lee (Rutgers, The State University of New Jersey)
Moderator : Inbo Han (CHA University)
KiBum Lee (Rutgers, The State University of New Jersey)

Transforming CNS injury therapeutics using a novel nanotechnology-enabled extracellular vesicle platform
KiBum Lee (Rutgers, The State University of New Jersey)

Axon guidance gene-targeted siRNA delivery system improves neural stem cell transplantation therapy after spinal cord injury
Seil Sohn (CHA University)

Current perspectives on neuropathic pain
Junseok Hur (Korea University)

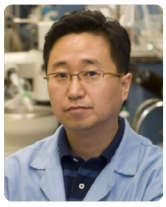
Advancing non-human primate disease models for superior translational research and enhanced clinical applicability
Seongjun Ryu (Eulji University)

Multimodal therapy strategy based on a bioactive hydrogel for repair of spinal cord injury
Inbo Han (CHA University)

C-reactive protein and unruptured intracranial aneurysm risk in Indonesia: a mendelian randomization study with real-world hospital-based study
Elvan Wiyarta (University of Indonesia Hospital) IBRO AWARDEE

S9-1

Transforming CNS injury therapeutics using a novel nanotechnology-enabled extracellular vesicle platform



KiBum Lee

Dept. of Chemistry & Chemical Biology, Rutgers University, 123 Bevier Road, Piscataway, NJ 08854-8087, USA

The dual challenge of treating acute damage while mitigating long-term neurodegeneration in CNS injuries like TBI and SCI remains a critical unmet need. To overcome the limitations of current therapies, we have been developing an integrated theragnostic platform that combines a potent regenerative therapy with a highly sensitive diagnostic tool for a comprehensive solution.
Our innovative approach merges two distinct nanotechnology strategies into a single, cohesive system. The therapeutic arm consists of a brain-mimetic bioorthogonal hydrogel that provides sustained, localized delivery of hypoxia-conditioned extracellular vesicles (EVs) derived from neural progenitor cells. These EVs are enriched with a powerful cocktail of neurotrophic and angiogenic factors. The diagnostic arm features a liquid biopsy chip that utilizes an aptamer-functionalized gold nanoarray and CRISPR-Cas13a biosensors. This system captures neuron-derived EVs from blood and performs amplification-free analysis of their miRNA cargo with femtomolar sensitivity.
This combined platform demonstrates significant therapeutic efficacy, including reduced lesion volume, enhanced neurogenesis, and marked motor function recovery in preclinical TBI models. Critically, the diagnostic component enables noninvasive, longitudinal monitoring of disease progression and therapeutic response by tracking specific biomarkers of neurodegeneration. By unifying advanced therapeutic delivery with precise, real-time biological feedback, our platform offers a paradigm shift in neurological care. It paves the way for personalized treatment strategies that can adapt to a patient's evolving condition, transforming the management of TBI from acute intervention to long-term neuroprotection.

Keywords : Nanotheragnostics, Extracellular vesicles, Neurotrauma, Liquid biopsy, and Neural Repair

S9-2

Axon guidance gene-targeted siRNA delivery system improves neural stem cell transplantation therapy after spinal cord injury

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Background Neural stem cells (NSCs) derived from the embryonic spinal cord are excellent candidates for the cellular regeneration of lost neural cells after spinal cord injury (SCI). Semaphorin 3 A (Sema3A) is well known as being implicated in the major axon guidance of the growth cone as a repulsive function during the development of the central nervous system, yet its function in NSC transplantation therapy for SCI has not been investigated. Here, we report for the first time that embryonic spinal cord-derived NSCs significantly express Sema3A in the SCI environment, potentially facilitating inhibition of cell proliferation after transplantation. Methods siRNA-Sema3A was conjugated with poly-l-lysin-coated gold nanoparticles (AuNPs) through a charge interaction process. NSCs were isolated from embryonic spinal cords of rats. Then, the cells were embedded into a dual-degradable hydrogel with the siRNA- Sema3A loaded-AuNPs and transplanted after complete SCI in rats. Results The knockdown of Sema3A by delivering siRNA nanoparticles via dual-degradable hydrogels led to a significant increase in cell survival and neuronal differentiation of the transplanted NSCs after SCI. Of note, the knockdown of Sema3A increased the synaptic connectivity of transplanted NSC in the injured spinal cord. Moreover, extracellular matrix molecule and functional recovery were significantly improved in Sema3A-inhibited rats compared to those in rats with only NSCs transplanted. Conclusions These findings demonstrate the important role of Sema3A in NSC transplantation therapy, which may be considered as a future cell transplantation therapy for SCI cases.

Keywords : Spinal cord injuries, Neural stem cells, Semaphorin-3A, Small interfering RNA, Axon guidance
Acknowledgements : This research was supported by a grant of Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by Ministry of Science, ICT and Future Planning (RS-2023-00209591), and Ministry of Education (RS-2023-00243616).

S9-3

Current Perspectives on Neuropathic Pain

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Neuropathic pain is framed within core pain physiology—transduction, transmission, modulation, and perception. I will clarify classification (nociceptive, neuropathic, nociplastic, mixed) and adopt the definition of neuropathic pain as pain caused by a lesion or disease of the somatosensory system. Clinically it presents with burning or electric-shock pain, paresthesia or dysesthesia, and allodynia or hyperalgesia in neuroanatomic distributions.
Pathophysiology spans multiple levels. Peripherally, injured afferents develop ectopic firing and ion-channel changes, with neuroimmune signaling between nociceptors and immune-glial cells driving sensitization. Centrally, glial activation, reduced inhibitory tone, and network plasticity stabilize persistent pain. This systems view explains clinical heterogeneity and variable treatment response. Management follows international guidelines and emphasizes mechanism-guided multimodal care. First-line options include SNRIs or TCAs, gabapentinoids, and topical agents (lidocaine or capsaicin), combined with exercise-based rehabilitation and psychological therapies. For refractory cases, interventional approaches—spinal cord or dorsal root ganglion stimulation and selective peripheral nerve stimulation—can be effective; tramadol or opioids are reserved with caution.
Recent advances include single-cell and spatial omics of human DRG and spinal cord, iPSC-derived nociceptor models, and in-vivo imaging that enable cell-type-specific target discovery. Biomarker-guided stratification using quantitative sensory phenotypes, evoked potentials, and markers of glial activation is informing precision trials. Emerging therapies span selective sodium-channel modulators, biased GPCR strategies, neuroimmune and glial-directed agents, and gene-based approaches to tune nociceptor excitability. Integrating physiology, classification, mechanisms, and guidelines points toward biologically grounded, clinically actionable precision analgesia.

Keywords : Neuropathic Pain; Pain Physiology; Pain Classification; Treatment Guidelines; Precision Analgesia

S9-4

Advancing non-human primate disease models for superior translational research and enhanced clinical applicability

Seongjun Ryu[1,2,3]

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[3]Visiting Faculty, Johns Hopkins University, School of Medicine, Solomon H. Snyder Department of Neuroscience, Baltimore, Maryland, USA orea

Non-human primate (NHP) models provide an essential translational bridge for elucidating complex pathophysiological processes in central nervous system (CNS) injury and for validating therapeutic strategies prior to clinical application. Using a photothrombosis (PT)-induced cortical stroke paradigm, we identified a novel astrocyte-driven mechanism linking oxidative stress to neuronal death. PT triggered an acute surge in H_2O_2, inducing astrocytic type I collagen (COL1) production through miR-29-mediated post-transcriptional and fucosylation-dependent post-translational regulation. This cascade activated integrin signaling, promoted glial barrier formation, fibrotic scarring, altered N-glycosylation, and led to neuronal loss and neurological deficits. Remarkably, astrocyte-specific silencing of COL1 or FUT8, or pharmacological treatment with KDS12025—a peroxidase enhancer that decomposes H_2O_2—effectively mitigated these pathological changes and improved functional recovery. KDS12025's neuroprotective effects were reproduced in an NHP cortical stroke model, confirming translational relevance. Together, Our studies establish advanced NHP models as a powerful platform for dissecting neuron–glia interactions, validating novel therapeutic targets such as astrocytic COL1 and FUT8, and accelerating the clinical translation of neuromodulatory interventions for CNS injuries.

Keywords : Non-human primate model, Ischemic stroke, Astrocytic collagen, Fucosylation, Brain Fibrosis

S9-5

Multimodal therapy strategy based on a bioactive hydrogel for repair of spinal cord injury

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Traumatic spinal cord injury results in permanent and serious neurological impairment, but there is no effective treatment yet. Tissue engineering approaches offer great potential for the treatment of SCI, but spinal cord complexity poses great challenges. In this study, the composite scaffold consists of a hyaluronic acid-based hydrogel, decellularized brain matrix (DBM), and bioactive compounds such as polydeoxyribonucleotide (PDRN), tumor necrosis factor-α/interferon-γ primed mesenchymal stem cell-derived extracellular vesicles (TI-EVs), and human embryonic stem cell-derived neural progenitor cells (NPC). The composite scaffold showed significant effects on regenerative prosses including angiogenesis, anti-inflammation, anti-apoptosis, and neural differentiation. In addition, the composite scaffold (DBM/PDRN/TI-EV/NPC@Gel) induced an effective spinal cord regeneration in a rat spinal cord transection model. Therefore, this multimodal approach using an integrated bioactive scaffold coupled with biochemical cues from PDRN and TI-EVs could be used as an advanced tissue engineering platform for spinal cord regeneration.

Keywords : Decellularized brain matrix, Hyaluronic acid hydrogel, Neural progenitor cell, olydeoxyribonucleotide, Spinal cord injury

S9-6 IBRO AWARDEE

C-Reactive Protein and Unruptured Intracranial Aneurysm Risk in Indonesia: A Mendelian Randomization Study with Real-World Hospital-Based Study

Elvan Wiyarta[1], Kento Oi[2], Linan Ge[2], Hannah Soetjoadi[3], David Pangeran[4], Rakhmad Hidayat[4], Mohammad Kurniawan[4]

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Background: C-reactive protein (CRP) is associated with various vascular diseases including unruptured intracranial aneurysm (UIA). Although observational studies suggest a link between CRP and UIA, the causal relationship in Indonesian populations remains uncertain. Objective: This study uses Mendelian Randomization(MR) and clinical validation to assess whether genetically elevated CRP levels influence UIA risk in Indonesian population. Methods: We performed a two-sample MR analysis using nine independent CRP-associated SNPs ($p < 5\times10^{-8}$, $r^2 < 0.01$) from large East Asian genome-wide association studies (GWAS). Outcome data were drawn from a meta-GWAS of UIA in East Asian populations. Causal estimates were calculated using inverse-variance weighted (IVW) analysis, with additional methods (MR-Egger, weighted median) used for sensitivity. Separately, we analyzed hospital records of 99 Indonesian patients (51 with UIA, 48 without), evaluating the association between CRP and UIA risk using multivariable logistic regression. Result: IVW analysis demonstrated a positive association between genetically proxied CRP levels and UIA risk (β=0.982, standard error[SE]=0.936), with consistent directional estimates across all models, although insignificant (p>0.29). MR sensitivity tests showed no evidence of heterogeneity or directional pleiotropy. Heterogeneity was low (Cochran's Q=3.25, p=0.918), and pleiotropy was negligible (MR-Egger intercept= -0.0057, p=0.965). In contrast, the hospital-based analysis revealed a significant association between elevated CRP and UIA risk. Logistic regression indicated that CRP was an independent predictor of UIA (adjusted OR = 1.43 per 1 mg/L increase, 95% CI: 1.11–1.93, p = 0.011). Conclusion: This study links genetic and clinical evidence on CRP and UIA. Modest MR findings contrast with a strong clinical association in Indonesians, underscoring the need for population-specific studies and GWAS in Indonesia.

Keywords : C-reactive protein, intracranial aneurysm, mendelian randomization, Indonesia, inflammation

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 10

Day 2 (August 25) **08:30-10:25** **Rm.204-205**

Synaptic balance in memory, homeostasis, and network stability

Organizer : Jong-Cheol Rah (Korea Brain Research Institute)
Moderator : Chul-Hoon Kim (Yonsei University)

Synaptic input-selective homeostasis safeguards developing cortical neurons toward set-point activity
Mingshan Xue (Baylor College of Medicine)

Cortico-hippocampal circuit interactions in shaping plasticity and memory functions
Jayeeta Basu (New York University)

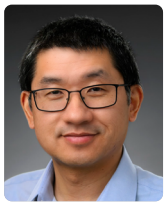
Disentangling morphological and synaptic mechanisms underlying network hyperexcitability in seizure disorders caused by mTOR hyperactivation
Matthew C. Weston (Virginia Tech)

Cholinergic modulation of thalamocortical gating mechanisms in short-term memory and its disruption in schizophrenia models
Jong-Cheol Rah (Korea Brain Research Institute)

Systems consolidation involves reorganization of hippocampal engram circuits
Sangyoon Ko (University of Toronto) Scitech Korea Awards

S10-1

Synaptic input-selective homeostasis safeguards developing cortical neurons toward setpoint activity



Zhao-Lin Cai[1,2], Colleen M. Longley[2,3], Dongwon Lee[1,2], Wu Chen[1,2], Mingshan Xue[1,2,3,4]

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The mammalian cerebral cortex achieves a remarkable balance between flexibility and stability. While dynamic neuronal activity enables the flexibility, the stability of cortical function arises from a set of homeostatic plasticity mechanisms that maintain the activity of individual neurons within a narrow range around their established setpoints in the face of perturbations. However, little is known about the mechanisms ensuring that cortical neurons progress from near-zero activity at birth to their mature setpoint activity levels. Here we discover a synaptic input-selective homeostatic mechanism that counteracts perturbations to the excitability of developing layer 2/3 pyramidal cells in the mouse primary visual cortex, facilitating their progression toward destined setpoint activity levels. By overexpressing an inward rectifying potassium channel Kir2.1 in a subset of layer 2/3 pyramidal cells, we silence these neurons from their birth through the early postnatal period. However, during postnatal development these initially silenced Kir2.1-expressing neurons gradually overcome this perturbation and ultimately reach the activity levels comparable to unmanipulated neighboring layer 2/3 pyramidal cells. By selectively stimulating distinct synaptic inputs, we find that excitatory inputs from layer 4 and layer 2/3 remain unchanged, but excitation from layer 5 is drastically enhanced in Kir2.1-expressing neurons. This synaptic potentiation occurs through increasing quantal amplitudes and unsilencing silent synapses and requires the insertion of GluA2-containing AMPA receptors. Thus, these results reveal a cell-autonomous homeostatic synaptic plasticity with unexpected input selectivity that safeguards developing cortical neurons toward their mature setpoint activity levels in vivo. Our findings suggest that the setpoint activity level may be encoded as part of neuronal identity and maintained by homeostatic monitoring and controlling mechanisms during development.

Keywords : Synaptic transmission, homeostatic plasticity, optogenetics.

S10-2

Cortico-hippocampal circuit interactions in shaping plasticity and memory functions

Jayeeta Basu

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The cortico-hippocampal circuit forms stable yet flexible representations of the external environment (place maps), and associated contextual cues (reward locations) to support encoding and recall of memories and adaptive learned behaviors. We know little about the role of long-range glutamatergic and GABAergic inputs from the entorhinal cortex in shaping hippocampal activity underlying multisensory memory processing. Our work uncovers how non-linear coding at single neuron and neural ensemble levels is modulated by long-range and local excitatory, inhibitory, and disinhibitory circuit interactions driven by the lateral entorhinal cortex (LEC). LEC conveys contextually salient input to the hippocampus and is particularly affected in early stages of Alzheimer's disease. Optogenetic circuit mapping with *ex vivo* somatic and dendritic physiology highlights divergent compartment and pathway-specific circuit mechanisms recruited by LEC input in hippocampal CA1 vs. CA3. In CA1, LEC glutamatergic (*Bilash et al., Cell Reports 2023)* and GABAergic input (*Basu et al. Science 2016*), disinhibit dendritic spikes by suppressing dendrite-targeting interneurons, inducing heterosynaptic input timing-dependent plasticity, but in CA3, these LEC inputs gate perisomatic inhibition to boost somatic spikes driven by coincident recurrent network activity (*Robert et al., 2025, accepted Science*). *In vivo* two-photon imaging of hippocampal place cells during goal-directed navigation behavior shows task-selective activity dynamics that stabilize with context-dependent learning (*Zemla et al., 2022, Cell Reports*) and differences in dendritic vs. somatic place coding stability (*Moore et al., 2025, Nature Comm*). Chemogenetic silencing of LEC inputs to CA3 during spatio-contextual learning impairs behavioral performance and associated stabilization of place maps (*Robert et al., 2025*, *accepted Science),* whereas LEC supports memory recall and post-learning place map stability in CA1 (*Hopkins in prep*).

Keywords : Cortico-hippocampal Circuitry, Disinhibition, Place Cell Stability, Learning, and Memory

S10-3

Disentangling morphological and synaptic mechanisms underlying network hyperexcitability in seizure disorders caused by mTOR hyperactivation

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Gene variants that hyperactivate PI3K-mTOR signaling in the brain lead to epilepsy and cortical malformations in humans. Some gene variants associated with these pathologies only hyperactivate mTORC1, but others, such as *PTEN, PIK3CA*, and *AKT*, hyperactivate both mTORC1- and mTORC2-dependent signaling. Previous work established a key role for mTORC1 hyperactivity in mTORopathies, however, whether mTORC2 hyperactivity contributes is not clear. To test this, we have inactivated mTORC1 and/or mTORC2 downstream of *Pten* deletion in several mouse models of *Pten* loss-of-function (LOF) in the cortex and hippocampus. Spontaneous seizures and epileptiform activity generally persist despite mTORC1 or mTORC2 inactivation alone, even when some improvements or cellular features are rescued. Only inactivating both mTORC1 and mTORC2 simultaneously normalizes brain activity, morphological, and electrophysiological changes caused by *Pten* loss. These results suggest that hyperactivity of both mTORC1 and mTORC2 can cause epilepsy, and that targeted therapies should aim to reduce activity of both complexes.

Keywords : mTOR, epilepsy, mTORC1, mTORC2

S10-4

Cholinergic modulation of thalamocortical gating mechanisms in short-term memory and its disruption in schizophrenia models

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Short-term memory (STM) relies on dynamic interactions between the prefrontal cortex (PFC) and the mediodorsal thalamus (MD), supported by recurrent thalamo-cortico-thalamic loops. However, the thalamofrontal synapses exhibit strong short-term depression, posing a challenge for sustaining high-frequency information flow during delay periods. We show that acetylcholine (ACh) enhances PFC excitability and enables effective signal transfer despite the intrinsic synaptic filtering. Using behaviorally engaged mice performing visually or auditorily guided delayed-response tasks, we demonstrate that muscarinic ACh receptor activity is essential for both task performance and for maintaining direction-selective neural representations in PFC. Furthermore, prolonged NMDAR hypofunction — a condition modeling schizophrenia — leads to impaired thalamofrontal synaptic release and degraded STM performance. Notably, restoring thalamocortical release efficiency normalizes STM, establishing a causal link. Our findings reveal that cholinergic modulation is critical for enabling persistent cortical activity through filtering synapses, and that disruption of this mechanism may underlie cognitive symptoms in schizophrenia.

Keywords : Short-term memory, Prefrontal cortex, Mediodorsal thalamus, Acetylcholine, Schizophrenia

S10-5 Scitech Korea AWARDEE

Systems consolidation involves reorganization of hippocampal engram circuits

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Episodic memories—high-fidelity representations of past events that initially depend on the hippocampus—do not maintain their precision indefinitely. An advantage of this time-dependent decline in precision is the emergence of event-linked gist memories that guide future behavior in novel yet related situations (that is, generalization). Prevailing models of systems consolidation propose that memory reorganization accompanies this loss of memory precision; however, the precise locus of this reorganization remains unclear. Here we report that time-dependent rewiring of hippocampal engram circuits actively regulates the shift in memory precision associated with systems consolidation. Using engram labeling tools in mice, we demonstrate that the passage of time does not erase hippocampal engrams; rather, it reorganizes DG–CA3–CA1 engram connectivity, enabling engram neurons to become broadly active and support behavior in situations distinct from the original training conditions. This reorganization depends on adult hippocampal neurogenesis; suppressing hippocampal neurogenesis prevents engram rewiring and preserves precise, event-linked memories. Conversely, promoting hippocampal neurogenesis accelerates rewiring and facilitates the emergence of event-linked gist memories within the hippocampus. These findings indicate that models of systems consolidation require updating to incorporate intra-hippocampal circuit reorganization as a key mechanism underlying qualitative shifts in memory precision.

Keywords : Engram, Hippocampus, Neurogenesis

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 11

Day 2 (August 25) **08:30-10:25** **Rm.107-109**

Neural codes across sensory systems: insights into perception and behavior

Organizer : Jeehyun Kwag (Seoul National University)
Moderator : Jeehyun Kwag (Seoul National University)

Stimulus information guides the emergence of behavior-related signals in primary somatosensory cortex during learning
Michael M. Kohl (University of Glasgow)

Decoding olfactory bulb output: A behavioural assessment of rate, synchrony, and respiratory phase coding
Izumi Fukunaga (Okinawa Institute of Science and Technology)

Neural variability structure in primary visual cortex is optimized for consistent representation of visual similarity
Hyeyoung Shin (Seoul National University)

Egocentric neural coding of space in the retrosplenial cortex guides goal-directed navigation
Jeehyun Kwag (Seoul National University)

Functional synchronization of the intermediate hippocampus and medial prefrontal cortex after learning spatial navigation in VR space
Heung-Yeol Lim (Seoul National University) Scitech Korea AWARDEE

S11-1

Stimulus information guides the emergence of behavior-related signals in primary somatosensory cortex during learning

Michael Kohl[1,2]

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Neurons in the primary cortex carry sensory- and behavior-related information, but it remains an open question how this information emerges and intersects together during learning. Current evidence points to two possible learning-related changes: sensory information increases in the primary cortex or sensory information remains stable, but its readout efficiency in association cortices increases. We investigated this question by imaging neuronal activity in mouse primary somatosensory cortex before, during, and after learning of an object localization task. We quantified sensory- and behavior-related information and estimated how much sensory information was used to instruct perceptual choices as learning progressed. We find that sensory information increases from the start of training, while choice information is mostly present in the later stages of learning. Additionally, the readout of sensory information becomes more efficient with learning as early as in the primary sensory cortex. Together, our results highlight the importance of primary cortical neurons in perceptual learning.

Keywords : sensory coding, decision making, mouse, information theory, two-photon imaging

S11-2

Decoding olfactory bulb output: A behavioural assessment of rate, synchrony, and respiratory phase coding

Izumi Fukunaga

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The olfactory system is a well-known model for studying the temporal encoding of sensory stimuli due to its rhythmic stimulus delivery through respiration. Sniff-locked activity is pervasive in the primary olfactory area, the olfactory bulb, and is considered critical to structuring the output of its computation. We tested the behavioural importance of these temporal features using simple closed-loop optogenetics embedded in custom behavioural paradigms. We found that mice perceive differences in evoked spike counts and discriminate between synchronous vs. asynchronous activations of the output neurons. Surprisingly, they failed to distinguish the timing of evoked activity relative to the sniff cycle. These results suggest that, beyond the first steps of olfactory processing, sniff rhythms play a more nuanced role, with greater reliance on the spike rate and synchrony for the neural encoding of the environment, consistent with a gradual transformation of encoding format at successive stages of sensory processing.

Keywords : Temporal coding, Olfaction, Optogenetics, Synthetic perception, Psychophysics

S11-3

Neural variability structure in primary visual cortex is optimized for consistent representation of visual similarity

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How different neuronal populations construct a robust representation of the sensory world in the presence of neural variability is a mystery. We found that neural variability in mouse primary visual cortex observe a simple rule: For a given sensory stimulus, the mean and the variance of spike counts follow a linear relationship across neurons. To understand how this neural variability structure affects the sensory representation, we artificially varied the slope of the log-mean and log-variance relationship. We found that the structure of neural variability allows representations of distinct sensory information to be continuous while minimizing overlap, balancing the tradeoff between generalizability and discriminability. Further, representational similarity was most consistent between different sets of neurons, both within and across mice, when the slope was 1. These results suggest that the structure of neural variability may enable different brains to build a common representation of the sensory world.

Keywords : neural variability, neural code, visual inference, mouse visual cortex, extracellular electrophysiology
Acknowledgements : This work was supported by the Samsung Science and Technology Foundation (SSTF-BA2302-07), the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (RS-2024-00358070, RS-2024-00413689, RS-2023-00301976), and the Seoul National University New Faculty Startup Fund.

S11-4

Egocentric neural coding of space in the retrosplenial cortex guides goal-directed navigation

Jeehyun Kwag

Brain and Cognitive Sciences, Seoul National University, Seoul, Republic of Korea

Egocentric neural representations of environmental features, such as edges and vertices, are important for constructing a geometrically detailed egocentric cognitive map for flexible, goal-directed navigation. Neurons that encode environmental boundaries in an egocentric frame, such as egocentric boundary cells, have been previously identified. However, it remains unknown whether the brain also encodes discrete geometric features such as vertices and how they are used to guide goal-directed navigation.
Here, we identify a novel class of neurons in the granular RSC—egocentric vertex cells (EVCs)—that selectively fire near geometric vertices of an environment, with receptive fields anchored at fixed angles and distances relative to the animal's heading direction. These cells form a structured egocentric vector map of space. Notably, goal-directed navigation selectively enhances EVC activity at goal-proximal vertices, with increased firing rates and tuning strength persisting even in the absence of immediate reward. This suggests that EVCs may encode egocentric vectors of the goal location and contribute to reward prediction, consistent with RSC's known roles in spatial planning and value representation.
Our findings reveal a circuit mechanism by which egocentric spatial maps in the RSC are flexibly modulated by goal learning, supporting the transformation of environmental geometry into actionable, self-centered representations that guide navigation.

Keywords : Retrosplenial cortex, Egocentric vertex cell, Egocentric neural code, goal-directed navigation, Calcium imaging
Acknowledgements : RS-2024-00341894

S11-5 Scitech Korea AWARDEE

Functional synchronization of the intermediate hippocampus and medial prefrontal cortex after learning spatial navigation in VR space

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[2]Department of Neurobiology, University of Utah, Utah, USA

The formation and utilization of hippocampal cognitive map depend on interactions with the medial prefrontal cortex (mPFC). Previous studies have mainly focused on dorsal hippocampus, which lacks direct projections to mPFC. In contrast, the intermediate hippocampus (iHP) projects directly to mPFC and retains spatial coding capacities, making it ideal for transferring spatial representations into goal-directed actions mediated by mPFC. However, little is known about this iHP-mPFC network. To address this, we simultaneously recorded single-neuron activities in the iHP and mPFC using a hyperdrive with 24 tetrodes while rats learned a goal-directed navigation task in a 2D VR environment. In VR, a circular area surrounded by a visually rich environment had two goal zones in the West and East. Rats first learned to navigate toward the West to get a water reward. After reaching the learning criterion (>75% correct), the reward zone was reversed to the East, and rats were retrained. To identify learning-related changes in spatial representations, we analyzed each neuron's preferential firing to specific facing directions, known to be prominent in 2D VR. Initially, iHP had a greater proportion of directional cells (37%) than mPFC (22%), but the mPFC proportion increased significantly after learning, eliminating the regional difference (iHP, 34%; mPFC, 37%). To examine population-level directional tuning, we applied neural manifold analysis to directional tuning curves of all neurons in a session. The manifolds exhibited ring-like structures in both regions, reflecting precise directional coding. Cross-region decoding confirmed increased structural similarity of iHP and mPFC manifolds after learning. Trial-by-trial analysis revealed that ring-like manifolds evolved faster in iHP than in mPFC. These results suggest that iHP is a major source of spatial representations to mPFC, highlighting their interaction in learning and utilizing cognitive map for goal-directed navigation.

Keywords : Intermediate hippocampus, Medial prefrontal cortex, Spatial navigation, Learning and memory, Virtual reality
Acknowledgements : This research was supported by the NationalResearch Foundation of Korea Grants 2019R1A2C2088799, 2021R1A4A2001803,2022M3E5E8017723, RS-2024-00452391. This work was supported by Mid-Career Bridging Program through Seoul National University.

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 12

Day 2 (August 25) **10:35-12:30** **Premier Ballroom A**

Diverse aspects of social behaviors: recognition, remembering, and reacting

Organizer : Yong-Seok Lee (Seoul National University)
Takashi Kitamura (University of Texas Southwestern Medical Center)
Moderator : Takashi Kitamura (University of Texas Southwestern Medical Center)
Yong-Seok Lee (Seoul National University)

Social memory representation in the hippocampus
Teruhiro Okuyama (The University of Tokyo)

Social and neural drivers of aggressive arousal and escalation of aggressive behavior
Aki Takahashi (University of Tsukuba)

Starved yet social: decoding why worms aggregate and swarm on food, instead of dispersing
Navneet Shahi (Indian Institute of Science) IBRO AWARDEE

Decoding the Valence of Developmental Social Behavior: Dopamine Governs Social Motivation Deficits in Autism
Ying Li (Chinese Institute for Brain Research)

Egocentric coding of social, object and spatial geometry in the anterior cingulate cortex
Takashi Kitamura (University of Texas Southwestern Medical Center)

S12-1

Social memory representation in the hippocampus

Teruhiro Okuyama

Institute for Quantitative Biosciences (IQB), The University of Tokyo, Tokyo, Japan

For social animals, the ability to recognize and remember individual conspecifics is essential for appropriate social behavior. Using a social discrimination test (SDT), we previously demonstrated that ventral CA1 (vCA1) pyramidal neurons in the hippocampus serve as a critical substrate for social memory, forming what is known as a social memory engram. Notably, even when social memory appears lost after prolonged separation, optogenetic activation of these engrams can fully restore it. In addition, vCA1 social memory neurons are preferentially reactivated during sharp-wave ripples (SPW-Rs), and the spike sequences of these replays reflect the temporal order of neuronal activity during theta cycles in social interactions. Disruptions in social memory, even minor ones, can significantly impair social behaviors, a phenomenon evident in humans. For example, individuals with autism spectrum disorder (ASD) often face difficulties in social memory or its downstream processes such as typical social communication. Recently, we revealed that dysfunction of the autism-associated Shank3 gene, induced by *in vivo* genome editing specifically in vCA1, results in social memory impairments. In ASD model Shank3 knockout (KO) mice, we observed a reduction in the proportion of social memory neurons and disruptions in neuronal ensemble spike sequences during SPW-Rs, which correlate with impairments in social discriminatory behavior.

Keywords : Social memory, Ventral CA1, Hippocampus, ASD, SPW-R

S12-2

Social and neural drivers of aggressive arousal and escalation of aggressive behavior

Aki Takahashi[1]

Institute of Human Sciences, University of Tsukuba, Tsukuba, Japan

Violent incidents in human society are often triggered by social instigation and stress. In many animal species, a brief encounter with a potential rival, known as social instigation or aggression priming, has been shown to escalate subsequent aggressive behavior. This procedure is thought to enhance an internal state called “aggressive arousal”, which causes escalation of aggressive behavior. Interestingly, the level of aggressive arousal is influenced by prior stress experiences. For example, male mice that experienced post-weaning social isolation stress show a greater increase in aggression following social instigation. We have also found that the characteristics of the instigator significantly affect the effectiveness of social instigation. The neural mechanism underlying aggressive arousal has been investigated, and we identified the involvement of the dorsal raphe nucleus (DRN) in male mice. In particular, excitatory input from the lateral habenula (LHb) to the DRN appears to mediate aggressive arousal induced by social instigation. Both optogenetic and chemogenetic inhibition of the LHb-DRN projection suppressed instigation-heightened aggression. In contrast, optogenetic activation of this pathway increased inter-male aggression. In this talk, we will discuss the social factors that promote aggressive arousal and escalate aggressive behavior in male mice, as well as the underlying excitatory and inhibitory neural mechanisms.

Keywords : Aggression, Social instigation, Dorsal raphe nucleus, Mouse
Acknowledgements : This study was supported by Japan Science and Technology Agency (JST) FOREST Program Grant Number JPMJFR214A, Japan Society for the Promotion of Science (JSPS) KAKENHI Grant Numbers 22K19744, 22H02660, and a research grant from the Astellas Foundation for Research on Metabolic Disorders.

S12-3 IBRO AWARDEE

Starved yet social: decoding why worms aggregate and swarm on food, instead of dispersing

Navneet Shahi[1], Nisha Kumari[1,2], Sharveri Khapre[1,3], Dimple Dahiya[1], Egemen Sarıtekin[4], Aşkın Kocabaş[4], Kavita Babu[1]

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[2]Department of Biology, KU Leuven, Leuven, Belgium, Belgium
[3]Centre for Neuroscience and Cell Biology, Universidade De Coimbra, Coimbra, Portugal, Portugal
[4]Physics, Koç University, Sarıyer/İstanbul, Türkiye, Turkey

The ability of animals to group or disperse is rarely random. It reflects a complex integration of diverse sensory, physiological, and environmental cues (1-2). In *Caenorhabditis elegans*, favourable conditions promote dispersal, while stressors like food depletion or overpopulation trigger aggregation (3). Here, we describe a distinct behaviour termed swarming, where *C. elegans* move and feed in aggregates along the food boundary despite abundant resource availability. While environmental factors are widely studied to influence this behaviour, the underlying genetic and molecular mechanisms remain unclear. In this study, we uncover a novel role for the conserved calsyntenin ortholog CASY-1 in regulating collective behaviour (4). *casy-1* mutants exhibit persistent swarming even in the presence of abundant food, ultimately leading to self-starvation, a phenotype resembling compulsive group-seeking (5). Given that Calsyntenins have been implicated in neuropsychiatric conditions such as autism (6), we investigated how CASY-1 controls social behaviour in *C. elegans*. We show that CASY-1 constrains swarming by maintaining a balance between two antagonistic neuromodulators: serotonin and PDF-1 (7). In *casy-1* mutants, impaired PDF-1 signalling results in disinhibition of serotonin activity, promoting a dwelling-like state and persistent aggregation. Notably, genetic and optogenetic activation of PDF-1 signalling, or disruption of serotonin signalling in *casy-1* mutants, suppresses this behaviour. As CASY-1 requires its C-terminal vesicular trafficking domain for this function, we propose that it regulates either PDF-1 neuropeptide release or the localisation of its receptor, PDFR-1. Further, we highlight the role of impaired mechanosensation in *casy-1* mutants in stabilising swarm aggregates, by reducing aversion between them. Together, our findings define a circuit-level mechanism by which CASY-1 integrates neuromodulatory and sensory cues to regulate collective behaviour.

Keywords : Swarming, CASY-1, Serotonin, Neuromodulation, C. elegans
Acknowledgements : Acknowledgements/References for the cited literature are as follows:
1. Anstey et al., 2009 (PMID: 19179529)
2. Demir et al., 2020 (PMID: 32250243)
3. Ding et al., 2019 (PMID: 31021320)
4. Ikeda et al., 2008 (PMID: 18381821)
5. M. Toth, 2019 (PMID: 30101538)
6. Ranneva et al., 2017 (PMID: 28647593)
7. Flavell *et al.*, 2013 (PMID: 23972393)

S12-4

Decoding the Valence of Developmental Social Behavior: Dopamine Governs Social Motivation Deficits in Autism

Ying Li

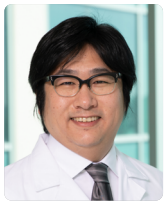
Chinese Institute for Brain Research, Beijing 102206, China.

The social motivation theory posits that core social deficits in autism spectrum disorder (ASD) arise from impaired social valence assignment during the social critical period, yet the specific dopaminergic mechanisms governing this process remain unclear. We combined high-resolution behavioral sequencing (Social-seq) with fiber photometry to resolve nucleus accumbens (NAc) dopamine during naturalistic juvenile interactions. Sex-divergent social strategies emerged: males exhibited peer play-dominant interactions with action-contingent dopamine release, while females favored environmental exploration with attenuated social dopamine. Shank3-deficient juveniles exhibited a triad of dopaminergic dysregulation—blunted signaling during social investigation, pathological inversion during active play, and hyper-responsive to non-social stimuli—recapitulating ASD-like phenotypes. Closed-loop activation of dopamine during play rescued social deficits, establishing a causal link between phasic dopaminergic signaling and social motivation. These findings identify NAc dopamine as a dynamic encoder of social valence and suggest that temporally precise modulation of dopaminergic circuits may offer therapeutic leverage for ASD-related social impairments.

Keywords : Autism, Social play, Social motivation, Dopamine, Deep-learning

S12-5

Egocentric coding of social, object and spatial geometry in the anterior cingulate cortex



Takashi Kitamura

Psychiatry, University of Texas Southwestern Medical Center, Dallas, USA

Animals perform action as a motor output in the self-perspective. For this to happen, the allocentric spatial map is transformed into an egocentric spatial map, and is then used by the animals to perform motor action by the secondary motor cortex (M2). Retrosplenial Cortex (RSC) is implicated in the transformation of allocentric to egocentric framework. However, it remains unclear how the information in the egocentric map is transformed for action. Anatomical studies have shown that Anterior Cingulate Cortex (ACC) receives input from RSC and is projected to M2 and is responsive to objects and social cues. These results suggest that ACC could be the site for map to action transformation. Therefore, we hypothesize that ACC could encode a wide variety of geometric features in egocentric fashion. To study the representational schema of the ACC, we expressed GCaMP6f in the ACC neurons using AAV infection and implanted a GRIN lens to monitor calcium activity in the ACC during spatial navigation. We demonstrated that a subset of ACC neurons encode border, convex and concave corners, doors to the compartment, object and social cue. We also observed that a majority of such geometry-encoding cells exhibits egocentric response. Importantly, these representations require multiple exposure to the environment for more than 2 weeks. Our data suggests that the ACC is potentially acting as a gateway to successful motor output by representing geometric features on the environment and the objects in an egocentric fashion, much like a contour map which provides a ‘birds eye view’ of the space to the animal.

Keywords : memory, spatial representation

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 13

Day 2 (August 25) **10:35-12:30** **Premier Ballroom B**

Synapse function and diseases

Organizer : Jun Xia (Hong Kong University of Science and Technology)
Moderator : Jun Xia (Hong Kong University of Science and Technology)

Synaptic RNA localisation and protein compositions in focal epilepsy
Julie Qiaojin Lin (Hong Kong University of Science and Technology)

Synaptic plasticity and memory dynamics
Akihiro Goto (Kyoto University)

Temporal dynamics of synapse remodeling, gliosis, and lipidomic alterations in seizure evolution of a mouse model of west syndrome
Kihoon Han (Korea University)

Transsynaptic mechanisms of synaptic inhibition
Jaewon Ko (Daegu Gyeongbuk Institute of Science and Technology)

Role of novel neuroligin-2 associated protein in inhibitory synapse formation and function
Jun Xia (Hong Kong University of Science and Technology)

S13-1

Synaptic RNA localisation and protein compositions in focal epilepsy

Zixin Sun, Julie Qiaojin Lin

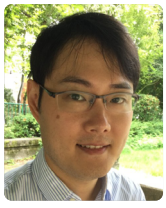
Bioscience and Biomedical Engineering Thrust, Systems Hub, Hong Kong University of Science and Technology (Guangzhou), Guangzhou, China

Focal epilepsy involves recurrent seizures originating from specific brain regions like the temporal lobes, driven by neuronal hyperexcitability and hypersynchronization. If left unstreated, this aberrant activity disrupts synaptic proteostasis and leads to drug-resistant epilepsy in over 30% of patients. Recent evidence indicates altered synaptic localization of mRNAs encoding disease-associated proteins in focal epilepsy, suggesting perturbations in synaptic mRNA localization and local translation within affected neurons. This study investigates whether abnormal electrical activity disrupts localized protein synthesis at epileptic foci, contributing to irreversible neuronal damage.
We analyzed synaptic mRNA and protein compositions in focal epilepsy using surgically resected frontal or temporal lobe tissues. Intraoperative electrophysiological mapping identified epileptic foci and adjacent non-focal regions. Synaptosome-enriched fractions were isolated via sucrose gradient centrifugation. Comparative transcriptomics and proteomics of synaptic fractions and whole tissues revealed significantly more mRNAs and proteins exhibiting cross-region differential expression within synapses compared to tissue homogenate, indicating synapses bear a substantial pathological burden during seizures. Specifically, synaptosomes from focal regions showed upregulated transcripts and proteins related to synaptic vesicles and mitochondrial structure/function. Notably, several transcripts enriched in focal epileptic synapses are known to undergo local translation, suggesting potential differential local translation between focal and non-focal regions.
Collectively, these findings elucidate specific synaptic molecular alterations associated with focal epilepsy, highlighting the synapse as a critical site of pathology. The results provide a foundation for developing therapeutic strategies targeting dysregulated synaptic mRNA translation.

Keywords : focal epilepsy, RNA localization, local protein synthesis, synapse, hyperexcitability

S13-2

Synaptic plasticity and memory dynamics



Akihiro Goto[1,2]

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[2]Thrust of Bioscience and Biomedical Engineering, Hong Kong University of Science and Technology(GZ), Guangzhou, China

Animals learn about their external environment and then take adaptive action based on that knowledge. During this process, new neural circuits are formed and adaptive behaviour is acquired by strengthening or weakening the synapses between specific neurons. This restructuring of neural circuits involves synaptic plasticity and associated changes in gene expression across multiple brain regions. However, the precise mechanisms underlying these processes are not fully understood.
Long-term potentiation (LTP) is a well-characterised phenomenon whereby the connection between neurons is strengthened in the long term. A recently developed optogenetic technique utilising chromophore-assisted laser inactivation (CALI) enables the selective and reversible cancellation of LTP using light (Goto et al., Science, 2021). Using this technique, our aim is to identify the brain regions and temporal dynamics involved in LTP induction. Specifically, we will investigate when and where LTP occurs following learning and during the updating of episodic memory across different memory-related brain regions.
Furthermore, gene expression plays a crucial role in synaptic plasticity. For instance, the expression of nuclear ERK activity accompanies LTP. By measuring such molecular markers after learning, we can examine the involvement of specific neuronal populations in memory processing. To this end, we have developed a fibre-bundle microendoscope experimental system that enables long-term FRET imaging in the brains of freely moving mice. Additionally, we perform simultaneous recordings across multiple brain regions using a multi-fibre system. Through these investigations, we aim to elucidate the role of synaptic plasticity in memory dynamics.

Keywords : Synaptic plasticity, CALI, FRET, episodic memory, LTP

S13-3

Temporal dynamics of synapse remodeling, gliosis, and lipidomic alterations in seizure evolution of a mouse model of West syndrome

Kihoon Han[1,2]

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[2]BK21 Graduate Program, Department of Biomedical Sciences, Korea University College of Medicine, Seoul 02841, Republic of Korea

Neurodevelopmental disorders can have long-lasting effects, causing not only early pediatric symptoms but also a range of neurological issues throughout adulthood. West syndrome is a severe neurodevelopmental disorder marked by infantile spasms, an early symptom that typically subsides with age. However, many patients progress to other seizure forms, known as seizure evolution, which is closely linked to poor long-term outcomes. Despite its clinical significance, the neurobiological mechanisms behind seizure evolution in West syndrome remain poorly understood. Recent genetic studies have consistently identified the *CYFIP2* p.Arg87Cys variant in West syndrome patients, and the *Cyfip2*$^{+/R87C}$ mouse model carrying this mutation has been shown to recapitulate key symptoms of the disorder, including infantile spasms. In this study, we aimed to gain deeper insight into seizure evolution by conducting longitudinal deep phenotyping of the *Cyfip2*$^{+/R87C}$ mouse model from the neonatal stage to seven months of age. We tracked seizure activity through behavioral and EEG recordings and employed multi-omic analyses, including tissue and single-cell level transcriptomics, ultrastructural analysis, proteomics, and lipidomics, to capture a comprehensive view of molecular and cellular changes. Our results showed that after an initial period of neonatal spasms, *Cyfip2*$^{+/R87C}$ mice entered a seizure-free phase, followed by spontaneous recurrent seizures in adulthood, ultimately leading to premature death. This progression was associated with synaptic remodeling, sequential activation of different glial cell types, lipid droplet accumulation in astrocytes, and significant proteomic and lipidomic changes in the brain. These findings suggest that seizure evolution in West syndrome involves complex, time-dependent interactions between neurons and glial cells, along with alterations in lipid metabolism.

Keywords : West syndrome, Seizure evolution, CYFIP2 Arg87Cys, Gliosis, Lipidome

S13-4

Transsynaptic mechanisms of synaptic inhibition

Jaewon Ko

Center for Synapse Diversity and Specificity, Department of Brain Sciences, Daegu Gyeongbuk Institute of Science and Technology (DGIST), Daegu, Republic of Korea

Synapses serve as fundamental information units of the brain, enabling the formation and precise regulation of intricate neural circuits. Synaptic cell-adhesion molecules (CAMs) are central organizers, orchestrating the structural alignment of pre- and postsynaptic membranes and coordinating the assembly of their respective machinery. These processes are essential for instructing cell-type specificity, neuronal specification, and the remarkable diversity of individual synapse functions. Over recent years, my laboratory has focused on identifying key synaptic CAMs and dissecting the mechanisms by which they sculpt distinct synaptic signaling pathways. Our hypothesis is that the number, location, and specific properties of diverse synapses are dictated by precise interactions between pre- and postsynaptic CAMs and their associated signaling molecules—a concept we term the molecular blueprint of neural circuit architecture. In this talk, I will present our latest studies that uncover the multipartite molecular complexes controlling transsynaptic inhibition, highlighting their broader implications for understanding the fundamental principles of neural circuit design.

Keywords : Synaptic inhibition, Synaptic adhesion, Amyloid precursor protein

S13-5

Role of Novel Neuroligin-2 Associated Protein in Inhibitory Synapse Formation and Function

Jun XIA

The Hong Kong University of Science and Technology (Guangzhou)

Synapses are highly specialized structures where one neuron contacting another neuron. There are two major types of synapses, the excitatory and inhibitory synapses, based on the types of neurotransmitters released from presynaptic terminals and neurotransmitter receptors at the postsynaptic terminals. In the brain, the excitatory synaptic transmission is mainly mediated by glutamate and its receptors, while the inhibitory synaptic transmission is mainly mediated by GABA and its receptors. The molecular mechanism responsible for the recruitment and regulation of receptors at postsynaptic terminal is not fully understood. Neuroligins, a family of transsynaptic cell adhesion molecules, were found to localize at synapses and capable of inducing synapse formation. Interestingly, different neuroligins were found to induce the formation of difference synapses. For example, neuroligin-1 was found to induce the formation of excitatory synapses, while neuroligin-2 induces the formation of inhibitory synapses. To provide insight into the formation and regulation of inhibitory synapses, we performed an extensive proteomic analysis of synaptic proteins by immunoprecipating proteins associating with different neuroligins. We identified a number of proteins that specifically located at different synapses. Detailed analysis found that some of these proteins are critical for synapses formation, maintaining excitatory and inhibitory synapses balance, and neuronal network activity. Their deficiency could lead to abnormal synaptic transmission and potential brain disorders.

Keywords : Neuroligin, Synapse, Inhibitory Synapse, Epilepsy, Autism

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 14

Day 2 (August 25) **10:35-12:30** **Premier Ballroom C**

Decoding the cerebellum in health and disease

Organizer : Kazuo Kitamura (University of Yamanashi)
Moderator : Kazuo Kitamura (University of Yamanashi)

Targeting the Cerebellum to Improve Parkinson's Disease Motor Deficits: Mechanisms and Clinical Implications
Jing-Ning Zhu (Nanjing University)

A cerebellar internal model for temporal prediction of rhythms
Masaki Tanaka (Hokkaido University)

Temporal dynamics of Purkinje cell-intrinsic excitability govern cerebellar systems consolidation
Sang Jeong Kim (Seoul National University)

Cerebellar Purkinje cell firing alterations contributes to aging-related declining motor coordination in mice
Alanna Watt (Mcgill University)

S14-1

Targeting the Cerebellum to Improve Parkinson's Disease Motor Deficits: Mechanisms and Clinical Implications

Xiao-Yang Zhang, Jing-Ning Zhu

School of Life Sciences, Nanjing University, China, China

While the cerebellum's role in Parkinson's disease (PD) has been historically underappreciated, emerging evidence highlights its reciprocal connections with the basal ganglia and potential involvement in PD pathophysiology. Here, we demonstrate that cerebellar nuclei send direct glutamatergic projections to dopaminergic neurons in the substantia nigra pars compacta (SNc), effectively ameliorating motor deficits in a PD rat model. Notably, low-frequency repetitive transcranial magnetic stimulation (rTMS) targeting the cerebellar cortex, which exerts strong inhibitory control over the cerebellar nuclei, produces sustained motor improvement in both Parkinsonian rats and human patients. Mechanistically, cerebellar rTMS may enhance dopaminergic neuron plasticity and survival via activation of the cerebello-nigral pathway. Our findings identify the cerebellum as a potent non-invasive neuromodulation target for PD, offering a novel circuit-based therapeutic paradigm.

Keywords : Cerebellum, Basal ganglia, Substantia nigra, Parkinson's disease, TMS
Acknowledgements : Supported by grants 32030044, 32171012, 82101332, 32200948, and 323B1008 from the National Natural Science Foundation of China; Project STI2030-Major Projects-2021ZD0202805 from the Ministry of Science and Technology of China; grant BK20240168 from the Natural Science Foundation of Jiangsu Province; and grants LNSN-202402, 020814380197, 020814380208, 2024300475 from Nanjing University.

S14-2

A cerebellar internal model for temporal prediction of rhythms

Masaki Tanaka

Physiology, Hokkaido University, Sapporo, Japan

Recent evidence suggests that the cerebellum contributes to a range of non-motor cognitive functions, but the underlying mechanisms remain largely unknown. To address this, we are investigating the role of the cerebellum in rhythm perception using non-human primates. During rhythm perception, the brain is believed to generate an internal model of the repeated stimuli, enabling precise timing predictions that facilitate the detection of rhythm changes and support motor synchronization. In our task, animals were trained to make an eye movement in response to the omission of regularly flashing visual stimuli. To detect a missing flash, they needed to learn the stimulus tempo, predict the next flash, and prepare an eye movement. We found that neurons in the cerebellum (dentate nucleus) and striatum (caudate nucleus), both linked to rhythm perception, showed periodic activity during the task. When the stimulus location and saccade target were varied independently, cerebellar neurons reflected stimulus location, whereas striatal neurons were modulated by the direction of planned movement. Moreover, when monkeys used either eye or hand movements to report omissions, many striatal neurons altered the periodic activity depending on the movement type, but cerebellar neurons did not. These findings suggest that, during rhythm perception, the cerebellum encodes sensory prediction, while the striatum supports motor preparation. Consistent with this, optogenetic manipulation of dentate nucleus activity impaired the detection of subtle changes in stimulus timing. Because Purkinje cells in the crus lobules, which project to the dentate nucleus, exhibited periodic simple and complex spike activity, plastic changes in the cerebellar cortex may play a role in forming internal models.

Keywords : Rhythm perception, Internal model, Temporal predition, Cerebellum, Non-human primate
Acknowledgements : Supported by JST-CREST (JPMJCR23P3) and MEXT (24H00064).

S14-3

Temporal dynamics of Purkinje cell-intrinsic excitability govern cerebellar systems consolidation

Sang Jeong Kim

Physiology, Seoul National University College of Medicine, Seoul, Republic of Korea

Systems consolidation, essential for long-term memory formation, orchestrates the reorganization of newly encoded memories from cortical networks into downstream circuits. Although synaptic mechanisms have been extensively characterized, the role of neuronal intrinsic excitability (IE) in this process remains relatively unexplored. Here, we utilized the optokinetic reflex, a representative cerebellum-dependent learning model, to investigate the causal link between neuronal IE and memory consolidation. By employing optogenetic manipulation of Purkinje cells (PCs), the sole output of the cerebellar cortex, we identified a crucial 90-minute post-learning window during which PC-IE typically undergoes a transient depression. Importantly, when optogenetic stimulation disrupted this natural decline by artificially elevating PC-IE, long-term memory formation was hindered; interventions outside this timeframe did not affect memory retention. Notably, abnormal PC-IE also did not alter basal ocular reflexes, indicating that its essential role is confined to adaptive states during consolidation rather than non-adaptive, basal conditions. Furthermore, elevated PC-IE eliminated the learning-induced intrinsic plasticity in flocculus-targeting neurons (FTNs) within the medial vestibular nucleus (MVN), a key downstream circuit involved in long-term memory storage. These findings underscore the precise temporal dynamics of IE as a critical mechanism in systems consolidation, emphasizing its vulnerability to disruptions.

Keywords : Memory, Consolidation, Optokinetic reflex, Purkinje cell, Intrinsic excitability

S14-4

Cerebellar Pu rkinje cell firing alterations contributes to aging-related declining motor coordination in mice

Eviatar Fields, Alanna Watt

Biology, McGill University, Montreal, Quebec, Canada

Aging is associated with the decline of many bodily functions including motor coordination. Aging-related impairment in motor coordination can result in falls, which reduce independence, health span and quality of life in the elderly. Consistent with this, we observed a progressive decline in motor coordination in aged mice on multiple motor coordination assays. The cerebellum is critically involved in motor coordination and balance, and cerebellar Purkinje cells play an important role in modulating motor output and coordinated movements. Purkinje cells fire high-frequency and high-regularity action potentials in healthy young adult mice. We wondered whether this firing remained stable across lifespan in aging mice. We performed juxtacellular recordings from Purkinje cells in acute cerebellar slices and observed a reduction in the rate of firing in aged animals without changes in firing regularity. To understand if reduced Purkinje cell firing rate caused impaired motor performance in aged mice, we used chemogenetics to modulate Purkinje cell firing. Reducing Purkinje cell firing rates in young mice impaired motor performance, while elevating Purkinje cell firing rates in aged mice improved motor performance. Our results suggest that Purkinje cell firing rate impacts motor coordination and that the aging-related reduction of Purkinje cell firing rate we observed contributes to impaired motor coordination and could contribute to declining health span and quality of life in the elderly.

Keywords : Cerebellum, Purkinje, Optogenetics, Aging

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 15

Supported By 아주대학교 의과대학 뇌질환융합연구센터

Day 2 (August 25) **10:35-12:30** **Rm.113-115**

Integrative approaches to neurodegeneration: insights from multiomics, inflammation, and cellular pathways

Organizer : Alexa Woo (Case Western Reserve University)
Moderator : David Kang (Case Western Reserve University)

Oligodendrocytes, a major contributor to aging and Parkinson's disease: Single-nuclei multiomic approach of human midbrain
Yoon-seong Kim (Rutgers, The State University of New Jersey)

Targeting the Resolution of Neuroinflammatory Signaling in Synucleinopathies.
Jae-Kyung Jamise Lee (University of Georgia)

Coniferaldehyde confers neuroprotection by restoring PKM2 and inhibiting JAK2/STAT3 in a 3-NP-induced Huntington's disease mouse mode
Ayooluwa Gabriel Ibiayo (Tzu Chi University) IBRO AWARDEE

Mitophagy and mitochondrial proteostasis: role of CHCHD10 in ALS and FTD
David Kang (Case Western Reserve University)

CHCHD2 dysfunction links the mitochondria-lysosome axis to proteinopathy and brain aging.
Alexa Woo (Case Western Reserve University)

S15-1

Oligodendrocytes, a major contributor to aging and Parkinson's disease: Single-nuclei multiomic approach of human midbrain

Yoon-Seong Kim[1], Levi Adams[1,2], Min-Kyung Song[1,3], Inhye Jeong[1], Yoshiaki Tanaka[4]

[1]Neurology, Rutgers University, Piscataway, NY, USA
[2]Biology, Bates College, Lewiston, ME, USA
[3]Nursing Science, Kyunghee University, Seoul, Republic of Korea
[4]Medicine, University of Montreal, Quebec, Canada

Aging is the primary risk factor for Parkinson's disease (PD), yet its effects on gene expression and chromatin regulation in the human brain remain poorly defined. Here, we present a single-nuclei multiomic analysis of postmortem midbrain tissue from young (n=9), aged (n=8), and PD (n=14) donors, profiling 69,289 high-quality nuclei. By integrating single-nuclei RNA-seq and ATAC-seq data, we constructed a combined pseudopathogenesis (cPP) trajectory to track molecular alterations across aging and disease progression.

We found that all major glial cell types are affected by aging, with microglia, oligodendrocytes, and oligodendrocyte precursor cells (OPCs) showing further perturbations in PD. In the substantia nigra, we identified three transcriptionally distinct oligodendrocyte subpopulations, including a novel disease-associated subtype with a high cPP score. Genes such as CARNS1 and RBFOX1 were altered by both aging and PD, while QDPR and SELENOP exhibited PD-specific dysregulation. These findings were validated using RNA-FISH in human substantia nigra tissue.

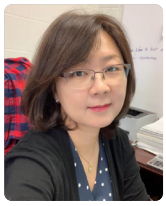
Peak-to-gene linkage analysis identified 89 PD-associated SNP loci with cell-type–specific regulatory changes, including five within the MAPT locus enriched in disease-associated oligodendrocytes. CellChat analysis revealed extensive remodeling of cell–cell communication networks during aging and PD.

Our results reveal cell-type–specific epigenomic and transcriptomic changes in the aging midbrain and uncover a previously unrecognized role for oligodendrocytes and OPCs in PD pathogenesis, highlighting their potential contribution to disease vulnerability and progression.

Keywords : Aging, Oligodendrocytes, OPC, Parkinson's disease, single-cell
Acknowledgements : This work is supported by NIH 1R01-NS100919, 1RF1-NS128607, and Rutgers Robert Wood Johnson Medical School Fund

S15-2

Targeting the Resolution of Neuroinflammatory Signaling in Synucleinopathies.



Jae-Kyung 'Jamise' Lee

Physiology and Pharmacology, University of Georgia, ATHENS, GA, USA

To advance understanding of the interplay between peripheral immune cells and α-synuclein (α-syn) pathology, this study focuses particularly on natural killer (NK) cells, a subset of innate immune lymphocytes. We previously demonstrated that NK cells are present in the brain parenchyma of individuals with Parkinson's disease (PD) and have the capacity to clear aggregated α-syn. In a preclinical mouse model of PD, depletion of NK cells worsened motor symptoms and increased α-syn pathology, suggesting a protective role for these cells. Here, we investigated whether systemic infusion of NK cells could mitigate α-syn pathology, neurodegeneration, and neuroinflammation in M83 transgenic mice using the PFF α-syn model. Mice received intrastriatal injections of recombinant PFF α-syn followed by systemic NK cell transfers. Motor deficits were assessed using clasping tests, and pathological outcomes were evaluated by quantifying phosphorylated α-syn (pSer129) and dopaminergic neuron loss. Our results demonstrated that NK cell treatment improved motor performance, reduced α-syn aggregation in the substantia nigra pars compacta (SNpc) and brainstem, and attenuated dopaminergic neurodegeneration. Mass cytometry (CyTOF) immune profiling revealed decreased CNS immune cell infiltration and dampened neuroinflammation, without evidence of aberrant peripheral immune activation. These findings indicate that NK cells can actively resolve neuroinflammation and limit α-syn pathology, supporting their potential as a novel immunotherapeutic strategy for PD.

Keywords : NK cells, neuroinflammation, α-synuclein, Parkinson's disease, immunotherapy
Acknowledgements : This study was supported by MJFF Research Grant ID MJFF-019068 and NIH/NINDS R01NS119610-01.

S15-3 IBRO AWARDEE

Coniferaldehyde confers neuroprotection by restoring PKM2 and inhibiting JAK2/STAT3 in a 3-NP-induced Huntington's disease mouse mode

Ayooluwa Gabriel Ibiayo[1], Peeraporn Varinthra[1], Mukundan Nagarajan[2], Ingrid Y Liu[1]

[1]Institute of Medical Sciences, Tzu Chi University, Hualien, Taiwan
[2]Molecular Biology and Human Genetics, Tzu Chi University, Hualien, Taiwan

Huntington's disease (HD) is a devastating neurodegenerative disorder characterized by progressive motor decline and neuronal loss, lacking effective disease-modifying therapies. The neurotoxin 3-nitropropionic acid (3-NP) is widely used to model HD pathologies. Coniferaldehyde (CFA) is a naturally occurring phenolic compound derived from dietary and medicinal plants, recognized for its anti-inflammatory, antioxidant, and free radical-scavenging properties. While its neuroprotective potential has been demonstrated in several disease models, its role in 3-NP-induced HD-like pathology remains undetermined. This study investigates CFA's potential as a disease-modifying neuroprotective agent in a 3-NP mouse model of HD, focusing on its underlying Janus kinase 2/signal transducer and activator of transcription 3 (JAK2/STAT3)-linked oxidative, metabolic, and inflammatory mechanisms. Neurological deficits, including motor coordination, were assessed by rotarod and open-field tests. Histological endpoints included Nissl and TUNEL staining for neuronal integrity and apoptosis, DHE fluorescence for ROS, and immunofluorescence for IL-6 and PKM2. In silico docking examined CFA's binding to STAT3, and Western blot quantified p-STAT3, GFAP, IL-1β, and iNOS levels in striatal lysates. CFA treatment improved 3-NP-induced motor deficits and preserved striatal neuron morphology, with a reduction in TUNEL-fluorescence intensity. CFA attenuated ROS accumulation, restored PKM2 expression, modulated astrocytic GFAP upregulation, and reduced inflammatory markers (IL-6, IL-1β, and iNOS). Molecular docking revealed high-affinity interactions of CFA within STAT3 domains, and CFA treatment decreased JAK2-mediated Tyr705 phosphorylation of STAT3. These findings demonstrate that CFA targets interconnected oxidative, metabolic, and inflammatory pathways, supporting its potential as a disease-modifying therapeutic candidate for HD.

Keywords : Coniferaldehyde, Huntington's disease, JAK2/STAT3 signaling, PKM2, Neuroinflammation

S15-4

Mitochondrial proteostasis and mitophagy: Role of CHCHD10 in ALS and FTD

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Mutations in CHCHD10 are associated with ALS-FTD spectrum disorders, which are characterized by cytoplasmic TDP-43 pathology. TDP-43 inclusions and FTD/ALS-linked CHCHD10 mutations similarly induce mitochondrial defects in respiration, fusion/fission, mtDNA stability, and cristae structure. In this study, utilizing CHCHD10 transgenic mouse variants (WT, R15L, & S59L), TDP-43 transgenic mice, human FTLD-TDP brains, isolated mitochondria, and recombinant proteins, we present in vivo evidence that CHCHD10 mutations drive disease-pertinent impairments in long-term synaptic plasticity and motor unit function, which are underpinned by CHCHD10 and phospho-TDP-43 pathologies originating from CHCHD10-mediated mitochondrial proteostasis and mitophagy. CHCHD10 colocalizes with phospho-TDP-43 in brains of mutant CHCHD10 transgenic mice and human FTLD-TDP patients, and insoluble CHCHD10 tightly correlates with insoluble TDP-43 in human brains. In vitro, recombinant CHCHD10 S59L enhances the size of TDP-43 aggregates, whereas recombinant CHCHD10 WT reduces TDP-43 aggregate size. Accordingly, CHCHD10 WT expression significantly mitigates TDP-43 pathology in TAR4 mice and rescues TDP-43-induced impairments in synaptic integrity and long-term synaptic plasticity. Additionally, we demonstrate that ALS/FTD-linked CHCHD10 mutations impair mitophagy flux and mitochondrial Parkin recruitment, whereas wild-type CHCHD10 (CHCHD10 WT) enhances these measures. Specifically, CHCHD10 R15L and CHCHD10 S59L mutations reduce PINK1 levels by increasing PARL activity, whereas CHCHD10 WT produces the opposite results through its stronger interaction with PARL, suppressing its activity. Importantly, FTD brains with TDP-43 pathology demonstrate disruption of the PARL-PINK1 pathway and that experimentally impairing mitophagy promotes TDP-43 aggregation. Thus, we provide herein new insights into mechanisms of ALS-FTD pathogenesis by CHCHD10 through both mitochondrial proteostasis and mitophagy.

Keywords : Mitophagy, Mitochondria, CHCHD10, Amyotrophic lateral sclerosis (ALS), Frontotemporal dementia (FTD)

S15-5

CHCHD2 dysfunction links the mitochondria-lysosome axis to proteinopathy and brain aging.

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Mutations in CHCHD2 are associated with Lewy body disorders (LBDs), including Parkinson's disease (PD). While the PD-linked CHCHD2 T61I mutation induces age-related PD-like phenotypes, the role of wild type (WT) CHCHD2 during brain aging remains unclear. Here, we demonstrate that CHCHD2 declines with age and that CHCHD2 WT expression protects against age-related neuroinflammation, dopaminergic neuron loss, insoluble protein accumulation, and aberrant mitochondrial and lysosomal ultrastructure. By contrast, CHCHD2 T61I accelerates such age-related phenotypes together with axonal degeneration and cognitive deficits. Mechanistically, we identify the mitochondria-lysosome axis, including lysosomal proteases cathepsin B (CTSB) and cathepsin L (CTSL), as critical players in CHCHD2-related changes. CHCHD2 T61I preferentially binds CTSB and CTSL and reduces their levels, inducing lysosomal membrane permeability and impairing a-synuclein fibril clearance. In humans, CTSB declines with CHCHD2 in LBD brains. Overall, these findings implicate CHCHD2 as a critical regulator of neuronal resilience to aging and disease through the mitochondria-lysosome axis.

Keywords : chchd2, mitochondria, lysosome, Parkinson's disease, Lewy body disease

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 16

Day 2 (August 25) **10:35-12:30** **Rm.116-118**

Recent advances in functional observation of ion channels and synaptic transmission

Organizer : Byung-Chang Suh (Daegu Gyeongbuk Institute of Science and Technology)
Moderator : Byung-Chang Suh (Daegu Gyeongbuk Institute of Science and Technology)
Yasushi Okamura (Osaka University)

In vivo and in vitro studies on turnover of voltage-gated ion channels at the axon initial segments of mammalian neurons
Yasushi Okamura (Osaka University)

Unique short-term synaptic plasticity between human cortical pyramidal neurons compared to other mammalian species such as mouse and non-human primate
Mean-Hwan Kim (Daegu Gyeongbuk Institute of Science and Technology)

Towards understanding GABAergic synaptic signaling
Ji Won Um (Daegu Gyeongbuk Institute of Science and Technology)

The ion channels modulating the reward circuit in the nucleus accumbens
Se-Young Choi (Seoul National University)

S16-1

In vivo and in vitro studies on turnover of voltage-gated ion channels at the axon initial segments of mammalian neurons

Daisuke Yoshioka[1], Kohei Yamamoto[1], Takafumi Kawai[1], Kenji Sakimura[2], Manabu Abe[2], Yoshifumi Okochi[1], Yasushi Okamura[1]

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The axon initial segment (AIS) is crucial for triggering action potentials and controlling neuronal excitability. It contains a high density of voltage-gated sodium and potassium channels, and sometimes GABA(A) receptors, receiving input from inhibitory neurons. AIS structure is flexible—its length and position can change depending on neural activity, disease, or aging. However, how its structure and ion channels are regulated is still not well understood.
To explore this, we studied how ion channels cluster at the AIS. Using genetic and imaging techniques, we examined the membrane expression of KCNQ2/3 and Nav1.6 channels in mouse neurons. We introduced a Halo-tagged KCNQ3 subunit into hippocampal neurons and found that a mutant with reduced activity was less targeted to the AIS. This suggests that KCNQ2/3 channel activity may influence its localization to the AIS.
We also investigated Nav1.6 channel turnover using a mouse model that distinguishes newly made proteins by fluorescent color changes. Our latest data show how Nav1.6 turnover varies over time and space, both in cell cultures and in living mice.

Keywords : voltage-gated sodium channel, KCNQ2/3 channel, axon initial segment, protein turnover

S16-2

Unique short-term synaptic plasticity between human cortical pyramidal neurons compared to other mammalian species such as mouse and non-human primate

Mean-Hwan Kim

Dept. of Brain Sciences, DGIST, Daegu, Republic of Korea

Evolutionary expansion of supragranular layers (i.e., Layers 2/3) in mammalian cortex is one of hallmark features to explain unique human intelligence such as creativity and social interaction. Six-layered mammalian cortex is composed of numerous cortical columns, where each column is functioning as individual modules to compute different cognitive tasks. Circuits dynamics within cortical column are governed by 1) local synaptic connections between multiple cell types in excitatory pyramidal and inhibitory interneurons, and 2) their short-term synaptic dynamics with circuit motifs such as recurrent excitation, and feedback inhibition, etc.
In this presentation, I will demonstrate short-term synaptic dynamics between excitatory pyramidal neurons, from excitatory to fast-spiking inhibitory interneurons respectively in layer 2/3 human cortex compared to mouse (temporal area, and V1) and non-human primate cortices (inferior temporal gyrus). Based on our finding of species-specific synaptic plasticity (i.e., temporal dynamics), we are currently building a computational model to provide mechanical understanding of species differences.

Keywords : evolution, cerebral cortex, cortical column, synaptic transmission, plasticity

S16-3

Towards understanding GABAergic synaptic signaling

JI WON UM[1,2]

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Synapses, the fundamental units of neural circuits, are essential for transferring, processing, and computing information in the brain. A precise balance between synaptic excitation and inhibition is crucial for proper brain function, and disruption of this balance has been implicated in various neurological disorders, including autism spectrum disorders (ASDs). In this talk, I will present recent findings that highlight collybistin, a GABAergic synapse-specific signaling protein, as a potential ASD causative factor. Novel mutations in the *ARHGEF9* gene encoding collybistin have been identified in individuals with ASD, underscoring its clinical relevance. Our data demonstrate that collybistin-mediated inhibitory synaptic function in the medial prefrontal cortex is critical for proper phosphorylation of gephyrin—a key scaffolding protein at inhibitory synapses—and for regulating ultrasonic communication in mice. We further show that ASD-associated collybistin mutations disrupt these processes, providing a mechanistic link between GABAergic synaptic dysfunction and behavioral phenotypes. These findings offer new insights into the molecular underpinnings of ASDs and suggest promising strategies for therapeutic intervention.

Keywords : GABAergic synapse, Gephyrin, Collybistin, Autism spectrum disorder, Phosphorylation

S16-4

The ion channels modulating the reward circuit in the nucleus accumbens

Se-Young Choi

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The nucleus accumbens (NAc) plays a pivotal role in reward-related behaviors, including motivation and decision-making, and is often referred to as the brain's "pleasure center." Consequently, the modulation of synaptic transmission of neural circuits connecting the NAc to higher-order neurons is believed to be crucial for memory and behaviors associated with reward and addiction. Given this, unidentified modulators that influence ion channel activity and synaptic transmission of the NAc neurons have garnered considerable attention. Recently, we demonstrated that both the knockdown of TRPA1 expression in the NAc and pharmacological inhibition of TRPA1 activity led to a reduction in drug-seeking behavior and reward responses in cocaine-exposed mice. We found that the neuronal activity of D1R-expressing medium spiny neurons is essential for the impact of TRPA1 KD on cocaine-CPP and synaptic transmission in the NAc core. Additionally, we observed that acetylcholine plays a regulatory role in effort-based motivated and reward behaviors, functioning as a modulator of NAc circuits via its effects on D1R-expressing medium spiny neurons. These findings offer new insights into the mechanisms linking ion channels to cocaine-induced reward behaviors and underscore the importance of ion channels as key regulators of reward processing, motivation, and addiction-related behavior.

Keywords : Ion channel, nucleus accumbens, synaptic transmission, reward circuit, addiction

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Symposium 17

Day 2 (August 25) **10:35-12:30** **Rm.204-205**

Transforming brain networks - neuromodulation strategies for neuropsychiatric disorders

Organizer : Hyang Woon Lee (Ewha Womans University)
Hao-Li Liu (National Taiwan University)
Moderator : Hao-Li Liu (National Taiwan University)

From bench to bedside - advancing neuromodulation therapy for intractable epilepsy
Hyang Woon Lee (Ewha Womans University)

Bidirectional neuronal control of epileptiform activities by repetitive transcranial focused ultrasound
Jinhyoung Park (Sungkyunkwan University)

Personalized virtual brain modeling to optimize brain stimulation towards clinical applications
Sora An (Ewha Womans University)

Focused ultrasound Neuromodulation for Epilepsy Treatment
Hao-Li Liu (National Taiwan University)

Human nerve tissue engineering approach for developing aging model: a novel tool for high-throughput screening of anti-aging molecules
Varsha Pai V (Manipal Centre for Biotherapeutics Research) IBRO AWARDEE

S17-1

From bench to bedside - advancing neuromodulation therapy for intractable epilepsy

Hyang Woon Lee

Ewha Womans University

Epilepsy, characterized by abnormal and excessive neural activity, presents a significant challenge in neurology, especially when it fails to respond to conventional medical treatments. This talk will introduce the ongoing field of seizure network modeling and the promising neuromodulation therapy using focused ultrasound (FUS). The main topic of this talk is the application of low-intensity focused ultrasound (LIFU) as a noninvasive neuromodulation strategy. Recent studies have demonstrated the potential of FUS to effectively modulate epileptic activity. For example, in-vivo animal research has demonstrated that FUS can suppress epileptic seizures by targeting specific neuron populations in the hippocampus. Furthermore, future clinical applications of neuromodulation therapies for various neuropsychiatric disorders, particularly epilepsy, have been proposed, highlighting its therapeutic potential. This talk aims to bridge the gap between computational neuroscience and clinical applications, providing insight into the transformation of neuromodulation therapies. Attendees will gain an understanding of how integrating seizure network modeling and focused ultrasound technology can pave the way for innovative treatments for intractable epilepsy.

Keywords: Neuromodulation, Epilepsy, Focused ultrasound, In-vivo animal research, Clinical applications

S17-2

Bidirectional neuronal control of epileptiform activities by repetitive transcranial focused ultrasound

Jinhyoung Park

Sungkyunkwan University

Repetitive stimulation procedures have been used in neuromodulation techniques to induce persistent excitatory or inhibitory brain activity. The directivity of modulation is empirically regulated by modifying the stimulation length, interval, and strength in electrical or magnetic stimulation methods. However, bidirectional neuronal modulations using ultrasound stimulations are rarely reported. This study presents bidirectional control of epileptiform activities with repetitive transcranial focused ultrasound stimulations in a rat model of drug-induced acute epilepsy. We found that repeated transmission of elongated (40 s), ultra-low pressure (0.25 MPa) ultrasound with long enough repetition interval length of 40 s can fully suppress epileptic activities in electro-encephalography and cerebral blood volume measurements, while the change in bursting intervals from 40 to 20 s worsens epileptic activities even with the same burst length. Furthermore, the suppression induced by 40 s long bursts was transformed to excitatory states by a subsequent transmission train repeating 500 ms long strong bursts with the interval of 30s. Bidirectional modulation of epileptic seizures with repeated ultrasound stimulation are achieved by regulating the changes in glutamate and γ-Aminobutyric acid levels, as confirmed by measurements of expressed c-Fos and GAD65 in immunohistochemistry and multitemporal analysis of γ-Aminobutyric acid levels and glutamate in the cerebrospinal fluid obtained via microdialysis before, during and after the ultrasound stimulation.

Keywords: Ultrasound brain stimulation, Epileptiform activity, Bidirectional neuromodulation, γ-Aminobutyric

S17-3

Personalized virtual brain modeling to optimize brain stimulation towards clinical applications

Sora An

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Neuromodulation therapies are increasingly explored as treatments for neurological and psychiatric conditions. However, individual variability in brain structure and dynamics limits the efficacy and generalizability of such interventions. In this work, we present a personalized virtual brain twin (VBT) modeling framework designed to simulate and optimize neuromodulation protocols tailored to each individual's anatomical and functional brain characteristics. We demonstrate two proof-of-concept applications of the proposed VBT framework. First, we apply the VBT framework to simulate deep brain stimulation (DBS) in patients with treatment-resistant depression. The individual model identifies the engagement of distinct white matter tracts and elicits event-related potentials (ERPs) depending on the stimulation sites, demonstrating the potential of this approach for personalized optimization of DBS. Second, we utilize the VBT to explore auricular vagus nerve stimulation (aVNS) strategies aimed at enhancing cognitive function in aging populations. The simulation reveals that the modulatory effects of aVNS may vary depending on individual structural or functional brain states, indicating the importance of personalized stimulation strategies in aging-related cognitive interventions. These findings demonstrate the potential of the VBT framework to support personalized neuromodulation, bridging computational modeling with clinical applications. This approach may evolve into a digital platform for predicting and optimizing therapeutic outcomes in neuromodulation.

Keywords : Virtual brain twin, Precision medicine, Brain stimulation therapies
Acknowledgements : This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (RS-2022-NR075832, RS-2023–00248701) and the Ministry of Science and ICT (MSIT) (RS-2022-NR070151, RS-2024–00461617) and by the Bio&Medical Technology Development Program of the NRF funded by the Korean government (MSIT) (RS-2024–00401794).

S17-4

Neuromodulatory focused ultrasound for epilepsy: cutting-edge advances and future directions

Hao-Li Liu

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Focused ultrasound (FUS) has emerged as a transformative neuromodulation and therapeutic tool for central nervous system (CNS) disorders. With advances in neuronavigation-guided focused ultrasound, precision-targeted interventions for blood-brain barrier opening (BBBO), neuromodulation have become increasingly feasible. Recent clinical trials have demonstrated the efficacy of FUS in treating conditions such as epilepsy and recurrent glioblastoma, while preclinical studies reveal promising neuromodulatory effects via mechanical-sensitive ion channel modulation. Besides, the integration of real-time acoustic emission feedback and advanced transducer array design has enhanced safety and efficacy, paving the way for expanded CNS applications. This presentation will explore the engineering and clinical advancements in FUS technology, its role in brain therapy, and the potential for future applications in CNS disorders.

Keywords : Focused ultrasound, phased array, neuronavigation, neuromodulation, epilepsy

S17-5 IBRO AWARDEE

Human nerve tissue engineering approach for developing aging model: a novel tool for high-throughput screening of anti-aging molecules

Varsha Pai V, Abhishek Kumar Singh

Manipal Centre for Biotherapeutics Research, Manipal Centre for Biotherapeutics Research, Manipal, Karnataka, India

Brain aging is a complex process characterized by cognitive decline, neurodegeneration, and reduced neural plasticity. Conventional 2D and animal models often fail to recapitulate the intricacies of human brain aging, highlighting the need for more accurate systems. This study presents a novel three-dimensional (3D) brain aging model using a neural tissue engineering approach involving Wharton's jelly-derived mesenchymal stem cells (WJ-MSCs) and polycaprolactone/gelatin (PCL/gelatin) scaffolds, which mimic the brain extracellular matrix. WJ-MSCs were isolated, characterized, and differentiated into neurons on electrospun PCL/gelatin for 20 days. The differentiated neurons were characterized by the expression analysis of neural markers such as Nestin, NeuN, Synapsin-1, PSD95, and PSA-NCAM. To induce aging, differentiated neuronal tissue was treated with D-galactose (300 mM), which triggered oxidative stress and cellular senescence. The scaffolds demonstrated high porosity, mechanical strength, and flexibility while maintaining cytocompatibility. 3D models presented reduced oxidative stress and apoptosis, enhanced autophagy, and increased expression of neuronal and autophagy markers (LC-3B, Beclin1, ULK, Nestin, Synapsin-1, PSD95, and PSA-NCAM). To validate the model's utility for therapeutic screening, we tested chlorogenic acid (CGA), a natural polyphenol which have been known for its anti-aging effects and antioxidant properties. Treatment with CGA significantly improved neuronal viability, reduced senescence markers, and promoted neuroprotection. This 3D aging model closely mimics physiological features of the human aging brain and offers a scalable, high-throughput-compatible system for studying neural aging and screening neuroprotective compounds such as CGA. It represents a significant advancement toward translational brain aging research.

Keywords : Nerve tissue engineering, Cellular senescence, Apoptosis, Oxidative stress, Autophagy
Acknowledgements : The authors acknowledge the Manipal Academy of Higher Education (MAHE), Manipal, Karnataka, India, for supporting the study. Varsha Pai is thankful to MAHE, Manipal, for providing the Dr. TMA Pai Research Fellowship. The study is supported by the Intramural Fund (MAHE/CDS/PHD/IMF/2023) provided by MAHE, Manipal.

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 18

Day 2 (August 25) **14:30-16:25** **Grand Ballroom**

The brain-body-microbiome axis: a key to regulate ingestion and beyond

Organizer : Greg Seong-Bae Suh (Korea Advanced Institute of Science and Technology)
Moderator : Greg Seong-Bae Suh (Korea Advanced Institute of Science and Technology)

Why do we self-medicate? Knowledge gained from animals in nature.
Michael A. Huffman (Kyoto University)

Gut microbial metabolites link dietary history to appetite regulation in *Drosophila*
Jing W. Wang (University of California, San Diego)

Bidirectional Modulation of the Gut-Microbiome-Brain Axis: Mechanistic and Translational Insights from Bottom-Up and Top-Down Approaches
Mauro Costa-Mattioli (Altos Labs)

Complex Interplay of Hormonal, Neuronal Responses by Gut-Brain Axis to a Deficit in Essential Amino Acids
Boram Kim (Korea Advanced Institute of Science and Technology)

Chronic exposure to air pollutants impaired memory performance via elevating gut microbial metabolites in a mouse model
Akhlaq Hussain (The Hong Kong Polytechnic University) IBRO AWARDEE

S18-1

Why do we self-medicate? Knowledge gained from animals in nature.

Michael A. Huffman

Institute of Tropical Medicine, Nagasaki University, Nagasaki, Nagasaki Prefecture, USA

The ability to self-medicate exists across the animal kingdom. Animals treat themselves and sometimes others with a wide variety of plants, minerals, and even other animals to protect against parasites, wounds, reproductive function, stress, and fatigue. The modes of medication are equally diverse, including passive prevention, ingestive-therapeutic treatment, topical preventative or therapeutic application of substances to skin, fur, or feathers, and fumigation of habitats. Similarities across distant taxa point to a long, evolutionarily stable continuum of medicative strategies for the maintenance of health. Instinctual and cognitive processes should play an interactive role, allowing an individual to access the complex and ever-changing resource base and navigate the infectious disease landscape in which it lives. Medicative behaviors can arise from a combination of instinct, associative learning, and social interactions. When an individual experiences malaise, gustatory responses have been shown to shift and develop into a preference for limited amounts of such toxic items, resulting in medicinal benefits. Animals living in multi-generational societies can learn from observing the behavior of the self-medicator about which part of a particular medicinal resource can be ingested and how, in the same way, dietary information is acquired by the young and maintained in a group as a cultural tradition. Subsequently, they can learn to associate similar relief if taken when sick themselves. The same combination of instinct and individual and social learning can explain the evolution and emergence of medication behaviors in a wide variety of animals, from apes to ants. Learning more about these medicating strategies in a variety of animal species will help us to better understand the interplay between instinct and cognition and their roles in our self-medicating behavior.

Keywords : Animals self-medication, Dietary selection, Homeostasis, Parasitosis, Evolution
Acknowledgements : I wish to wholeheartedly thank the conference organizers for the invitation to attend this conference, which otherwise would not have been possible. This work is a partial summary of nearly 40 decades of collaborative research efforts with many collaborators and many funding organizations around the globe, making it impossible to acknowledge and mention them all. My thanks go out to all of you.

S18-2

Gut microbial metabolites link dietary history to appetite regulation in *Drosophila*

Emma C. Spillman[1], Jing W. Wang[1,2,3]

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All metazoan guts harbor commensal communities, from a dozen bacterial species in Drosophila to hundreds in humans. Here, we condition flies with diets containing varying levels of protein and sugar to investigate the impact of dietary history on the interaction between commensal gut bacteria and feeding adaptation in Drosophila. We find that appetite increases with dietary protein, dependent on total gut bacteria content, and enhanced by a drug that promotes the growth of short-chain fatty acid (SCFA)-producing gut bacteria. Lactiplantibacillus is a potential source of butyrate, while *Acetobacter* produces acetate. Mono-association with *Acetobacter* or *Lactiplantibacillus* increases food intake. Mutant strains unable to produce acetate or butyrate have lesser effects. Finally, adding acetate or butyrate to conditioning diets recapitulates the appetitive effect of *Acetobacter* and *Lactiplantibacillus*, respectively. Our findings suggest that protein-enriched diets enhance appetite by promoting the interaction between commensal bacteria and the host, with bacterial SCFAs as a conduit.

Keywords : Gut-brain axis, Enteroendocrine cells, Neuropeptide, Short-chain fatty acids, Microbiome

S18-3

Bidirectional Modulation of the Gut-Microbiome-Brain Axis: Mechanistic and Translational Insights from Bottom-Up and Top-Down Approaches

Mauro Costa-Mattioli[1,2]

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[2]Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA.

The gut-microbiome-brain axis is a bidirectional communication system that plays a vital role in regulating host physiology and overall fitness. While extensive evidence from our lab and others supports *bottom-up* modulation—where gut microbes influence brain function and behavior—direct evidence for *top-down* modulation, in which the brain shapes the gut microbial ecosystem, has remained limited.

In this presentation, I will first focus on bottom-up modulation. I will show how the bacterium Lactobacillus reuteri consistently reverses social deficits across multiple mouse models of autism spectrum disorder (ASD). I also will discuss the underlying mechanisms and signals through which *L. reuteri* modulates brain function and behavior. Moving to clinical translation, I will share findings from our recent clinical trial in children with ASD, where *L. reuteri* treatment led to improvements in social behavior—highlighting the translational potential of this safe and well-characterized microbial strain.

I will finally switch focus to top-down modulation. Using a brain-targeted molecular genetic approach, I provide direct evidence that persistent (not acute) activation of the brain can act as a selective pressure that affects the stability and diversity of the gut microbial ecosystem. These findings provide a novel perspective on how neural activity can shape the microbial ecosystem. In conclusion, this work underscores the reciprocal nature of gut-brain interactions and reveals new opportunities for developing integrated microbial interventions to improve social function and overall health.

Keywords : Neurological disorders, Gut-Microbiome-Brain Axis, Social impairment, Microbial interventions.

S18-4

Complex Interplay of Hormonal, Neuronal Responses by Gut-Brain Axis to a Deficit in Essential Amino Acids

Boram Kim[1], Seongju Lee[1], Jong-Hoon Won[1], Hyeyeon Bae[1], Dongwoo Kim[1], Byungkwon Jung[1], Makoto I. Kanai[4], Yangkyun Oh[3], Won-Jae Lee[2], Greg S. B. Suh[1]

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[2]National Creative Research Initiative Center for Hologenomics School of Biological Sciences, Seoul National University, Seoul, Republic of Korea
[3]Department of Life Science, Ewha Womans University, Seoul, Republic of Korea
[4]Departments of Cell Biology, Neuroscience NYU Grossman School of Medicine New York, NY, USA

A deficit in protein can trigger a nutrient-specific appetite; however, the mechanism underlying this process remains poorly understood. Here, we found that a set of distinct neuronal and systemic mechanisms is activated in the microbiome-gut-brain axis to induce an essential amino acids (EAA) specific appetite. In Drosophila, EAA deprivation increases the expression of CNMa in the gut enterocyte, which activates enteric neurons and ellipsoid body neurons in the brain to promote the intake of EAAs. By contrast, CNMa inhibits the activity of sugar-sensing DH44 neurons, thereby reducing sugar intake. Protein deprivation in mice also results in an increased appetite for EAAs that occurred independently of FGF21 and required spinal pathway. Together, we propose the fundamental mechanisms underlying the maintenance of EAA homeostasis across species.

Keywords : Nutrient-specific appetite, Essential amino acids, Gut-brain axis, Post-ingestive nutrient sensing, Drosophila and mouse

S18-5 IBRO AWARDEE

Chronic exposure to air pollutants impaired memory performance via elevating gut microbial metabolites in a mouse model

Akhlaq Hussain, Suk-yu Yau

Rehabilitation Science, The Hong Kong Polytechnic University, Hong Kong, Hong Kong, China

Exposure to fine particulate matter (PM2.5) is epidemiologically linked to neurological disorders, yet the molecular mechanisms mediating its effects on brain function remain poorly understood. Here, we demonstrate that chronic PM2.5 exposure impairs cognition via a gut–liver–brain axis in C57BL/6J mice. Mice received intratracheal instillations of PM2.5 (2.5 μg/μl) or artificial lung fluid three times weekly for three weeks. PM2.5-exposed mice exhibited increased depression- and anxiety-like behaviors in the forced swim and open field tests, alongside deficits in working and spatial memory in the novel object recognition and Y-maze tasks. These behavioral impairments correlated with reduced adult hippocampal neurogenesis (Ki67□ and DCX□ cells), impaired long-term potentiation, and downregulation of synaptophysin and GluA1 in the hippocampus. Mechanistically, PM2.5 exposure elevated circulating levels of the gut microbiota-derived metabolite trimethylamine N-oxide (TMAO), concomitant with increased hippocampal endoplasmic reticulum (ER) stress. Pharmacological inhibition of TMAO synthesis with dimethyl butanol or dietary supplementation with resveratrol, which reduces ER stress, ameliorated both behavioral and hippocampal deficits. These findings reveal a mechanistic pathway by which PM2.5 induces cognitive impairment through the gut–liver–brain axis, highlighting potential therapeutic targets for pollution-induced neurotoxicity.

Keywords : PM2.5, hippocampal plasticity, gut–liver–brain axis, Trimethylamine N-oxide (TMAO), endoplasmic reticulum stress
Acknowledgements : Department of Rehabilitation Science, The Hong Kong Polytechnic University

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 19

Day 2 (August 25) **14:30-16:25** **Premier Ballroom A**

Taste sensing from the tongue to the brain

Organizer : Myunghwan Choi (Seoul National University)
Yong-taek Jeong (Korea University)
Moderator : Yong-taek Jeong (Korea University)

Channel Synapse Mediates Neurotransmission of Upper Airway Protective Chemoreflexes
Akiyuki Taruno (Kyoto Prefectial University)

Understanding and targeting the taste system of dangerous mosquitoes
Lisa S. Baik (Yale University)

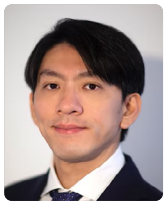
Regional, cell-type, and modal specification of taste bud organoids.
Yong-Taek Jeong (Korea University)

Taste bud connectome: patterns of connectivity in a dynamic sensory organ
Courtney Wilson (University of Colarado)

Cellular basis of non-sweet aftertaste in artificial sweeteners
Geehyun Kim(Seoul National University) Scitech Korea AWARDEE

S19-1

Channel Synapse Mediates Neurotransmission of Upper Airway Protective Chemoreflexes



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Neural reflexes to chemicals in the throat protect the lungs from aspiration and infection, and are thus crucial for survival. Dysfunction in these reflexes represents an unmet medical need. Despite their importance, the molecular and cellular mechanisms underlying these reflexes remain largely unclear. Meanwhile, the recent discovery of channel synapses between epithelial chemosensory cells and afferent nerves, characterized by synaptic vesicle-independent, CALHM1/3 channel-mediated neurotransmitter (ATP) release, has revealed a previously unknown mechanism of body-brain interactions through these synapses. In this study using mice, by combining a whole-body survey for channel synapses with single-cell transcriptome analyses, we discovered subclasses of the *Pou2f3*$^{+}$ chemosensory epithelial cell family, a.k.a. tuft cells, in the throat that communicate with vagal neurons via the channel synapse. These epithelial cells express Tas2Rs, a set of G protein-coupled receptors for diverse noxious chemicals, and trigger airway protective reflexes in response to luminal Tas2R ligands. Targeted optogenetic stimulation of these *Pou2f3*$^{+}$ chemosensory cells also initiated these reflexes. Furthermore, upon stimulation, these cells release ATP, and the associated reflexes were abolished by *Calhm3* knockout and pharmacological inhibition of ATP receptors on vagal neurons, demonstrating the involvement of the purinergic channel synapse for neurotransmission. Together, these findings identify *Pou2f3*$^{+}$ epithelial cells with channel synapses as previously unrecognized chemosensory end organs for airway protective reflexes and their molecular signaling pathways, advancing our understanding of airway defense mechanisms and offering distinct therapeutic targets.

Keywords : Cough, Swallow, Synapse, Bitter, Tuft

S19-2

Understanding and targeting the taste system of dangerous mosquitoes

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Mosquitoes are dangerous vectors of deadly diseases. The taste system controls many insect behaviors but is greatly understudied in mosquitoes. Little is known about how tastants are encoded in mosquitoes or how they regulate critical behaviors. Here we examine how taste stimuli are encoded by the *Aedes albopictus* mosquito, a highly invasive disease vector. We investigate how taste cues influence biting, feeding, and egg laying. We find that neurons of the labellum, the major taste organ of the head, differentially encode a wide variety of human and other cues. We identify three functional classes of taste sensilla with an expansive coding capacity. Unexpectedly, in addition to excitatory responses we discover strikingly prevalent inhibitory responses, which are predictive of biting behavior. Certain bitter compounds suppress physiological and behavioral responses to sugar, suggesting their use as potent stop signals against appetitive cues. Complex cues, including human sweat, nectar, and egg-laying site water, elicit distinct response profiles from the neuronal repertoire. We identify key tastants on human skin and in sweat that synergistically promote biting behaviors. Transcriptomic profiling identifies taste receptors that might be targeted to disrupt behaviors. Our study sheds light on key features of the taste system that suggest new ways of manipulating chemosensory function and controlling mosquito vectors.

Keywords : Mosquitoes, Gustation, Chemosensation, Vector Biology, Behavior
Acknowledgements : This work was supported by NIH Grants F32DC019250 and K99DC021504 Dr. Lisa S. Baik and R01 DC02174, R01 DC04729, and R01 DC11697 to Dr. John R. Carlson

S19-3

Regional, cell-type, and modal specification of taste bud organoids.

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Humans can recognize and distinguish at least five basic taste modalities: sweet, bitter, salty, sour, and umami. This ability stems from the cellular heterogeneity of taste buds, the primary sensory organs for gustation. Although taste cells have been classified into distinct types based on their morphology, gene expression, and response to tastants, the molecular heterogeneity, developmental programs, and mechanisms by which these cells acquire modality-specific functions remain incompletely understood.
Here, using taste bud organoid models, we reconstruct the differentiation trajectories of individual taste cell lineages. This approach has allowed us to precisely delineate cell type-specific differentiation programs and to induce taste cell formation even in the anterior lingual epithelium, which harbors taste buds rarely. Furthermore, we propose novel strategies to direct the differentiation of Type II taste cells toward specific taste modalities, offering new insights into the fundamental processes of taste cell development and function.

Keywords : Taste buds, organoids, stem cells, differentiation

S19-4

Taste bud connectome: patterns of connectivity in a dynamic sensory organ

Courtney Wilson

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Mammalian taste buds contain 50-100 epithelial-derived taste cells which are renewed repeatedly and allow for the detection of five basic taste qualities: sweet, bitter, umami, salty, and sour. Approximately half of the taste cells in a bud are glial-like, while others express receptors that respond to one or more taste modalities and synapse onto taste nerves carrying taste information to the CNS. The degree of specificity of connectivity between taste cells and afferent nerve fibers has consequences for taste quality coding as well as the process of taste cell renewal. We mapped the “connectome” of several mouse taste buds using Serial Blockface Electron Microscopy (sbfSEM), which allows the volumetric examination of whole and partial taste buds at high resolution. In our detailed reconstruction of nerve fibers and taste cells, we find that afferent nerve fibers tend to receive synapses from taste cells of a single type, suggesting that some taste fibers carry information pertaining to one taste quality. A few fibers in each bud, however, receive synapses from cells of differing types, indicating that at least some fibers carry multimodal taste quality information. Taste bud renewal complicates this picture somewhat: while taste bud cells are renewed continuously, taste nerve fibers are long-lived and must adapt to an ever-changing peripheral sensory organ. Nerve fibers presumably disconnect from dying taste cells and reconnect to newly mature taste cells. Our datasets contain several cells whose ultrastructural features are consistent with apoptosis. The nerve fibers in contact with these dying cells show synapses in various stages of degradation. Interestingly, many of these nerve fibers appear to be fragments that no longer connect to the main intragemmal nerve fiber network. This suggests that nerve fiber fragmentation may be a part of the nerve remodeling process.

Keywords : Taste, Connectome
Acknowledgements : I would like to thank my colleagues who contributed to the project design, tissue preparation, data analysis, and advice: Dr. Tom Finger, Dr. Rob Lasher, Dr. Ruibiao Yang, Yannick Dzowo, Dr. Ernesto Salcedo, and Dr. Jack Kinnamon. I would also like to thank our collaborators Dr. Graham Kidd and Emily Benson at the Cleveland Clinic in Cleveland, Ohio, USA for imaging the tissue blocks.

S19-5 Scitech Korea AWARDEE

Cellular basis of non-sweet aftertaste in artificial sweeteners

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Artificial sweeteners convey stronger sweetness with much lower calories compared to natural sugars and thus highly demanded among patients suffering from diabetes and obesity. However, unpleasant non-sweet aftertaste is reported from certain artificial sweeteners, discouraging their usage. Here we suggest that the aftertastes of artificial sweeteners are encoded by the sour sensing type III taste bud cells, thereby reporting a novel functional role of them. Using in-vivo functional imaging of genetically-targeted type III cells in fungiform taste buds, we observed that a subpopulation of sour-sensing type III cells exhibits calcium activity in response to sweet offset, which can be referred as “sweet OFF response”. Series of pharmacological inhibition experiments suggested that certain sweeteners hyperpolarize type III cells via opening pH sensitive potassium channels, and the washout of sweeteners cause rebound potential via t type voltage gated calcium channels. Analogous to the off-response in auditory neurons and thalamic neurons, we suggest that sweet off-response is a post inhibitory rebound. Since pH sensitive potassium channels are involved in sweet OFF responses, we tested the hypothesis that direct increase of pH might cause a similar OFF response. Application and washout of alkaline substance triggered OFF response, inhibited by the same pharmacological agents. This further supports the involvement of pH sensitive potassium channels in sweet OFF response and suggests that type III taste cells are able to encode alkaline stimuli along the canonical acidic stimuli. In line with the psychophysics studies upon unpleasant aftertaste of the sweeteners, mice expressed aversion against the “OFF responsive” sweeteners. Taken together, these results suggests that unpleasant aftertaste of certain sweeteners are due to OFF response elicited by type III cells and emphasize a novel functional role of type III taste bud cells.

Keywords : Artificial sweetener, Aftertaste, Alkaline, Type III taste bud cells, In vivo calcium imaging
Acknowledgements : This work was supported by Samsung Science and Technology Foundation under Project Number SSTF-BA2002-14 and the NRF of Korea grant funded by the Korea government (2020R1A5A1018081).

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 20

Supported By

Center for Cognition and Sociality ibs

Day 2 (August 25) **14:30-16:25** **Premier Ballroom B**

Updates on autism models and potential rescue strategies

Organizer : Xiang Yu (Peking University)
Mihyun Bae (Korea Advanced Institute of Science and Technology)
Moderator : Xiang Yu (Peking University)
Mihyun Bae (Korea Advanced Institute of Science and Technology)

Behavioral Improvement Through *In Vivo* Base Editing in a Mouse Model of Snijders Blok-Campeau Syndrome
Zilong Qiu (Shanghai Jiao Tong University)

From mouse to cell models of autism
Toru Takumi (Kobe University)

New therapeutic methods for ASD
Mihyun Bae (Institute for Basic Science)

Using oxytocin to treat autism: insights from animal models
Xiang Yu (Peking University)

S20-1

Behavioral Improvement Through *In Vivo* Base Editing in a Mouse Model of Snijders Blok-Campeau Syndrome

Zilong Qiu

Songjiang Research Institute, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Snijders Blok-Campeau Syndrome (SNIBCPS) is a rare neurodevelopmental disorder caused by mutations in the *CHD3* gene. Here, we report a *de novo* single-nucleotide variant (c.C3073T, p.R1025W) in *CHD3* identified in a child with SNIBCPS, which leads to accelerated degradation of the CHD3 protein. Using a *Chd3*$^{R1025W/+}$ knock-in mouse model, we observed impaired vocalization, cognition, and autism-like behaviors. To address these deficits, we developed an improved TadA-embedded adenine base editor (TeABE) and delivered into the mouse brain via Adeno-associated virus (AAV). Base editing *in vivo* significantly restored CHD3 protein levels in the mouse brain and ameliorated various behavioral abnormalities. Furthermore, we validated the AAV-mediated delivery efficacy of TeABE in nonhuman primate, highlighting its translational potential. These findings establish *in vivo* base editing as a promising therapeutic strategy for SNIBCPS and pave the way for clinical applications targeting brain disorders.

Keywords : Snijders Blok-Campeau Syndrome, CHD3, base editing, mouse, monkey

S20-2

From mouse to cell models of autism

Toru Takumi

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Substantial evidence suggests that chromosomal abnormalities, including copy number variations (CNV), contribute to autism risk. The duplication of human chromosome 15q11-13 is one of the most frequent cytogenetic abnormalities associated with autism spectrum disorder (ASD). Using chromosome engineering, we established a mouse model with a 6.3-Mb duplication of the conserved region on mouse chromosome 7. This *15q dup* mouse is the first CNV model of ASD and a founder mouse for the forward genetics of a developmental brain disorder. Our multi-dimensional approach reveals that 15q dup mice exhibit not only impaired social behavior but also spine phenotypes, serotonin abnormalities, and excitatory/inhibitory imbalance. Using synapse phenotypes, we identified a critical gene within the duplication. To collect a systematic CNV model, we developed a next-generation chromosome engineering technique. With this technique, we established a library of ES cell models with CNVs observed in ASD. I will discuss our recent analyses, primarily focusing on CNV cell models, and outline our new direction in understanding the pathophysiology of ASD.

Keywords : autism, ES cell, CNV, mouse model, chromosome

S20-3

New therapeutic methods for ASD

Mihyun Bae

Center for Synaptic Brain Dysfunctions, IBS, Daejeon, Republic of Korea

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition with diverse etiologies, and the heterogeneous nature of disease presentation and risk genes have made treatment especially difficult. Fortunately, excitatory/inhibitory (E/I) imbalance in neural circuits has emerged as a convergent pathophysiological mechanism. In this study, we investigated therapeutic strategies aimed at restoring E/I balance in genetically validated mouse models of ASD. Through a combination of pharmacological and/or genetic interventions, we modulated inhibitory tone and excitatory drive. Behavioral assays revealed significant improvements in core ASD-like phenotypes, including social interaction deficits and repetitive behaviors, following treatment. Electrophysiological recordings confirmed a normalization of synaptic activity toward physiological E/I ratios. Our findings highlight the therapeutic potential of targeting E/I imbalance as a unifying mechanism in ASD and provide a translational framework for future clinical intervention strategies.

Keywords : ASD, E/I imbalance, Therapeutics

S20-4

Using oxytocin to treat autism: insights from animal models

Xiang Yu

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Oxytocin plays diverse functional roles, contributing to regulation of socio-emotional and socio-sexual behaviors, sensory processing, learning and memory, modulation of stress and pain systems, as well as homeostatic, metabolic and autonomic responses. Reduction in oxytocin level, as well as SNPs in oxytocin receptor, are associated with autism. Oxytocin nasal spray has been clinically tested for autism treatment in a number of trials, with mixed results. More mechanistic insight from animal studies can contribute towards more effective treatment strategies. In previous work, we show that pleasant social touch can increase the firing of oxytocin neurons in the paraventricular hypothalamus (PVH), as well as promote social interaction and preference for the social touch context (Yu et al., Neuron, 2022, PMID: 35045339). This effect is blocked in oxytocin knockout mice, and can be mimicked by chemogenetic activation of PVH oxytocin neurons. Here, we further show that a genetic autism model has oxytocin system deficits, starting from early development and extending until adulthood. Intraperitoneal injection (i.p.) injection of oxytocin and chemogenetic activation of PVH oxytocin can rescue the oxytocin neuronal firing rates, as well as social interaction and sensory processing deficits. These results underscore restoration of oxytocin neuronal firing as a potential strategy for autism treatment.

Keywords : Autism, Oxytocin, PVH, ASD
Acknowledgements : We thank Prof. Toru Takumi for autism mouse model. We thank colleagues at Peking University for suggestions and comments. This work was funded by grants from the National Science Foundation of China, and the Ministry of Science and Technology of China.

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 21

Day 2 (August 25) **14:30-16:25** **Rm.113-115**

Innovations in imaging- and sequencing-based approaches in neurosciences

Organizer : Chang Ho Sohn (Korea Advanced Institute of Science and Technology)
Moderator : Chang Ho Sohn (Korea Advanced Institute of Science and Technology)

Multiscale molecular imaging and phenotyping of the human brain based on polymer hydrogel
Juhyuk Park (Seoul National University)

Fixative eXchange (FX)-seq: Scalable Single-nucleus RNA Sequencing Analysis of PFA-fixed or FFPE Tissue
Chang Ho Sohn (Korea Advanced Institute of Science and Technology)

Longitudinal optical imaging of the deep brain through the intact mouse skull
Wonsik Choi (Korea University)

Engineering interventional neuro-omics: where viral vectors meet 3D spatial biology
Min Jee Jang (University of Illinois)

Presynaptic mitochondrial capture mechanism during synapse formation
Kazuki Tsujimura (The University of Tokyo) IBRO AWARDEE

S21-1

Multiscale molecular imaging and phenotyping of the human brain based on polymer hydrogel

Juhyuk Park

Department of Materials Science and Engineering, Seoul National University, Seoul, Republic of Korea

Understanding the spatial organization, morphology, and connectivity of cells is fundamental to uncovering how biological systems function and where they deteriorate. However, current technologies fall short in capturing the detailed architecture of individual cells within the larger, intact structure of human organs. This limitation becomes particularly evident when studying complex systems like the human brain, where preserving fine-scale cellular details across large tissue volumes is essential. To address this challenge, we developed an advanced polymer hydrogel-based platform that employs mELAST technology, combined with specialized mechanical devices and computational tools. This innovative system enables the simultaneous acquisition of multiscale, multidimensional data from individual cells embedded within intact, slab-scale human brain tissues, preserving structural integrity throughout the process.
We demonstrated the remarkable capability of this platform by examining Alzheimer's disease pathology across various scales, showcasing its effectiveness in capturing intricate cellular changes and mapping neural connectivity within human brain tissues. By providing clear, high-resolution images of complex tissue structures, this system allows for a more comprehensive understanding of disease mechanisms. Ultimately, our platform represents a significant advancement in the study of complex biological systems, offering valuable insights into normal function and disease progression. Furthermore, it opens new possibilities for developing next-generation therapeutic strategies through detailed, multiscale analysis of cellular networks and interactions.

Keywords : Tissue clearing, Brain imaging, Hydrogels, Molecular phenotyping, Alzheimer's disease
Acknowledgements : This work was supported by the NIH (1-DP2-ES027992, U01MH117072), the Institute for Basic Science (IBS-R026-D1), JPB Foundation (PIIF and PNDRF), and NCSOFT Cultural Foundation, under supervision of Prof. Kwanghun Chung at MIT.

S21-2

Fixative eXchange (FX)-seq: Scalable Single-nucleus RNA Sequencing Analysis of PFA-fixed or FFPE Tissue

Chang Ho Sohn

Graduate School of Medical Science and Engineering, KAIST, Daejeon, Republic of Korea

Despite widespread availability of clinical formalin-fixed paraffin-embedded (FFPE) samples for human genomic studies, single-nucleus RNA sequencing (snRNA-seq) of these samples has been challenging due to low reverse transcription (RT) yields. Here, we present Fixative-eXchange (FX)-seq, a scalable snRNA-seq method for heavily paraformaldehyde (PFA)-fixed and FFPE samples that enhances RT yield by removing PFA crosslinks while preventing RNA leakage through regiospecific crosslinking. We validated our protocol by analyzing over 500k nuclei across multiple samples, including PFA-fixed tissue, FFPE blocks, and FFPE/H&E-stained sections from mouse brain and human clinical cancer specimens. This revealed diverse mouse brain cell types, rare tumor populations, and cancer-specific transcriptome changes in pathologically annotated FFPE sections. Application to perfused and PFA-fixed mouse brain tissues enabled precise regional dissection for snRNA-seq, yielding reproducible transcriptome data across various cell types without bias toward glia cells. FX-seq advances basic and clinical research by enabling single-nucleus transcriptome profiling of PFA-fixed and FFPE specimens.

Keywords : single nucleus RNA seq, FFPE, single cell transcriptomics
Acknowledgements : This work was supported by grants from Institute for Basic Science (IBS-D01-026), National Research Foundation (NRF) of Korea, funded by the Ministry of Science and ICT (RS-2021-NR061245, RS-2021-NR055513, and RS-2024-00441161).

S21-3

Longitudinal optical imaging of the deep brain through the intact mouse skull

Wonshik Choi

Department of Physics, Korea University

Optical imaging of deep brain structures *in vivo* is fundamentally challenged by strong light scattering and aberrations from the skull and brain tissues. Here, we present an imaging approach that enables high-resolution visualization of neuronal and myelination dynamics through the intact mouse skull. Using a reflection matrix imaging framework combined with computational adaptive optics at a wavelength of 1.3 μm, we precisely measure and correct complex skull-induced aberrations. This method preserves diffraction-limited resolution at depths corresponding to cortical layer 4, enabling label-free tracking of cortical myelination from 3 to 10 postnatal weeks in the same animals. The non-invasive nature of the technique avoids surgical perturbation of neural development and allows repeated measurements over weeks, offering unprecedented opportunities to study brain maturation, learning-related myelination, and neurodegenerative processes. Our results establish a powerful optical platform for chronic deep-brain imaging through intact scattering barriers, paving the way for broad applications in neuroscience research.

Keywords : Reflection matrix imaging, Adaptive optics, Deep brain imaging, Myelination, Non-invasive microscopy

S21-4

Engineering interventional neuro-omics: where viral vectors meet 3D spatial biology

Min Jee Jang

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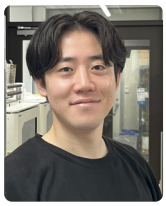
Spatial omics has emerged as a revolutionary technology in modern biology, providing crucial insights into the molecular architecture of intact biological systems with unprecedented detail. Moving beyond its traditional observational nature, recent incorporation of genetic technologies has opened new avenues for interventional omics, enabling researchers to capture cellular connectivity, perturbation responses, and dynamic molecular processes alongside gene expression readouts. Despite its transformative potential, the field remains in its infancy, facing significant challenges including dependence on transgenic animals, poor sensitivity and coverage, and limited scalability. Aiming to advance interventional omics at the whole-brain level, I will introduce our multifaceted efforts in engineering systemic viral vectors and 3D spatial omics technologies. First, we have engineered a series of adeno-associated virus (AAV) vectors for highly efficient, brain-targeted gene delivery across the blood-brain barrier. This viral toolkit provides unprecedented access to the entire brain, enabling systematic introduction of diverse genetic and molecular tools without requiring transgenic animals. Second, we have developed a highly sensitive spatial transcriptomics platform capable of detecting both endogenous and AAV transcripts in intact 3D brain tissues. This integrated approach allows us to simultaneously map natural gene expression patterns and genetically encoded information in their native 3D tissue contexts. Our current efforts focus on enhancing the target specificity of viral gene delivery while expanding the depth and scalability of our 3D spatial omics platform. With the rapid expansion of genetic technologies—exemplified by recent developments of molecular barcoding, lineage tracing, and activity recording systems—our integrated platform will provide essential infrastructure for next-generation neuroscience research.

Keywords : Spatial transcriptomics, Viral vectors, AAV, Gene delivery
Acknowledgements : This work is supported by NARSAD Young Investigator grant (28907) from Brain and Behavior Research Foundation and Roy J. Carver Cheritable Trust grant (25-6023).

S21-5 IBRO AWARDEE

Presynaptic mitochondrial capture mechanism during synapse formation



Kazuki Tsujimura[1], Kota Ando[1], Kotaro Hirayama[1], Tomoyuki Yoshida[2], Christian Hoffmann[3], Dragomir Milovanovic[3], Yusuke Hirabayashi[1]

[1]Graduate School of Engineering, The University of Tokyo, Tokyo, Japan
[2]Faculty of Medicine, University of Toyama, Toyama, Japan
[3]Molecular Neuroscience, German Center for Neurodegenerative Disease, Berlin, Germany

Synapses play a central role in neural activity as sites of information transmission, and their properties must be tightly regulated. Mitochondria are actively transported along axons, but as neurons mature, they become preferentially localized to presynaptic sites. There, mitochondria modulate synaptic transmission by regulating cytosolic Ca²□ dynamics. Notably, only about half of excitatory presynaptic boutons in the cerebral cortex contain mitochondria, suggesting that their presence or absence shapes the properties of individual presynaptic boutons, thereby contributing to synaptic diversity and neural circuit complexity. While proper presynaptic localization of mitochondria is crucial for neural network function, the fundamental mechanism by which transported mitochondria are specifically arrested at presynaptic sites remains uncler.

In this study, we developed a novel Live Correlative Light and 3D Electron Microscopy (Live-3D CLEM) method by integrating live fluorescence imaging with 3D electron microscopy. By combining this method with synapse induction via synaptic adhesion molecules, which allows spatiotemporal control of synapse formation, we tracked presynaptic development in primary cultured cortical neurons. Live-3D CLEM captured the moment mitochondria stalled at developing presynaptic sites and allowed analysis of the associated ultrastructure. Through this analysis, we revealed that clustered synaptic vesicles (SVs) were associated with stalled mitochondria, suggesting a shared mechanism for SV clustering and mitochondrial capture. Furthermore, we established a reductionist system reconstituting SV-like vesicle clusters in non-neuronal cells and showed they are sufficient to retain mitochondria outside neurons. In this symposium, we will discuss how SV clustering compartments capture mitochondria. Our findings propose a novel model for regulating mitochondrial localization within axons, offering insights into synaptic diversity and function.

Keywords : Mitochondria, Presynaptic sites, Synaptic vesicle cluster, Live-3D CLEM

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 22

Day 2 (August 25) **14:30-16:25** **Rm.204-205**

Hurting inside and out: sensing pain and nausea

Organizer : Seungwon (Sebastian) Choi (University of Texas Southwestern Medical Center)
Hojoon Lee (Northwestern University)
Moderator : Hojoon Lee (Northwestern University)

Neural basis of motion sickness
Hojoon Lee (Northwestern University)

Molecular dissection of area postrema and its role in nausea
Chuchu Zhang (University of California, Los Angeles)

Analysis of spinal output circuits in chronic pain
Seungwon (Sebastian) Choi (University of Texas Southwestern Medical Center)

Feeling the pressure: PIEZO ion channels in urinary mechanosensation
Kara Marshall (Baylor College of Medicine)

S22-1

Neural basis of motion sickness

Hojoon Lee

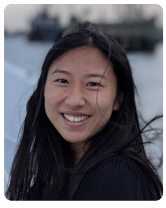
Department of Neurobiology, Northwestern University, Evanston, Illinois, USA

Nausea is evoked by the interoception of distressful physiological changes occurring within the body. When these signals reach the brain and are interpreted as a potential threat or disruption to homeostasis, the unpleasant sensation of nausea arises. However, there remains a critical gap in the fundamental understanding of how distress is sensed by the brain and how this is communicated to other physiological systems. I will present our recent work focusing on motion sickness (originating in the brain) rather than chemically induced nausea (originating in the viscera), thereby providing an orthogonal view into the cellular and circuit mechanisms of nausea.

Keywords : Nausea, Motion, Brainstem, NTS
Acknowledgements : This work was supported in part by the Whitehall Foundation and the Brain Research Foundation.

S22-2

Molecular dissection of area postrema and its role in nausea



Chuchu Zhang

Physiology, UCLA, Los Angeles, California, USA

Nausea is an unpleasant sensation of visceral malaise often accompanied by vomiting. Nausea responses are evolutionarily beneficial behaviors to avoid or expel toxins, but they can also be maladaptive, as therapeutics for cancer and diabetes induce nausea as a major side effect. Current anti-emetic drugs have only limited efficacy, so, new strategies for nausea are needed and may be enabled by a mechanistic understanding of how the sensation of nausea arises, which is largely unknown. Known as the “chemoreceptor trigger zone” for nausea, the area postrema was identified by classical lesion studies as a brain structure that mediates nausea responses. Unlike other parts of the nervous system, neurons in the area postrema occupy a unique anatomical location outside the blood-brain-barrier, allowing them to be regulated by humoral factors. Using single-nucleus RNA-sequencing combined with genetic approaches for cell-selective activation, ablation, and gene knockout and rescue, we have recently identified a population of the area postrema excitatory neurons that, in response to emetic cues, induce nausea-associated aversive behaviors in mice. Clinically relevant receptors were identified in these aversion promoting neurons, such as receptors for glucagon-like peptide 1 (GLP1) and cytokine GDF15. These neurons project to the midbrain aversive learning pathway, providing a circuit-based mechanism for the observed responses. Finally, we also identified area postrema inhibitory neurons that projected locally and elicited inhibitory currents in the nausea-promoting area postrema excitatory neurons. Targeted activation of the area postrema inhibitory neurons counteracted nausea-associated poison responses evoked by area postrema excitatory neurons. Altogether, we have uncovered the basic organization of area postrema nausea circuitry and provided a framework towards understanding, predicting, and therapeutically controlling nausea.

Keywords : nausea, intereoception, circumventricular organ, visceral sensation, aversive

S22-3

Analysis of spinal output circuits in chronic pain

Seungwon (Sebastian) Choi

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Pain is initiated by the activation of nociceptors that innervate the skin and internal organs. Nociceptive signals are propagated into the spinal cord and then transmitted to the brain by spinal cord projection neurons (PNs). These spinal PNs are attractive therapeutic targets for pain treatment because nociceptive signals emanating from the periphery are channeled through these spinal cord output neurons *en route* to the brain to produce pain sensations. Spinoparabrachial (SPB) neurons, a major population of spinal PNs that innervate the lateral parabrachial nucleus of the pons, represent an ideal neuronal population for developing new approaches to treat pain because they convey touch and pain information to higher brain centers that control the affective aspects (i.e., emotional "feelings") of touch and pain. Previously, we showed that *Tacr1*$^{+}$ and *Gpr83*$^{+}$ SPB neurons form two largely-nonoverlapping subdivisions of the SPB pathway that cooperate to convey tactile, thermal and noxious signals from the spinal cord to the brain. To further define the contribution of each SPB subdivision to pain sensation and associated behavioral responses to noxious stimuli, we have begun to examine the effects of acute silencing of *Tacr1*$^{+}$ and *Gpr83*$^{+}$ SPB neurons, individually or simultaneously, on nocifensive behaviors. In addition, to determine if neuropeptide signaling mediated by either TACR1, GPR83 or both in the spinal cord is required for pain transmission, we also have begun to examine acute and neuropathic pain behaviors following spinal cord-specific deletions of the *Tacr1* and *Gpr83* genes using mouse lines that harbor conditional alleles of *Tacr1* and *Gpr83* in conjunction with spinal cord specific Cre lines. Collectively, these behavioral analyses will provide insights into the functions of *Tacr1*$^{+}$ and *Gpr83*$^{+}$ SPB neurons and neuropeptide signaling mediated by the TACR1 and GPR83 GPCRs in acute and neuropathic pain and may reveal novel therapeutic targets for treating pain.

Keywords : pain, parabrachial nucleus, spinal cord

S22-4

Feeling the pressure: PIEZO ion channels in urinary mechanosensation

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Mechanical force sensation is critical for driving physiology. For example, bladder stretch alerts us to find a bathroom and intiates reflexes that sustain urination. Despite their importance, the mechanosensory systems that govern internal processes are not well understood. We previously discovered that the mechanosensory ion channel PIEZO2 is essential to detect bladder filling and drives urinary reflexes. Normal reflex function and urinary control is impaired with aging or common pathologies like bladder pain and inflammation, which cause many difficulties and a lower quality of life in humans. Specifically, we find that PIEZO1 activity in smooth muscle contributes to age-related urinary dysfunction, and we can modulate mechanosensory function through dietary fatty acid supplementation to rescue these deficits. Mechanosensation becomes painful in the context of cystitis and inflammation, but find paradoxically we found that signaling through PIEZO2 in neurons seems to inhibit pain phenotypes. This indicates low-threshold inputs from the bladder inhibit nociceptive activity. This opens up new questions about how low-threshold mechanical force sensation is integrated with chemosensory signals in the context of bladder inflammation, and all together highlights the importance of understanding mechanosensation in healthy and disease states.

Keywords : Bladder, Mechanosensation, PIEZO1, PIEZO2, Pain

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 23

Day 2 (August 25) **14:30-16:25** **Rm.206-207**

Neuromodulation in the brain: new understanding and emerging methods

Organizer : Jung Ho Hyun (Daegu Gyeongbuk Institute of Science and Technology)
Jae-Ick Kim (Ulsan National Institute of Science of Technology)
Moderator : Jung Ho Hyun (Daegu Gyeongbuk Institute of Science and Technology)

Illuminating the brain: new tools to unravel how neuronal networks generate complex behaviors
Olivia Andrea Masseck (University of Cologne)

Modulatory synapses in the brain: new biological features and functions of dopaminergic and serotonergic synapses
Jae-Ick Kim (Ulsan National Institute of Science of Technology)

Rapid eye movement sleep is initiated by basolateral amygdala dopamine signaling in mice
Emi Hasegawa (Kyoto University)

Serotonergic Modulation of Structural Knowledge for Flexible Behavior
Jung Ho Hyun (Daegu Gyeongbuk Institute of Science and Technology)

S23-1

Illuminating the brain: new tools to unravel how neuronal networks generate complex behaviors

Olivia Andrea Masseck[1,2]

[1]Neuromodulatory Circuits, University of Cologne, Cologne, NRW, Germany
[2]Synthetic Biologie, University of Bremen, Bremen, Bremen, Germany

Understanding how neuronal networks generate complex behavior is one of the central goals of neuroscience. Neurotransmitters and neuromodulators play a crucial role in information flow between neurons, and deciphering their dynamics as well as their effects on neuronal activity is key to understanding their behavioral relevance. In this talk, I will introduce PinkyCaMP, a new red-shifted genetically encoded calcium indicator (GECI) based on mScarlet (Fink et al. 2024). PinkyCaMP outperforms existing red-shifted calcium sensors in brightness, photostability, and optogenetic compatibility. It is well tolerated by neurons, showing no toxicity or aggregation, both in culture and in vivo. Additionally, I will present sDarken, a novel family of genetically encoded serotonin (5-HT) sensors based on the native 5-HT_{1A} receptor and circularly permuted GFP (Kubitschke et al., 2022). sDarken sensors exhibit high fluorescence in the unbound state and decrease fluorescence upon 5-HT binding. Variants with different serotonin affinities enhance versatility in serotonin imaging. These sensors demonstrate excellent membrane expression, high specificity, and a superior signal-to-noise ratio, enabling detection of endogenous serotonin release and in vivo imaging. To overcome the limitations of intensity-based fluorescent measurements, we are now implementing fluorescence lifetime imaging (FLIM) as a novel readout for serotonin dynamics.

Keywords : genetically encoded calcium sensors, serotonin, liftetime, imaging
Acknowledgements : Thank you to the incredible team of the Masseck Lab, our collaboration partners, and the funding agencies for their invaluable support.

S23-2

Modulatory synapses in the brain: new biological features and functions of dopaminergic and serotonergic synapses

Jae-Ick Kim

Department of Biological Sciences, Ulsan National Institute of Science and Technology, Ulsan, Republic of Korea

Diffuse modulatory systems, such as the dopaminergic and serotonergic systems, are essential in the brain for broadly regulating diverse neural functions, including motor control, reward processing, emotions, and mood. Despite their functional importance, the comprehensive biological features and functions of modulatory synapses in the central nervous system remain poorly understood. In this talk, we introduce novel biological principles and functions of serotonergic and dopaminergic synapses in the hippocampus and striatum, respectively. First, using electrophysiology, optogenetics, immunohistochemistry, and confocal imaging, we demonstrate that synaptic transmission from raphe nuclei di-synaptically influences neuronal activity in hippocampal CA1 neurons. Importantly, this raphe-driven synaptic transmission critically regulates hippocampal synaptic plasticity through VGLUT3-dependent glutamate co-transmission. Furthermore, this modulation is predominantly mediated by CCK-expressing interneurons in the hippocampus. In the second part of the talk, we present evidence indicating that dopaminergic presynaptic boutons in the striatum are primarily engulfed by microglia, but not astrocytes. Additionally, this microglia-dependent engulfment of dopaminergic boutons is dynamically regulated by the activation state of dopamine neurons and significantly affects the functional properties of dopamine synapses in the striatum. Together, these findings reveal previously unrecognized mechanisms by which modulatory synapses dynamically shape neural circuitry and function, offering potential insights into the pathophysiology of various neurological disorders.

Keywords : Raphe-driven glutamate co-transmission, CCK interneurons, Dopamine boutons engulfment, Microglia, Striatum
Acknowledgements : This research was supported by the Mid-Career Researcher Program (NRF-2023R1A2C1006489) and the Bio & Medical Technology Development Program (NRF-2021M3A9G8022960, NRF-2022M3E5E8017907) of the National Research Foundation (NRF) funded by the Korean government (MSIT).

S23-3

Rapid eye movement sleep is initiated by basolateral amygdala dopamine signaling in mice

Emi Hasegawa[1], Ai Miyasaka[2], Katsuyasu Sakurai[2,3], Yoan Cherasse[2], Yulong Li[4], Takeshi Sakurai[2,3]

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[2]International Institute for Integrative Sleep Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba City, Ibaraki, Japan
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[4]School of Life Sciences, Peking University, Yiheyuan Road, Haidian District,Beijing, China

The sleep cycle alternates between REM (rapid eye movement) and NREM (non-rapid movement) sleep, which is a highly characteristic feature of sleep. However, the mechanisms by which this cycle is generated are totally unknown. We found that a periodic transient increase of dopamine (DA) level in the basolateral amygdala (BLA) during non-rapid eye movement (NREM) sleep terminates NREM sleep and initiates REM sleep. DA acts on dopamine receptor D2 (Drd2)-expressing neurons in the BLA to induce a transition from NREM to REM sleep. This mechanism also plays a role in cataplectic attack, which is a pathological intrusion of REM sleep into wakefulness in narcoleptics. These results show a critical role of DA signaling in the amygdala in REM sleep regulation and provide a neuronal basis of sleep cycle generation.

Keywords : Mice, REM sleep, Dopamine, Amygdala, Cataplexy

S23-4

Serotonergic Modulation of Structural Knowledge for Flexible Behavior

Jung Ho Hyun

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[3]Center for Synapse Diversity and Specificity, DGIST, Daegu 42988, Republic of Korea

Cognitive flexibility is fundamental to high-level brain function, yet underlying neuronal mechanisms remain unclear. While orbitofrontal cortex (OFC) lesions impair choice behavior and serotonin depletion disrupts reversal learning (RL), how flexibility is encoded by neurons is unknown. The key question is understanding how new information updates without losing existing memories. We examined DRN-OFC circuits using high spatiotemporal resolution techniques. Optogenetic stimulation of serotonergic inputs facilitated RL, while inhibition slowed learning. Serotonin depolarizes the membrane potential and enhances OFC network activity. Miniscope and two-photon Ca2+ imaging showed serotonin boosted Ca2+ transients at dendritic spines. Serotonergic inputs triggered rapid reorganization of OFC ensemble activity when task rules changed, accelerating adaptation to new contingencies. OFC neurons encoded task rules hierarchically, distinguishing local stimulus-reward associations from global task contexts. These results suggest serotonin-primed neurons exhibit increased excitability following a non-Hebbian hyperexcitable model, leading to expanded ensemble sizes and memory linking between events. Thus, cognitive flexibility is encoded via state-dependent mechanisms orchestrated by serotonergic modulation, rather than specific cell types or pathways. These findings provide insights into cognitive learning and psychiatric disorders characterized by inflexibility.

Keywords : Cognitive flexibility, OFC, Serotonin, Reversal learning, Ensemble

August 24(Sun)- 27(Wed), 2025

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Symposium 24

Supported By 아주대학교 AJOU UNIVERSITY

Day 3 (August 26) **08:30-10:25** **Premier Ballroom A**

Convergent mechanisms for axon regeneration and CNS repair

Organizer : Kevin (Kyung) Park (University of Texas Southwestern Medical Center)
Byung Gon Kim (Ajou University)
Moderator : Byung Gon Kim (Ajou University)

Axon regeneration and functional rewiring after adult central nervous system injury
Kai Liu (Hong Kong University of Science and Technology)

Targeting Microtubule Dynamics to Promote Axon Regeneration
Eun Mi Hur (Seoul National University)

Path toward vision restoration through promoting optic nerve regeneration and reconnection
Kevin K. Park (University of Texas Southwestern Medical Center)

Immune modulation of CNS fibrosis
Jae Kyu Lee (University of Miami)

Neuro-immune interaction in post-stroke plasticity and functional recovery
Byung Gon Kim (Ajou University)

S24-1

Axon regeneration and functional rewiring after adult central nervous system injury

Kai Liu

Division of Life Science, Department of Chemical and Biological Engineering, SIAT-HKUST Joint Laboratory for Brain Science, State Key Laboratory of Nervous System Disorders, The Hong Kong University of Science and Technology

In contrast to the peripheral nervous system, axons in the adult mammalian central nervous system typically do not undergo spontaneous regeneration following injury. Axon regeneration failure poses a significant barrier to achieving functional recovery following neurotrauma, such as injuries to the spinal cord or optic nerve. Our study has mostly focused on the intrinsic mechanisms that regulate axon regeneration. We aim to build a research program investigating axon regeneration at the molecular, cellular, and system levels. Our research group has made discoveries in understanding the cell signaling pathways and mechanisms that control the process of axon regeneration. These findings offer a chance to investigate the role of regenerating axons, rebuild disrupted neural circuits, and develop potential therapeutic approaches following central nervous system injury.

Keywords : Axon regeneration, Retinal ganglion cells, Visual pathway injury, Spinal cord injury

S24-2

Targeting Microtubule Dynamics to Promote Axon Regeneration

Eun Mi Hur

College of Veterinary Medicine, Seoul National University, Seoul, Republic of Korea

In contrast to the central nervous system, neurons in the peripheral nervous system regenerate axons spontaneously after injury. Microtubules are the building blocks of axons, and axon regeneration occurs through polymerization of microtubules. Neuronal microtubules are heavily modified by various post-translational modifications (PTMs), which have been suggested to regulate the stability and dynamics of the polymer, as well as the interaction with a myriad of microtubule-associated proteins. In this study, we found that peripheral nerve injury induces specific changes in tubulin PTMs and alters the levels of multiple enzymes mediating tubulin PTMs. Moreover, modulating the expression levels of these enzymes by overexpression or knock-down approaches altered the speed of regenerative axon growth both in primary cultures and *in vivo* after sciatic nerve injury. These findings suggest that tubulin PTM controls intrinsic axon growth capacity and that targeting the regulatory mechanism of tubulin PTMs might provide ways to promote axon regeneration.

Keywords : Microtubule, Axon, Regeneration, Posttranslational modification, Nerve injury
Acknowledgements : This work was supported by the Research Institute for Veterinary Science at Seoul National University and the National Research Foundation funded by the Korean government (MSIT) (RS-2024-00338713, RS-2021-NR057184, Bio&Medical Technology Development Program RS-2021-NR056922, and the Comparative Medicine Disease Research Center SRC program RS-2021-NR060088).

S24-3

Path toward vision restoration through promoting optic nerve regeneration and reconnection

Kevin Park[1], Noah Mathe[2]

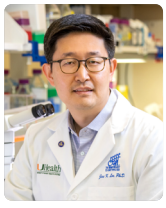
[1]Ophthalmology and Neuroscience, Peter O'Donnell Jr. Brain Institute, University of Texas Southwestern Medical Center, Dallas, USA
[2]Ophthalmology and Neuroscience, University of Texas Southwestern Medical Center, Dallas, USA

Optic nerve injury leads to irreversible vision loss due to the limited regenerative capacity of retinal ganglion cells (RGCs) in mammals. Understanding and enhancing optic nerve regeneration is a critical step toward developing effective therapies for blinding diseases such as glaucoma and optic neuropathies. In this study, we use mouse models to investigate the molecular and cellular mechanisms underlying optic nerve regeneration. By combining targeted genetic manipulations, viral vector-mediated gene delivery, and single-cell transcriptomic profiling, we identify key pathways and cell types involved in promoting axonal regrowth and reconnection after injury. Additionally, we assess functional recovery using electrophysiological and behavioral assays to correlate anatomical regeneration with visual function. Our findings highlight novel regenerative pathways and suggest combinatorial strategies that significantly enhance RGC survival and axon regeneration. This work contributes to the broader effort of CNS repair research and establishes a foundation for future translational approaches aimed at vision restoration.

Keywords : Axon regeneration, Visual system, Neuroprotection, Axon guidance, Non-coding RNA
Acknowledgements : This work was supported by grants from the National Eye Institute (NEI) R01EY032542, P30EY030413 (K.K.P), and Challenge Grant from Research to Prevent Blindness (K.K.P).

S24-4

Immune modulation of CNS fibrosis



Jae Kyu Lee

Miami Project To Cure Paralysis, University of Miami School of Medicine, Miami, Florida, USA

Fibrosis is a critical pathological feature in spinal cord injury (SCI) and other neurological disorders, contributing significantly to impaired recovery and long-term dysfunction. This process, characterized by excessive extracellular matrix deposition and scar formation, is intricately regulated by the innate immune system. The dynamic interplay between macrophages and fibroblasts shape the fibrotic response, mediating both protective and detrimental outcomes. This presentation explores the underlying mechanisms through which the immune system orchestrates fibrosis in the context of SCI, focusing on the role of macrophages and fibroblast subtypes. Additionally, it examines parallels in other neurological conditions, such as multiple sclerosis and stroke, to identify common immune pathways influencing fibrosis and scar resolution. This research highlights potential therapeutic strategies aimed at modulating the immune response to mitigate fibrosis, enhance neural regeneration, and improve functional outcomes. Understanding the immune-fibrosis axis opens new avenues for targeted interventions, offering hope for better recovery trajectories in patients with neurological injuries and diseases. This investigation underscores the importance of interdisciplinary approaches to deciphering the complexities of immune system involvement in central nervous system repair and fibrosis regulation.

Keywords : spinal cord injury, fibrosis, macrophages, fibroblasts, regeneration

S24-5

Neuroimmune interaction in post-stroke plasticity and functional recovery

Hyung Soon Kim[1], Byung Gon Kim[2]

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[2]Department of Brain Science, Department of Neurology, Ajou University School of Medicine, Suwon, 16499, Republic of Korea

Emerging evidence suggests that neuroimmune regulation determines stroke severity, tissue damage, and long-term functional outcomes through coordinated peripheral-central nervous system interactions. The complex interplay between nervous and immune systems fundamentally shapes neuroplasticity and outcomes following ischemic stroke. Within this neuroimmune landscape, arginase-1 (Arg1) serves as a critical mediator of immune cell phenotypes, particularly in anti-inflammatory macrophages associated with inflammation resolution and tissue repair. However, its precise role in orchestrating neuroimmune crosstalk during poststroke recovery remains incompletely understood. This study elucidates how Arg1-mediated neuroimmune interactions influence poststroke recovery and inflammatory milieu. Arg1 expression increases in a time-dependent manner, peaking at 7 days after photothrombotic stroke in mice, with cellular mapping revealing predominant expression in LysM-positive infiltrating macrophages. Using conditional knockout (cKO) mice, we examined how macrophage-expressed Arg1 modulates neuroimmune communication. Unexpectedly, Arg1 cKO in LysM-positive macrophages significantly enhanced skilled forelimb motor function recovery, revealing a detrimental role in neuroimmune regulation. Mechanistically, Arg1 deficiency promoted beneficial neuroimmune interactions by reducing pathological microglial synaptic elimination and enhancing tissue repair processes. In vitro experiments demonstrated that macrophage Arg1 activity directly modulates microglial synaptic phagocytosis, providing evidence for this neuroimmune interaction. These findings highlight the significance of peripheral-central immune crosstalk in stroke pathophysiology and demonstrate that precise neuroimmune regulation is crucial for optimal recovery. Our results position neuroimmune interface modulation as a fundamental therapeutic strategy, with Arg1 representing a key regulatory node determining stroke outcomes.

Keywords : Neuro-immune interaction; Stroke; Arginase-1; Functional recovery; Synapse elimination

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Symposium 25

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한국뇌연구원 Korea Brain Research Institute

Day 3 (August 26) **08:30-10:25** **Premier Ballroom B**

Decoding neuro-glial interactions: the critical role of ion channels from molecules to behaviors

Organizer : Hyun-Ho Lim (Korea Brain Research Institute)
Moderator : C. Justin Lee (Institute for Basic Science)

Bestrophins: structure, function and diseases
Tingting Yang (Columbia University)

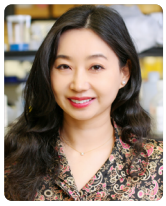
Molecular insight into the structural and functional modulation of bestrophin1 channel
Hyun-Ho LIm (Korea Brain Research Institute)

Bestrophin-1 mediated tonic GABA release from reactive astrocytes in kainate-injected hippocampus
Jin Bong Park (Seoul National University)

Bestrophin channels regulate food swallowing in C.elegans
Kyuhyung Kim (Daegu Gyeongbuk Institute of Science and Technology)

S25-1

Bestrophins: structure, function and diseases



Aaron Owji, Alec Kittredge, Jiali Wang, Yu Zhang, Tingting Yang

Ophthalmology, Columbia University, New York, USA

Bestrophins are a family of Ca^{2+}-activated anion channels with important (patho)physiological implications in the eye and the brain. In particular, bestrophin-1 (Best1) is predominantly expressed in the retinal pigment epithelium (RPE), and mutations in the human *BEST1* gene result in a spectrum of macular degenerative diseases collectively known as bestrophinopathies; bestrophin-2 (Best2) is located in non-pigmented epithelium (NPE) of the ciliary body, participating in the regulation of intra-ocular pressure (IOP). By cryogenic electron microscopy (cryo-EM), we solved the high-resolution structures of wild-type human Best1 and Best2 in various states, elucidating the gating mechanisms of these channels that underlie their distinct electrophysiological characteristics. Intriguingly, we identified key enzymes in glutamate metabolism as interacting regulators of bestrophin channels: 1) glutamine synthetase (GS) extends the ion conducting pathway of BEST2 through its central cavity and inhibits BEST2 channel function in the absence of intracellular glutamate, but sensitizes BEST2 to intracellular glutamate, which promotes the opening of BEST2 and thus relieves the inhibitory effect of GS; 2) both isoforms of glutamic acid decarboxylases (GAD65 and GAD67) interact with Best1 and promote Best1-mediated Cl^- currents, while only GAD65 tunes the functions of Best1 as a GABA receptor and a neurotransmitter conducting channel. These findings shed light on the physiological roles and regulations of bestrophins in the neural system, and inspire new strategies and targets for the treatment of bestrophin-associated diseases.

Keywords : Bestrophin, Calcium-activated anion channel, Anion transport, Glutamate metabolism, Retinal disease
Acknowledgements : National Institute of General Medical Sciences (NIGMS), National Eye Institute (NEI), Research to Prevent Blindness (RPB), Irma T. Hirschl Trust, Schaefer Research Scholars Program, Simons Foundation, Center on Membrane Protein Production and Analysis (COMPPÅ), National Center for Cryo-EM Access and Training (NCCAT), Columbia Cryo-EM Core

S25-2

Molecular insight into the structural and functional modulation of bestrophin1 channel

Hyun-Ho Lim

Neurovascular Unit Research Group, Korea Brain Research Institute, Daegu, Republic of Korea

Bestrophin 1 (BEST1) channels are calcium-activated Cl^- channels involved in diverse physiological processes, including gliotransmitter release in astrocytes. Interestingly, BEST1 orthologs share high amino acid sequence identity in the N-terminal region (~370 residues), but exhibit only marginal identity in the C-terminal region (~150-200 residues). While human and chicken BEST1 orthologs have been extensively studied, the structural and functional properties of mouse BEST1 (mBEST1) remain poorly understood. To address this gap, we characterized mBEST1 using whole-cell patch-clamp recordings, surface biotinylation assays, and single-particle cryo-electron microscopy (cryo-EM). Additionally, to investigate the molecular basis underlying the functional differences between human and mouse BEST1 channels, we performed immunoprecipitation-mass spectrometry (IP–MS) to identify proteins that specifically interact with hBEST1. This analysis revealed PYCR3, the terminal enzyme in proline biosynthesis, as a specific binding partner of hBEST1. The interaction was further validated through co-immunoprecipitation, size-exclusion chromatography, and split-GFP reconstitution assays. The functional consequences of the hBEST1–PYCR3 interaction were evaluated using whole-cell patch-clamp recordings, and we also determined the structure of the hBEST1-PYCR3 complex at a resolution of ~3 Å. In this symposium, I will present recent advances from my laboratory on the structural and functional characterization of BEST1 channels and discuss their physiological and mechanistic implications.

Keywords : Bestrophin, Cryo-electron microscopy, Whole-cell patch-clamp, Chloride, gliotransmitter

S25-3

Bestrophin-1 Mediated Tonic GABA Release from reactive astrocytes in kainate-injected hippocampus

Jin Bong Park

Department of Veterinary Medicine, College of Veterinary Medicine Seoul National University, Seoul, Republic of Korea

Tonic inhibition mediated by extrasynaptic $GABA_A$ receptors ($GABA_ARs$) is essential for maintaining the brain's excitation/inhibition (E/I) balance. This form of inhibition is regulated by a low, sustained release of GABA from astrocytes. Disruption of this delicate balance can lead to neurological disorders, including epileptic seizures. However, the specific contribution of astrocyte-derived tonic GABA release to epilepsy has remained largely unexplored. In this talk, I will present evidence that pharmacological blockade or genetic deletion of Bestrophin-1 (Best1)—a GABA-permeable channel expressed in astrocytes—impairs tonic $GABA_AR$-mediated inhibition. This disinhibition of CA1 pyramidal neurons enhances seizure susceptibility in a kainic acid (KA)-induced mouse model of epilepsy. Strikingly, astrocyte-specific overexpression of Best1 in KA-injected Best1 knockout mice restores tonic $GABA_A$ inhibition and markedly suppresses seizure activity.
These findings demonstrate that tonic GABA release from reactive astrocytes provides a key compensatory mechanism for restoring E/I balance in the epileptic hippocampus. We propose that tonic astrocytic GABA release of Best1 is a promising therapeutic target for modulating aberrant inhibitory tone in epilepsy.

Keywords : Best1, astrocytes, extrasynaptic GABAAR, hippocampus, epilepsy

S25-4

Bestrophin channels regulate food swallowing in *C*. elegans

Kyuhyung Kim

Department of Brain Sciences, DGIST, Daegu, Republic of Korea

Interoception, the process of sensing internal signals from the body, is essential for maintaining homeostasis and survival. Various ion channels, including the PIEZO channel, have been implicated in interoception; however, how different ion channels contribute to this process and interact with cellular signaling pathways remains largely unknown. In *C. elegans*, the PIEZO channel, encoded by *pezo-1* and expressed in the pharyngeal-intestinal valve (PI valve), detects food accumulation in the anterior intestinal lumen and triggers rhythmic pharyngeal plunges—a process that regulates intestinal food movement (Park et al., 2024). However, how PIEZO channels translate mechanical cues into cellular signals remains poorly understood, particularly the mechanisms by which mechanically activated channels regulate downstream signaling events mediating physiological responses. Here, we show that the evolutionarily conserved calcium-activated chloride channels Bestrophins (BESTs) regulate PIEZO-dependent pharyngeal plunge. Among the 26 bestrophin genes in *C. elegans*, we found that *best-1* and *best-9* are co-expressed in the PI valve. We also found that *best-9 best-1* double mutants, but not *best-1* or *best-9* single mutants, exhibit prolonged and deep pharyngeal plunges, which are restored by the expression of *best-1* or *best-9* cDNA under the control of their respective promoters. Furthermore, overexpression of *best-1* or *best-9* in the PI valve decreases the frequency and depth of pharyngeal plunges, leading to defects in food swallowing. These results indicate that *best-1* and *best-9* act redundantly to inhibit pharyngeal plunging in the PI valve. Additionally, optogenetic activation of the PI valve in double mutants results in significantly deeper pharyngeal plunges compared to wild-type worms. This study uncovers a mechanistic link between BEST channels and PIEZO-dependent mechanosensation, providing insights into how BEST channels regulate interoceptive processes.

Keywords : Piezo, bestrophin, interoception, *C. elegans*, food swallowing

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 26

Day 3 (August 26) **08:30-10:25** **Premier Ballroom C**

Neuroscience-inspired AI: computational insights into biological and artificial intelligence

Organizer : Sungho Hong (Institute for Basic Science)
Jae Kwon (Max Planck Institute)
Moderator : Sungho Hong (Institute for Basic Science)

Digital Brain for NeuroAI
Kenji Doya (Okinawa Institute of Science and Technology)

Training neural networks using random noise
Se-Bum Paik (Korea Advanced Institute of Science and Technology)

Advancing Spiking Neural Networks for Sequential Modeling
Dongqi Han (Microsoft Research Asia)

Transformer as a hippocampal memory consolidation model based on NMDAR-inspired nonlinearity
Jea Kwon (Max Planck Institute)

SUBTLE: An Unsupervised Platform with Temporal Link Embedding that Maps Animal Behavior
Sunpil Kim (Institute for Basic Science)

S26-1

Digital Brain for NeuroAI

Kenji Doya

Neural Computation Unit, Okinawa Institute of Science and Technology Graduate University, Onna Village, Okinawa, Japan

Following the conclusion of the Brain/MINDS project (2014-2024), a new six-year program Brain/MINDS 2.0 has started. A remarkable feature of this program is that the Digital Brain plays a central role in integrating structural and dynamic brain data from multiple species for understanding brain functions and tackling neuropsychiatric disorders. This talk will present what is the Digital Brain of Brain/MINDS 2.0, how we can build that using AI technologies, and how that can contribute to NeuroAI deveopment. Building Digital Brain requires fresh talents from math, computation, AI and brain sciences, as well as broad international collaborations. In this symposium, we hope to extend our network with researchers in Korea, China, and beyond.

Keywords : digital brain, Brain/MINDS, data-driven science, computational modeling
Acknowledgements : This work is supoorted by Japan Agency for Medical Research and Development (AMED) grant JP23wm0625001.

S26-2

Training neural networks using random noise

Se-Bum Paik

Brain and Cognitive Sciences, KAIST, Daejeon, Republic of Korea

Randomness, often regarded as mere noise or an unwanted signal, is in fact a fundamental component of natural systems, including the brain. In this talk, I propose a novel perspective on the essential role of random noise in neural network development and training, grounded in a computational neuroscience approach. First, I examine the role of spontaneous, seemingly random neural activity in shaping the brain's capacity for learning. Even before environmental interaction, the brain engages in intrinsic activity patterns — resembling random noise — that refine and optimize its circuits in preparation for future learning. Through computational modeling, we demonstrate that pretraining neural networks with random noise can greatly increase the learning efficiency as well as generalization abilities without weight transport, enabling a biologically plausible error backpropagation algorithm. Second, I show that such pretraining facilitates uncertainty calibration within neural circuits, enabling robust detection of unfamiliar or novel inputs. Together, these findings highlight the constructive role of randomness in brain function and challenge the conventional view that structured external input is the primary driver of learning and cognition.

Keywords : computational neuroscience, neural network, random noise, pretraining, generalization
Acknowledgements : This work was supported by the National Research Foundation of Korea (NRF) grants (NRF2022R1A2C3008991 to S.P.) and by the Singularity Professor Research Project of KAIST (to S.P.).

S26-3

Advancing Spiking Neural Networks for Sequential Modeling

Dongqi Han

Microsoft Research Asia, Microsoft, Shanghai, China

Spiking neural networks (SNNs) offer a promising pathway toward developing artificial neural networks that are both energy-efficient and biologically plausible. Their inherent ability to model temporal dynamics makes them particularly well-suited for sequential data. However, systematically applying SNNs to sequential modeling tasks—such as time-series forecasting and natural language processing—remains a challenge. In this talk, I present three contributions aimed at advancing the application of SNNs to sequential modeling. First, we propose a framework for time-series forecasting using SNNs, leveraging the temporal efficiency of spiking neurons. Experimental results show that our SNN-based Transformer architecture achieves performance comparable to or surpassing that of conventional forecasting methods across various benchmarks. Second, we identify the incompatibility of traditional positional encoding techniques with SNNs. Inspired by central pattern generators (CPGs) in the human brain—which generate rhythmic outputs without rhythmic inputs—we introduce a novel positional encoding method for SNNs, which is simple yet consistently brings performance gain. Finally, we propose several strategies for approximating relative positional encoding in spiking Transformers while preserving the discrete, binary nature of spikes. Together, these contributions advance the potential of SNNs for energy-efficient sequential modeling.

Keywords : Spiking Neural Network, Central Pattern Generator, Deep Learning, Leaky Integrate-and-Fire Neuron, Artificial Intelligence

S26-4

Transformer as a hippocampal memory consolidation model based on NMDAR-inspired nonlinearity

Dong Kyum Kim[1], Jea Kwon[1], Meeyoung Cha[1], C. Justin Lee[2]

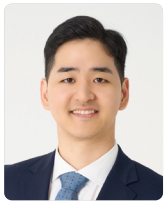
[1]Data Science for Humanity, Max Planck Institute for Security and Privacy, Bochum, Germany
[2]Center for Cognition and Sociality, Institute for Basic Science, Daejeon, Republic of Korea

The hippocampus plays a critical role in learning, memory, and spatial representation, processes that depend on the NMDA receptor (NMDAR). Inspired by recent findings that compare deep learning models to the hippocampus, we propose a new nonlinear activation function that mimics NMDAR dynamics. NMDAR-like nonlinearity shifts short-term working memory into long-term reference memory in transformers, thus enhancing a process that is similar to memory consolidation in the mammalian brain. We design a navigation task assessing these two memory functions and show that manipulating the activation function (i.e., mimicking the Mg^{2+}-gating of NMDAR) disrupts long-term memory processes. Our experiments suggest that place cell-like functions and reference memory reside in the feed-forward network layer of transformers and that nonlinearity drives these processes. We discuss the role of NMDAR-like nonlinearity in establishing this striking resemblance between transformer architecture and hippocampal spatial representation.

Keywords : NMDAR, Transformer, Nonlinearity, Hippocampus, Memory Consolidation

S26-5

SUBTLE: An Unsupervised Platform with Temporal Link Embedding that Maps Animal Behavior



Jea Kwon[1], Sunpil Kim[1], Dong-Kyum Kim[2], Jinhyeong Joo[1,3], SoHyung Kim[1], Meeyoung Cha[2,4], C. Justin Lee[1,3]

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While huge strides have recently been made in language-based machine learning, the ability of artificial systems to comprehend the sequences that comprise animal behavior has been lagging behind. In contrast, humans instinctively recognize behaviors by finding similarities in behavioral sequences. Here, we develop an unsupervised behavior-mapping framework, SUBTLE (spectrogram-UMAP-based temporal-link embedding), to capture comparable behavioral repertoires from 3D action skeletons. To find the best embedding method, we devise a temporal proximity index (TPI) as a new metric to gauge temporal representation in the behavioral embedding space. The method achieves the best TPI score compared to current embedding strategies. Its spectrogram-based UMAP clustering not only identifies subtle inter-group differences but also matches human-annotated labels. SUBTLE framework automates the tasks of both identifying behavioral repertoires like walking, grooming, standing, and rearing, and profiling individual behavior signatures like subtle inter-group differences by age. SUBTLE highlights the importance of temporal representation in the behavioral embedding space for human-like behavioral categorization.

Keywords : Unsupervised behavior mapping, Spectrogram-UMAP, Temporal proximity index, Behavior embedding space
Acknowledgements : The authors would like to thank Dae-Gun Kim and Jungjoon Park from ACNTNOVA for their helpful discussions and experimental support on the AVATAR system. D. K. K. and M. C. were supported by IBS under Grant Number IBS-R029-C2. J. K., S. K., J. H. J., S. H. K., and C. J. L. were supported by IBS under grant number IBS-R001-D2.

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 27

Day 3 (August 26) **08:30-10:25** **Rm.113-115**

Decoding Inhibition: the interplay of GABA, chloride, and astrocytes in neural function in health and disease

Organizer : Verena Untiet (University of Copenhagen)
Heejung Chun (Yonsei University)
Moderator : Verena Untiet (University of Copenhagen)
Heejung Chun (Yonsei University)

Astrocytic tonic Inhibition as a therapeutic Target for motor dysfunction in neurodevelopmental disorders
Bo-Eun Yoon (Dankook University)

Astrocytes control neuronal activity by modulating extracellular ion concentrations
Verena Untiet (University of Copenhagen)

Reactive astrocytes drive tau pathology via autophagy dysfunction and MAO-B upregulation in Alzheimer's disease
Heejung Chun (Yonsei University)

S27-1

Astrocytic tonic Inhibition as a therapeutic Target for motor dysfunction in neurodevelopmental disorders

Jong Min Joseph Kim[1,5], Moonsun Sa[2,5], Junsung Woo[2], Yoo Sung Kim[1], Won-Seok Lee[1], Joo Ok Min[1], Dong-Wook Kang[3], Hyun-Woo Kim[3], C. Justin Lee[2,*], Bo-Eun Yoon[1,4*]

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[5]These authors contributed equally

Astrocytes are key players in motor coordination, modulating neuronal excitability through tonic GABA release, and represent a potential therapeutic target for movement and psychiatric disorders characterized by an altered excitation/inhibition balance. In ADHD genetic model, we observed gait instability, reflected by an abnormal base of support, and altered behavioral patterns, notably frequent transitions to head-raising-like behavior without progression to rearing-like behavior. Treatment with SNAP5114, a GAT-3 inhibitor that modulates tonic inhibition, alleviated these abnormalities. These findings indicate that tonic inhibition plays a role in the pathophysiology of this neurodevelopmental disorder and that its modulation may represent a promising therapeutic strategy for addressing motor deficits in psychiatric disorders.

Keywords: Motor coordination, Tonic inhibition, GAT-3, ADHD, Cerebellum

S27-2

Astrocytes control neuronal activity by modulating extracellular ion concentrations

Verena Untiet

Center for Translational Neuromedicine, University of Copenhagen, Copenhagen, Denmark, Denmark

Neuronal excitability is tightly controlled by chloride (Cl^-), the principal ion mediating inhibition in the brain. We show in naturally behaving mice that astrocytes actively regulate Cl^- homeostasis in a brain state-dependent manner—maintaining high intracellular Cl^- during sleep and exhibiting dynamic fluctuations during wakefulness in response to sensory and motor activity. Optogenetic manipulation of astrocytic Cl^- alters neuronal responses, revealing astrocytes as modulators of the excitation/inhibition (E/I) balance via extracellular Cl^- buffering. Cl^- release occurs via $GABA_AA$ receptors and tracks with brain state, challenging the long-held view of static extracellular Cl^- levels. Disrupting Cl^- accumulation or release from astrocytes lowers seizure thresholds, identifying astrocytic Cl^- dynamics as a key regulator of network excitability and a promising target for epilepsy therapy.

Keywords : Inhibition, GABA, Chloride, Astrocyte, brain states
Acknowledgements : This work was funded by the Novo Nordisk Foundation, the Independent Research Fund Denmark and the Lundbeck Foundation.

S27-3

Reactive astrocytes drive tau pathology via autophagy dysfunction and MAO-B upregulation in Alzheimer's disease

Heejung Chun

College of Pharmacy, Yonsei University, Incheon, Republic of Korea

Reactive astrocytes emerge among the earliest pathological changes in Alzheimer's disease (AD), yet their role in the development of later-stage tau pathology remains unclear. Here, we demonstrate that reactive astrocytes actively contribute to tau aggregation and cognitive dysfunction through impaired autophagy and elevated monoamine oxidase-B (MAO-B). Neuronal expression of human 3-repeat (3R) tau alone did not induce neurofibrillary tangles (NFTs) or memory deficits. However, under neuroinflammatory conditions that induce robust astrocytic reactivity, hTau3R expression led to increased NFTs and cognitive impairment. Adenovirus-induced reactive astrocytes exhibited disrupted autophagic flux, and astrocyte-specific knockdown of ATG5 exacerbated tau pathology and MAO-B expression. Notably, genetic or pharmacological inhibition of astrocytic MAO-B significantly reduced tau accumulation and behavioral deficits. Together, our findings uncover a mechanistic link between astrocytic dysfunction and tauopathy, establishing reactive astrocytes as key pathological amplifiers and suggesting astrocytic autophagy and MAO-B as potential therapeutic targets in AD.

Keywords : Reactive astrocytes, Alzheimer's disease, tau pathology, autophagy, monoamine oxidase-B (MAO-B)
Acknowledgements : This research was supported by the Yonsei University Research Fund of 2024 (2024-22-0131).

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 28

Supported By KAIST GSMSE 의과학대학원
뇌 체성 돌연변이 연구단
Center for Brain Somatic Mutations

Day 3 (August 26) **08:30-10:25** **Rm.204-205**

Epilepsy:from gene to circuit

Organizer : Won Seok Chang (Yonsei University)
Eunee Lee (Yonsei University)
Moderator : Won Seok Chang (Yonsei University)

Understanding Neurodevelopmental and Seizure Patterns in Monogenic Epilepsies
Se Hee Kim (Yonsei University)

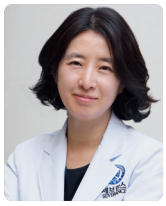
The intersection between autism and epilepsy in SCN2A-related neurodevelopmental disorders
Kevin Bender (University of California, San Francisco)

Neurosurgical approach for intractable epilepsy from bench to clinic
Won Seok Chang (Yonsei University)

Electrophysiological hallmarks of epilepsy and autism in the human neocortex
Jaeyoung Yoon (Harvard University)

S28-1

Understanding Neurodevelopmental and Seizure Patterns in Monogenic Epilepsies



Se Hee Kim

Pediatric Neurology, Severance Children's Hospital, Seoul, Republic of Korea

Monogenic epilepsies are a clinically and biologically heterogeneous group of disorders that often begin in early childhood and are associated with a wide spectrum of neurodevelopmental outcomes. Advances in genomic diagnostics have enabled the identification of a growing number of pathogenic variants, yet major gaps remain in understanding how specific genetic mechanisms contribute to seizure patterns and long-term developmental trajectories.
This lecture will explore how genetic variant types—such as single nucleotide variants (SNVs) and copy number variants (CNVs)—and gene functional categories, particularly channelopathies versus non-channelopathies, relate to epilepsy severity, cognitive outcomes, and developmental milestones in affected children. Emerging evidence suggests that certain genetic mechanisms may influence the timing and severity of seizures, the likelihood of achieving early motor and language milestones, and the risk of intellectual disability.
By integrating insights from clinical cohorts and basic neuroscience research, we aim to identify biomarkers and early developmental indicators that can predict long-term outcomes. Special attention will be given to how early seizure characteristics, anti-seizure medication burden, and failure to achieve key milestones can inform prognosis and guide treatment strategies.
This session will highlight the need for mechanism-based approaches in the care of children with monogenic epilepsies and underscore the importance of interdisciplinary collaboration between clinicians, geneticists, and neuroscientists in developing precision therapies.

Keywords : Epilepsy, Developmental epileptic encephalopathy, Genetic
Acknowledgements : This study was supported by the Korea Health Industry Development Institute (KHIDI, RS-2023-00266971), and a Faculty Research Grant of Yonsei University College of Medicine (6-2024-0119).

S28-2

The intersection between autism and epilepsy in SCN2A-related neurodevelopmental disorders

Kevin Bender

University of California, San Francisco

Dysfunction in the gene SCN2A, which encodes the neuronal sodium channel NaV1.2, is a major risk factor for a range of neurodevelopmental disorders, including epileptic encephalopathy, autism spectrum disorder, and developmental delay. Broadly, these different neurodevelopmental disorders result from different effects on NaV1.2 function, with gain-of-function missense variation that enhance NaV1.2 function associated with early onset epilepsy and loss-of-function missense or protein truncating variation that dampen NaV1.2 function associated with autism and developmental delay. And yet, a subset of children with SCN2A loss-of-function variants also develop seizures, albeit far later in development than those with gain-of-function variants. These seizures are of neocortical origin, where NaV1.2 is expressed in excitatory pyramidal cell dendritic domains. Here, I will discuss recent progress from the lab in understanding why loss-of-function in NaV1.2 in neocortical dendrites can promote epilepsy, how studies across model systems can help shed light on disorder etiology, and how restoration of SCN2A expression in loss-of-function conditions can help restore normal cortical function.

Keywords: epilepsy, autism, ion channel, neocortex, electrophysiology

S28-3

Neurosurgical Approach for Intractable Epilepsy: From Bench to Clinic

Won Seok Chang

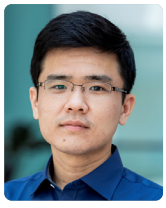
Department of Neurosurgery, Severance Epilepsy Center, Yonsei University College of Medicine, Seoul, Republic of Korea.

Intractable epilepsy—defined as persistent seizures despite adequate trials of antiseizure medications—affects approximately one-third of patients with epilepsy, profoundly impacting quality of life and increasing the risk of injury even sudden unexpected death in epilepsy (SUDEP). For these patients, neurosurgical intervention remains a cornerstone of treatment, offering the possibility of seizure freedom or significant reduction in seizure burden. Over the past decade, advances in both diagnostic and therapeutic modalities have reshaped the neurosurgical landscape, enabling more precise, individualized, and less invasive approaches. In this presentation, a comprehensive overview of the translational journey from bench to clinic in the surgical management of intractable epilepsy will be provided, with a particular emphasis on stereoelectroencephalography (sEEG) radiofreqneucy thermal coagulation(RFTC) and focused ultrasound (FUS). sEEG has revolutionized presurgical evaluation by allowing safe and accurate three-dimensional mapping of epileptogenic networks, even in deep or eloquent cortical areas. We will review innovations in sEEG trajectory planning, integration of high-resolution structural and functional imaging with arc centered stereotactic robotic system, and efficacy of development and preclinical evaluation of RFTC implanted sEEG. In parallel, focused ultrasound is emerging as a versatile tool in epilepsy care. Preclinical studies and early-phase clinical trials have demonstrated its potential in applications of low-intensity FUS to transiently open the blood–brain barrier (BBB), facilitating localized delivery of antiseizure drugs, gene therapy vectors, or neuromodulatory agents. These approaches hold promise for patients who are poor candidates for open surgery or in whom minimally invasive alternatives are preferred. Drawing from experimental models, translational research, and early human experience, this presentation will explore the mechanistic insights, technical refinements, and safety considerations that underpin these innovations. Case examples will illustrate how sEEG and FUS can be integrated into a stepwise treatment algorithm, potentially expanding the pool of patients eligible for surgical intervention
By bridging basic science discoveries and clinical application, these neurosurgical advances are redefining the treatment paradigm for intractable epilepsy, with the ultimate goal of delivering safer, more effective, and more personalized care.

Keywords : Intractable epilepsy, stereoencephalography, radiofrequency thermal coagulation, focused ultrasound, preclinical

S28-4

Electrophysiological hallmarks of epilepsy and autism in the human neocortex



Jaeyoung Yoon[1], Brielle Ferguson[1,2]

[1]F.M. Kirby Neurobiology Center, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA
[2]Department of Genetics, Harvard Medical School, Boston, MA, USA

Research on the physiology and pathophysiology of the human brain is challenging due to the limitations on the experimental methods appropriate for human subjects, or the inherent dissimilarities of animal models to the human system. Combining the advantages of high-resolution techniques and human studies, we examined the neuronal intrinsic and synaptic properties with patch clamp electrophysiology in acute human brain slices. Neocortical tissue was resected from patients with tumor or intractable epilepsy, some of whom were additionally diagnosed with autism spectrum disorder (ASD). In epilepsy with focal cortical dysplasia type I (FCD I), the synaptic drive of fast-spiking interneurons (FSINs) was shifted from progressively increasing excitation to net inhibition, thus compromising the cortical excitation-inhibition (E-I) balance. In ASD, local and long-range excitatory cortical connectivity were inversely affected, but without changes in the E-I balance. Corroborating findings from in vivo and in vitro experiments are presented, and future directions are discussed.

Keywords : Synaptic physiology, Excitation-inhibition balance, Epilepsy, Autism spectrum disorder, Human brain slice

August 24(Sun)- 27(Wed), 2025

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KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 29

Supported By 한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

Day 3 (August 26) **08:30-10:25** **Rm.206-207**

Decoding the neurobiology of acupuncture through modern neuroscientific approaches

Organizer : Min-Ho Nam (Korea Institute of Science and Technology)
Hi-Joon Park (Kyung Hee University)
Moderator : Min-Ho Nam (Korea Institute of Science and Technology)
Hi-Joon Park (Kyung Hee University)

Neuroanatomical organization of electroacupuncture in modulating gastric function in mice and humans
Shenbin Liu (Fudan University)

Central role of hypothalamic circuits for acupuncture's anti-parkinsonian effects
Min-Ho Nam (Korea Institute of Science and Technology)

Neurobiological mechanism of acupuncture in Parkinson's disease through gut-brain axis modulation
Hi-Joon Park (Kyung Hee University)

Vascular endothelial cell-secreted protein acts as a bridge for early periphery-to-brain inflammatory signaling
Qiuzi Wu (Peking University) IBRO AWARDEE

S29-1

Neuroanatomical organization of electroacupuncture in modulating gastric function in mice and humans

Shenbin Liu

State Key Laboratory of Brain Function and Disorders, MOE Frontiers Center for Brain Science, Institutes of Brain Science, Huashan Hospital, Fudan University, Shanghai, 200032, China

Somatosensory-vagal reflexes evoked by electroacupuncture (EA) can modulate visceral functions. However, the underlying principles and neural mechanisms remain poorly understood, hindering further optimization. Here, we identified key neural components essential for EA topographically driving the somatosensory-vagal-gastric reflex in mice. EA drove this reflex via activation of a subset of TRPV1$^+$ nociceptors marked by the expression of Adra2a and located exclusively in deep fascial tissues. Through TRPV1$^+$ fibers, EA activated a subtype of gastro-projecting Oxtr$^+$ fibers originating from the dorsal motor nucleus of the vagus (DMV). Genetic ablation of TRPV1$^+$ fibers or Oxtr$^+$ DMV neurons attanuated EA-induced gastric reflexes. Conversely, optogenetic activation of these neurons was sufficient to drive gastric motility in mice. Using similar stimulation parameters, we demonstrated that EA successfully improved gastric functions in patients with dysmotility-like functional dyspepsia. Our findings thus provide a neural anatomical basis for EA topographically to promote and treat gastric motility disorders.

S29-2

Central role of hypothalamic circuits for acupuncture's anti-parkinsonian effects

Ju-Young Oh[1,2], Hyowon Lee[3], Hi-Joon Park[1,2*], Min-Ho Nam[2,3*]

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Despite clinical data stretching over millennia, the neurobiological basis of the effectiveness of acupuncture in treating diseases of the central nervous system has remained elusive. Here, using an established model of acupuncture treatment in Parkinson's disease (PD) model mice, we show that peripheral acupuncture stimulation activates hypothalamic melanin-concentrating hormone (MCH) neurons via nerve conduction. We further identify two separate neural pathways originating from anatomically and electrophysiologically distinct MCH neuronal subpopulations, projecting to the substantia nigra and hippocampus, respectively. Through chemogenetic manipulation specifically targeting these MCH projections, we demonstrate their respective roles in mediating the acupuncture-induced motor recovery and memory improvements following PD onset, as well as the underlying mechanisms mediating recovery from dopaminergic neurodegeneration, reactive gliosis, and impaired hippocampal synaptic plasticity. Collectively, we find these MCH neurons constitute not only a circuit-based explanation for the therapeutic effectiveness of traditional acupuncture, but also a potential cellular target for treating both motor and non-motor PD symptoms.

Funding: RS-2022-NR071818, RS-2024-NR121316, RS-2025-25413720

Keywords : Acupuncture, Parkinson’s disease, Lateral hypothalamus, Melanin-concentrating hormone, Neural circuits

S29-3

Neurobiological mechanism of acupuncture in Parkinson's disease through gut-brain axis modulation

Hi-Joon Park[1,2], Min-Ho Nam[2,3], Ju-Young Oh[1], Hyowon Lee[2], Mijung Yeom[1], Su-Yang Park[1], Sun-Young Jang[1], Seung-Tae Kim[4], Inwha Baek[5]

[1]Acupuncture & Meridian Science Research Center, College of Korean Medicine, Kyung Hee University, Seoul, 02447, Republic of Korea, [2]Department of KHU-KIST Convergence Science Technology, Graduate School, Kyung Hee University, Seoul, 02447, Republic of Korea, [3]Brain Science Institute, Korea Institute of Science and Technology (KIST), Seoul, 02792, Republic of Korea, [4]Department of Korean Medical Science and Division of Meridian and Structural Medicine, School of Korean Medicine, Pusan National University, Yangsan, 626313, Republic of Korea, [5]College of Pharmacy, Kyung Hee University, Seoul, 02447, Republic of Korea

Parkinson's disease (PD) is increasingly recognized as a multi-system disorder involving bidirectional brain–gut communication. Here, we identify melanin-concentrating hormone (MCH) neurons in the lateral hypothalamus and zona incerta as critical regulators of this axis. In a mouse PD model, acupuncture selectively activated MCH neurons projecting to the dorsal motor nucleus of the vagus (DMV), engaging vagal efferents to restore gut barrier integrity, reduce intestinal inflammation, and normalize microbiota composition, leading to motor improvement. Cell-type-specific chemogenetic activation of MCH neurons reproduced these effects, whereas inhibition abolished them. Subdiaphragmatic vagotomy eliminated both gastrointestinal and behavioral benefits, confirming the $MCH^{LH/ZI}$→DMV→vagus nerve→gut pathway as essential. These findings establish a top-down hypothalamic–brainstem circuit through which acupuncture exerts anti-parkinsonian effects, providing a mechanistic basis for integrated central–peripheral therapeutic strategies.

Funding: NRF-2021R1A2C2006818; RS-2024-00409969; RS-2022-NR071818
Keywords : Acupuncture, Parkinson's disease, melanin concentrating hormone releasing neuron, gut-brain axis, vagus nerve

S29-4 IBRO AWARDEE

Vascular endothelial cell-secreted protein acts as a bridge for early periphery-to-brain inflammatory signaling

Qiuzi Wu[1], Miao Qi[1,2], Qi Qin[1], Yi Dai[1,2], Xiang Yu[1]

[1]State Key Laboratory of Membrane Biology, School of Life Sciences, Peking-Tsinghua Center for Life Sciences, and Peking University McGovern Institute, Peking University, Beijing, China
[2]Academy for Advanced Interdisciplinary Studies, Peking University, Beijing, China

Acute pathogenic infections, if not effectively controlled, have a high probability of transforming into systemic inflammation, leading to breakdown of the blood-brain barrier (BBB), intense inflammatory response in the brain and impairment of brain function. Previous studies have mostly focused on the role of glial cells in the development and progression of neuroinflammation, while little attention has been paid to other neurovascular unit components, especially vascular-associated cells. Here we found that knockout of *Tlr4* in vascular endothelial cells (VECs) significantly and consistently reduced the neuroinflammation induced by lipopolysaccharide (LPS) injection. By combining the results of multi-omics, and further screening in *in vitro* assays, we found the SERPIN to be the most promising candidate. *Serpin* increased rapidly and dramatically after LPS challenge, and predominantly expressed in brain VECs during the early stages of neuroinflammation. Acute injection of recombinant SERPIN protein directly into the brain markedly promoted the expression of proinflammatory cytokines as well as the activation of microglia. Transcriptome sequencing revealed that SERPIN injection significantly activated the host innate immune response and diverse immune signaling cascades. In contrast, expression of proinflammatory cytokines and microglial activation after LPS injection were reduced in *Serpin* knockout mice, suggesting attenuation of the level of neuroinflammation. Notably, *Serpin* knockout alleviated LPS-induced hypothermia and sickness behavior, and protected against high-dose LPS-induced mortality. In summary, our work identified SERPIN secreted by brain VECs as a key signaling molecule bridging peripheral inflammation and neuroinflammation. The strategic location of SERPIN-expressing cells makes it a promising new molecular drug target that enables early intervention at the source of neuroinflammation, without the need to cross the BBB.

Keywords : Neuroinflammation, Vascular endothelial cells, SERPIN, Microglia
Acknowledgements : We are grateful to colleagues at PKU and members of the YuX laboratory for suggestions and comments. This work was supported by grants from the Ministry of Science and Technology of China (2021ZD0202500, to X.Y.)

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 30

Day 3 (August 26) **10:35-12:30** **Premier Ballroom B**

Precise dissection of structural and functional features in visual system

Organizer : Jiayi Zhang (Fudan University)
Hailan Hu (Zhejiang University)
Moderator : Wei Li (National Institutes of Health)
Jiayi Zhang (Fudan University)

Functionally distinct GABAergic amacrine cell types regulate spatiotemporal encoding in the mouse retina
Keisuke Yonehara (National Institute of Genetics)

Linking single-cell transcriptomes with physiological phenotypes
Sheng Liu (Sun Yat-sen University)

Altered Visuomotor Responses in Achiasmatic Vax1AA/AA Mice
Jin Woo Kim (Korea Advanced Institute of Science and Technology)

How robust is the retina? Visual responses in a severely disorganized circuit
Chieko Koike (Ritsumeikan University)

VIVIT: Resolving trans-scale volumetric biological architectures via ionic glassy tissue
Kexin Yuan (Tsinghua University)

and the National Natural Science Foundation of China (32030049, to X.Y.).

S30-1

Functionally distinct GABAergic amacrine cell types regulate spatiotemporal encoding in the mouse retina

KEISUKE YONEHARA

Dept. of Gene Function and Phenomics, National Institute of Genetics, Mishima, Japan

GABA (γ-aminobutyric acid) is the primary inhibitory neurotransmitter in the mammalian central nervous system. GABAergic neuronal types play important roles in neural processing and the etiology of neurological disorders; however, there is no comprehensive understanding of their functional diversity. Here we perform two-photon imaging of GABA release in the inner plexiform layer of mouse retinae using the GABA sensor iGABASnFR2. By applying varied light stimuli to isolated retinae, we reveal over 40 different GABA-releasing neuron types. Individual types show layer-specific visual encoding within inner plexiform layer sublayers. Synaptic input and output sites are aligned along specific retinal orientations. The combination of cell type-specific spatial structure and unique release kinetics enables inhibitory neurons to sculpt excitatory signals in response to a wide range of behaviorally relevant motion structures. Our findings emphasize the importance of functional diversity and intricate specialization of GABAergic neurons in the central nervous system.

Keywords : Retina, GABA, Two-photon imaging, Visual Processing, Inhibitory neurons
Acknowledgements : iGABASnFR2 plasmids and AAVs were a gift from the GENIE Project, Janelia Research Campus, Howard Hughes Medical Institute. This work was supported by grants from the Lundbeck Foundation (DANDRITE-R248-2016-2518; R344-2020-300), Novo Nordisk Foundation (NNF15OC0017252; NNF20OC0064395), European Research Council Starting Grant (638730), KAKENHI (20K23377; 22K21353; 23H04241; 24H02311).

S30-2

Linking single-cell transcriptomes with physiological phenotypes

Qiang Xu, Wanjing Huang, Zhao-Zhe Hao, Ruifeng Liu, Lei Tang, Jing Su, Sheng Liu

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou 510060, China

Understanding the neural basis of vision requires a comprehensive atlas depicting the morphological, functional, and transcriptomic features of the neurons in the visual system. High-throughput single-cell sequencing technology has established a transcriptomic cell atlas and revealed novel neuron types. However, their functions, morphological features, and spatial distributions, which are the fundamental phenotypes of neurons, are illusive.
To overcome this hurdle, we used an optimized Patch-seq technique, which simultaneously obtains the light response, morphology, and gene expression features of retinal ganglion cells (RGCs) at the single-cell resolution. Using this technique, we characterize the transcriptomic, morphological, and functional features of 472 high-quality RGCs. This dataset provides the functional and morphological annotations of 33 transcriptomic RGC types, including 14 previously reported and 19 novel cell clusters. We also identified differentially expressed genes among ON, OFF, and ON-OFF RGCs, such as Vat1l, Slitrk6, and Lmo7, providing candidate marker genes for future functional studies.
Compared with rodents, the primate visual system exerts high cognitive ability and strong information processing capacity. Using a specifically developed technique for the single-cell isolation in adult primates, we established a single-cell RNA-sequencing atlas of the macaque primary visual cortex, containing 133,454 cells that cover all major cortical cell classes. We also identified primate-specific neuron types that involve the visual learning and plasticity. Comparisons of our dataset with humans and mice revealed that glutamatergic neurons may be more diverse across species than GABAergic neurons and non-neuronal cells. The multi-modality interrogation of the neurons in both rodent and primate visual systems paves the way for a comprehensive and systematic study of visual signal processing, facilitating the precision treatments of damaged RGC.

Keywords : RGCs, Patch-seq, Morphology, Electrophysiology, RNA

S30-3

Altered Visuomotor Responses in Achiasmatic *Vax1*$^{AA/AA}$ Mice

Kwang Wook Min[1,2], Jin Woo Kim[1]

[1]Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Daejeon, Republic of Korea
[2]Dongsan Medical Center, Keimyung University, Daegu, Republic of Korea

In binocular animals with stereoscopic vision, retinal ganglion cell (RGC) axons project bilaterally to brain targets by forming a commissural structure known as the optic chiasm (OC). Previously, we demonstrated that the homeodomain protein Ventral Anterior Homeobox 1 (Vax1) plays essential roles in OC formation, acting both cell-autonomously in optic pathway cells and non-cell-autonomously in growing RGC axons. To assess the physiological relevance of Vax1 transfer, we generated *Vax1*$^{AA/AA}$ mice expressing a mutant Vax1 protein (Vax1^{AA}) that retains transcriptional activity but lacks the ability to undergo intercellular transfer. In these mice, RGC axons fail to uptake Vax1^{AA} protein from optic stalk (OS) cells and are unable to reach the midline. Consequently, RGC axons project exclusively to ipsilateral brain regions, resulting in abnormal oculomotor responses despite normal retinal activity. These findings provide direct physiological evidence for the necessity of intercellular Vax1 transfer and highlight the importance of bilateral RGC projections in visuomotor function.

Keywords : optic chiasm, optic nerve, retinal ganglion cell, Vax1, visuomotor response

S30-4

How Robust is the Retina? Visual Responses in a Severely Disorganized Circuit

Chieko Koike[1,2,3]

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Robustness in neural circuits—the capacity to maintain function despite structural disruptions—is a fundamental property of biological systems, yet remains difficult to study in most parts of the central nervous system. The retina, as an anatomically and functionally discrete CNS structure, provides an ideal model due to its measurable input-output relationships. It is highly organized into layers that are believed to be essential for proper transmission and refinement of visual signals. While many developmental studies have examined gene mutations in the retina, fewer have addressed the functional consequences. This raises a key question: how much visual function can be retained when retinal structure is severely compromised?
We examined the impact of afadin deficiency on retinal development and function. Afadin is an actin-binding scaffold protein that links nectins to the actin cytoskeleton and is essential for the formation and maintenance of adherens junctions. Its loss caused severe disorganization of outer retinal lamination, with reductions and mislocalization of photoreceptors, their outer segments, and synaptic structures. As expected, electroretinogram (ERG) recordings showed no detectable a- or b-waves.
Multi-electrode array (MEA) recording is a powerful method for evaluating population-level activity in retinal output neurons. Using this approach, we unexpectedly detected small but discernible local field potentials, suggesting residual retinal activity. Further analysis revealed more intriguing findings: we classified retinal ganglion cells based on light-evoked firing patterns and mapped receptive fields.
These findings suggest that developmental plasticity or compensatory mechanisms may allow partial preservation of retinal signaling without structural integrity. Our results provide new insight into the robustness of retinal circuits and show that visual processing can persist—even partially—under profoundly disorganized conditions.

Keywords : retina, afadin, robustness, visual processing, retinal ganglion cells
Acknowledgements : This work was supported by JSPS KAKENHI (24390019, 22KK0137, 23K15920, 22K20698), JST PRESTO, the Takeda Science Foundation, the Kobayashi Foundation, and R-GIRO.

S30-5

VIVIT: Resolving trans-scale volumetric biological architectures via ionic glassy tissue

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Biological structures across scales integrate seamlessly to perform essential functions. While various histological methods were developed to reveal these intricate structures, preserving the integrity of large-volume architectures while revealing microstructures with high resolution remains a major challenge. Here, we introduce VIVIT, a 3D histological method leveraging the chemical properties of ionic liquids. VIVIT transforms biological tissue into an ionic glassy state, which enables optical clearing with minimal distortion and high transparency, preserves tissue from low-temperature crystal damage, and amplifies fluorescent signals from both genetically encoded and immunostained labels, thus yielding precise and reliable mapping of fluorescent signals within intact 3D architectures. Using VIVIT, we demonstrated the link between the modality of synaptic inputs to multisensory thalamic neurons and the targets of their brain-wide outputs, and identified aspects of inhibitory control in the human cortex. VIVIT thus offers opportunities to elucidate the organizational principles underlying trans-scale biostructures.

Keywords : VIVIT, Optical clearing, Ionic liquids, Trans-scale, 3D

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 31

Supported By 한국뇌연구원 Korea Brain Research Institute

Day 3 (August 26) **10:35-12:30** **Premier Ballroom C**

Frontiers in addiction: linking neural mechanisms to public health strategies

Organizer : Ja Wook Koo (Korea Brain Research Institute)
Heh-In Im (Korea Institute of Science and Technology)
Moderator : Ja Wook Koo (Korea Brain Research Institute)

Innovative approaches for treating drug overdose: insights from preclinical and community research
Sandra Comer (Columbia University)

Cocaine-induced Modification of Prefrontal Output Connectivity
Suk-Ho Lee (Seoul National University)

Neural circuit and social mechanism of drug addiction
Yingjie Zhu (Chinese Academy of Sciences)

Striatal Cholinergic Interneurons Control Physical Nicotine Withdrawal via Muscarinic Receptor Signaling
Heh-In Im (Korea Institute of Science and Technology)

Therapy or threat? Behavioural insights into kratom's dual role in addiction from a zebrafish study
Nur Sabrina Abdul Basit (Monash University Malaysia) IBRO AWARDEE

S31-1

Innovative approaches for treating drug overdose: insights from preclinical and community research

Sandra Comer

Psychiatry, Columbia University, New York, NY USA, USA

Drug-related overdoses, mainly due to fentanyl and other synthetic opioids, are a leading cause of death in North America. Although the most recent data are showing decreases in drug-related mortality, the numbers are still incredibly high, and the incidence of non-fatal overdoses far exceeds these numbers. Although effective medications are available for treating opioid overdose (OD), novel approaches are clearly needed. The current presentation will include preclinical data to support the development of biologics and devices for treating opioid OD and a behavioral intervention for maximizing the effectiveness of naloxone. For treatment of acute OD, we are developing a monoclonal antibody (mAb) that targets fentanyl. Our preclinical data demonstrate that our lead mAb (HY6-F9) reverses fentanyl-induced respiratory depression at rates and magnitudes similar to naloxone, an opioid antagonist. An advantage of HY6-F9, however, is that it should not produce withdrawal in people who are physically dependent on opioids and its effects are longer lasting. Another novel approach that we are developing to treat acute OD is a device that sends electrical currents through patches placed on the skin of the neck to stimulate the phrenic nerve, which controls the diaphragm, a muscle that plays a major role in breathing. The ultimate goal will be to create a portable device that can be used in the community, similar to an Automated External Defibrillator (AED). Like the AED, our Automated External Respiration System (AERS) will be developed for use by untrained people to automatically maintain breathing until medical personnel can arrive or the overdose wears off. Our data collected in pigs have demonstrated that this approach is safe and effective in producing a rapid and sustained reversal of severe fentanyl-induced respiratory depression. These approaches may provide additional options for clinicians and bystanders to reduce the mortality associated with drug use.

Keywords : Drug overdose, Opioid, Device, Monoclonal antibody, Phrenic nerve
Acknowledgements : I would like to acknowledge my collaborators including Dr. Pravetoni and his team at the Univ Washington and Univ Minnesota for developing the fentanyl mAb, Dr. Levin and his team at Coridea LLC for developing the AERS device and Dr. Guedes at Univ Minnesota for testing it in pigs, Dr. Jones at Columbia Univ for the naloxone behavioral intervention, and NIDA for supporting all of this research.

S31-2

Cocaine-induced Modification of Prefrontal Output Connectivity

Suk-Ho Lee[1,2], Jaehan Kwon[1], Jiwon Ryu[2], Hyun Jin Kim[3]

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Glutamatergic projection from the medial prefrontal cortex (mPFC) to the nucleus accumbens core (NAcC) has been proposed as a final common pathway for cocaine-induced early locomotor sensitization (LS) as well as reinstatement of cocaine seeking behavior after extinction training. Addictive drugs trigger reward-related behavior by inducing unbalanced activity of direct and indirect pathways of mesocorticolimbic system, but adaptive plastic changes at mPFC-NAcC synapses associated with cocaine addiction remains little understood. To elucidate cocaine-induced connectivity changes of prelimbic (PL) pyramidal neurons (PNs) to NAcC, we studied the correlation of the connectivity change with behavioral sensitization. NAcC-projecting pyramidal neurons in the PL cortex were segregated into D1- and D2-receptor positive PNs. Although the connections between D1/D2-PN and direct/indirect pathway were unbiased in naïve animals, repeated cocaine injection biased the connections toward direct pathway through presynaptic mechanisms. This cocaine-induced rewiring accompanied LS. Both of the rewiring and LS was prevented by prelimbic infusion of riluzole that reduced intrinsic excitability of PL neurons. These findings indicate that cocaine-induced rewiring of PL-to-NAcC connection well correlates with early behavioral sensitization, and that the rewiring and LS can be prevented by reducing the excitability of PL neurons.

S31-3

Neural circuit and social mechanism of drug addiction

Yingjie Zhu

Brain Institute, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, Guangdong, China

Drug addiction is characterized by compulsive drug-seeking behavior despite adverse consequences. Addictive substances produce euphoria by acting on the brain's reward system, inducing persistent changes in neural circuits that drive the progression of addiction. The vulnerability to addiction is influenced by a complex interplay of biological, psychological, and social factors. In this talk, I will present our latest findings on the cellular and circuit architecture of the lateral septum in reward processing and how maladaptive changes in this circuit contribute to methamphetamine sensitization. I will also discuss how social factors impact addiction susceptibility by remodeling the mesocortical and mesolimbic dopaminergic pathways, and explore potential therapeutic strategies that could be developed based on these insights.

Keywords : drug addiction, dopamine, vulnerability, lateral septum, social rank

S31-4

Striatal Cholinergic Interneurons Control Physical Nicotine Withdrawal via Muscarinic Receptor Signaling

Heh-In Im

Korea Institute of Science and Technology

Striatal cholinergic interneurons (ChIs) provide acetylcholine tone to the striatum and govern motor functions. Nicotine withdrawal elicits physical symptoms that dysregulate motor behavior. Here, the role of striatal ChIs in physical nicotine withdrawal is investigated. Mice under RNAi-dependent genetic inhibition of striatal ChIs (ChIGI) by suppressing the sodium channel subunit NaV1.1, lessening action potential generation and activity-dependent acetylcholine release is first generated. ChIGI markedly reduced the somatic signs of nicotine withdrawal without affecting other nicotine-dependent or striatum-associated behaviors. Multielectrode array (MEA) recording revealed that ChIGI reversed ex vivo nicotine-induced alterations in the number of neural population spikes in the dorsal striatum. Notably, the drug repurposing strategy revealed that a clinically-approved antimuscarinic drug, procyclidine, fully mimicked the therapeutic electrophysiological effects of ChIGI. Furthermore, both ChIGI and procyclidine prevented the nicotine withdrawal-induced reduction in striatal dopamine release in vivo. Lastly, therapeutic intervention with procyclidine dose-dependently diminished the physical signs of nicotine withdrawal. The data demonstrated that the striatalChIs are a critical substrate of physical nicotine withdrawal and that muscarinic antagonism holds therapeutic potential against nicotine withdrawal.

S31-5 IBRO AWARDEE

Therapy or Threat? Behavioural Insights into Kratom's Dual Role in Addiction from a Zebrafish Study

Nur Sabrina Abdul Basit, Satoshi Ogawa

School of Medicine, Monash University Malaysia, Bandar Sunway, Selangor, Malaysia

Kratom (Mitragyna speciosa) is a Southeast Asian plant traditionally used for its stimulant and analgesic properties. Its global use is increasing, particularly for self-managing pain and opioid withdrawal. Notably, kratom has gained traction among individuals recovering from opioid addiction as a self-directed alternative to alleviate withdrawal and reduce reliance on stronger opioids. Mitragynine, the plant's primary alkaloid, is believed to mediate many of its psychoactive effects via opioid and monoaminergic pathways. However, the pharmacological complexity of kratom (containing multiple active alkaloids) remains poorly understood, especially in relation to its effects on emotional regulation and central nervous system activity. This underscores the need for preclinical studies using in vivo models to clarify its neurobehavioral profile. This study employed the zebrafish (Danio rerio) larval model to assess acute behavioural effects of kratom decoction and purified mitragynine. The light-dark paradigm serves as a sensitive assay for changes in anxiety-like behaviour and arousal, offering insight into underlying neural modulation. The results demonstrated distinct behavioural signatures across treatment groups. Mitragynine consistently reduced overall activity, particularly during light phases. In contrast, kratom decoction elicited dose-dependent and more variable responses. Notably, the decoction's effects did not replicate those of mitragynine alone, suggesting that other alkaloids in the whole-plant extract influence its net impact. These findings highlight the importance of studying kratom in its traditional form, as decoction better represents real-world use. Solely evaluating purified mitragynine may overlook critical interactions, leading to incomplete conclusions regarding kratom's therapeutic potential and addiction risk.

Keywords : Kratom, Addiction, Mitragynine, Zebrafish, Neural activity

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Symposium 32

Supported By

KIST Brain Science Institute
Korea Institute of Science and Technology

Day 3 (August 26) **10:35-12:30** **Rm.113-115**

Connecting the Dots: illuminating the brain from connectivity to function

Organizer : Jinhyun Kim (Korea Institute of Science and Technology)
Jong-Hyun Park (Korea Institute of Science and Technology)
Moderator : Jinhyun Kim (Korea Institute of Science and Technology)
Jong-Hyun Park (Korea Institute of Science and Technology)

Energetics and competitive neural and vascular interactions shape blood-flow dynamics in cortex
David Kleinfeld (University of California, San Diego)

High-resolution imaging of astrocyte structure and function
U. Valentin Nägerl (Goettingen University)

Visualizing brain-wide connectivity with fluorescence micro-optical sectioning tomography
Qingming Luo (Hainan University)

Live imaging of neuroglia-like interaction in the taste bud
Myunghwan Choi (Seoul National University)

Imaging neuronal activity in the cerebellar cortex of behaving mice
Bernd Kuhn (Okinawa Institute of Science and Technology)

S32-1

Energetics and competitive neural and vascular interactions shape blood-flow dynamics in cortex

David Kleinfeld[1], Jacob Duckworth[1], Thomas Broggini[2], Karishma Chhabria[1], Massimo Vergassola[1]

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The pial arteriole network distributes blood across the brain through branches that rhythmically ungulate with a resting-state resonance near 0.1-Hz. We tested the hypothesis that ongoing spatiotemporal patterns of vaso-oscillations are shaped through competition among neurovascular inputs. Using transcranial optical imaging of neocortex in awake mice, we observed that rhythmic sensation is enhanced by extracting power from vaso-oscillators. This establishes that arterioles are active oscillators and not passive resonators. Next, using visual sensation, vibrissa sensation, and/or medullary input, we probed vaso-dynamics in response to single and paired rhythmic inputs. All told, arterioles resonantly amplified the underlying neural activity. Sensory drive with a fundamental or harmonic rate nearest to the resting-state frequency predominates, albeit medullary input can supersede sensation. Lastly, we observed that the resonnce is diminished by suppressing expression of the inward rectifier channel that mediates neuronal-to-vascular communication. We conclude that the amplitude and pattern of vasomotion, which modulates the perfusion of blood, movement of interstitial fluid, and informs the interpretation of fMRI, reflects the spectral composition of stimuli relative to ongoing activity.

Keywords : Vasomotion, Oscillators, Resonance, Neurovascular
Acknowledgements : United States National Institutes of Health (U24 EB028942, R35 NS097265, and U19 NS123717)

S32-2

High-resolution imaging of astrocyte structure and function

U. Valentin Nägerl

Department of Anatomy and Cell Biology, University Medical Center Göttingen/University of Göttingen, Göttingen, 37075, Germany

Progress in microscopy has historically driven major advances in neuroscience. STED microscopy, renowned for breaking the diffraction barrier of light microscopy, is a prime example. It enables visualization of anatomical structures and nanoscale dynamics that are beyond the reach of conventional light microscopy—from the intricate architecture of neurons and glial cells to the organelles and molecules within them. Similarly, light-sheet microscopy has proven invaluable for high-speed imaging with minimal phototoxicity, capturing rapid or transient events with high sensitivity, contrast, and spatial resolution.
In the first part of my talk, I will review our contributions to the development of live-tissue STED imaging and its application to astrocytes and the extracellular space of the brain. Specifically, we combined super-resolution morphological imaging with confocal calcium imaging in living organotypic mouse hippocampal slices. This approach enabled us to uncover the structural basis of astrocytic calcium signals at tripartite synapses, characterized by nanoscale morphological specializations—namely, nodes and shafts.
Next, I will present unpublished work using lattice light-sheet microscopy, which allowed us to capture spontaneous and evoked calcium activity in these structures with unprecedented temporal resolution. Notably, we observed that calcium signals propagated in a saltatory manner from node to node, with occasional failures at branch points.
I will conclude by presenting numerical simulations that explore how nanoscale astrocytic morphology influences the spread of calcium activity.

Keywords : STED microscopy, Live-cell super-resolution imaging, Extracellular space, Astrocytes, Calcium imaging

S32-3

Visualizing brain-wide connectivity with fluorescence micro-optical sectioning tomography

Qingming LUO[1,2]

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The brain is the most complex and significant organ, but little is known regarding to the mechanisms of its function, which is related to brain anatomy. Conventional anatomical methods based on brain slices fail to reconstruct the neural projection in axial direction at single-cell resolution. To solve the problem, my lab has spent more than ten years developing Brain-wide Positioning System (BPS), a novel solution combining microscopic optical imaging and physical sectioning to obtain the tomographic information of a whole brain with sub-micron voxel resolution. BPS includes several generations of Micro-Optical Sectioning Tomography (MOST) and fluorescence MOST (fMOST). In this talk, I will introduce the principles of BPS and demonstrate how to locate and visualize the labelled neurons and neuronal networks in the whole brain. The pipeline includes whole-brain sample preparation, whole-brain optical imaging, and massive brain image processing and reconstruction. BPS may play a crucial role and usher in a new era of Brainsmatics. Brainsmatics refers to the integrated, systematic approaches of measuring, analyzing, managing, and displaying brain spatial data, including but not limited to the concepts of digital mapping and visualization of the brain neuronal/vascular networks, brain atlas, brain connectome and projectome, brainnetome, neuroinformatics, and neuroimaging. Brainsmatics will provide comprehensive and systematic information to understand the brain, defeat the brain disease, and develop the brain-inspired intelligence.

Keywords : Brainsmatics, fMOST, MOST, Brain-wide Positioning System, connectome

S32-4

Live imaging of neuroglia-like interaction in the taste bud

Myunghwan Choi

School of Biological Sciences, Seoul National University, Seoul 08826, Republic of Korea

The sense of taste generally shows diminishing sensitivity to prolonged sweet stimuli, referred to as sweet adaptation. Yet, its mechanistic landscape remains incomplete. Here, we report that glia-like type I cells provide a distinct mode of sweet adaptation via intercellular crosstalk with chemosensory type II cells. Using the microfluidic-based intravital tongue imaging system, we found that sweet adaptation is facilitated along the synaptic transduction from type II cells to gustatory afferent nerves, while type I cells display temporally delayed and prolonged activities. We identified that type I cells receive purinergic input from adjacent type II cells via P2RY2 and provide inhibitory feedback to the synaptic transduction of sweet taste. Aligning with our cellular-level findings, purinergic activation of type I cells attenuated sweet licking behavior, and P2RY2 knockout mice showed decelerated adaptation behavior. Our study highlights a veiled intercellular mode of sweet adaptation, potentially contributing to the efficient encoding of prolonged sweetness.

Keyword : microscopy, taste, sweet adaptation

S32-5

Imaging neuronal activity in the cerebellar cortex of behaving mice

Bernd Kuhn

Optical Neuroimaging Unit, OIST Graduate University, Onna, Okinawa/Japan, Japan

The cerebellar cortex receives massive sensory and motor input and integrates these inputs. The result of this integration refines coordination and timing of motor activity. Purkinje neurons with their fan-shaped dendritic tree and about 70000 spines (mouse) play a crucial role in this neuronal circuit as the sole output of the cerebellar cortex. We use voltage and calcium imaging to study their activity during behavior in detail. I will show dendritic coincidence detection on a millisecond time scale in response to sensory input and population Ca^{2+} activity of Purkinje dendrites and interneurons during a tongue interception task.

Keywords : Cerebellum, voltage imaging, Ca2+ imaging, two-photon microscopy, Purkinje neurons

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 33

Day 3 (August 26) **10:35-12:30** **Rm.116-118**

Neuroscience of schizophrenia: from structure to function

Organizer : Minah Kim (Seoul National University)
Moderator : Jun Soo Kwon (Hanyang University)

Structural abnormalities of the brain and its clinical implications in schizophrenia
Sung Woo Joo (Asan Medical Center)

Reactive astrocyte dysfunction in schizophrenia
Minah Kim (Seoul National University)

Surface-based techniques for brain shape analysis in schizophrenia
Ilwoo Lyu (Pohang University of Science and Technology)

Electrophysiological studies of schizophrenia using mismatch negativity
Daisuke Koshiyama (The University of Tokyo)

Exploring the interplay between macrostructural and microstructural brain abnormalities in psychosis
Sun-Young Moon (Seoul National University)

S33-1

Structural abnormalities of the brain and its clinical implications in schizophrenia

Sung Woo Joo

Department of Psychiatry, ASAN Medical Center, Seoul, Republic of Korea

Schizophrenia is a chronic psychiatric disorder characterized by delusions, hallucinations, and disorganized behavior, typically emerging during adolescence or early adulthood. Numerous studies have identified structural brain abnormalities in individuals with schizophrenia. Notably, reductions in cortical thickness—particularly in the frontal and temporal lobes—have been consistently reported, alongside volume reductions in several subcortical regions including the hippocampus, amygdala, and thalamus. However, the link between these structural abnormalities and clinical symptoms remains unclear. One major challenge is the substantial clinical heterogeneity among patients who are broadly categorized under the single diagnostic label of schizophrenia. Another challenge lies in the limited reproducibility of group-level differences when applied to individual patients. These issues have led to a growing interest in quantifying brain structural deviations at the individual level rather than relying solely on group comparisons. Normative modeling is one promising approach, which quantifies individual deviations in brain structure by leveraging large-scale neuroimaging datasets from the general population. Recent developments have also introduced network-based models that account for inter-regional cortical connectivity. Among them, structural network models such as Morphometric Inverse Divergence (MIND) have been proposed, which utilize fine-grained morphometric features across cortical regions. In this presentation, I will review previously reported cortical structural abnormalities in schizophrenia and highlight recent methodological advances, with a focus on normative models and MIND-based structural network approaches.

Keywords : schizophrenia, cerebral cortex, normative model, structural connectivity

S33-2

Reactive astrocyte dysfunction in schizophrenia

Minah Kim

Department of Psychiatry, Seoul National University College of Medicine, Seoul, Republic of Korea

Emerging evidence suggests that impaired astrocytic function, particularly involving glutamate dysregulation and neuroinflammation, is central to the pathophysiology of schizophrenia. Despite its significance, direct in vivo visualization of reactive astrocytes in schizophrenia remains scarce. This study aimed to assess the presence of reactive astrocytes and their association with positive symptoms in schizophrenia using positron emission tomography (PET) with the [^{18}F]THK5351 tracer, which binds to monoamine oxidase B (MAO-B). A total of 33 individuals diagnosed with schizophrenia and 35 demographically matched healthy controls underwent [^{18}F] THK5351 PET scans. Standardized uptake value ratios (SUVr) were computed for the anterior cingulate cortex (ACC) and hippocampus, designated as primary regions of interest (ROIs), as well as for additional limbic structures considered secondary ROIs. Group comparisons were conducted, followed by correlational analyses between SUVr values and positive symptom scores from the Positive and Negative Syndrome Scale (PANSS) in the schizophrenia group. Results indicated that schizophrenia patients exhibited significantly elevated SUVr in the bilateral ACC and the left hippocampus relative to controls. No significant group differences were observed in the secondary ROIs. Notably, higher SUVr in the ACC was positively correlated with PANSS positive symptom scores. These findings offer the first in vivo PET imaging evidence of reactive astrocyte involvement in schizophrenia, particularly in relation to positive symptoms. The ACC may represent a promising neurobiological target for interventions aimed at alleviating these symptoms.

Keywords : glutamate, neuroinflammation, reactive astrocyte, positive symptoms, schizophrenia

S33-3

Surface-based techniques for brain shape analysis in schizophrenia

Ilwoo Lyu

Graduate School of Artificial Intelligence, POSTECH, Pohang, Republic of Korea

This talk will explore advanced surface-based techniques for brain shape analysis with a focus on cortical folding patterns. Specifically, we will discuss methods for skeletonizing these folds to simplify the brain's structural representation and shape quantification techniques for assessing local folding development. Also, we will cover sulcal labeling as a tool for identifying structural variations across individuals. The talk will explore the applications of these methods in neurodegenerative research particularly in understanding diseases/disorders like schizophrenia. Finally, we will highlight opportunities to bridge these techniques with neurodegenerative studies, offering insights into future research directions in this evolving field.

Keywords : Cortical surface, Sulcal patterns

S33-4

Electrophysiological studies of schizophrenia using mismatch negativity

Daisuke Koshiyama, Reiji Shioda, Taiki Kishigami, Kenji Kirihara, Kiyoto Kasai

Department of Neuropsychiatry, The University of Tokyo, Tokyo, Japan

Auditory mismatch negativity (MMN) has been repeatedly reported to be reduced in amplitude in patients with schizophrenia and is a biological index of electroencephalography (EEG) reflecting glutamatergic neuronal dysfunction, a leading pathological hypothesis for schizophrenia. We found that MMN amplitude is already reduced before the onset of schizophrenia and is associated with overall levels of social adjustment. We also found that MMN is hierarchically related to social adjustment level via negative symptoms and cognitive dysfunction. In order to investigate whether reduced MMN amplitude reflect altered deviance detection or altered adaptation, we deconstructed MMN into the deviance detection component and the adaptation component. We found that the deviance detection component, but not adaptation component was impaired in patients with schizophrenia. We also estimated the sources of MMN reduction in patients with schizophrenia using EEG, identified the sources in the frontal and temporal cortices, and provided spatial information of neural networks underlying MMN. These studies bridge animal and clinical studies and greatly contribute to establish MMN as a biological index to understand the pathophysiology and develop novel therapeutics of schizophrenia.

Keywords : mismatch negativity, schizophrenia, event-related potentials, electroencephalography (EEG)
Acknowledgements : This study was supported by JSPS KAKENHI (JP22K15760, JP24K02378, JP25K19073), by the Takeda Science Foundation, by the Narishige Neuroscience Research Foundation, by the Watanabe Foundation, and by UBE Foundation.

S33-5

Exploring the interplay between macrostructural and microstructural brain abnormalities in psychosis

Sun Young Moon

Department of Public Health Services & Psychiatry, Bundang Seoul National University Hospital, Seongnam, Republic of Korea

Schizophrenia is a serious mental disorder that carries a significant burden of disease. However, the neurobiological foundations of this disorder remain largely unclear. Historically, post-mortem studies have revealed a widespread reduction in brain volumes and an increase in ventricular size. With the introduction of neuroimaging techniques, researchers have identified evidence of accelerated brain volume loss in patients with schizophrenia, with the frontotemporal regions being the most affected. Recently, advanced neuroimaging methods such as texture analysis, diffusion tensor imaging, and diffusion kurtosis imaging have garnered increased research interest. These advanced techniques allow for the investigation of sensitive microstructures in both cerebral gray and white matter, thus providing valuable insights that could enhance our understanding of the pathophysiology of schizophrenia. Microstructural properties are not only sensitive, but are thought to precede the macrostructural volume/thickness changes, which pose them as an interesting candidate marker to monitor disease progression or the response to specific treatments. In the current session, the properties of texture analysis, diffusion tensor imaging, and diffusion kurtosis imaging to examine microstructural properties of the underlying tissue are briefly introduced, followed by a comprehensive review of recent studies that focused on investigating gray/white matter microstructures in patients with schizophrenia. And then, the proposed mechanisms by which microstructural changes interact with later macrostructural changes (e.g., cortical reorganization, progression of disease, restructuring of the gray matter cortical lamina, etc.) are discussed.

Keywords : Schizophrenia, Structural neuroimaging, Microstructural changes, Texture analysis, Diffusion kurtosis imaging

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The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 34

Day 3 (August 26) **10:35-12:30** **Rm.206-207**

Local mRNA translation in axon development, health and function

Organizer : Yongcheol Cho (Daegu Gyeongbuk Institute of Science and Technology)
Moderator : Yongcheol Cho (Daegu Gyeongbuk Institute of Science and Technology)

Local mRNA translation in axons sustains synapse-specific neurotransmission
Hovy H. Wong (The Chinese University of Hong Kong)

Regulation of local translation and cytoplasmic viscosity in axons of aging neurons
Marco Terenzio (Okinawa Institute of Science and Technology)

Regulation of axonal translation via control of ribosomal protein mRNA localization in regenerating axons
Jung Eun Shin (Dong-A University)

Regulation of neural epitranscriptome during neuronal differentiation and synaptogenesis
Ki-Jun Yoon (Korea Advanced Institute of Science and Technology)

S34-1

Local mRNA translation in axons sustains synapse-specific neurotransmission

Hovy Ho-Wai Wong[1,2,3]

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For > 60 years, memory formation has been linked to protein synthesis (PS), with the prevalent view that this occurs in the cell body. However, recent studies have found hundreds of mRNAs in axons, suggesting that presynaptic PS controls neural communication. Here we show that local PS in axons sustains neurotransmission in mouse visual cortex.
Neurotransmission was suppressed within minutes after PS blockade. To localize the PS need, we selectively manipulate pre- or postsynaptic neurons with intracellular drug loading. We found synaptic response deficits and exaggerated paired-pulse ratio after presynaptic blockade with M7 cap analog, indicating synaptic release is boosted by presynaptic PS. Using 2-photon laser microsurgery to sever axon from cell body, we showed that axonal PS sustained neurotransmitter release. To understanding the dynamics of axonal PS, we live imaged RNA localization and translation. Taking advantage of FAM-puromycin incorporation as proxy for PS, we captured the rapid and localized activity-dependent mRNA translation at presynaptic boutons. Interestingly, endogenous RNA revealed persistent and discrete docking patterns at individual presynaptic sites, suggesting bouton-specific regulation. In agreement, PS sustained neurotransmission at synapses from excitatory cells to excitatory cells, but not to inhibitory cells. Axonal PS can therefore fine-tune excitatory: inhibitory balance. We also found that axonal PS is required in high- but not low-frequency neurotransmission, suggesting a role in high-fidelity information transfer and memory formation. Local PS in axon is thus a previously unappreciated principle for supporting neurotransmission at specific synapse types.
PS has emerged as a promising candidate target for treating disorders like autism and Alzheimer's, yet the focus has historically been postsynaptic. Our results highlight the potential for disease interventions that rely on synapse-type-specific local translation in axons.

Keywords : Synapse, Neurotransmission, Local protein synthesis, MRNA localization, Axon
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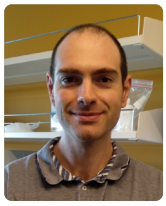
S34-2

Regulation of local translation and cytoplasmic viscosity in axons of aging neurons



Maria Fransiska Emily[1], Laurent Guillaud[1], Sandra De la Fuente Ruiz[1], Riya Agrawal[2], Susan Boerner[1], Yuto Akimoto[1], Tara Helmi Turkki[1], Marco Edoardo Rosti[2], Marco Terenzio[1]

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Axonal translation plays a role in maintaining axonal morphology and regeneration after axonal injury. Mitochondria are trafficked along axons and provide energy required for several intracellular mechanisms including molecular transport and local translation. Decline in mitochondria activity is one of the hallmarks of aging. However, it is still unclear whether this decline corresponds to a similar reduction in the extent of axonal translation in aging neurons. We utilized microfluidic devices to separate cell body and axons of DRG neurons. Using live imaging, we found a significant decrease in the number of active mitochondria and in the percentage of moving mitochondria in axons of sensory neurons isolated from late-adulthood mice. This decrease was mirrored by an ATP-dependent decrease in axonal cytoplasm viscosity. RNA granules stained by G3BP1 were also fewer in number and forming bigger aggregates in sensory neurons isolated from late-adulthood mice. Functionally, this resulted in a decrease in axonal translation as well in the number of translational hotspots in aging neurons. We also showed that attempting to increase ATP synthesis had a positive effect on axonal translation in aging neurons. We think that this research sheds a light on axonal translation in aged neurons and its relationship with energy sources inside the axonal compartment, which might present an opportunity for therapy in the future.

Keywords : Aging, RNA granules, mRNA translation, Translational regulation

S34-3

Regulation of axonal translation via control of ribosomal protein mRNA localization in regenerating axons

Jung Eun Shin

Molecular Neuroscience, Dong-A University College of Medicine, Busan, Republic of Korea

Axonal mRNA localization and local translation support axon regeneration, but how ribosomes are supplied to regenerating axons remains unclear. Here, we investigate an RNA-binding protein-mediated mechanism that controls the axonal localization of mRNAs encoding ribosomal proteins (RP-mRNA), and thereby regulates axonal translation in regenerating axons. The RNA-binding protein NONO (p54nrb), known for its role in nuclear RNA retention, has also been associated with intellectual disability and neurodegeneration. In mouse dorsal root ganglia (DRG), NONO is selectively expressed in neuronal nuclei. Using RNA immunoprecipitation sequencing, we identify RP-mRNAs as the most enriched transcripts bound to NONO. Knockdown of *Nono* in cultured DRG neurons enhances injury-induced axonal localization of RP-mRNAs and increases local ribosomal protein expression. This correlates with elevated axonal translation capacity after injury in neurons lacking NONO, demonstrating a negative role for NONO in regulating axonal ribosomes. *In vivo*, sciatic nerve crush injury leads to significantly enhanced axon regeneration in *Nono* knockout mice compared to controls, indicating that NONO functions as a negative regulator of regeneration. In sum, our results reveal a novel mechanism by which NONO restricts axonal RP-mRNA trafficking and local translation. These findings suggest that suppressing NONO activity may provide therapeutic benefit for promoting axonal regeneration and functional recovery after nerve injury.

Keywords : Axon regeneration, Nono, Local translation, ribosome, RNA-binding protein

S34-4

Regulation of neural epitranscriptome during neuronal differentiation and synaptogenesis

Ki-Jun Yoon[1,2]

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[2]KAIST Stem Cell Center, Korea Advanced Institute of Science and Technology (KAIST), Republic of Korea.

Recent discoveries of widespread mRNA chemical modifications raise the question of whether this mechanism plays a post-transcriptional regulatory role in the development and function of the brain. N6-methyladenosine (m6A), installed by the Mettl3/Mettl14 methyltransferase complex, is the most prevalent internal mRNA modification that controls various aspects of mRNA metabolism, including stability, translation, splicing, and localization. Neurons are distinctly polarized cells where mRNA can be transported and localized in distal structures like axons and dendrites. However, how m6A modification influences such RNA localization in developing neurons has not been understood well. We demonstrated that the ablation of Mettl14 in postmitotic neurons reduces m6A content and impairs axonal projection during corticogenesis. Our RNA-seq analysis and single-molecule in situ hybridization experiments revealed that specific mRNA targets were mislocalized in the neurites of postmitotic neurons with m6A loss-of-function. Furthermore, we identified YTHDF2 as the reader protein responsible for mRNA transportation in interhemispheric callosal axons in the developing brain. YTHDF2 interacts with motor proteins, translational regulators, and microtubules to facilitate the efficient distal transport of m6A-tagged transcripts. Not only m6A modification, but we have explored other post-transcriptional regulations, such as poly-A tail modifications in neurons. The mixed tailing of guanosine residues within poly-A tails has been reported to safeguard mRNAs from rapid deadenylation, yet its role in neuronal contexts remains poorly understood. In this study, we discovered that two cytoplasmic proteins, TENT4A and TENT4B, selectively stabilize mRNAs targeted to dendrites and synapses via mixed tailing, playing a crucial role in normal neuronal differentiation and synaptic function. These findings unveil a multi-layered post-transcriptional regulation mechanism for localizing mRNAs to distal neuronal compartments, which is essential for proper neuronal function.

Keywords : Neurodevelopment, mRNA localization, Epitranscriptomics, Synaptic functions, RNA modifications

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 35

Supported By

Center for Cognition and Sociality ibs

Day 3 (August 26) **14:30-16:25** **Grand Ballroom**

Synaptic development, function, and brain disorders

Organizer : Eunjoon Kim (Korea Advanced Institute of Science and Technology)
Moderator : Eunjoon Kim (Korea Advanced Institute of Science and Technology)

From human genetics to animal models to potential novel therapeutics for schizophrenia
Morgan Sheng (Massachusetts Institute of Technology)

Control of neurodevelopmental gene expression programs and circuit assembly by spontaneous neuronal activity in the mouse visual cortex
Peter Scheiffele (University of Basel)

Disease mechanisms and intervention strategies for SNAREopathies, syndromes caused by mutations in presynaptic genes
Matthijs Verhage (Vrije University)

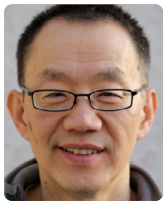
GluN2A mediates ketamine-induced antidepressant effects
Yelin Chen (Shanghai Institute of Organic Chemistry)

Cortical mechanisms underlying sensory hypersensitivity in *Adnp*-mutant mice
Heera Moon (Korea Advanced Institute of Science and Technology)

Perturbed cell fate decision by schizophrenia-associated AS3MTd2d3 isoform during corticogenesis
Seunghyun Kim (Pohang University) Scitech Korea AWARDEE

S35-1

From human genetics to animal models to potential novel therapeutics for schizophrenia



Morgan Sheng

Stanley Center for Psychiatric Research, Broad Institute, Cambridge, MA 02142, USA

Recent years have seen tremendous progress in discovery of human genetic variants that increase the risk for schizophrenia and related psychiatric illnesses. In particular, loss-of-function genetic mutations with high penetrance have facilitated the construction of animal models with human genetics validity, from which we have gained new insights into the mechanisms of disease. Heterozygous mutant mice in schizophrenia risk gene GRIN2A, which encodes a subunit of NMDA receptors, show multiple molecular and neurobiological abnormalities that overlap with features of human schizophrenia. The GRIN2A genetic animal model responds to known anti-psychotic drugs and can be leveraged for discovery of novel targets for treatment of schizophrenia.

Keywords : schizophrenia, NMDA receptor, therapeutics, animal model, human genetics

S35-2

Control of neurodevelopmental gene expression programs and circuit assembly by spontaneous neuronal activity in the mouse visual cortex

Peter Scheiffele

Biozentrum, University of Basel, Basel, Switzerland

Neurodevelopmental disorders are frequently accompanied by sensory abnormalities that are thought to arise from alterations in cortical circuit assembly during development. However, the fundamental mechanisms directing neocortical synapse formation in the mammalian brain are only beginning to be understood. The formation of sensory cortical circuits is largely completed at the onset of sensation, with individual cortical neurons exhibiting specific and selective response properties that undergo only minor refinement thereafter. Before sensation, all sensory systems exhibit spontaneous patterned activity that propagates through ascending sensory pathways. Simultaneously, transcriptional programs unfold that specify cortical cell types and may instruct wiring patterns. The structure and spatio-temporal dynamics of spontaneous patterned activity are thought to have a major impact on wiring. However, the molecular mechanisms engaged by spontaneous activity are unknown.
We will discuss our recent studies using spatial transcriptomics, long-read single molecule sequencing and longitudinal in vivo two-photon calcium imaging of individual neurons in primary visual cortex of newborn mice to map the developmental emergence of neuronal cell types, transcript isoform programs, and spontaneous patterned activity. Our experiments identified an array of developmentally regulated neuronal components in upper layer neurons, including ion channels and synaptic adhesion molecules. Moreover, we uncovered broad transcript splice isoform programs that are dependent on the pattern of spontaneous activity in vivo. This work demonstrates how spontaneous activity in developing sensory systems instructs wiring and gene expression and provides a foundation for understanding of how disorder-associated genetic alterations modify developmental processes underlying the function of mature cortical networks.

Keywords : neurodevelopmental disorders, synapse, spontaneous activity, adhesion molecules, visual processing
Acknowledgements : This work was supported by grants from the European Research Council and the Swiss National Science Foundation.

S35-3

Disease mechanisms and intervention strategies for SNAREopathies, syndromes caused by mutations in presynaptic genes

Matthijs Verhage[1,2]

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[2]Functional Genomics, Amsterdam University Medical Center, Amsterdam, Netherlands

SNAREopathies are syndromes caused by mutations in presynaptic genes that together drive synaptic vesicle exocytosis and synaptic transmission. SNAREopathies are characterized by developmental delay, intellectual disability, epilepsy, and are among the most common monogenic neurodevelopmental disorders. We have studied SNAREopathies, especially caused by mutations in STXBP1/Munc18-1 and SYT1, in patient cohorts, in mouse models and in cultured IPSC-derived neurons from these patients. While mutations in SYT1 lead to functional deficits, all pathogenic STXBP1 mutations cause protein instability, reduced cellular levels, reorganization of the synaptic proteome, changes in neuronal network activity, hyper-excitability, EEG abnormalities and cognitive deficits. We have used the observed cellular and mouse model phenotypes to design new intervention strategies. We have used IPSC-derived patient neurons, new EEG analyses, and *in silico* modeling to establish cell-based diagnostics for SNAREopathies and develop personalized treatment decisions based on the emerging predictivity of such in vitro models and EEG-biomarkers. Finally, we have established the EU consortium ESCO (www.stxbp1eu.org), to serve as a coordinating platform for a natural history study (NHS) and clinical trials for STXBP1-related disorders. ESCO works together with the European Medicine Agency using *in silico* trial simulations with real world data from our NHS to design innovative clinical trials that maximize power and data usability for the limited patient population. ESCO aims to nest different trial modalities in a single NHS serving as a grand historical/concurrent control and providing (Bayesian) priors. In this way, ESCO expects to be able to evaluate many emerging candidate therapies (repurposing, small molecule, RNA-based, gene-replacement) with a limited patient cohort.

Keywords : neurodevelopmental disorder, IPSC, STXBP1, SYT1, Munc18

S35-4

GluN2A mediates ketamine-induced antidepressant effects

Yelin Chen

SIOC, Chinese Academy of Sciences, Shanghai, China

Ketamine was thought to induce rapid antidepressant responses by inhibiting GluN2B-containing N-methyl-d-aspartic acid (NMDA) receptors (NMDARs), which presents a promising opportunity to develop better antidepressants. However, adverse side effects limit the broader application of ketamine and GluN2B inhibitors are yet to be approved for clinical use. It is unclear whether ketamine acts solely through GluN2B-dependent mechanisms. The present study reports that the loss of another major NMDAR subunit, GluN2A, in adult mouse brains elicits robust antidepressant-like responses with limited impact on the behaviors that mimic the psychomimetic effects of ketamine. The antidepressant-like behavioral effects of broad NMDAR channel blockers, such as ketamine and MK-801 (dizocilpine), were mediated by the suppression of GluN2A, but not by the inhibition of GluN2B. Moreover, treatment with ketamine or MK-801 rapidly increased the intrinsic excitability of hippocampal principal neurons through GluN2A, but not GluN2B. Together, these findings indicate that GluN2A mediates ketamine-triggered rapid antidepressant-like responses.

Keywords : GluN2A, ketamine, depression

S35-5

Cortical mechanisms underlying sensory hypersensitivity in *Adnp*-mutant mice

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Sensory dysfunction is reported in over 90% of individuals with autism spectrum disorder (ASD), yet the underlying neural mechanisms remain poorly understood. In the present study, *Adnp*-heterozygous (Adnp HT) mice, a well-established ASD model, were found to exhibit somatosensory hypersensitivity. An unbiased brain-wide activity screen identified hyperactivation of the anterior cingulate cortex (ACC) as being strongly associated with this sensory phenotype. Electrophysiological recordings from ACC neurons in Adnp HT mice revealed increased intrinsic excitability and an excitatory/inhibitory imbalance, suggesting potential contributors to ACC hyperactivity. Omics analyses further characterized the molecular alterations underlying this neural dysfunction. Chemogenetic inhibition of ACC neurons significantly alleviated sensory hypersensitivity in Adnp HT mice. Moreover, targeted inhibition of a specific subpopulation of ACC neurons, those responsive to electric foot shocks, restored both mild tactile reactivity and nociceptive behavior. These findings highlight the ACC as a key region involved in sensory hypersensitivity in ASD. A distinct neuronal ensemble within the ACC appears to be responsible for processing somatosensory and noxious stimuli, and its dysfunction plays a critical role in the manifestation of sensory abnormalities in ASD models.

Keywords : Autism, Hypersensitivity, Anterior cingulate cortex, electrophysiology

S35-6 Scitech Korea AWARDEE

Perturbed cell fate decision by schizophrenia-associated AS3MTd2d3 isoform during corticogenesis

Seunghyun Kim[1], Youngsik Woo[1], Dahun Um[1], Inseop Chun[1], Su-Jin Noh[1], Hyeon Ah Ji[1], Namyoung Jung[1], Bon Seong Goo[1], Jin Yeong Yoo[1], Dong Jin Mun[1], Tran Diem Nghi[1], Truong Thi My Nhung[1], Seung Hyeon Han[1], Su Been Lee[1], Jong-Cheol Rah[2], Seung Tae Baek[1,3], Ki-Jun Yoon[4], Min-Sung Kim[1,3], Tae-Kyung Kim[1,3], Sang Ki Park[1,3]

[1]Department of Life Sciences, Pohang University of Science and Technology, Pohang, Republic of Korea
[2]Sensory & Motor Systems Research, Korea Brain Research Institute, Daegu, Republic of Korea
[3]Institute for Convergence Research and Education in Advanced Technology, Yonsei University, Seoul, Republic of Korea
[4]Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Daejon, Republic of Korea

The neurodevelopmental theory of schizophrenia highlights early brain abnormalities in its etiology. Genome-wide association studies have linked schizophrenia to genetic variants of the AS3MT gene, particularly increased expression of the AS3MTd2d3 isoform. To elucidate how this isoform contributes to schizophrenia pathogenesis, we generated a transgenic mouse model (AS3MTd2d3-Tg) that ectopically expresses AS3MTd2d3 in cortical neural stem cells. AS3MTd2d3-Tg mice displayed enlarged lateral ventricles, impaired sensorimotor gating, and reduced sociability, mirroring schizophrenia-related phenotypes. Single-cell RNA sequencing of developing brains and single-nucleus RNA sequencing of adult AS3MTd2d3-Tg brains revealed disrupted neural stem cell fate decisions, premature neuronal differentiation, and a reduction of layer 2/3 excitatory (Tshz2+) neurons in the anterior cingulate cortex. Mechanistically, AS3MTd2d3 protein localized to the centrosome, causing mitotic spindle misorientation and altered progenitor division. This was partially mediated through misregulation of Nucleophosmin 1 (NPM1), a centrosomal partner involved in mitosis. Human brain organoid and protein structure analysis identified exposed hydrophobic residues (V129, F131) in AS3MTd2d3 as critical for its aberrant centrosomal localization and function. Our findings provide insight into how AS3MTd2d3 may disrupt early corticogenesis and contribute to schizophrenia pathophysiology, suggesting a potential developmental and molecular mechanism linking genetic risk to neuroanatomical and behavioral abnormalities.

Keywords : Schizophrenia, AS3MTd2d3 Isoform, Neurodevelopment, Mitotic Spindle Orientation, Centrosome Localization
Acknowledgements : This work was supported by National Research Foundation of Korea grants (RS-2023-00260454, RS-2024-00353657 to S.K.P.; RS-2023-00265581 to T.-K.K., S.K.P.; RS-2024-00410124 to S.K.), Samsung Science & Technology Foundation (SSTF-BA2102-09 to T.-K.K.), Multitasking Macrophage Research Center (RS-2023-00217798 to T.-K.K.), KBSI (RS-2021-NF000572 to T.-K.K.), and KBRI (24-BR-03-01 to J.-C.R., S.K.P.)

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 36

Day 3 (August 26) **14:30-16:25** **Premier Ballroom A**

Computational neuroethology of social and cognitive behaviors

Organizer : Jeongjin Kim (Korea Institute of Science and Technology)
Ain Chung (Korea Advanced Institute of Science and Technology)
Moderator : Jeongjin Kim (Korea Institute of Science and Technology)
Ain Chung (Korea Advanced Institute of Science and Technology)

1. Ethological and neural dynamics of collective foraging behavior in mice
   Jee Hyun Choi (Korea Institute of Science and Technology)
2. Mechanistic theory of social foraging
   Ahmed El Hady (Max Planck Institute)
3. Computational neuroethological approaches for neurological disease
   Seng Bum Michael Yoo (Sungkyunkwan University) Scitech Korea AWARDEE
4. Chaotic worms: integrative insights from the dynamics of animal behavior
   Greg Stephens (Vrije University)
5. Neural substrate of visual valence in the primate amygdala
   Gwangsu Kim (Massachusetts Institute of Technology)

S36-1

Ethological and neural dynamics of collective foraging behavior in mice: insights from burst-based neurophysiology in naturalistic settings

Jee Hyun Choi

Korea Institute of Science and Technology

Collective foraging is essential for survival in social animals but is often challenged by free-riders who exploit group efforts. The evolution of cooperation depends on individual differences in risk-taking and willingness to collaborate, yet the neural mechanisms underlying such naturalistic social behaviors remain poorly understood. To address this, we combine computational ethology with systems neuroscience, tracking neural activity corresponding to behaviorally defined syllables, brief action units identified from continuous observation. Traditional spike-aligned analyses, particularly averaged firing rates, lack temporal precision and fail to capture directional information flow between brain regions. In contrast, transient beta and gamma bursts in local field potentials, lasting tens to hundreds of milliseconds, carry oscillatory phase information that reveals circuit-level interactions and their directionality. We developed a platform to study collective foraging in group-housed mice within a colosseum-like arena containing a mobile, snack-bearing robot spider. Using automated tracking and classification, behavioral roles such as “workers” and “freeriders” emerge over time. Our setup integrates synchronized multimodal data streams including high-resolution video, burst-based telemetry EEG, RF tagging, vocalization tracking, and environmental monitoring, enabling precise alignment of ethologically defined behaviors with temporally resolved neural dynamics. I will present data showing that transient beta and gamma bursts mark collective behavioral transitions, and that burst-phase coupling across the prefrontal cortex, nucleus accumbens, and basolateral amygdala reflects the flow of task-relevant information. This work demonstrates how burst-level electrophysiology combined with computational ethology can reveal the fast-timescale neural dynamics that support cooperation, role differentiation, and adaptive social organization in ecologically valid contexts.

Keywords : Natural behaviors, Social interaction, Burst-level electrophysiology, Collective foraging, mPFC-BLA-NAc circuit

S36-2

Mechanistic theory of social foraging

ahmed elhady

Collective Behavior, University of Konstanz, Konstanz, Germany

Abstract: Foraging is a ubiquitous behaviour performed by all animals as search for food is crucial for survival. When the animal is foraging throughout its environment searching for resources, it is employing a variety of cognitive computations from decision making to planning to learning in addition to adjusting its bodily dynamics. Foraging as a behavior allows studying cognitive dynamics in a natural context and opens up the opportunity for evolutionary comparison across species. In this talk, I will provide a quantitative framework for an integrative understanding of patch foraging focusing on recently developed mechanistic theoretical models, that delineate the potential decision strategies an animal might employ to decide when and how to leave a patch of food across environments with different statistics. I will discuss how these models can be extended to the social foraging realm. These theoretical models can be fit to field data from a variety of species , to unravel the diversity of foraging strategies across environments. Closing the loop between theoretical models, field studies and large scale naturalistic experiments will shape the future of social foraging studies

Keywords : Foraging , Theoretical modelling , Behavior, Decision Making

S36-3

A Mixture of Neural Dynamics Underlies Discrete Behavioral Transitions

Seng Bum Michael Yoo

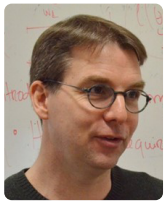
Department of Biomedical Engineering, Sungkyunkwan University, Gyeonggi-do, South Korea

The premise of computational ethology is to discretize the continuous stream of behavior into prominent primitives and investigate the neural dynamics underlying each of these primitives. A considerable question is whether neural dynamics themselves can be discretized in parallel with behavioral primitives. To address this, we studied neural population activity in macaque monkeys as they engaged in 3D virtual reality games. We classified behavior according to two distinct objectives by projecting behaviors into a high-dimensional state-space: maximizing reward or maximizing information. We then estimated the flow field of the neural population to test whether separate neural dynamics governed each behavioral objective. Our results showed that mixtures of two neural dynamics underpinned the seemingly distinct behaviors, with the relative contributions correlating with the degree to which each objective was achieved. These findings suggest that neural dynamics flexibly combine rather than discretely switch, enabling behavior to reflect a graded integration of multiple objectives.

Biography: (CV attached)

S36-4 Scitech Korea AWARDEE

Chaotic worms: integrative insights from the dynamics of animal behavior



Greg Stephens

Department of Physics, VU Amsterdam, Amsterdam, Netherlands &
Biological Physics Theory Unit, OIST Graduate University, Okinawa, Japan

How do we quantitatively capture the breadth of animal behavior, from rapid body twitches to aging? What principles characterize living movement? Research in our group seeks to answer these questions with a modern biophysics approach and model systems ranging from the nematode *C. elegans* and *Drosophila* larvae to social behavior in zebrafish and insect collectives. We combine theoretical ideas with quantitative experiments, to understand behavior from high-resolution posture sequences. I demonstrate our approach in the wiggling of a "simple" worm where we find a low-dimensional and chaotic phase space, spanned by three sets of unstable orbits, broadly interpretable as forward, reverse and turning locomotion. Despite the range of timescales exhibited by every living system, we construct a Markov worm dynamics which is remarkably predictive of long-time behavior. Overall, our work provides an integrative perspective from which we can interogate mechanistic understanding.

Biography: Greg Stephens obtained his Ph.D in theoretical physics from the University of Maryland with a dissertation in general relatively under the guidance of Bei-Lok Hu. He held postdoctoral positions at Los Alamos National Laboratory with Wojciech Zurek and Garret Kenyon, and, after a change in research direction to the physics of living systems, with William Bialek at Princeton University. He is currently an associate professor of physics at Vrije Universiteit Amsterdam and an adjunct professor at OIST Graduate University. He maintains research groups in both the Netherlands and Japan with interests centered upon organism-scale biophysics.

S36-5

Neural substrate of visual valence in the primate amygdala

Gwangsu Kim, Alina Peter, James DiCarlo

[1]McGovern Institute, Massachusetts Institute of Technology, Cambridge, USA

The amygdala is known to encode the valence of sensory stimuli, particularly through conditioned learning with rewards or punishment. However, the neural mechanism by which valence is assigned to unconditioned visual inputs—those lacking explicit value association—remains unclear. Here, we report that primate amygdala neurons systematically assign valence to unconditioned naturalistic visual inputs in the absence of explicit value conditioning. Electrophysiological recordings were obtained from the primate amygdala and inferior temporal cortex (IT) during the presentation of 400 naturalistic images across 16 categories including faces, animals, and natural scenes. A subset of amygdala neurons (~20%) exhibited reliable visual tuning even comparable to IT neurons. Furthermore, the amygdala responses were predictable using task-optimized deep neural network models of IT, reflecting functional circuits for processing unconditioned visual inputs. Next, we investigated whether some visually reliable amygdala neurons jointly encode valence. Valence neurons were identified by their statistically significant differential responses to positive or negative unconditioned stimuli (positive: juice, water; negative: air puffs). We found that a significant subpopulation of visual amygdala neurons (~26%) simultaneously encoded valence. Notably, our regression analyses showed that the cross-modal valence tuning of these visuo-valent neurons was linearly predictable from their visual tuning profiles ($R^2 \approx 0.8$ when holding out a neuron, $R^2 \approx 0.55$ when holding out a recording session). The visual-valence associations quantified each image's contribution to activating neural populations with specific valence signs, uncovering a category-specific structure in valence assignment. These findings suggest that the amygdala is engaged in systematically processing valence of unconditioned visual stimuli, alongside its role in explicit value learning.

Keywords : Amygdala, Visual system, Emotion, Deep neural network, Computational neuroscience
Acknowledgements : This work was supported by a grant from The Simons Foundation International (GK)

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 37

Day 3 (August 26) **14:30-16:25** **Premier Ballroom B**

Cross-regional brain circuit development: from neural differentiation to functional brain networks

Organizer : Keiko Tanaka-Yamamoto (Korea Institute of Science and Technology)
Yoko Yazaki-Sug (Okinawa Institute of Science and Technology)
Moderator : Keiko Tanaka-Yamamoto (Korea Institute of Science and Technology)
Yoko Yazaki-Sug (Okinawa Institute of Science and Technology)

1. Mitotic bookmarking in brain development
   Yan Song (Peking University)
2. Excavating growth cone architecture from the developing neocortex with volumeEM
   Yu Nakanishi (The University of Tokyo) IBRO AWARDEE
3. Opposite fine disorganization of the neocortex associated with Down Syndrome and Autism Spectrum Disorder
   Songhai Shi (Tsinghua University)
4. Dynamics auditory to motor circuits for developmental song learning in zebra finches
   Yoko Yazaki-Sugiyama (Okinawa Institute of Science and Technology)
5. The role of salience and action mode networks during the development of an internal-external functional brain axis in humans
   Seok-Jun Hong (Sungkyunkwan University)

S37-1

Mitotic bookmarking in brain development

Yan Song

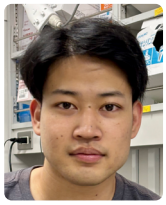
[1]School of Life Sciences, Peking University, Beijing, China
[2]Peking-Tsinghua Center for Life Sciences, Peking University, Beijing, China

In brain development, neural stem cells (NSCs) undergo asymmetric cell divisions to replicate themselves and meanwhile produce differentiating siblings. It remains obscure how NSCs preserve their self-renewing fate memory across mitosis. Even less is known how NSC-specific fate memory is selectively erased in the differentiating daughter cells. By developing a new pipeline for enriching mitotic versus interphase cells from developing brain, followed by low-input omics analysis, we recently identified TBP (TATA binding protein) as a crucial mitotic bookmarker for preserving NSC fate memory. Importantly, TBP achieves its mitotic retention through recruiting the chromatin remodeler EP400, which in turn increases local chromatin accessibility via depositing histone variant H2A.Z. Our unpublished work further reveals, immediately after NSC asymmetric cell divisions, how cell fate memory is differentially propagated to sibling daughter cells adopting distinct cell fates. Together, our latest discoveries unveil fundamental principles underlying the preservation or erasure of cell fate memory in brain development.

Keywords : Neural stem cell, Epigenetic memory, Cell fate decision, Mitotic bookmarking, Cell fate memory

S37-2 IBRO AWARDEE

Excavating Growth Cone Architecture from the Developing Neocortex with VolumeEM



Yu Nakanishi[1], Hiroyuki Hioki[2], Nobuhiko Ohno[3,4], Yusuke Hirabayashi[1]

[1]School of Engineering , The University of Tokyo, Tokyo, Japan
[2]Graduate School of Medicine, Juntendo University, Tokyo, Japan
[3]Division of Histology and Cell Biology, Jichi Medical University, Tokyo, Japan
[4]Division of Ultrastructural Research, National Institute for Physiological Sciences, Tokyo, Japan

During brain development, neurons form intricate neural circuits by extending axons and precisely regulating the direction and speed of growth. Growth cones, located at the tips of growing axons, are thought to play a critical role in this process by extending filopodia, but their structure and roles in a living brain remain largely unknown. Recent studies in 3D neuronal cultures showed a significant reduction in the number of filopodia compared to that in 2D cultures. This challenges traditional views on the role of filopodia in axon growth. However, to our knowledge, the 3D ultrastructure of the growth cone in a living brain has never been captured, and its filopodial structure remains elusive. The limited resolution of fluorescence microscopy prevents detailed visualization of growth cone ultrastructure, especially in its axial resolution. While EM provides the required lateral and axial resolution, its restricted field of view has made capturing growth cones located far from the cell body particularly challenging. To overcome this, we developed a genetically encoded tagging system to identify specific neurons in the developing mouse neocortex for EM analysis. By combining this technique with serial block-face scanning electron microscopy (SBF-SEM), we successfully captured the 3D ultrastructure of in vivo growth cones for the first time. Remarkably, we found that at a specific developmental stage, most growth cones in the corpus callosum lacked filopodia. We would like to discuss organelle organization within growth cones uncovered by our analysis.

Keywords : Growth cone, Ultrastructure, Volume EM, SBF-SEM

S37-3

Opposite fine disorganization of the neocortex associated with Down Syndrome and Autism Spectrum Disorder

Song-Hai Shi

Tsinghua University, School of Life Sciences, Beijing, China

Abnormal neocortical development and organization have been implicated in Down syndrome (DS) and autism spectrum disorder (ASD); yet, the exact nature and origin of the defects remain elusive. Here we show that opposite dysregulation of the fine structural and synaptic organization of neocortical excitatory neurons are distinctively associated with these two disorders. In *Ts65Dn* mice, a common model for DS, clonally related excitatory neurons originated from the same radial glial progenitor (RGP) become laterally clustered with excessive synaptic connectivity. In contrast, in three well-characterized mouse models of unrelated ASD high-risk genes, clonally related excitatory neurons become laterally dispersed with reduced synaptic connectivity. Accordantly, the expression of clustered protocadherins is oppositely perturbed in DS and ASD neocortices, restoration of which reverses the defects. Together, these results suggest that exquisite generation and organization of neocortical excitatory neurons is a crucial converging process vulnerable in different neurodevelopmental disorders.

Keywords : Neocortex, Development, Neural circuit, Neurodevelopmental disorders

S37-4

Dynamics auditory to motor circuits for developmental song learning in zebra finches

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Like human infants learn to speak, juvenile songbirds learn to sing during the developmental critical period. In zebra finches, a commonly used songbird model, only males learn to sing an individually unique song by memorizing their tutor's song (TS) and then matching their vocalizations to TS memories via auditory feedback. We found that fractions of neurons in the zebra finch higher auditory area, caudomedial nidopallium (NCM) become to show highly selective auditory responsiveness to TS after tutoring. Recently, we found the transient axonal projections into the song premotor area, HVC, from the NCM neurons activated by hearing TS. In contrast to the dense NCM axonal projections observed in HVC in the juveniles in sensorimotor song learning period, significantly smaller amount of NCM-HVC projections were found in the older juveniles in the end of song learning period. Ablating NCM neurons responding to TS prevented juveniles from learning TS. To further examine whether early song experiences and their timing affect the time course of NCM-HVC projection dynamics, we raised the juveniles with two tutors sequentially. We found that the sequentially tutored juveniles learned songs from the second tutor (T2) beyond the normal learning period with auditory isolation in between the experience with the first tutor (T1). We further visualized the NCM neurons responsive to each tutor's song in sequentially tutored birds. The projections from NCM neurons responding to T2 song were found in HVC within 12 hrs after being exposed to it. Notably, projections remained in HVC from both NCM neurons activated by hearing T1 or T2 songs in adulthood when NCM-HVC projections were rarely found in normally raised birds. Taken together, our results suggest that early song learning experiences and their timing shape the dynamic auditory-motor neuronal circuits and song learning time course.

Keywords : vocal learning, development, songbird, sensorimotor
Acknowledgements : This research is supported by the KAKENHI Grants #23K27284 and #24H02316

S37-5

The role of salience and action mode networks during the development of an internal-external functional brain axis in humans

Seok-Jun Hong

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How large-scale functional networks crystallize over human development remains a central problem in systems neuroscience. Here, I present evidence that the thalamus orchestrates this process. Leveraging high-resolution resting-state fMRI from more than 800 participants spanning infancy to early adulthood, we traced continuous thalamocortical gradients and uncovered a staged reorganization. In the earliest months, thalamic connectivity is broadly distributed across primary sensorimotor cortices; however, with maturation, it progressively converges on the ventral attention (salience) network. This shift sharpens the boundary between externally oriented sensory regions and internally oriented associative cortices, effectively laying down an internal–external processing axis. We argue that the emergent ventral attention hub integrates salience detection with action-mode control, linking task-driven collaboration among exteroceptive areas to episodic memory consolidation. These findings position the thalamus as a developmental switchboard that redirects cortical processing from action-centred exteroception toward introspective cognition, providing a mechanistic framework for investigating neurodevelopmental disorders marked by disrupted attention, memory, and self-referential thought.

Keywords : Large-scale functional networks, Human brain development, Generative modeling, Thalamus, internal-external axis

Acknowledgements : NRF-2022R1C1C1007095, RS-2023-00217361, RS-2024-00398768

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 38

Day 3 (August 26) **14:30-16:25** **Premier Ballroom C**

Molecular probing of cognitive processes

Organizer : Haruhiko Bito (The University of Tokyo)
Xiao-Hong Xu (Fudan University)
Moderator : Haruhiko Bito (The University of Tokyo)
Xiao-Hong Xu (Fudan University)

1. Rational engineering of XCaMP-C, a versatile genetically-encoded Ca2+ indicator for all-optical interrogation, multiplex and quantitative Ca2+ imaging
   Hajime Fujii (The University of Tokyo)
2. Brain-wide protein profiling using 3D immunolabeling techniques
   Young-Gyun Park (Korea Advanced Institute of Science and Technology)
3. Visualizing Neuroinflammation: Genetically Encoded cGAMP Sensors Reveal Innate Immune Dynamics
   Jianzhi Zeng (Shenzhen Bay Laboratory)
4. An insular cortical circuit required for itch sensation and aversion
   Xiao Min Zhang (Sun Yat-sen University)
5. Molecular mechanisms mediating engram ensemble retrievability state in mice
   Sungmo Park (The Hospital for Sick Children) Scitech Korea AWARDS

S38-1

Rational engineering of XCaMP-C, a versatile genetically-encoded Ca^{2+} indicator for all-optical interrogation, multiplex and quantitative Ca^{2+} imaging

Hajime Fujii[1], Keisuke Ota[1], Yayoi Kondo[1], George Cai[1,2], Richard Song[1,3], Haobo Song[1], Michiko Okamura[1], Hayato Kondo[1], Masatoshi Inoue[1,4], Haruhiko Bito[1]

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Understanding neuronal activities and biochemical signaling within complex neural circuits is a key challenge in neuroscience. The development of G-CaMPs/GCaMPs and their improved mutants has made GECI imaging essential for quantitative cellular studies. Recently, three new demands have emerged that the state-of-the-art GECIs do not fully address. First, all-optical interrogation, which integrates GECI imaging with optogenetic photomanipulation, requires GECIs that have unambiguously separable two-photon cross-section from light-sensitive channelrhodopsins. Second, advances in single-cell sequencing demand a much higher degree of multiplexity in recording of activities from diverse neuronal types. Third, detailed insights into biochemical signaling emphasize the need to quantitatively analyze local Ca^{2+} signaling dynamics in subcellular compartments. To address these challenges, we have developed a new cyan variant XCaMP-C, which offers (1) fast imaging completely free of crosstalk with optogenetic actuators, (2) the potential for more than 4-fold multiplex imaging of diverse neuronal types, and (3) precise quantification of Ca^{2+} transient dynamics in small sub-neuronal compartments. XCaMP-C allows Ca^{2+} imaging at 820 nm with minimal crosstalk from rsChRmine, significantly improving the resolution of all-optical interrogation without averaging and demonstrating horizontal functional connections at single-cell resolution in layer 2/3 of the mouse cortex in vivo. Additionally, XCaMP-C supports 6-color Ca^{2+} imaging in one-photon imaging, representing one of the highest multiplexity reports to date, and enables quantitative Ca^{2+} fluorescence lifetime imaging, revealing the heterogeneity of Ca^{2+} levels in dendrites and soma. Our progress paves the way towards deeper insights into complex and hierarchical neuronal network computations at the subcellular level and offers a new quantitative framework for recording in vivo Ca^{2+} signaling dynamics in brain health and disease.

Keywords : Ca2+ imaging, optogenetics, all-optical interrogation, GECI, FLIM
Acknowledgements : Grant/Support KAKENHI 23K06344, 25H00437, 22H05160 and AMED-SICORP JP25jm0210097

S38-2

Brain-wide protein profiling using 3D immunolabeling techniques

Young-Gyun PARK

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Proteins are major functioning molecules of biological systems. Immunolabeling proteins in whole brains can reveal the types of cells, synapses, and neurites that comprise neural circuitry, providing the information necessary to mechanistically understand brain functions and dysfunctions. However, whole-brain immunolabeling faces challenges of speed, cost, and heterogeneity. In this talk, I will present 3D immunolabeling techniques I developed to address these challenges. As presented in the talk, these techniques will demystify neural underpinnings embedded in the 3D landscape of nervous systems.

Keywords : 3D histology, Immunostaining, whole brain

S38-3

Visualizing Neuroinflammation: Genetically Encoded cGAMP Sensors Reveal Innate Immune Dynamics

Jianbo Zhao[1,2,3,4], Guihua Zhang[1], Ying Yu[1], Pengfei Che[1], Zhihang Ren[1], Zhenglong Shen[1], Yulong Li[1,2,3,5,6,7], & Jianzhi Zeng[1,*]

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Neuroinflammation is a key pathological feature shared by many neurodegenerative disorders and is characterized by persistent activation of immune signaling pathways. One of the major molecular drivers of this process is the cGAS–cGAMP–STING pathway, which detects leaked mitochondrial DNA and activates downstream innate immune responses. Despite its critical role, the spatiotemporal dynamics of neuroinflammation remain poorly understood, largely due to limitations in detection methods. To address this gap, we leveraged the intramolecular conformational changes that occur when cGAMP binds to STING, engineering a suite of genetically encoded intensiometric cGAMP sensors. In vitro characterization revealed that these sensors exhibit remarkable sensitivity, with >2000% ΔF/F0 response to cGAMP and EC50 values ranging from 10 to 500 nM. Sensor-expressing cells reported endogenous cGAMP signals evoked by transfected DNA, mitochondrial DNA, and herpes simplex virus type 1. By delivering the sensors into the mouse nervous system via adeno-associated virus (AAV) or transgenic expression, we successfully tracked neuronal cGAMP dynamics that correlated with disease progression in an LPS induced-inflammation disease model. This versatile toolkit provides unprecedented opportunities to dissect the role of pathological neuroinflammation across neurodegenerative disorders, offering new insights into their progression and potential therapeutic targets.

Keywords : Neuroinflammation, cGAS-cGAMP-STING, cGAMP sensor

S38-4

An insular cortical circuit required for itch sensation and aversion

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Itch encompasses both sensory and emotional dimensions, with the two dimensions reciprocally exacerbating each other. However, whether a shared neural circuit mechanism governs both dimensions remains elusive. Here, we report that the anterior insular cortex (AIC) is activated by both histamine-dependent and -independent itch stimuli. The activation of AIC elicits aversive emotion and exacerbates pruritogen-induced itch sensation and aversion. Mechanistically, AIC excitatory neurons project to the GABAergic neurons in the dorsal bed nucleus of the stria terminalis (dBNST). Manipulating the activity of the AIC→dBNST pathway affects both itch sensation and itch-induced aversion. Our study discovers the shared neural circuit (AIC→dBNST pathway) underlying the itch sensation and aversion, highlights the critical role of the AIC as a central hub for the itch processing, and provides a framework to understand the neural mechanisms underlying the sensation and emotion interaction.

Keywords : itch, aversion, insula, dBNST

S38-5 Scitech Korea AWARDEE

Molecular mechanisms mediating engram ensemble retrievability state in mice

Sungmo Park[1], Joseph Lee[1,2], Jung Hoon Jung[3,1], Asim Rashid[1], Paul Frankland[1,2], Sheena Josselyn[1,2]

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Engram ensembles, the cellular substrates of memory, exist on a spectrum of retrievability states, ranging from active to silent. While sensory cues typically reactivate engram neurons to induce memory retrieval, silent engrams fail to respond to these cues, though they can be artificially reactivated through optogenetic stimulation. In this study, we investigated the molecular mechanisms regulating engram silencing and un-silencing in forgetful TgCRND8 (Tg) mice, characterized by high endocytosis of GluA2-containing AMPA receptors (AMPARs) at the post-synaptic membrane. During context threat training, engram ensembles formed normally in the dorsal hippocampus CA1 of Tg mice but subsequently became silent. Remarkably, administering a peptide that interferes with GluA2-AMPAR endocytosis selectively during engram activation—whether through training, memory retrieval attempts, or optogenetic stimulation—restored engram activity and enabled memory retrieval. Similarly, in wild-type mice, LTD (Long-term depression)-type stimulation silenced engram ensembles, but the same peptide reactivated them when applied during engram activation. These findings elucidate the molecular processes underlying the dynamic states of engram retrievability, demonstrating the critical role of GluA2-AMPAR trafficking in memory silencing and reactivation. Our results offer novel insights into memory restoration mechanisms and suggest potential therapeutic approaches for memory impairments.

Keywords : memory, AMPAR trafficking , silent engram, retrievable, dorsal hippocampus

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 39

Day 3 (August 26) **14:30-16:25** **Rm.113-115**

Next-generation genetically encoded sensors and actuators for brain exploration

Organizer : Sangkyu Lee (Institute for Basic Science)
Moderator : Sangkyu Lee (Institute for Basic Science)

1. Evolving towards the highest-performance biosensors of neuronal signalling and metabolism
   Robert E. Campbell (The University of Tokyo)
2. Voltage imaging reveals biophysical basis of associative plasticity rules
   Pojeong Park (Daegu Gyeongbuk Institute of Science and Technology)
3. Large-scale in vivo imaging of neuronal firing with a high-contrast voltage indicator
   Sungmoo Lee (Stanford University) Scitech Korea Awardee
4. Genetically encoded biosensors and actuators for neurotransmitter receptors
   Jihye Seong (Seoul National University)
5. Sculpting neural circuits via engineered neuron-astrocyte interactions
   Sangkyu Lee (Institute for Basic Science)

S39-1

Evolving towards the highest-performance biosensors of neural signalling and metabolism

Robert E. Campbell

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The rapidly growing selection of high performance fluorescent protein (FP)-based biosensors is revolutionizing our ability to spy on the otherwise invisible chemistry of neural signalling and metabolism. In this seminar I will describe our most recent efforts to use protein engineering to make the next generation of genetically encoded biosensors with improved properties and an expanded range of potential applications. Key to this effort is our reliance on the use of iterative cycles of directed protein evolution which reliably lead to us to biosensors with the highest levels of performance. These biosensors include ones for inorganic ions such as calcium ion, potassium ion, and sodium ion, and metabolites such as lactate, pyruvate, and citrate. By creating biosensors with different colors and specificities, we are opening up new opportunities for researchers to use multiplexed imaging to investigate the spatiotemporal interplay of neural activity and metabolism in model organisms.

Keywords : Fluorescence , Protein engineering, Biosensors, Neural activity, Metabolism

S39-2

Voltage imaging reveals biophysical basis of associative plasticity rules

Pojeong Park

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Neurons convert synaptic inputs arriving onto dendrites into action potentials that propagate outward along axons. Back-propagating action potentials (bAPs) also go from soma into dendrites and interact with synaptic inputs to strengthen or weaken individual synapses, a key process in learning and memory. Our understanding of the molecular and biophysical mechanisms driving dendritic integration and synaptic plasticity remains limited. To bridge this gap, we developed molecular, optical, and computational tools for all-optical electrophysiology in dendrites. Our techniques have enabled to map sub-millisecond voltage dynamics throughout the dendritic trees of CA1 pyramidal neurons in acute brain slices and in live animals. In my talk, I will discuss our recent findings on history-dependent bAP propagation in distal dendrites, driven by locally generated Na^+ spikes (dSpikes). We observed that collisions of dSpikes with synaptic inputs can trigger N-methyl-D-aspartate receptor (NMDAR)-dependent plateau potentials, crucial elements in associative memory. These results, combined with numerical simulations, paint an intuitive picture connecting dendritic biophysics to associative plasticity rules.

Keywords : Voltage imaging, Synaptic plasticity, Dendritic non-linearity, Spike back-propagation

S39-3 Scitech Korea AWARDEE

Large-scale in vivo imaging of neuronal firing with a high-contrast voltage indicator

Sungmoo Lee[1], Guofeng Zhang[1,9], Laura C. Gomez[2,3], Can Dong[1], Guilherme Testa-Silva[4], Yukun Hao[1,5], Atsuki Hiramoto[4], Yue Sun[6], Richard H. Roth[6], Dongyun Jiang[1], Jun Ding[6], Thomas R. Clandinin[1], Botond Roska[4,7], Lisa Giocomo[1,8], Daniel Feldman[2], Na Ji[2,3], Michael Z. Lin[1,5]

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Fluorescent genetically encoded voltage indicators (GEVIs) directly report changes in neuronal transmembrane potential with changes in fluorescence intensity. Recently, we reported a positively tuned GEVI, ASAP4e, that exhibits exceptional photostability and responsivity while detecting spikes with similar signal-to-noise ratios (SNRs) as ASAP3. To further enhance optical spike detection, we performed multiparametric structure-guided mutagenesis of ASAP4. The resulting ASAP6 is faster and more responsive than ASAP4 while maintaining high photostability and consistent performance across multiple 1- and 2-photon imaging methods. With ASAP6, we demonstrate kilohertz-rate 1-photon imaging of spiking activity in awake behaving mice at densities exceeding 400 neurons/mm². Directly comparing ASAP6 and the calcium indicator GCaMP8f using frame rates matched to their activation kinetics, we find that ASAP6 detects single action potentials with similar SNR but higher temporal precision than GCaMP8f. Thus, ASAP6 enables large-scale action potential imaging in genetically defined neurons in vivo with improved spike timing accuracy.

Keywords : voltage imaging, GEVI, voltage indicator, fluorescent protein, CA1

Acknowledgements : This work was supported by the Stanford Department of Bioengineering and NIH grants 1UM1MH136462, 1RM1NS132981, 1RF1NS131075, and 1R01NS123681.

S39-4

Genetically encoded biosensors and actuators for neurotransmitter receptors

Jihye Seong

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Neurotransmission serves as the fundamental mechanism governing brain function. At synapse, neurotransmitters bind to their specific receptors, which are often G protein-coupled receptors (GPCRs), activating precisely regulated signaling cascades that orchestrate complex brain functions. To advance our understanding of these processes, we develop genetically encoded biosensors and optogenetic actuators, for real-time monitoring and precise control of neurotransmitter receptors. First, we engineered multi-color biosensors enabling real-time monitoring of dopamine receptors subtypes DRD1 and DRD2, revealing differential functional crosstalk in DRD1-DRD2 heterodimers. We are applying the biosensors to investigate the complex functions of neurotransmitter heterodimers. Second, we created optogenetic actuators (OptoXRs) for precise spatiotemporal control of receptor activity. In particular, we engineered OptoDRD2, a light-responsive chimeric receptor incorporating the light-sensitive component of rhodopsin with the intracellular signaling domain of DRD2. When expressed in excitatory neurons of the lateral globus pallidus in mice, OptoDRD2 activation enhanced motor function, uncovering a previously unrecognized role for DRD2 signaling in this region. We are further engineering OptoXRs for the more precise control of specific neurotransmission. Together, these technologies provide powerful tools for investigating the complex dynamics of neurotransmitter receptor function in the brain, with significant implications for understanding both normal neural circuit function and neurological disorders.Fluorescent biosensor

Keywords : Fluorescent biosensor, Optogenetic actuator, Neurotransmitter receptor, GPCR, dopamine receptor
Acknowledgements : This work is supported by National Research Foundation of Korea (NRF) grant RS-2023-00227950, RS-2024-00407331, RS-2024-00338426, RS-2024-00403094.

S39-5

Sculpting neural circuits via engineered neuron-astrocyte interactions

Sangkyu Lee

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Information flow through synapses in the central nervous system is regulated by both the rapid electrochemical activity and the slower structural remodeling, involving complex interplays between neurons and glial cells. While remarkable advances have enabled precise control of synaptic activity, methods for structural editing of synaptic connections remain limited. Here, we present SynTrogo (Synthetic Trogocytosis), a synthetic molecular approach for targeted synapse elimination through engineered neuron-astrocyte interactions, harnessing the natural proximity of astrocytes to synapses. By introducing synthetic ligand and receptor proteins in two cell populations, we induce their tight interactions, triggering 'Trogocytosis', where one cell nibbles membrane fragments of others. Using immunohistochemistry, correlative light and electron microscopy (CLEM) imaging, electrophysiological analysis, we demonstrate that induced physical binding of neurons and astrocytes in the hippocampus enables astrocytes ingest synaptic components, leading to reduced synaptic connectivity through selective synapse elimination. Unexpectedly, the remaining synapses undergo substantial remodeling, exhibiting enlarged pre- and post-synaptic structures, reorganization of synaptic components and organelles, as well as enhanced synaptic plasticity and memory. This study elucidates how the brain adaptively reshapes neural circuits following astrocyte-mediated synapse pruning and provides a technical foundation of connectome editing through engineered neuron-astrocyte interactions.

Keywords : Neuron-astrocyte interaction, Protein engineering, Synthetic trogocytosis, Synaptic pruning

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 40

Day 3 (August 26) **14:30-16:25** **Rm.116-118**

Basic and translational researches on myelination and demyelination

Organizer : Hwan Tae Park (Dong-A University)
Hyun-Jeong Yang (University of Brain Education)
Moderator : Hwan Tae Park (Dong-A University)

1. The role of oligodendrocyte lineage cells in the hypothalamus
   Dong Ho Woo (Korea Institute of Toxicology)
2. Searching for Novel Myelination-Promoting Factors in the Central Nervous System
   Hyun-Jeong Yang (University of Brain Education)
3. Oligodendroglial precursor cells orchestrate immune crosstalk at the onset of multiple sclerosis
   Qi Wang (Sun Yat-sen University) IBRO AWARDEE
4. Nerve-specific gene therapy for CMT1A: safety, efficacy and biomarker characterization in sheep
   Nicolas Tricaud (Inserm)
5. Differential subcellular distribution of cell adhesion molecules in neurons guides myelin targeting
   Elior Peles (Weizmann Institute of Science)

S40-1

The role of oligodendrocyte lineage cells in the hypothalamus

Ye-Ji Kim[1,3], Duhyeon Park[2,3], Daeui Park[2,3], Dong Ho Woo[1,3]

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Oligodendrocytes are known for their role in myelin formation and efficient neurotransmission, but numerous studies highlight their heterogeneity. The specific molecular and cellular mechanisms of hypothalamic oligodendrocyte lineage cells under overnutrition conditions remain unknown. This study aims to investigate the long-term effects of a high-fat diet (HFD) on oligodendrocyte health by comparing oligodendrocytes after 4 and 20 weeks of HFD feeding. To investigate how external overnutrition conditions influence oligodendrocyte lineage cells, we also compared the hypothalamus of ob/ob mice, which have a leptin mutation. Weight increased from 25.4±0.5g at 4 weeks to 50.2±1.2g at 20 weeks. Concurrently, blood TNF rose from 18.3±3.2 to 27.4±2.4, while the number of leukocytes decreased. Blood CD45+ cells decreased significantly, dropping by 40% at 4 weeks and by 60% at 20 weeks. In contrast, NK1.1+ cell counts remained unchanged. CD3+ T cells also decreased, with similar reductions observed at both the 4-week and 20-week time points. At 20 weeks, blood TNF levels remained stable in mice on a normal diet but decreased by 50% in those on a high-fat diet. This suggests that external blood factors might influence the brain. In the hypothalamic region at 20 weeks, HFD-induced obesity increased the number of GFAP-positive cells but not Iba-1-positive cells in the α2 and β1 hypothalamic subregions. At 20 weeks, the number of hypothalamic Olig2+ cells remained unchanged, while GFAP+ cell counts increased dramatically. Interestingly, Olig2+ cell changes were also observed in the irrelevant area. I would like to discuss changes in areas other than the relevant area

Keywords : oligodendrocyte, hypothalamus, high fat diet, obesity, inflammation
Acknowledgements : This research was supported by the Korea Institute of Toxicology, Republic of Korea (Grant Nos. 1711195891 and KK-2515), a National Research Council of Science & Technology (NST) grant by the Korean government (MSIT) (No. GTL24021-000), and Korea Institute of Marine Science & Technology Promotion(KIMST) funded by the Ministry of Oceans and Fisheries(RS-2025-02292973).

S40-2

Searching for Novel Myelination-Promoting Factors in the Central Nervous System

Hyun-Jeong Yang[1,2], Youngja Hwang Park[3,4], Dalnim Kim[1,2], Ahreum Lee[1,2], Minkuk Park[5], Eugene Koh[6], Gakyung Lee[5]

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Myelin is a lipid-rich sheath that insulates neuronal axons, facilitating saltatory conduction. In the central nervous system (CNS), oligodendrocytes are responsible for forming this myelin sheath. Environmental enrichment, including social interaction, promotes not only synaptic but also myelin plasticity. Since myelination occurs over an extended period after birth—continuing into adulthood—it is particularly vulnerable to environmental stressors such as social isolation. Disruption of myelination during early life can increase the risk of psychiatric symptoms in adulthood. Recent studies have also suggested links between myelination, gut metabolites, and behavior, although the mechanisms remain unclear. To identify myelination-promoting factors via the gut–brain axis, we performed gut metabolomics in a post-weaning social isolation (PWSI) mouse model and identified a novel myelin-enhancing factor. To investigate its mechanism, we assessed social behavior, myelin levels in the medial prefrontal cortex (mPFC), and lipid composition in the myelin-rich corpus callosum of PWSI mice with or without this factor. We found that it enhanced myelination by promoting oligodendrocyte maturation, supporting mitochondrial metabolism, and altering myelin lipid composition, ultimately improving social behavior. Our findings suggest that promoting myelination through gut-derived factors may serve as a therapeutic strategy for psychiatric disorders.

Keywords : Myelin, Post-weaning social isolation, Oligodendrocyte, gut, Medial prefrontal cortex
Acknowledgements : This work was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2020R1I1A3A04038150), Korea Basic Science Institute (National research Facilities and Equipment Center) grant funded by the Ministry of Education (2023R1A6C101A045), and the NRF grant funded by the Korea government (MSIT 2020R1A2C2103067).

S40-3 IBRO AWARDEE

Oligodendroglial precursor cells orchestrate immune crosstalk at the onset of multiple sclerosis

Qi Wang, Chenju Yi

Research Centre, Seventh Affiliated Hospital, Sun Yat-sen University, Shenzhen, Guangdong, China

The immunomodulatory cellular network that triggers early inflammation and demyelination, the key steps in multiple sclerosis (MS) pathogenesis remains poorly characterized. Here, we demonstrate that overactivation of Wnt pathway promotes pathological transformation of oligodendrocyte precursor cells (OPCs) to replicate pathological OPCs in human MS. In mouse experimental autoimmune encephalomyelitis (EAE), pathological OPCs attract $CD4^+$ T-helper 1 (Th1) cells into the spinal cord and brain through CC-chemokine ligand 4 (CCL4), whilst OPCs cooperate with Th1 cells inducing transformation of cytotoxic macrophages that execute early demyelination. Simultaneously, Th1 cells and cytotoxic macrophages upregulate Wnt signaling and CCL4 expression in OPCs, thus exerting positive feedback onto the OPC-immune cascade and establishing a vicious cycle propagating EAE pathogenesis. Breaking this cascade by targeting CCL4 reduces immune cell infiltration, alleviates demyelination, and attenuates EAE severity. Our findings demonstrate a closely coordinated network of OPCs and immune cells therefore providing an alternative insight into MS pathophysiology.

Keywords : Multiple sclerosis, Oligodendrocyte precursor cells, Wnt pathway, Immune crosstalk, CCL4
Acknowledgements : This work was supported by grants from the National Nature Science Foundation of China, Guangdong Basic and Applied Basic Research Foundation and Shenzhen Fundamental Research Program. We also thank Prof Fu-Dong Shi from Tianjin Medical University General Hospital for the MS brain tissues.

S40-4

Nerve-specific gene therapy for CMT1A: safety, efficacy and biomarker characterization in sheep

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PMP22 overexpression leads to defective myelination, secondary axonal loss and muscle atrophy in CMT1A. We recently developed an AAV9 expressing PMP22-targeted siRNA that restores normal protein expression and improves phenotype in mouse and rat disease models. The vector is delivered locally around nerves using perineural injection route, which is standard care in regional anesthesia. Treating the main nerves of arms and legs aims to bring full benefit to all limb muscles and to largely alleviate disease burden. After non-human primates, we investigated safety and molecular efficacy in adult sheep, which have larger nerves and a plurifasciculated nerve structure similar to humans. Such as in NHP, treating all targeted nerves in humans showed no local or systemic toxicity in sheep. Immune response remained limited to antibody production. Biodistribution was mostly limited to treated nerves with low liver and spleen transduction and very low or absent transduction in DRG, spinal cord, heart, kidney, lung and brain. To reliably correlate vector dose with molecular efficacy on a large scale, PMP22 protein level was used as a biomarker and measured along treated sheep nerves using Simple Western™ technology. The study involved a total of 820 samples from more 70 nerves (sciatic, peroneal, tibial, sural, caudal, radial, median, thoracic, ulnar) and 16 sheep. Results show that gene therapy enables a dose-dependent PMP22 protein decrease in all treated nerves but also their branches. A single nerve treatment allowed to decrease PMP22 over at least 30 cm of nerve. However, whatever the dose used PMP22 decrease never reached more than 50% decrease, preventing animals to develop HNPP, a demyelinating condition due to too low PMP22 expression. Perineural delivery of AAV9 in one or several nerves appears to be a fully translatable, efficient and safe therapeutic avenue to treat CMT diseases as well as other peripheral nerve disorders.

Keywords : Myelin, peripheral neuropathies, gene therapy

S40-5

Differential subcellular distribution of cell adhesion molecules in neurons guides myelin targeting

Bharath Vijayaragavan[1,2], Bassima Ibrahim[1,2], Nimrod Elazar[1,2], Yuki Ogawa[3], Anya Vainstein[1,2], Matthew N. Rasband[3], Yael Eshed-Eisenbach[1,2] and Elior Peles[1,2]

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Myelin forms preferentially around axons while avoiding neuronal cell bodies and dendrites, but the underlying basis of such subcellular targeting is still unknown. Myelination in the central nervous system involves complex intercellular contacts between oligodendrocytes and their underlying axons. Oligodendrocyte-axon contact is mediated by the binding of glial cell adhesion molecules 4 and 1 (Cadm4 and Cadm1) to Cadm3 and Cadm2 present in axons. Neuronal Cadms also regulate the avoidance of oligodendrocytes from wrapping around non-axonal structures such as neuronal cell bodies and dendrites. Proteomic analysis of cultured hippocampal neurons aimed at defining their cell surface interactome revealed the presence of all four Cadm proteins. Using endogenous genomic tagging, we found that Cadm4 and Cadm1 are restricted to the somatodendritic compartment in motor neurons, whereas Cadm3 and Cadm2 are present in all neuronal compartments, including the axon. Nevertheless, despite the presence of Cadm3 and Cadm2 in cell bodies and dendrites, Cadm4 only binds to axons. This was attributed to the presence of Cadm4 in the somatodendritic compartment. Neuronal deletion of both Cadm4 and Cadm1, or increased expression of Cadm3 in the neuronal soma and dendrites, enabled the binding of Cadm4 to all neuronal compartments and led to somatodendritic ensheathment by oligodendrocytes. Our results demonstrate that the differential subcellular distribution of cell adhesion molecules of the Cadm family in neurons contributes to the preferential targeting of oligodendrocytes to axons.

Keywords:Oligodendrocyte, Axon, Myelin targeting, Cadm/SynCAM, Cell recognition

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 41

Day 3 (August 26) **14:30-16:25** **Rm.206-207**

Pleiotropic roles of mitochondria in neurobiology

Organizer : Seok-Kyu Kwon (Korea Institute of Science and Technology)
Moderator : Jun Young Heo (Chungnam National University)
Seok-Kyu Kwon (Korea Institute of Science and Technology)

1. Hitch-hiking of mRNAs on mitochondria
   Angelika Harbauer (Max Planck Institute)
2. A Mitochondrial Switch of Cell Fate Decision in Early Corticogenesis
   Sang Ki Park (Pohang University of Science and Technology)
3. Organellar pathogenesis in Neurodegenrative diseases
   Kyu-Sun Lee (Korea Research Institute of Bioscience and Biotechnology)
4. Correlative organelle microscopy with multimodal data to study mitochondria in lipid related neuronal developmental disorders
   Ji Young Mun (Korea Brain Research Institute)
5. In situ localization of ER-mitochondria tethering proteins at the nanometer scale
   Takumi Sakano (The University of Tokyo) IBRO AWARDEE

S41-1

Hitch-hiking of mRNAs on mitochondria

Angelika Harbauer

MPRG Neurometabolism, MPI for Biological Intelligence, Martinsried, Germany

Neurons with their elaborate and extended morphology must employ homeostatic mechanisms that allow neuronal mitochondria to exist far away from the cell body while still retaining a functional proteome. This process, called “Mitostasis”, is most likely a finely tuned concert of mitochondrial transport, local protein synthesis and local degradation by proteasomal and autophagic mechanisms. Modulation of these processes may prove beneficial in the treatment of neurodegenerative diseases. However, the processes that allow local translation of mRNAs encoding for mitochondrial proteins are only partially understood. Using the transcript of PTEN-induced kinase 1 (PINK1) as a model substrate, we have discovered that this RNA associates with mitochondria specifically in neurons and uses mitochondria as a means of transport into axons and dendrites. This is a neuron specific mechanism driven by selective expression of an mRNA anchoring complex at the outer mitochondrial membrane which we termed mitochondrial hitch-hiking. To get an unbiased insight into the amount of mitochondrial RNA hitch-hiking, we performed RNAseq of mitochondria isolated from retinal ganglion cell axons and motorneuron axons. This revealed a cell-type specific adaption of the amount of RNA hitch-hiking not only of the mRNA encoding Pink1, but of an entire class of proteins involved in mitophagy, synaptic and cytoskeletal processes, that may be driven by the local availability (or absence) of these transcripts. This suggests fundamental difference in axonal biology between glutamatergic and cholinergic axons.

Keywords : Mitochondria, Cytoskeleton, Local translation, Mitophagy, RNA transport

S41-2

A Mitochondrial Switch of Cell Fate Decision in Early Corticogenesis

Sang Ki Park, TRAN DIEM NGHI

Department of Life Sciences, POSTECH, Pohang, Republic of Korea

Embryonic neural stem and progenitor cells (NSPCs) inhabit a specialized niche adjacent to the lateral ventricle, where apical membrane receptors mediate access to essential signaling molecules in the primordial cerebrospinal fluid. However, how these signals are transduced to regulate NSPC fate is poorly elucidated. We identify EPHA2 as a critical mediator in this process. EPHA2 is enriched selectively in NSPCs and disruption of its ligand-independent, but not canonical ephrin-dependent, pathway impairs NSPC self-renewal by inducing premature cell cycle exit. Mechanistically, we demonstrate that ligand-independent EPHA2 signaling promotes dephosphorylation of ECSIT, the mitochondrial complex I assembly factor, at threonine 179 by protein phosphatase 2A. This enables ECSIT’s mitochondrial localization and supports complex I activity essential for NSPC maintenance. Notably, maternal NAD+ supplementation rescues progenitor loss and mitigates aberrant neurogenesis caused by EPHA2 pathway disruption. These findings delineate an EPHA2-ECSIT-mitochondria axis that bridges the extracellular microenvironment with intracellular metabolism to sustain the NSPC pool during neocortical development.

Keywords : EPHA2 signaling, ECSIT, mitochondrial Complex I, neocortical development, neural stem and progenitor cells (NSPCs)
Acknowledgements : This work was supported by the National Research Foundation of Korea (NRF) K-Brain Project (RS-2023-00265581 to S.K.P.), the Innovation Research Center (RS-2023-00260454 to S.K.P.), and the Mid-career Researcher Program (RS-2024-00353657 to S.K.P.).

S41-3

Organellar pathogenesis in Neurodegenerative diseases

Kyu-Sun Lee

Metabolism and Neurophysiology Research Group, KRIBB, Daejeon 34141, Korea

Mitochondrial dysfunction represents a pivotal characteristic of numerous neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. These conditions, distinguished by unique clinical and pathological features, exhibit shared pathways leading to neuronal damage, all of which are closely associated with mitochondrial dysfunction. Growing evidence from genetic, biochemical, and cellular investigations associates impaired quality-control mechanisms, such as mitophagy, with the initial phases of disease progression. PINK1 is a representative kinase that regulates mitophagy through the phosphorylation and activation of various substrates. In particular, it regulates mitophagy by phosphorylating parkin, an E3-ubiquitin ligase, and our research team recently discovered that it is also involved in pexophagy, a peroxisome-specific autophagy. In particular, our results show that interactions between CHIP1 and pexophagy-regulated molecules are important. These findings contribute to understanding of the molecular mechanisms underlying orgalle turnover and may have implications for therapeutic strategies targeting neurodegenerative diseases.

Keywords : PINK1, CHIP1, Peroxisome, Mitochondria, Neurodegenerative diseases

S41-4

Correlative organelle microscopy with multimodal data to study mitochondria in lipid related neuronal developmental disorders

Ji Young Mun

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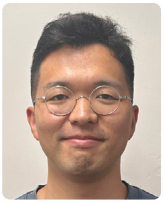
Lipid metabolism plays a fundamental role in brain development, serving not only as an energy source but also as a key regulator of membrane biogenesis, intracellular signaling, and organelle communication. However, how imbalanced lipid profiles influence mitochondrial function during neurodevelopment remains poorly understood. In this study, we investigated mitochondrial dynamics in neural stem cells exhibiting a distinct lipid remodeling pattern, characterized by a selective increase in triacylglycerol (TG) levels without corresponding changes in other lipid species. This lipid remodeling suggests that remaining lipid precursors are primarily utilized for membrane synthesis and neutral lipid accumulation. Mitochondria exhibited dynamic responses to this altered lipid environment. Using volume electron microscopy, correlative light and electron microscopy (CLEM), and live-cell imaging, we observed marked alterations in mitochondrial morphology, including impaired fission-fusion dynamics and disrupted organelle distribution during neural differentiation. Transcriptomic analysis further revealed the activation of stress-responsive mitochondrial pathways associated with oxidative phosphorylation, redox imbalance, and lipid peroxidation. Together, these findings highlight the sensitivity of mitochondrial function to lipid imbalance during early neurodevelopment and underscore the multifaceted role of mitochondria as a metabolic hub that buffers, adapts to, or exacerbates lipid-induced cellular stress. Our study provides mechanistic insights into how disrupted lipid homeostasis may impair mitochondrial function and contribute to neurodevelopmental disorders.

Keywords : Mitochondria, Dynamics, Lipid, NSC, CLEM

S41-5 IBRO AWARDEE

In situ localization of ER-mitochondria tethering proteins at the nanometer scale



Takumi Sakano[1], Koki Nakamura[1], Toshiyuki Oda[2], Yusuke Hirabayashi[1]

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Traditionally, intracellular organelles have been considered to function independently. However, recent advances in electron microscopy have revealed that organelles often come into close proximity within tens of nanometers without fusing, forming specialized structures known as organelle contact sites. Among these, mitochondria-endoplasmic reticulum contact sites (MERCS) are particularly crucial for regulating essential cellular processes. In neuronal dendrites, MERCS play a key role in activity-dependent calcium dynamics, where calcium is released from the ER and buffered by mitochondria to support proper neuronal signaling. Therefore, regulating the size and spatial distribution of MERCS is critical for neuronal function. Genetic approaches have identified several key proteins essential for MERCS formation; notably, among these proteins, the ER membrane protein PDZD8 has been shown to be critical for proper brain function. PDZD8 is thought to physically tether the two organelles to form these contacts. However, the spatial mechanisms underlying tethering protein-mediated MERCS formation remain largely unclear, primarily due to the lack of tools for nanoscale protein localization analysis. To address this gap, we employed a genetically encoded gold nanoparticle labeling method using MTn tags, enabling electron microscopy–based visualization of target proteins. Using this approach, we successfully visualized the nanoscale localization of PDZD8 in HEK293T cells. Furthermore, we extended our analysis to another MERCS tethering protein, VAPB, and intriguingly found that PDZD8 and VAPB exhibit distinct spatial preferences within MERCS. We would like to discuss how the spatial distribution of tethering proteins contributes to the structure and function of MERCS.

Keywords : Electron microscopy, Organelle contact, Gold nanoparticle labeling, Ultrastructure
Acknowledgements : Prof. Masahide Kikkawa and Associate Prof. Chieko Saito

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 42

Day 4 (August 27) **09:00-10:55** **Grand Ballroom**

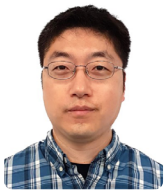
Unlocking pathophysiological and novel therapeutic mechanisms for mood disorders: insights from synapse research

Organizer : Ji-Woon Kim (Kyung Hee University)
Moderator : Ji-Woon Kim (Kyung Hee University)

1. Role of phospholipase Cη1 in lateral habenula astrocytes in depressive-like behavior in mice
   Jeongyeon Kim (Korea Brain Research Institute)
2. Functional nano-organization of central synapses and rapid antidepressant action
   Ege T. Kavalali (Vanderbilt University)
3. Mechanism of rapid antidepressant action
   Lisa M. Monteggia (Vanderbilt University)
4. Neurophysiological effects of psilocybin on the cortical and claustral circuits
   Juhyun Kim (Korea Brain Research Institute)
5. Stress-induced spontaneous high-frequency firing in the hippocampus promotes synaptic diversity and memory encoding through entropy expansion
   Yuheng Yang (Yamaguchi University) IBRO AWARDEE

S42-1

Role of phospholipase Cη1 in lateral habenula astrocytes in depressive-like behavior in mice



Sukwoon Song [#1], Miseon Kang [#1], Jiyoung Lee [#1], Yong Ryoul Yang [2], Ho Lee [3], Jae-Ick Kim [4], Beomsue Kim [5], Hoon-Seong Choi [6], Eun-Bin Hong [7,8], Min-Ho Nam [7], Pann-Ghill Suh [9], Jeongyeon Kim [10]

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[9]Korea Brain Research Institute, Daegu, Republic of Korea.
[10]Emotion, Cognition and Behavior Research Group, Korea Brain Research Institute, Daegu, Republic of Korea.

Phospholipase C (PLC) enzymes play crucial roles in intracellular calcium-signaling transduction. Several brain PLC subtypes have been extensively studied, implicating them in psychiatric disorders such as depression, epilepsy and schizophrenia. However, the role of the recently identified PLCη remains largely unknown. We found that PLCη1 is prominently expressed in lateral habenula (LHb) astrocytes. Here, to investigate its physiological role, we generated astrocyte-specific PLCη1 conditional knockout (cKO) mice (Plch1$^{f/f}$; Aldh1l1-Cre^{ERT2}). In these cKO mice, we observed a reduction in cellular morphological complexity metrics, such as total process length, as well as a decrease in the passive membrane conductance of LHb astrocytes. Additionally, neuronal function was impacted by the cKO, as the synaptic efficacy and firing rates of LHb neurons increased, while extrasynaptic long-term depression was impaired. Both tonic α-amino-3-hydroxy-5-methyl-4-isoxazolepdlropionic acid receptor/N-methyl-D-aspartate receptor (AMPAR/NMDAR) currents and extracellular glutamate levels were reduced. Interestingly, chemogenetic activation of astrocytes restored the reduced tonic AMPAR/NMDAR currents in cKO mice. Furthermore, LHb astrocyte-specific deletion of PLCη1 via AAV-GFAP-Cre injection induced depressive-like behaviors in mice, which were reversed by chemogenetic activation of LHb astrocytes. Finally, we found that restraint stress exposure decreased Plch1 mRNA expression in the LHb. These findings suggest that PLCη1 could be a potential therapeutic target for depression and highlight the critical role of astrocytes in the etiology of neuropsychiatric disorders.

Keywords : Phospholipase C, Lateral habenula, Astrocyte, Depression

S42-2

Functional nano-organization of central synapses and rapid antidepressant action

Ege T. Kavalali

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Major depressive disorder affects millions worldwide, yet current treatments require prolonged administration. In contrast, ketamine produces rapid antidepressant effects by blocking spontaneous NMDA receptor signaling, which lifts the suppression of protein synthesis and triggers homeostatic synaptic plasticity. Here, I will discuss the role of mGluR signaling in this process by demonstrating how mGluR and NMDA receptor driven Ca2+ signals interact at nanoscale and promote rapid antidepressant-like effects. These findings highlight mGluR signaling as a promising therapeutic target for rapid antidepressant action, harnessing the complex nanoscale organization of synapses.

Keywords : Calcium signaling, rapid antidepressant action, metabotropic glutamate receptors, NMDA receptors, spontaneous neurotransmitter release

S42-3

Mechanism of rapid antidepressant action

Lisa M. Monteggia

Vanderbilt University

Ketamine produces rapid and sustained antidepressant effects in patients with major depressive disorder and treatment resistant depression. The rapid action of ketamine provides an opportunity to elucidate the types of acute synaptic plasticity changes that can be recruited to counter depression symptoms. Work over the past decade converges on a synaptic mechanism for ketamine's rapid antidepressant action. Specifically, ketamine by blocking NMDA receptors, inhibits the phosphorylation of eukaryotic elongation factor 2 kinase (eEF2K), resulting in the desupression of protein synthesis of BDNF and specific synaptic proteins, promoting the insertion of AMPA receptors. This cascade produces a novel form of synaptic plasticity in the hippocampus, specifically at CA3-CA1 synapses, that we hypothesize underlies the rapid antidepressant action. More recently, we have begun to link these rapid effects to the sustained action of ketamine and will present on downstream mechanisms involved in the prolonged antidepressant action.

S42-4

Neurophysiological effects of psilocybin on the cortical and claustral circuits

Juhyun Kim

Emotion, Cognition and Behavior Research Group, Korea Brain Research Institute, Daegu, Republic of Korea

Psychedelics are hallucinogenic drugs that induce non-ordinary mental states and expanded consciousness. Substances like psilocybin, MDMA, and LSD show potential as neurotherapeutics, though their neural mechanisms remain unclear. A recent fMRI study found that psilocybin acutely affects the claustrum, a brain region linked to the cortex. Since the claustrum and cortex are interconnected, we hypothesized that psilocybin alters neuronal activity in both. We injected psilocybin (1–3 mg/kg) into male and female mice and analyzed c-Fos activation. Results showed a significant increase in claustrum activation in both sexes. In the cortex, c-Fos cell density varied by region. We further examined parvalbumin and somatostatin interneurons using cell type-specific markers and found regional differences in their activation. Anterior cortical areas showed increased c-Fos density, while posterior areas showed changes in a subset of interneurons. Activation patterns also differed slightly between sexes. These findings suggest psilocybin's effects are regionally, cell type-, and sex-specific.

Keywords : Psilocybin, Claustrum, Sensory cortex, Psychedelics, Circuits
Acknowledgements : This research was supported by Korea Brain Research Institute (KBRI, 24-BR-02-02 & 24-BR-04-04) and basic science research program through the National Research Foundation of Korea (NRF, RS-2023-00248148) funded by Ministry of Science and ICT.

S42-5 IBRO AWARDEE

Stress-induced spontaneous high-frequency firing in the hippocampus promotes synaptic diversity and memory encoding through entropy expansion

Yuheng Yang[1], Junko Ishikawa[1], Dai Mitsushima[1,2]

[1]Department of Physiology, Yamaguchi University Graduate School of Medicine, Ube, Yamaguchi, Japan
[2]The Research Institute for Time Studies, Yamaguchi University, Ube, Yamaguchi, Japan

The formation of long-term memory depends on activity-dependent synaptic plasticity in the hippocampal CA1 region. Although artificial high-frequency stimulation is known to induce plasticity (Bliss & Lomo 1973), the endogenous neuronal firing patterns that naturally trigger synaptic changes during memory encoding remain poorly understood. We recently identified a novel firing pattern, termed the "super burst", which spontaneously emerges in the CA1 region of freely moving rats during emotionally salient experiences. These transient high-frequency firings across multiple neurons precede an increase in sharp-wave ripple activity, suggesting a role in encoding stress-related memories. To assess their functional significance, we developed a real-time detection and closed-loop intervention system. Allowing super bursts to occur led to significant increases in the amplitude and frequency of both excitatory (mEPSC) and inhibitory (mIPSC) synaptic currents in CA1 pyramidal neurons, indicating enhanced synaptic diversity by excitatory/inhibitory synapses. In contrast, selective suppression of super bursts attenuated these synaptic changes, suggesting a causal role in driving plasticity. Furthermore, entropy analysis revealed significantly higher information diversity in the amplitude and frequency domains in stressed animals compared to those deprived of super bursts. Behaviorally, the super burst-deprived group showed reduced freezing responses, indicating impaired memory formation. These findings support a novel hypothesis that super bursts induce bidirectional synaptic strengthening at both excitability and inhibitory synapses, expanding the dimensionality of synaptic diversity. This mechanism may play a critical role in enhancing the balance and precision of memory traces during encoding under emotionally charged conditions. These results offer potential therapeutic targets for stress-related neuropsychiatric disorders such as PTSD and depression.

Keywords : Hippocampus CA1, Super burst, Synaptic plasticity, Entropy, Memory encoding
Acknowledgements : This work was supported by the Kao Health Science Foundation (2024) and the Uehara Memorial Foundation (2025). We thank Dr. Ishikawa and Dr. Mitsushima for their guidance and critical feedback on electrophysiological protocols.

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 43

Supported By

Day 4 (August 27) **09:00-10:55** **Premier Ballroom A**

Astrocyte heterogeneity from neural networks to behaviors

Organizer : Ruotian Jiang (Sichuan University)
Wuhyun Koh (Institute for Basic Science)
Moderator : Ruotian Jiang (Sichuan University)
Kyungchul Noh (Ajou University)

1. A novel form of region-specific astrocyte morphological plasticity involved in instinct behaviors
   Ruotian Jiang (Sichuan University)
2. Divergent roles of prefrontal astrocytes in social dominance behavior and victory
   Kyungchul Noh (Ajou University)
3. Prefrontal cortex astrocytes modulate distinct neuronal populations to control anxiety-like behavior
   Xinzhu Yu (University of Illinois)
4. An astroglial basis of major depressive disorder: molecular, cellular, and circuit heterogeneity
   Xiong Cao (Southern Medical University)
5. Astrocytic phagocytosis during sleep controls systems consolidation
   Won-Suk Chung (Korea Advanced Institute of Science and Technology)

S43-1

A novel form of region-specific astrocyte morphological plasticity involved in instinct behaviors

Bin Zhou, Mengchan Su, Qingran Li, Ruotian Jiang

Department of Anesthesiology , West China Hospital of Sichuan University , Chengdu, China

Astrocytes in the mammalian brain exhibit intricate morphology, with their fine processes such as branchlets and leaflets constituting a significant portion of the cell volume and representing as contact points with neurons. The classical tripartite synapse theory emphasizes the astrocyte-synapse interactions through perisynaptic processes (PAPs), in which astrocytes ensheathe pre- and post- synaptic structure to maintain synaptic neurotransmitter and ion homeostasis. However, how astrocytes interact with neuron cell body remains largely unknown. Here, by using electron microscopy and high-resolution morphological reconstruction, we identified astrocytic lamellar structures enveloping neuronal somata, termed perisomatic astrocytic sheets (PASs), in the hypothalamus. We report the detailed 3D structure of the PASs, the molecular mechanism underlying its morphological dynamics, as well as its role in regulating instinct behaviors in mice.

Keywords : astrocytes, hypothalamus , instinct behaviors , synapses, morphology

S43-2

Divergent roles of prefrontal astrocytes in social dominance behavior and victory

Kyungchul Noh[1,2], Woo-Hyun Cho[1,3], Yoon-Jung Kim[2], Minkyu Hwang[4], Ja-Hyun Baik[5], Se-Young Choi[1], Sung Joong Lee[1]

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[2]Pharmacology, Ajou University School of Medicine, Suwon , Republic of Korea
[3]Institute for Neurological Therapeutics , Rutgers-Robert Wood Johnson Medical School, NJ, USA
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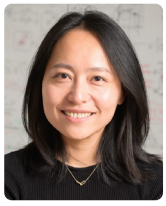
Winning can make you more likely to succeed in future competitions, thanks to something called the “winner effect”. This boost in confidence and dominance comes from memories of past victories. But how does the brain create and store these winning memories, and how do they shape social status? In this symposium, I will discuss a recent research highlighting the role of certain brain cells, called astrocytes, in the prefrontal cortex – a part of the brain important for decision-making and social behavior. By recording astrocyte activity during social competition, we found that these astrocytes are activated after a win, helping the brain lock in memories of success. This activation depends on a signal from another brain area called the ventral tegmental area, which sends a dopamine to reinforce the memory. Interestingly, enhancing astrocyte activity strengthened winning memories, while suppressing it made those memories weaker. These findings reveal how the brain’s chemistry supports the “winner effect” and helps establish social hierarchies.

Keywords : Astrocytes, Prefrontal cortex, Dopamine, Winner effect, Social hierarchy

S43-3

Prefrontal cortex astrocytes modulate distinct neuronal populations to control anxiety-like behavior



Eunyoung Kim[1,#], Hairuo Du[1,#], Yanqi Tan[2], Brandon L. Brown[3], Yaowen Chang[4], Blanca Díaz-Castro[5], Jonathan V. Sweedler[2], and Xinzhu Yu[1,6,7]

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[2]Department of Chemistry, Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign, Urbana, Illinois, USA
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[#]These authors contributed equally.

Accumulating evidence has supported diverse regulatory functions of astrocytes in different neural circuits as well as various aspects of complex behaviors. However, little is known about how astrocytes regulate different neuronal subpopulations that are linked to specific behavioral aspects within a single brain region. Here, we show that astrocytes in the medial prefrontal cortex (mPFC) encode anxiogenic environmental cues in freely behaving mice. Silencing mPFC astrocyte Ca^{2+} signaling heightens anxiety-like behavior and triggers opposing functional responses in excitatory and inhibitory neurons. Moreover, neuronal subpopulations tuned to anxiety-like behavior are differentially modulated by mPFC astrocytes at single cell and network levels. Using cell type-specific proximity biotinylation approaches, we identified significant intracellular and intercellular proteomic alterations in mPFC astrocytes and at the astrocyte-neuron interface associated with anxiety. Collectively, our findings uncover mechanisms underpinning the heterogenous astrocyte-neuron interaction that is behaviorally relevant and offer critical insights into the pathophysiology of emotional disorders.

Keywords : Prefrontal cortex, astrocytes, neurons, anxiety

S43-4

An astroglial basis of major depressive disorder: molecular, cellular, and circuit heterogeneity.

Xiong Cao

Key Laboratory of Mental Health of the Ministry of Education, Guangdong Province Key Laboratory of Psychiatric Disorders, Department of Neurobiology, School of Basic Medical Sciences, Southern Medical University, Guangzhou, 510515, China.

Major depressive disorder is a common psychiatric disorder and a leading cause of disability worldwide. Astrocytes play a role in the maintenance of the function of the central nervous system, both physiologically and pathologically. Accumulated evidence indicates that the astrocyte is an essential contributor to the pathophysiology of major depressive disorder, including blood-brain barrier integrity, gap junctions, gliotransmission, glutamate homeostasis, and energy metabolism. Here, we comprehensively summarize an astroglial basis for major depressive disorder based on molecular, cellular, and circuit properties, suggesting that astrocytes appear to be highly sensitive to stress and are likely to be uniquely positioned to stress responses.

Keywords : Astrocyte, Major depressive disorder, ATP, Neural circuit

S43-5

Astrocytic phagocytosis during sleep controls systems consolidation

Chi Hong Shin[1,2], Jeonghyun Park[1], Sungbin Kim[1,3] Jisu Lee[1,2], Eunjoon Kim[1,3], Jaekyung Kim[1], Won-Suk Chung[1,2]

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[2]Center for Vascular Research, Institute for Basic Science (IBS), Daejeon 34141, Republic of Korea
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Memories are initially stored in the hippocampal circuits and are subsequently transferred to the cortex for long-term storage, a process known as systems consolidation. A key aspect of systems consolidation is the delayed reorganization of memories within the cortex. After initial learning, synapse remodeling and potentiation in the cortex do not occur immediately, but rather emerge at later stages of systems consolidation. Despite recent advances in our understanding of this process, how such delayed memory transfer is achieved at the levels of circuits and synapses remains incompletely understood.
Previous studies have implicated sleep as a crucial player in systems consolidation, as newly encoded memory traces in the hippocampus are repeatedly reactivated during sleep, thereby reorganizing the connectivity of cortical memory-storing neurons, or engram cells. For example, the reactivation of hippocampal neurons during slow wave sleep (SWS) as well as rapid eye movement (REM) sleep results in potentiation as well as elimination of cortical synapses after learning. These findings highlight the important role of sleep in regulating interregional connectivity during systems consolidation. However, how sleep precisely controls cortical synapse remodeling and how this process contributes to memory transfer, remain elusive.
Glial cells are central players in driving synapse remodeling and plasticity. Among their diverse functions, we have previously shown that astrocytes refine neural circuits and maintain synapse homeostasis by selectively eliminating redundant synapses through phagocytosis. Notably, astrocytes phagocytose synapses in a neural activity-dependent manner, offering a plausible mechanism for synapse remodeling during systems consolidation, a hypothesis that we sought to investigate in this study. Thus, in this talk, I will discuss our recent findings on the mechanisms and physiological importance of astrocyte-mediated circuit remodeling during sleep-dependent systems consolidations.

Keywords : Sleep, Systems Consolidation, Astrocyte, Phagocytosis, Synapse Elimination

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 44

Supported By

Day 4 (August 27) **09:00-10:55** **Premier Ballroom B**

Audiovisual processing in rodents and marmosets

Organizer : Seung-Hee Lee (Korea Advanced Institute of Science and Technology)
Soo Hyun Park (Korea Advanced Institute of Science and Technology)
Moderator : Seung-Hee Lee (Korea Advanced Institute of Science and Technology)
Soo Hyun Park (Korea Advanced Institute of Science and Technology)

1. Orthogonalization of spontaneous and stimulus-driven activity by hierarchical neocortical areal network in primates
   Kenichi Ohki (The University of Tokyo)
2. Synaptic molecules tune neuronal feature selectivity: novel in vivo imaging techniques and gene therapy development
   Ingie Hong (Johns Hopkins University)
3. Dynamic visual processing in marmoset extrastriate cortex
   Soo Hyun Park (Korea Advanced Institute of Science and Technology)
4. Dendritic and circuit computation for flexible decision-making
   Ninglong Xu (Chinese Academy of Sciences)
5. Balancing flexibility and stability during auditory reversal learning
   Seung-Hee Lee (Korea Advanced Institute of Science and Technology)

S44-1

Orthogonalization of spontaneous and stimulus-driven activity by hierarchical neocortical areal network in primates.

Kenichi Ohki[1, 2, 3]

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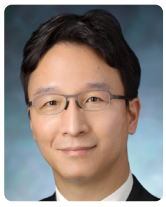
[2]International Research Center for Neurointelligence (WPI-IRCN), The University of Tokyo, Tokyo, Japan
[3]Institute for AI and Beyond, The University of Tokyo, Tokyo, Japan

How biological neural networks reliably process information in the presence of spontaneous activity remains controversial. In mouse primary visual cortex (V1), stimulus-evoked and spontaneous activity show orthogonal (dissimilar) patterns, which is advantageous for separating sensory signals from internal noise. However, studies in carnivore and primate V1, which have functional columns, have reported high similarity between stimulus-evoked and spontaneous activity. Thus, the mechanism of signal-noise separation in the columnar visual cortex may be different from that in rodents. To address this issue, we compared spontaneous and stimulus-evoked activity in marmoset V1 and higher visual areas. In marmoset V1, spontaneous and stimulus-evoked activity showed similar patterns as expected. However, in marmoset higher visual areas, spontaneous and stimulus-evoked activity were progressively orthogonalized along the cortical hierarchy, eventually reaching levels comparable to those in mouse V1. These results suggest that orthogonalization of spontaneous and stimulus-evoked activity is a general principle of cortical computation.

Keywords : Visual cortex, Primate, Marmoset, Mouse, Spontaneous activity

S44-2

Synaptic molecules tune neuronal feature selectivity: novel in vivo imaging techniques and gene therapy development



Ingie Hong

Department of Neurology, Johns Hopkins University, Baltimore, MD, USA

Our brains use ion channel receptors and diverse neuronal cell types to orchestrate neuronal information processing, the basis for intelligent behavior. While neuronal molecules like receptors and kinases have been well-characterized in reduced systems, the impact of these molecules on sensory responses and *in vivo* computation is largely unexplored. In this seminar, I will introduce my work developing in vivo two-photon imaging techniques and novel kinase biosensors, which have provided unprecedented insights into the dynamics of cortical information processing. These approaches allow us to dissect how molecular components of neurons influence network activity and behavior. Our visual cortex uses molecules in synapses to learn and recognize the objects around us. We demonstrate that parvalbumin-positive (PV) interneurons, unlike excitatory neurons, express calcium-permeable AMPA receptors (CP-AMPARs) due to low *GRIA2* expression. This mammalian-conserved transcriptional suppression of *GRIA2* leads to reduced orientation selectivity of PV interneurons in the visual cortex. Replacing CP-AMPARs with calcium-impermeable AMPARs increased their orientation selectivity. Similar effects were observed in spatial selectivity of PV neurons in the hippocampus, our brain's navigational system, highlighting CP-AMPARs' general role in sensory processing across modalities. Global knockout of *Gria2* led to abundant CP-AMPARs in excitatory neurons and a loss of selectivity, potentially explaining why *GRIA2* mutations in humans lead to profound intellectual disability. These findings reveal that CP-AMPARs maintain the low feature selectivity of PV interneurons and demonstrate the power of connecting critical neuronal molecules to their role in shaping the key axes of brain activity. Understanding these mechanisms may unravel the molecular logic of our intelligence and open a new field of neurocomputational therapeutics.

Keywords : two photon microscopy, GABAergic neurons, visual processing, intellectual disability, synaptic plasticity
Acknowledgements : I would like to thank Juhyun Kim, Thomas Hainmueller, Thomas Kim, Yoichi Araki, and Richard Huganir for their excellent contributions. This work was supported by R37NS036715 (R.L.H.), R01NS085121 (S.B.), KBRI Basic Research Program (24-BR-02-02 to J.Ki.), CRC-TRR 384/1 2024-514483642 (M.B. and H.S.), and U01DA056556 (I.H. and R.L.H.).

S44-3

Dynamic visual processing in marmoset extrastriate cortex

Soo Hyun Park

Brain and Cognitive Sciences, KAIST, Daejeon, Republic of Korea

Previous single-unit studies in the macaque inferotemporal cortex during video watching have revealed that neighboring neurons exhibit dissimilar video-driven responses that covary with a distinct set of areas across the entire brain. These findings raise the question of how the localized regions of the visual cortex are organized, especially under more naturalistic conditions such as free viewing of dynamic videos. We addressed this question in the marmoset extrastriate visual cortex. We used an endoscopic PRISM probe to monitor the activity and spatial arrangement of a local population of visual neurons. To make the workflow more efficient, we developed a new lens implant that combines an endoscopic PRISM probe with an injection cannula yoked to a lens (“lennula”). The new implant enables a targeted delivery of a genetically encoded calcium indicator directly into the imaging field. We carried out daily recordings in two awake, behaving marmoset monkeys and monitored the activity and spatial arrangement of a local population of visual neurons. During each recording session, we imaged neuronal activity from 60 to 130 neurons within the field of view, which was approximately 800 micrometers in each dimension. From each neuron, we measured calcium responses during both active viewings of videos and periods of quiescent rest. In both animals, we observed that individual neurons exhibited similar response time courses to the repeated presentation of the same videos. The head-mounted miniscope, in combination with the lennula implant, provides a straightforward method for examining the spatial organization of functional networks over mesoscopic scales in marmosets.

Keywords : Vision, Dynamic, Imaging, Natural, Monkey
Acknowledgements : This work was supported by the Korea Advanced Institute of Science and Technology(KAIST) grant (No. G04230052) and the National Research Foundation of Korea(NRF) grant (RS-2024-00406240) funded by the Korea government (MSIT), and supported by the POSCO Science Fellowship of POSCO TJ Park Foundation.

S44-4

Dendritic and circuit computation for flexible decision-making

Ning-long Xu

Institute of Neuroscience, CEBSIT, Chinese Academy of Sciences, Shanghai, China

Decision-making and problem-solving require the ability to flexibly select actions based on rules and contexts in response to sensory inputs. Despite extensive psychological and theoretical studies, the neuronal and circuit mechanisms enabling this cognitive flexibility remains poorly understood. We have been tackling this challenge by leveraging quantitative cognitive tasks in head-fixed mice combined with modern neural circuit interrogation tools. In this talk, I will present our recent advances revealing how cortical circuits and single neurons enable rule-dependent flexible decision-making. We demonstrate that specific cross-region cortical circuits mediate rule inference, while dendritic computations in individual cortical neurons dynamically transform sensory inputs into motor outputs in a rule-dependent manner. These findings provide new mechanistic insights to the biological basis of intelligence and cognitive flexibility.

Keywords : Decision-making, Dendritic computation, Circuit computation, Flexibiliby

S44-5

Balancing flexibility and stability during auditory reversal learning

Seung-Hee Lee[1,2]

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[2]Center for Synaptic Brain Dysfunctions, Institute for Basic Science , Daejeon, Republic of Korea

The ability to flexibly modify behavior in response to changing environmental contingencies is fundamental to adaptive decision-making. However, how distributed brain circuits coordinate such rapid adaptation remains unclear. Here, we show that the posterior parietal cortex (PPC) facilitates auditory reversal learning via parallel projections to the auditory cortex (AC) and inferior colliculus (IC). Inactivation of the AC selectively impaired auditory reversal learning, while IC inactivation disrupted stable auditory discrimination. Dual retrograde tracing revealed anatomically segregated PPC neurons projecting to AC (PPC_{AC}) and IC (PPC_{IC}). Projection-specific calcium imaging revealed PPC_{AC} neurons flexibly encode stimulus-outcome contingencies, whereas PPC_{IC} neurons maintain stable representations of response outcomes. Optogenetic inactivation demonstrated distinct functional roles: silencing PPC_{AC} selectively impaired contingency updating, while silencing PPC_{IC} disrupted stable response execution after rule reversal. Thus, parallel PPC projections differentially coordinate flexible rule updating and stable motor execution, balancing flexibility and stability to support cognitive flexibility.

Keywords : auditory reversal learning, posterior parietal cortex, auditory cortex, inferior colliculus, cognitive flexibility
Acknowledgements : This work has been supported by grants to S.H.L. from the Institute for Basic Science (IBS-R002-A2).

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 45

Day 4 (August 27) **09:00-10:55** **Premier Ballroom C**

Brain cell atlas and technology

Organizer : Shiping Liu (BGI-Research)
Ying Lei (BGI-Research)
Moderator : Linqing Feng (Zhejiang Lab)

1. eLemur: A cellular-resolution 3D atlas of the mouse lemur brain
   Jinhyun Kim (Korea Institute of Science and Technology)
2. The human protein atlas, a neuroscience resource
   Jan Mulder (Karolinska Institute)
3. Cerebral cortex connectomics
   Moritz Helmstaedter (Max Planck Institute)
4. From connectome to functional study for somatorsensory-system
   Yangang Sun (Chinese Academy of Sciences)
5. Decoding the Macaque Claustrum: Single-Cell Transcriptomics Meets Whole-Brain Connectivity
   Ying Lei (BGI-Research)

S45-1

eLemur: A cellular-resolution 3D atlas of the mouse lemur brain

Jinhyun Kim

Brain Science in Stitute, Korea Institute of Science and Technology, Seoul, Republic of Korea

The gray mouse lemur (Microcebus murinus), one of the smallest living primates, emergesas a promising model organism for neuroscience research. This is due to its genetic similar-ity to humans, its evolutionary position between rodents and humans, and its primate-likefeatures encapsulated within a rodent-sized brain. Despite its potential, the absence ofa comprehensive reference brain atlas impedes the progress of research endeavors in thisspecies, particularly at the microscopic level. Existing references have largely been con-fined to the macroscopic scale, lacking detailed anatomical information. Here, we pres-ent eLemur, a unique resource, comprising a repository of high-resolution brain-wideimages immunostained with multiple cell type and structural markers, elucidating thecyto- and chemoarchitecture of the mouse lemur brain. Additionally, it encompasses asegmented two-dimensional reference and 3D anatomical brain atlas delineated intocortical, subcortical, and other vital regions. Furthermore, eLemur includes a com-prehensive 3D cell atlas, providing densities and spatial distributions of non-neuronaland neuronal cells across the mouse lemur brain. Accessible via a web-based viewer(https://eeum-brain.com/#/lemurdatasets), the eLemur resource streamlines data shar-ing and integration, fostering the exploration of different hypotheses and experimentaldesigns using the mouse lemur as a model organism. Moreover, in conjunction with thegrowing 3D datasets for rodents, nonhuman primates, and humans, our eLemur 3D dig-ital framework enhances the potential for comparative analysis and translation research, facilitating the integration of extensive rodent study data into human studies.

Keywords : Mouse Lemur, Primate, Brain Atlas, 3D cell atlas, web-based database

S45-2

The Human Protein Atlas (HPA) a neuroscience resource.

Jan Mulder

Department of Neuroscience, Karolinska Institute, Stockholm, Sweden

The Human Protein Atlas (HPA) project (http://www.proteinatlas.org) is initiated in 2003, two years after the completion of the human genome projects. The mission of the HPA is to create a public accessible online resource that provides detailed information on the expression and distribution of all proteins in all major organs and tissues in health and disease. The brain section of HPA provides information on regional distribution of protein expression across 200 micro-dissected regions of the healthy human brain. Recently added high resolution spatial transcriptomics data provides a detailed overview of protein expression in the main cell types in selected brain regions including cerebral cortex and cerebellum. Applying high resolution spatial mapping technologies (Stereo_seq) on brain samples from frontotemporal dementia patients with a progranulin mutation (FTD-GRN) revealed several molecular changes in astrocytes that could be confirmed with antibody-based approaches. The main challenges in the field of high-resolution spatial transcriptomics is cell-segmentation. Especially the identification and characterization of small non-neuronal cells with complex morphologies that express low number of transcripts (compared to neurons) is challenging. A method based on single-cell-co-expression provides way to group and allocate single spots to cell types and reveal the cellular and molecular organization of the brain in health and diseases.

Keywords : Human brain, Spatial transcriptomics, Cerebellum, Neurodegenerative disorders, Bioinformatics
Acknowledgements : The Human Protein Atlas project is funded by the Knut and Alice Wallenberg foundation. Additional funding from the Swedish research council (VR 2023-02656) , Alzheimerfonden, Hjärnfonden, Alzheimer Nederland and StratNeuro have been used for the presented work.

S45-3

Cerebral Cortex Connectomics

Moritz Helmstaedter

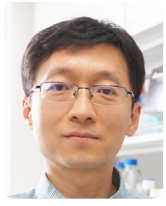
Connectomics, Max Planck Institute for Brain Research, Frankfurt Am Main, Germany, Germany

The mapping of neuronal connectivity is one of the main challenges in neuroscience. Only with the knowledge of wiring diagrams is it possible to understand the computational capacities of neuronal networks, both in the sensory periphery, and especially in the mammalian cerebral cortex. Our methods for dense circuit mapping are based on 3-dimensional electron microscopy (EM) imaging of tissue, which allows imaging nerve tissue at nanometer-scale resolution across substantial volumes, extending to more than one millimeter on the side, followed by AI-based image analysis to obtain dense connectivity maps, or connectomes. With these we have mapped local circuitry in mouse and human cortex, determining learning-related synaptic traces, inhibitory axonal development, and discovering an expanded interneuron-to-interneuron network in the human cortex. Most recently we completed the connectomic reconstruction of a cortical column. We are currently screening cortical connectomes across age, disease states and experience to obtain a deeper understanding of their relevance for individual behavioral performance and brain pathology.

Keywords : Connectomics, Neuronal Connectivity, Relation between artificial and biological intelligence

S45-4

From connectome to functional study for somatosensory system



YanGang Sun

Institute of Neuroscience, Center for Excellence in Brain Science and Intelligence Technology, Chinese Academy of Sciences, Shanghai, China

Somatosensory information includes multiple modalities, and the neural circuit mechanism of these multimodal sensory information processing is an important issue in the field of neuroscience. Spinal projection neurons are core nodes in somatosensory information processing. Our research revealed the neural circuit mechanism by which pain and itch sensations ascend to the brain through spinal cord projection neurons. We further used single-cell sequencing, single-cell morphology reconstruction and other technologies to analyze the structural basis of somatosensory information processing.

Keywords : Connectome, Cell atlas, Pain, Somatosensation, spinal cord

S45-5

Decoding the Macaque Claustrum: Single-Cell Transcriptomics Meets Whole-Brain Connectivity

Ying Lei[3,5], Yuxuan Liu[4,9], Mingli Wang[1,6], Nini Yuan[1], Yujie hou[2], Lingjun Ding[3,5], Zhiyong Zhu[3,5], Zihan Wu[7], Chao Li[1], Jianhua Yao[7], Longqi Liu[3,5], Wu Wei[4,6], Henry Kennedy[2], Zhiming Shen[1,8]

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Claustrum orchestrates brain functions via its connections with numerous brain regions, but its molecular and cellular organization remains unresolved. Single-nucleus RNA sequencing of 227,750 macaque claustral cells identified 48 transcriptome-defined cell types, with most glutamatergic neurons similar to deep-layer insular neurons.Comparison of macaque,marmoset,and mouse transcriptomes revealed macaque-specific cell types. Retrograde tracer injections at 67 cortical and 7 subcortical regions defined four distinct distribution zones of retrogradely labeled claustral neurons. Joint analysis of whole-brain connectivity and single-cell spatial transcriptome showed that these four zones containing distinct compositions of glutamatergic (but not GABAergic) cell types preferentially connected to specific brain regions with a strong ipsilateral bias. Several macaque-specific glutamatergic cell types in ventral vs. dorsal claustral zones selectively co-projected to two functionally related areas—entorhinal cortex and hippocampus vs. motor cortex and putamen, respectively. These data provide the basis for elucidating the neuronal organization underlying diverse claustral functions.

Keywords : claustrum, non-human primates, insula, spatial transcriptome, connectome

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 46

Day 4 (August 27) **09:00-10:55** **Rm.116-118**

Emerging mechanisms in white matter injury: autoimmunity, vascular dysfunction, and lipid metabolism

Organizer : Sun Ah Park (Ajou University)
Moderator : Sun Ah Park (Ajou University)

1. Single-cell immune profiling reveals distinct CSF and blood signatures distinguishing MOGAD from MS and NMOSD in treatment-naïve patients
   Charlotte Ng (Korea Institute of Science and Technology) Scitech Korea AWARDEE
2. CNS Autoimmune (Diseases involving White Matter
   Young Nam Kwon (Yonsei University)
3. Hereditary Vascular Dysfunctions Resulting in White Matter Ischemic Disorders
   Jay Chol Choi (Jeju National University)
4. Survival signaling pathways of oligodendrocyte lineage cells in ischemic white matter injury.
   Jun Young Choi (Ajou University)
5. Cell-Autonomous Lipid Metabolism Defects in PS1-Mutant Astrocytes Exacerbate Alzheimer's Pathology
   Zeng Li (Duke-NUS Medical School)

S46-1 Scitech Korea AWARDEE

Single-cell immune profiling reveals distinct CSF and blood signatures distinguishing MOGAD from MS and NMOSD in treatment-naïve patients

Charlotte Ng[1,2], Takahisa Mikami[3], Rodrigo Castaneda[1], Narae Park[1], KwanHee Lee[1,2], Joo Hong Min[4], ByeongJun Kim[4], ChulJoo Lee[1], Michael Levy[3], JinWoo Park[6], Rafael TaeHo Han[1,8]

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Autoimmune demyelinating diseases, specifically multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), are neuroinflammatory disorders involving immune-mediated attacks on the central nervous system that present with similar clinical features but are driven by distinct immune mechanisms. Current diagnostic markers, including MRI-detected lesions and autoantibody titers, inadequately assess therapeutic responses or disease progression, highlighting the need for biomarkers reflecting disease-specific immune activity. To address this gap, we leveraged single-cell RNA sequencing and TCR/BCR repertoire analysis of cerebrospinal fluid (CSF) and blood from treatment-naive patients. MOGAD exhibits a distinct immune profile, with peripheral enrichment of cytotoxic CD8+ T cells (GZMB, GZMK) and reduced CD8+ central memory T cells in the CSF. The CSF in MOGAD is moderately enriched for Th17-like CD4+ T cells (IL6ST, IL6R), including activated HLA-DR+ CD4+ T cells. The TCR repertoire in MOGAD is highly diverse with low clonality, suggesting broad, polyclonal T cell activation rather than antigen-driven responses. In contrast, MS and NMOSD display convergent immune features, including CSF enrichment of CXCR3+ Th1-like CD4+ T cells and marked depletion of effector CD8+ TEM and TEMRA cells in the CSF. Both diseases show reduced TCR diversity and highly expanded T cell clones, consistent with antigen-driven immune activity. NMOSD is distinguished from MS by mild CSF enrichment of CD8+ central memory T cells. Across all three diseases, CSF enrichment of Tregs is consistently observed, indicating a shared compensatory immunosuppressive response. These findings highlight MOGAD's unique immunological identity and advance disease-specific therapeutic approaches to improve clinical outcomes in neuroinflammatory demyelination diseases.

Keywords : Single-cell rna sequencing, Multiple sclerosis, Neuromyelitis optica spectrum disorder, Myelin oligodendrocyte glycoprotein antibody-associated disease, TCR/BCR repertoire
Acknowledgements : This work was supported by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (RS-2024-00346245, RS-2023-KH139821, RS-2023-00209436).

S46-2

CNS Autoimmune Diseases involving White Matter

Young Nam Kwon

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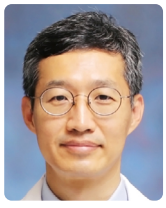
Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) is an autoimmune inflammatory demyelinating disorder of the central nervous system (CNS), mediated by immunoglobulin G antibodies targeting the MOG protein expressed on the surface of oligodendrocytes. MOGAD has emerged as a distinct disease entity, separate from multiple sclerosis (MS) and aquaporin-4 (AQP4) antibody-positive neuromyelitis optica spectrum disorder (NMOSD), owing to its unique clinical, radiologic, and immunologic characteristics. The gold standard for diagnosis is a cell-based assay (CBA) employing full-length human MOG as the antigen, which has been shown to provide greater sensitivity and specificity compared to short-length MOG constructs. The use of IgG1-specific secondary antibodies further enhances diagnostic accuracy. Detection of MOG-IgG in both serum and cerebrospinal fluid (CSF) highlights the relevance of intrathecal immune responses in certain patients. Clinically, MOGAD presents with a spectrum of phenotypes, including optic neuritis, transverse myelitis, and acute disseminated encephalomyelitis (ADEM). Approximately 40–60% of adult patients exhibit a relapsing disease course. Persistent MOG-IgG positivity is associated with increased relapse risk, while seronegative conversion may indicate a more favorable prognosis. Management includes high-dose corticosteroids and immunomodulatory therapies during the acute phase, followed by maintenance immunotherapy in high-risk individuals. Ongoing research into MOG isoforms and differential antibody reactivity aims to inform individualized treatment strategies. This presentation provides an updated overview of the pathophysiology, diagnostic approaches, clinical manifestations, and immunotherapy strategies for MOGAD, integrating recent international and Korean data.

Keywords : MOGAD, CNS, autoimmune disease, myelin oligodendrocyte glycoprotein, autoantibody

S46-3

Hereditary Vascular Dysfunctions Resulting in White Matter Ischemic Disorders



Jay Chol Choi

Department of Neurology, Jeju National University College of Medicine, Jeju, Republic of Korea

Hereditary vascular dysfunctions affecting the brain's small vessels represent a distinct and clinically important subset of cerebrovascular diseases. Among them, disorders leading to white matter ischemia are notable for their early onset, progressive course, and genetic origin. Unlike sporadic small vessel diseases driven by aging and vascular risk factors, hereditary forms often affect younger individuals and offer valuable insights into the mechanisms of cerebral microangiopathy. A key example is CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy), the most common monogenic small vessel disease, caused by mutations in the NOTCH3 gene. Clinically, CADASIL presents with recurrent strokes, migraine with aura, psychiatric symptoms, and cognitive decline. Despite its genetic basis, the disease shows marked phenotypic variability, even within families, complicating diagnosis and clinical management. Recent studies suggest NOTCH3 variants may be more prevalent in Asian populations than previously recognized, pointing to potential ethnic susceptibility or underdiagnosis. MRI features—particularly anterior temporal lobe and external capsule involvement—are highly specific and aid in distinguishing CADASIL from sporadic forms. The presence of granular osmiophilic material in vessel walls remains a pathologic hallmark. This talk will explore CADASIL as a model for understanding hereditary small vessel disease, emphasizing the need for integrated clinical, imaging, and genomic approaches to improve diagnosis and care across diverse populations.

Keywords : Small vessel disease, CADASIL, NOTCH3, Cerebral ischemia

S46-4

Survival signaling pathways of oligodendrocyte lineage cells in ischemic white matter injury.

Jun Young Choi

Brain Science and Neurology, Ajou University School of Medicine, Suwon, Gyeonggi-do, Republic of Korea

Brain white matter is vulnerable to ischemic insult due to its anatomical and cellular features, particularly involving oligodendrocytes. About 50% of individuals over 60 have ischemic white matter injury (IWMI), compared to 10% with Alzheimer's. Ischemic white matter injury has a range of clinical manifestations, from normal appearances to severe vascular dementia or Parkinsonism. Despite its importance, basic research is lacking in identifying therapeutic targets for IWMI. Given the pathomechanism and neuropathologic findings of IWMI, oligodendrocyte lineage cells represent important cellular targets, from reducing ischemic-induced oligodendrocyte death to promoting remyelination processes. Here, I'd like to talk about the role of Toll-like receptor 2 (TLR2) in ischemic oligodendrocyte death and IWMI. Oligodendrocytes express TLR2. The deletion of TLR2 in oligodendrocytes has demonstrated an aggravation of ischemic oligodendrocyte death in both in vitro and in vivo focal IWMI models. A synthetic TLR2 agonist has shown potential in rescuing ischemic oligodendrocyte death in vitro and reducing focal IWMI size in vivo. One of the endogenous ligands that activates TLR2 in oligodendrocytes is high-mobility group box 1 (HMGB1), which is released from dying oligodendrocytes. Inhibition of autocrine HMGB1-TLR2 signaling could worsen ischemic oligodendrocyte death and focal IWMI. Additionally, the HMGB1-TLR2 axis may facilitate the migration of oligodendrocyte precursor cells into the lesion, representing the initial step for remyelination processes. However, additional exogenous HMGB1 did not lead to a reduction in focal IWMI size in vivo. These data indicate that TLR2 is a necessary and sufficient factor for protecting oligodendrocytes and focal IWMI from ischemic insult, whereas HMGB1 is a necessary but insufficient factor for focal IWMI. Further exploration of TLR2 signaling pathways in oligodendrocytes could unveil new therapeutic targets for IWMI.

Keywords : Oligodendrocyte, White matter, Stroke, Toll-like receptor 2
Acknowledgements : This work was supported by NRF grants (RS-2019-NR-040055 and RS-2024-00335969) and a grant from KHIDI (RS-2021-KH113820)

S46-5

Cell-Autonomous Lipid Metabolism Defects in PS1-Mutant Astrocytes Exacerbate Alzheimer's Pathology

Lifeng Qiu[1, 2#], Qiaoyang Sun[3#], Pei-Yen Lim[4], Jolene Wei Ling Lee[1,6], Wei Zhou[3], Brijesh Kumar Singh[5], Jayne Tan[12], Pin Li[2], Shuo-Chien Ling[6,14], Su-Chun Zhang[6,13], Adeline S.L. Ng[6,7], Eng-King Tan[3,6,7], Amaury Cazenave-gassiot[4,2,9,10,11], & Zeng Li[1,6, 8,*]

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Alzheimer's disease (AD) is a complex neurodegenerative disorder characterized by progressive cognitive decline. While neuronal dysfunction is central to AD pathogenesis, growing evidence implicates astrocytes as key contributors to disease progression. However, the cell-autonomous mechanisms driving astrocyte dysfunction in AD, particularly in the context of *Presenilin 1 (PS1)* mutations, remain poorly understood. Here, we generated cerebral organoids (COs) from an AD patient-derived induced pluripotent stem cell (iPSC) line harboring the *PS1* mutation (MT) and its isogenic CRISPR-corrected control (Ctrl). Astrocytes were isolated and analyzed using single-cell RNA sequencing (scRNA-seq), bulk RNA-seq, and lipidomic profiling. Functional assays assessed lipid accumulation, mitochondrial respiration, cytokine secretion, and Aβ42 uptake. Astrocyte-neuron co-cultures were used to evaluate their impact on Aβ pathology. Transcriptomic and lipidomic analyses revealed that PS1 MT astrocytes exhibit disrupted lipid metabolism, with significant accumulation of cholesterol esters (CEs) and triacylglycerols (TAGs). Functional characterization demonstrated that mutant astrocytes display increased lipid storage, elevated mitochondrial respiration, altered cytokine release, and impaired Aβ42 clearance. Furthermore, co-culture with PS1 MT astrocytes exacerbated amyloid-beta accumulation in neurons. Our study uncovers a PS1 mutation-driven astrocyte dysfunction linked to lipid dysregulation, mitochondrial abnormality, and defective Aβ clearance, providing mechanistic insights into how astrocytes contribute to AD progression.

Keywords : Alzheimer's disease, astrocytes, PS1, scRNA-seq, lipidomic

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 47

Day 4 (August 27) **12:30-14:25** **Premier Ballroom A**

Recent insights into molecular orchestration of synaptic transmission and neural circuit modulation

Organizer : Yukiko Goda (Okinawa Institute of Science and Technology)
Huang Ma (Zhejiang University)
Moderator : Yukiko Goda (Okinawa Institute of Science and Technology)
Huang Ma (Zhejiang University)

1. Cognitive aging and its sex-specific regulation: mechanisms and insights
   Huan Ma (Zhejiang University)
2. Cortico-hippocampal CA1 direct circuits for learning and memory
   Xiaohui Zhang (Beijing Normal University)
3. An actin-regulatory pathway governing the maintenance of presynaptic homeostatic plasticity
   Seungbok Lee (Seoul National University)
4. Presynaptic metabolism of phosphoinositides
   Shigeo Takamori (Doshisha University)
5. Unique dynamics and distinguishable subsets of spontaneously recycled inhibitory synaptic vesicles
   Chungwon Park (The Hong Kong University of Science and Technology) IBRO AWARDEE
6. Synapse-astrocyte interactions in fine-tuning of synaptic strengths
   Yukiko Goda (Okinawa Institute of Science and Technology)

S47-1

Cognitive aging and its sex-specific regulation: mechanisms and insights

Jing Qu, Huan Ma

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Deciphering the complex interplay between neuronal activity and mitochondrial function is pivotal in understanding brain aging, a multifaceted process marked by declines in synaptic function and mitochondrial performance. Here, we unveiled a novel age-related coupling between neuronal excitation and mitochondrial DNA transcription (E-TC_{mito}), which operates distinctively compared to classic excitation-transcription coupling in the nucleus (E-TC_{nuc}). Utilizing custom-engineered biosensors specifically designed for monitoring mitochondrial transcriptional activity, we demonstrated that E-TC_{mito} repurposes molecules traditionally associated with E-TC_{nuc} to modulate mitochondrial DNA expression, closely aligning with synaptic activation sites. This activity-driven modulation, which diminishes during natural aging, dynamically governs mitochondrial mass and quality, thereby sustaining synaptic resilience to neuronal activity challenges. Crucially, loss of E-TC_{mito} led to notable aging-related functional impairments, including decreased neuronal energy reserves and disrupted memory. However, enhancing E-TC_{mito} in aged mouse brains significantly revitalized these functions while concurrently reducing cellular senescence, suggesting a promising strategy to combat brain aging. Moreover, we identify accelerated mitochondrial dysfunction and cellular senescence as a female-predominant process in the human brain during midlife. These findings establish a novel sex-specific framework for understanding cognitive aging and highlight a potential therapeutic strategy to preemptively target female-pronounced aging, thereby preventing severe age-related deterioration later in life.

Keywords : Aging, synaptic Plasticity, mitochondria, cellular senescence, memory

S47-2

Cortico-hippocampal CA1 direct circuits for learning and memory

Xiaohui Zhang

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The hippocampus (HP) and parahippocampal regions (PHR) from complex connection networks for learning and memory. The PHR is composed of the peri-, post- and ento-rhinal cortices (PER, POR, EC) as well as the pre- and para-subiculum. In the PHR-HP network, besides the generally-known “PER/POR-EC-HP (dentate gyrus) ” major pathway, recent evidence has also supported existence of direct connections from the PER or EC to the HP-CA1 and their important roles in regulating functions of learning and memory. In my lecture, I would present our two findings on the PHR-HP CA1 direct circuits in the mouse study. First, we have revealed that medial and lateral parts of EC form distinct direct circuits with dorsal HP CA1 (dCA1) principal cells and then differentially regulate associative learning function and transfer spatial and non-spatial inputs to dCA1. Second, PER neurons send their direct projections to dCA1 as well, but preferentially form their synaptic connections selectively on a specific group of dCA1 inhibitory neurons (INs). This novel PER-dCA1 INs direct pathway participates in the regulation of memory retrieval and generalization in recognition of object or context.

Keywords : Cortico-hippocampal CA1 circuit, Entorhinal cortex, Perirhinal cortex, associative learning, recognition memory
Acknowledgements : This work is supported by the grants from the STI2030-Major Project 2022ZD0204900 and the the National Natural Science Foundation of China (32071025).

S47-3

An actin-regulatory pathway governing the maintenance of presynaptic homeostatic plasticity

Eunsang Cho, Hyun Gwan Park, Seunghwan Song, Seungbok Lee

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Presynaptic homeostatic plasticity (PHP) is a highly conserved mechanism that stabilizes synaptic transmission within the physiological range in response to perturbations of neural. At the larval neuromuscular junction (NMJ) of *Drosophila melanogaster*, inhibition of glutamatergic neurotransmitter receptors triggers a retrograde enhancement of presynaptic release to restore normal postsynaptic responses. This process consists of two temporally distinct phases, a rapid induction phase and a long-term maintenance phase. The maintenance phase is initiated by ELKS/Bruchpilot (Brp)-driven active zone (AZ) remodeling during the induction phase; however, the underlying mechanisms remain poorly understood. Here, we present evidence that retrograde Ephrin-Eph signaling is specifically required for the maintenance, but not the induction, of PHP. We further demonstrate that two Cdc42-specific guanine nucleotide exchange factors, RhoGEF3 and Ephexin, act downstream of the Eph receptor. Finally, we show that RhoGEF3- and Ephexin-mediated signaling converge on Cdc42 to regulate the induction and maintenance of AZ remodeling through actin polymerization. Together, our results identify Eph-dependent Cdc42 signaling as a key regulator of Brp-driven AZ remodeling and highlight the critical role of actin cytoskeleton dynamics in sustaining PHP.

Keywords : Presynaptic homeostatic plasticity; RhoGEF3/Cdc42 signaling; Actin regulation; Brp; Active zone remodeling

S47-4

Presynaptic metabolism of phosphoinositides

Shigeo Takamori

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Efficient synaptic vesicle (SV) recycling is essential for sustaining synaptic transmission. While the multiple roles of phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) in SV recycling are well documented, presynaptic regulation of phosphatidylinositol 4-phosphate (PI(4)P) synthesis and its potential role in SV recycling remain poorly understood. Recently, we identify phosphatidylinositol 4-kinase IIIα (PI4KIIIα) as the key enzyme responsible for both the maintenance and activity-dependent production of presynaptic PI(4)P. Notably, unlike previously believed, we find that SVs are nearly devoid of PI(4)P but are rich in phosphatidylinositol (PI) and that PI(4)P synthesis is triggered upon SV fusion as vesicular PI is delivered to the plasma membrane. Furthermore, under condition where PI(4)P levels are selectively reduced without affecting basal PI(4,5)P2 levels, SV exo-endocytosis is significantly impaired, primarily due to reduced conductivity of voltage-gated Ca2+ channels. This reveals a PI(4,5)P2-independent homeostatic mechanism in which continuous PI(4)P production, driven by SV fusion, sustains efficient synaptic transmission.

Keywords : Synaptic transmission, PI(4)P, Calcium channel, SV recycling
Acknowledgements : This study was supported by JSPS Core-to-Core Program A (JPJSCCA20220007), JSPS KAKENHI (24K02126), reserach grants from the Takeda Foundation and the Naito Foundation to ST.

S47-5 IBRO AWARDEE

Unique dynamics and distinguishable subsets of spontaneously recycled inhibitory synaptic vesicles

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Spontaneous synaptic transmission operates in an activity-independent manner, distinguished from activity-evoked synaptic transmission. Previous researches primarily using glutamatergic excitatory synapses revealed peculiar features of spontaneous synaptic transmission, such as a distinct set of vesicle fusion machinery proteins and spatially segregated release sites. However, the dynamic properties of spontaneous synaptic vesicles activity-independently releasing neurotransmitters remain poorly understood, especially in inhibitory synapses. In the study, we investigate the dynamics and exocytosis of spontaneously recycled GABAergic synaptic vesicles in rat primary hippocampal neuron cultures via a three-dimensional real-time tracking of a single GABAergic synaptic vesicle spontaneously labeled with a quantum dot-conjugated anti-vesicular GABA transporter antibody in the presence of tetrodotoxin. Our results demonstrate that the dynamics of spontaneously recycled GABAergic synaptic vesicles differ from those of the vesicles recycled via evoked release, and a considerable portion of the spontaneously recycled vesicles undergoes evoked release under sustained stimulation, showing unique dynamic features. In addition, they can be divided into two distinct subsets, tethered and untethered vesicles, which show differences in spatial distribution inside presynaptic terminals and in fusion competency during the final dwell immediately before fusion. Interestingly, the final dwell time of the tethered vesicles was significantly shortened under the knockdown of synaptotagmin-2, indicating its suppressive role in spontaneous vesicle fusion. Our putative models of the dynamics and exocytosis of spontaneously recycled GABAergic synaptic vesicles based on the results imply a possibility of the difference in release sites between the two subsets of spontaneously recycled vesicles and hence the difference in fusion competency between them.

Keywords : Spontaneous synaptic transmission, Spontaneously recycled GABAergic synaptic vesicles, Tethered vesicles, Untethered vesicles, Synaptotagmin-2
Acknowledgements : We thank the members of Park lab for helpful discussion and comments. This work was supported by the Research Grants Council of Hong Kong (Grants 16102322 and N_HKUST648/24 to H.P.) and by the Innovation and Technology Commission (ITCPD/17-9 to H.P.), the Industry Academic Cooperation Foundation Fund, CHA University Grant (CHA-202500040001 and CHA-202500030001 to S.J.).

S47-6

Synapse-astrocyte interactions in fine-tuning of synaptic strengths

Yukiko Goda

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Recent studies have highlighted the contribution of astrocyte network in shaping synaptic circuit activity with consequences on behavior in various brain areas. Yet, precisely how astrocytes interact with synapses and how they modify individual synaptic strengths, especially in local circuits, remains to be fully understood. We have sought to clarify the cellular organization and the molecular basis that shape tripartite synapses in the hippocampus by focusing on a class of cell adhesion proteins. The amyloid precursor protein (APP) has been intensely studied for its role in Alzheimer's disease, but its physiological function remains unclear. In neurons, APP and its homologs, the amyloid precursor-like proteins are present at synapses and promote synaptogenesis. Astrocytes also express APP although a role for astrocytic APP remains unclear. We have studied the expression and function of astrocytic APP in mouse astrocytes *in vitro* and *in vivo*. Interfering with astrocytic APP expression compromises astrocyte morphological elaboration with potential consequences on synapse function. Our findings underscore the emerging theme of synaptic strength regulation by astrocyte processes.

Keywords : Astrocyte process, APP, synaptic plasticity
Acknowledgements : MEXT KAKENHI JP24H02309, JSPS Core-to-Core Program JPJSCCA20220007, JST JPMJPF2205, JSPS P19728 and internal research fund of Okinawa Institute of Science and Technology Graduate University and RIKEN Center for Brain Science.

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Symposium 48

Day 4 (August 27) **12:30-14:25** **Premier Ballroom B**

The molecular, cellular and circuitry mechanism of pain and itch

Organizer : Yongjing Gao (Nantong University)
Guang-Yin Xu (Soochow University)
Moderator : Yongjing Gao (Nantong University)

1. Thermosensitive TRP channels in itch and Pain
   Makoto Tominaga (Nagoya City University)
2. Mechanisms linking peripheral injury repair and neuropathic pain
   Yun Wang (Peking University)
3. Purinergic receptors and chronic pain
   Guang-Yin Xu (Soochow University)
4. Neuronal circuitry and plasticity of pain
   Yong Ho Kim (Gachon University)
5. NEUROINFLAMMATION AND NEUROPATHIC PAIN
   Yong-Jing Gao (Nantong University)
6. FTO demethylase modulates neuropathic pain through m6A-mediated presynaptic control of Cav2.2 channels
   Jianxiong Wei (Xi'an Jiaotong University) IBRO AWARDEE

S48-1

Thermosensitive TRP channels in itch and Pain

Makoto Tominaga

Nagoya Advanced Research and Development Center, Nagoya City University, Nagoya, Japan

TRP channels are non-selective cation channels having relatively high Ca^{2+} permeability, and comprise six related protein families (TRPC, TRPV, TRPM, TRPA, TRPML, TRPP) in mammals. Among the huge TRP super family of ion channels, some have been proven to be involved in thermosensation detecting ambient temperatures from cold to hot. There are now eleven thermosensitive TRP channels. A capsaicin receptor TRPV1 which is activated by heat stimulus over 43 degree C was reported in 1997. Another TRP channel, TRPA1 is also well known to be involved in pruriception and nociception. Although TRPA1 was initially reported to be activated by noxious cold stimuli, its temperature sensitivity is still controversial. We found that some thermosensitive TRP channels make a complex with Ca^{2+}-activated chloride channel, anoctamin1 (ANO1), also known as TMEM16A and are involved in various physiological functions. Interaction between TRPV4 and ANO1 is involved in water efflux in choroid plexus of mouse brain, salivary/lacrimal grands and sweat grand. And TRPV1 (TRPA1)/ANO1 interaction was found to be involved in the enhancement of pruriceptive and nociceptive signals through further depolarization upon chloride efflux in peripheral sensory neurons. This interaction could be one of the reasons why TRP channels have high Ca^{2+} permeability, and a target for the development of novel antipruriceptive and antinociceptive agents. I will also talk about the evolution of thermosensitive TRP channels since animals on the earth are thought to evolve by changing their chemical and temperature sensitivity in the evolutional process. TRPV3 and TRPV4, warmth-activated TRP channels, are well expressed in skin keratinocytes and reported to be involved in itch sensation. Thus, I will summarize the involvement of thermosensitive TRP channels in itch and pain.

Keywords : TRP channels, pruriception, nociception, temperature, sensory neurons

S48-2

Mechanisms linking peripheral nerve injury repair and neuropathic pain

Yun Wang

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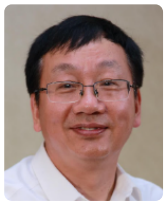
Peripheral nerve injuries, often resulting from trauma, falls, gunshot wounds, sports-related incidents, and iatrogenic damage, are frequently overlooked compared to acute pain associated with soft tissue and skeletal injuries. However, timely intervention is critical, as delays or improper treatment can lead to dysfunction in muscles or tissues innervated by the affected nerve and may also precipitate chronic neuropathic pain. Patients suffering from such injuries may endure severe pain during routine activities like dressing, washing their face, or even feeling a gentle breeze, which significantly elevates the risk of depression and anxiety. Unfortunately, conventional analgesics, including non-steroidal anti-inflammatory drugs and opioids, often prove ineffective for this type of pain. Thus, addressing peripheral nerve injuries requires a focus on the interplay between repair and pain, yet there is a notable absence of suitable animal models for studying these mechanisms.
To tackle this challenge, we have developed two innovative rat models utilizing chemogenetics, single-cell sequencing, and Patch-Seq, combined with morphological and behavioral studies, to elucidate the molecular mechanisms that connect injury repair and pain. In the early stages of injury, pharmacological interventions targeting these molecular pathways can enhance nerve regeneration and mitigate pain. It is crucial to investigate the shared mechanisms underlying the regeneration and repair of peripheral nerve injuries and to identify effective strategies for early intervention and nerve repair. These studies aim to offer new insights and directions for early intervention and long-term rehabilitation of peripheral nerve injuries.

Keywords: peripheral Nerve Injury, repair and pain linking mechanism, dorsal root ganglia

S48-3

Purinergic receptors and chronic pain



Guang-Yin Xu

Institute of Neuroscience, Soochow University, Suzhou 215123, China

Chronic pain is a chronic disease that severely impairs patients' quality of life. Although people have gained certain understanding of the pathological mechanisms of chronic pain over the past two to three decades, the clinical treatment of chronic pain remains a great challenge. In recent years, our laboratory has focused on a series of studies on the purinergic receptor signal transduction system. The results show that purinergic receptors are involved in the transmission of somatic pain and visceral pain at the peripheral and spinal synaptic levels. However, at the central nervous system level (such as the hypothalamic paraventricular nucleus), they only mediate the transmission of visceral pain but not somatic pain. Therefore, we innovatively put forward the concept of a "pain sorting center". This concept can not only describe the differences in central transduction mechanisms between somatic pain and visceral pain, but also provide new molecular targets, specific brain regions (target regions) and their neural circuits (target circuits) for clinical specific intervention in intractable visceral pain.

Keywords : Purinergic receptors, chronic pain, epigenetic regulation, neural circuits, pain sorting center

S48-4

Analgesic action of GLP-1 and novel endogenous peptides via direct TRPV1 inhibition without thermoregulatory side effects

Yong Ho Kim[1, 2]

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Endogenous metabolic peptides can modulate pain. We discovered that glucagon-like peptide-1 (GLP-1) exerts potent analgesic effects by directly inhibiting TRPV1. GLP-1 and related peptides (exendin 9–39, exendin 20–29) bind a specific extracellular site on TRPV1. This interaction blocks capsaicin-induced TRPV1 activation in sensory neurons without affecting proton responses. In pain models, GLP-1–related peptides attenuate capsaicin-induced acute and chronic pain behaviors. Unlike conventional TRPV1 antagonists, these peptides do not trigger hyperthermia or disturb thermoregulation. This suggests a novel analgesic strategy: direct, biased TRPV1 inhibition that relieves pain without thermoregulatory side effects.

We identified additional endogenous peptide candidates that similarly target the TRPV1 extracellular domain. These candidates were structurally optimized to maximize TRPV1 inhibition and stability without causing thermoregulatory side effects. In preclinical neuropathic and inflammatory pain models, including primates, the optimized peptides produced substantial analgesia without altering core body temperature. We are developing these peptides as a new class of pain therapeutics.

In summary, our work highlights an intrinsic analgesic mechanism and a forward-looking therapeutic strategy. Nutrient- and signal-linked endogenous peptides serve as templates to design selective, safe TRPV1 modulators, suggesting innovative treatments for chronic pain.

Keywords : TRPV1; GLP-1; Analgesia; Endogenous Peptides; Thermoregulation

S48-5

NEUROINFLAMMATION AND NEUROPATHIC PAIN

Yue-Juan Ling, Xiao-Bo Wu, De-Li Cao, Ling-Jie Ma, Yong-Jing Gao

Institute of Pain Medicine and Special Environmental Medicine, Nantong University, Jiangsu, China

Neuropathic pain caused by nerve injury is a common clinical condition with limited treatment options. Neuroinflammation mediated by cytokines and chemokines contributes to its development. Our previous studies have shown that chemokines such as CCL2, CXCL1, CXCL10, and CXCL13 mediate interactions between astrocytes and neurons, promoting central sensitization in the spinal cord. These inflammatory mediators also participate in peripheral sensitization. We recently found that follistatin (FST), a secreted protein that binds TGF-β superfamily cytokines, is released from A-fiber neurons and enhances Nav1.7-mediated hyperexcitability in nociceptive neurons through IGF1R binding, contributing to peripheral sensitization. These findings suggest that modulating neuroinflammatory processes may provide new therapeutic approaches for neuropathic pain.

Keywords : Neuropathic pain, Neuroinflammation, Astrocytes, Microglia, Neuron-glia interaction
Acknowledgements : This work was supported by the STI2030-Major Projects (2022ZD0204700) and the National Natural Science Foundation of China (32030048, 82271256, and 31871064) to Yong-Jing Gao.

S48-6 IBRO AWARDEE

FTO Demethylase Modulates Neuropathic Pain Through m6A-Mediated Presynaptic Control of Cav2.2 Channels

Jianxiong Wei[1], Ye Sun[2], Zhi-Xia Zhao[2], Xinqi Liu[1], Hongxiu Chen[1], Xu-Hui Li[2], Lingli Liang[1]

[1]Health Science Center, Xi'an Jiaotong University, Xi'an/Shaanxi, China
[2]Frontier Institute of Science and Technology, Xi'an Jiaotong University, Xi'an/Shaanxi, China

Neuropathic pain, a debilitating condition, involves complex pathological processes including synaptic dysfunction. N6-methyladenosine (m6A), the most abundant internal mRNA modification in eukaryotes, plays a critical role in synaptic plasticity through demethylase-regulated local translation, as demonstrated by recent in vitro studies. However, it's in vivo implications in neuropathological conditions remain unclear. Given the medial prefrontal cortex (mPFC)'s key role in pain modulation, we investigated whether m6A and its demethylases contribute to pain regulation. Using a spinal nerve ligation (SNL)-induced neuropathic pain model, we observed a significant reduction in mPFC m6A levels 14 days post-SNL. MeRIP-Seq analysis revealed distinct patterns of hypomethylated and hypermethylated genes in SNL mice. Notably, SNL upregulated the expression of m6A demethylases FTO and ALKBH5 in the cytoplasm of bilateral mPFC neurons. Further experiments demonstrated that conditional knockout of FTO in either mPFC pyramidal or GABAergic neurons alleviated SNL-induced pain hypersensitivity. Conversely, FTO overexpression in pyramidal neurons, but not GABAergic neurons, induced pain hypersensitivity in naïve mice. Electrophysiological recordings showed that FTO knockdown reversed SNL-induced reductions in the frequency and amplitude of EPSCs in layer V pyramidal neurons. By integrating MeRIP-Seq (sham vs. SNL) and RNA-Seq (control vs. FTO-overexpressed) data, we identified hundreds of potential FTO targets in neuropathic pain regulation. Ultimately, we revealed that mPFC FTO modulates neuropathic pain via a presynaptic mechanism by regulating the expression and function of the N-type calcium channel Cav2.2. These findings highlight FTO as a promising therapeutic target for neuropathic pain management.

Keywords : Neuropathic pain, mPFC, m6A, FTO, Cav2.2
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KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 49

Day 4 (August 27) **12:30-14:25** **Premier Ballroom C**

Emergence, maintenance, and entrainment of circadian clocks: from molecules to networks

Organizer : Jihwan Myung (Taipei Medical University)
Moderator : Jihwan Myung (Taipei Medical University)

1. Impact of the emergence of circadian clock on the developmental physiology in mammals
   Kazuhiro Yagita (Kyoto Prefectural University)
2. PPIase Facilitates Robust Circadian Rhythms via Dual Regulation of PERIOD Protein Dynamics in Drosophila
   Eun Young Kim (Ajou University)
3. Early emergence of peripheral clocks through abrupt bifurcation in the mouse embryo
   Jihwan Myung (Taipei Medical University)
4. Revealing the dynamic eocoding of light in the mice SCN using in vivo calcium imaging
   Shih-Kuo Chen (National Taiwan University)

S49-1

Impact of the emergence of circadian clock on the developmental physiology in mammals

Kazuhiro Yagita

Department of Physiology and Systems Bioscience,
Kyoto Prefectural University of Medicine, Kyoto, Japan

In mammals, in addition to the central clock located in the suprachiasmatic nucleus (SCN), circadian oscillators are present in virtually all peripheral tissues. These so-called peripheral clocks play essential roles in regulating local physiology. We previously demonstrated that circadian oscillations can be autonomously established during the in vitro differentiation of embryonic stem (ES) cells, and that these oscillations are subsequently lost upon reprogramming into induced pluripotent stem (iPS) cells. These findings highlight a strong link between circadian clock function and cellular differentiation status. Using this system, we have been investigating how circadian temporal organization emerges during development. Our results indicate that the initiation of circadian rhythmicity is precisely regulated during differentiation, both in vivo and in vitro. Furthermore, we observed species-specific differences in the timing of clock emergence, with murine cells exhibiting earlier onset of rhythmicity compared to human cells. During the circadian clock-suppressed stage of the embryo, the segment clock oscillates and constructs the somite segments. Interestingly, ectopic activation of circadian key components Clock/Bmal1 in the segmentation clock oscillating embryonic organoids, gastruloids, disrupted the ultradian rhythm and somite-like segment formation. These findings indicate that the circadian clock oscillation may interfere with the segmentation clock oscillation and somitogenesis in the embryos, and suggest that the strict suppression of circadian clock development may be important for the intact development. These findings suggest that in vitro differentiation systems can recapitulate not only morphological but also physiological aspects of development, such as the establishment of circadian rhythms. This approach highlights how the analysis of biological rhythms can provide new insights into developmental physiology using dish-based models.

Keywords : circadian clock, development, stem cells, differentiation, circadian rhythm

S49-2

PPIase Facilitates Robust Circadian Rhythms via Dual Regulation of PERIOD Protein Dynamics in Drosophila

So Who Kang[1,2,4], Hong Thuan Tran[1,2], Gaeun Lee[1,2,4], Jestlin Tianthing Ng[1,3,4], Su Bin Lim[1,3,4], Eun Young Kim[1,2,4]

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The circadian clock enables organisms to anticipate and adapt to 24-hour environmental changes by regulating behavior and physiology. This cell-autonomous molecular clock is driven by transcriptional-translational feedback loops (TTFLs) involving core clock proteins. In Drosophila, CLOCK (CLK) and CYCLE (CYC) activate transcription of period (per) and timeless (tim), with PERIOD (PER) serving as the core repressor. The activity, localization, and stability of PER are regulated by various post-translational modifications, including phosphorylation, ubiquitination, and O-GlcNAcylation. Additionally, peptidyl-prolyl cis/trans isomerization acts as a molecular timer, modulating protein function and cellular processes. Our previous studies identified Dodo (Dod), a homolog of mammalian PIN1, as a regulator of PER stability via its interaction with phosphorylated PER isoforms. Building on this, we performed an RNAi-based behavioral screen of 21 annotated PPIases in Drosophila, identifying CG5808, termed Drosophila Peptidyl-Prolyl cis/trans Isomerase-like 4 (dPPIL4), as critical for circadian rhythm regulation. Knockdown of dppil4 in clock cells lengthened the circadian period and reduced rhythmicity, accompanied by decreased PER levels. Mechanistically, dPPIL4 modulates PER dynamics by enhancing both synthesis and degradation. Knockdown of dppil4 reduced per transcription by downregulating phosphorylation of RNA polymerase II at Ser5, essential for transcription elongation. Additionally, dPPIL4 stabilized Cullin1 of the SCF complex, facilitating PER degradation. These findings underscore the dual role of dPPIL4 in maintaining high-amplitude PER oscillations, essential for robust circadian rhythms.

Keywords : Circadian rhythm, Peptityl-prolyl cis/trans isomerase, Period, Amplitude, Drosophila
Acknowledgements : This research was supported by National Research Foundation of Korea (NRF) grants funded by the Korean government (Ministry of Science and ICT; grant numbers 2017R1A2B2010334, 2019R1A5A2026045, and RS-2023-00208490). Drosophila stocks obtained from the Bloomington Drosophila Stock Center (NIH P40OD018537) and Vienna Drosophila Resource Center (VDRC, www.vdrc.at) were used in this study.

S49-3

Early Emergence of Peripheral Clocks through Abrupt Bifurcation in the Mouse Embryo

Jihwan Myung[1,2]

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[2]Graduate Institute of Medical Sciences, Taipei Medical University, Taipei, Taiwan

The mammalian circadian system is traditionally viewed as hierarchical, with the suprachiasmatic nucleus (SCN) centrally synchronizing peripheral oscillators. Developmentally, this suggests peripheral tissues await SCN maturation to exhibit rhythmicity. However, although neural development continues postnatally, circadian clocks arise earlier during embryogenesis, potentially supporting developmental homeostasis. Using PER2::LUC bioluminescence imaging and temporal transcript sampling in mouse embryos, we identified circadian oscillations emerging in the fourth ventricular choroid plexus at embryonic day 12.5 (E12.5), preceding the SCN clock, which emerges at E15.5. Simultaneous time-differential imaging showed that the embryonic heart similarly initiates an autonomous circadian clock prior to SCN rhythmicity, with molecular oscillations in genes regulating cardiac excitability beginning by E13.5. Notably, circadian rhythmicity in heart rate becomes phase-locked to PER2::LUC expression peaks well before the development of sympathetic or parasympathetic innervation. These early peripheral clocks exhibit an abrupt, nonlinear onset characteristic of a saddle-node on invariant circle (SNIC) bifurcation, distinct from the Hopf bifurcation dynamics typically observed in mature circadian oscillators, suggesting these early peripheral clocks "switch on" at specific embryonic stages. Our findings indicate that circadian system development diverges from the classical hierarchical model and instead follows emergence driven by sudden onsets in key loci critical for fluid homeostasis, suggesting a role for diffusive signaling mechanisms during early embryonic development.

Keywords : Circadian clock emergence, SNIC bifurcation, Choroid plexus, Embryonic cardiac rhythm, Suprachiasmatic nucleus
Acknowledgements : This work was financially supported by the National Science and Technology Council (NSTC) (110-2314-B-038-162, 111-2314-B-038-008, 112-2314-B-038-063, 113-2314-B-038-121) and by the Higher Education Sprout Project of the Ministry of Education (MOE) in Taiwan.

S49-4

Revealing the dynamic eocoding of light in the mice SCN using in vivo calcium imaging

ShihKuo Chen

Life Science, National Taiwan University, Taipei, Taiwan

The circadian clock, a conserved mechanism across species, regulates most physiological processes by aligning with the environmental light-dark cycle through a process known as circadian photoentrainment. This synchronization occurs when light exposure at specific times leads to distinct phase shifts, such as phase delays during early night, phase advances in late night, and a midday period with no shift, known as the dead zone. In mammals, including mice, intrinsically photosensitive retinal ganglion cells (ipRGCs) play a key role in transmitting light signals to the suprachiasmatic nucleus (SCN), a central clock composed of around 20,000 neurons. Although the intracellular molecular signaling pathways influencing clock gene expression after light exposure are well understood, the neuronal circuits responsible for the distinct light response phases are less clear. Using in vivo two-photon microscopy and gradient-index (GRIN) endoscopes, we identified seven unique light response patterns in SCN neurons. Under 90 seconds of light exposure, SCN neurons exhibited transient, delayed, and sustained activation or inhibition. Most SCN neurons could show either activation or inhibition responses at different trials, even within the same ZT period. However, while individual neurons exhibited highly variable responses to light across trials, the proportion of activation and inhibition among all recorded neurons was similar between zeitgeber times (ZT) 16 and 22. Notably, we observed a small group of neurons consistently activated by light at ZT 16 and another subset inhibited at ZT 22. By employing the targeted recombination in active populations (TRAP) system to label neurons responding to light at ZT 16, we demonstrated that their activation could induce phase delays at any circadian time, overcoming the typical midday dead zone in photoentrainment. Together, we propose a dynamic bi-stable network model for circadian photoentrainment in the mammalian SCN.

Keywords : SCN, ipRGC, calcium imaging, in vivo

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 50

Supported By CUREVERSE 큐어버스

Day 4 (August 27) **12:30-14:25** **Rm.113-115**

Decoding GPCR signaling: innovations in neuroscience research

Organizer : Ka Young Chung (Sungkyunkwan University)
Moderator : Jihye Seong (Seoul National University)

1. Molecular mechanism of β-arrestin 2 interaction with phosphorylated GPCRs and phosphatidylinositol 4,5-bisphosphate
   Ka Young Chung (Sungkyunkwan University)
2. Structural and pharmacological analysis of serotonin receptor
   Kuglae Kim (Yonsei University)
3. Illuminating spatial organization of GPCR signaling in the living cell
   Yonghoon Kwon (Gwangju Institute of Science and Technology)
4. An expanded palette of ATP and adenosine sensors for multiplex imaging
   Zhaofa Wu (Chinese Academy of Sciences)
5. In vivo multiplex imaging of dynamic neurochemical networks with designed far-red dopamine sensors
   Yu Zheng (Peking University) IBRO AWARDEE

S50-1

Molecular mechanism of β-arrestin 2 interaction with phosphorylated GPCRs and phosphatidylinositol 4,5-bisphosphate

Ka Young Chung

School of Pharmacy, Sungkyunkwan University, Suwon, Republic of Korea

G protein-coupled receptors (GPCRs), the key regulators of cellular signaling, transduce signals through G proteins or arrestins. G protein- or arrestin-mediated signal transduction induces distinct functional consequences, and therefore the molecular mechanisms of the interaction between GPCR-G protein or GPCR-arrestin have been of great interest. Phosphorylated residues of G protein-coupled receptors bind to the N-domain of arrestin, resulting in the release of its C-terminus. This induces further allosteric conformational changes, such as polar core disruption, alteration of interdomain loops, and domain rotation, which transform arrestins into the receptor-activated state. It is widely accepted that arrestin activation occurs by conformational changes propagated from the N- to the C-domain. However, recent studies have revealed that the binding of phosphatidylinositol 4,5-bisphosphate (PIP_2) to the C-domain transforms arrestins into a pre-active state. While the mechanism of arrestin binding to GPCRs with a phosphorylated C-terminal tail (C-tail) is well understood, little is known about arrestin interactions with GPCRs that possess a short C-tail and a long phosphorylated intracellular loop 3 (ICL3). Here, we explored the interaction between β-arrestin 2 (βarr2) and the dopamine receptor D2 (D2R), a critical receptor for brain function, which features an exceptionally long ICL3 but no C-tail. We also examined the mechanisms underlying PIP_2-induced βarr2 pre-activation. Our results provide new insights into structural dynamics of GPCR- βarr complex, especially in understanding the D2R-βarr2 and PIP_2-βarr2 interaction.

Keywords : Arrestin, Dopamine, Phosphatidylinositol 4,5-bisphosphate, Structure, HDX-MS
Apply for Scitech Korea Best Oral Presentation Awards : NPoster

S50-2

Structural and pharmacological analysis of serotonin receptor

Kuglae Kim

Yonsei University

S50-3

Illuminating Spatial Organization of GPCR Signaling in the Living Cell

Yonghoon Kwon

Department of Life Sciences, Gwangju Institute of Science and technology , Gwangju, Republic of Korea

G-protein-coupled receptors (GPCRs), the largest family of signalling receptors, as well as important drug targets, are known to activate extracellular-signal-regulated kinase (ERK)—a master regulator of cell proliferation and survival. However, the precise mechanisms that underlie GPCR-mediated ERK activation are not clearly understood. Here we investigated how spatially organized β_2-adrenergic receptor (β_2AR) signalling controls ERK activity by utilizing subcellularly targeted ERK activity biosensors. We demonstrate that β_2AR-mediated ERK activity is spatially compartmentalized based on the observation that we found the ERK activity at endosomes, but not at the plasma membrane. This pool of ERK activity depends on active, endosome-localized $G\alpha_s$ and requires ligand-stimulated β_2AR endocytosis. We further identify an endosomally localized non-canonical signalling axis comprising $G\alpha_s$, RAF and mitogen-activated protein kinase kinase, resulting in endosomal ERK activity that propagates into the nucleus. Selective inhibition of endosomal β_2AR and $G\alpha_s$ signalling blunted nuclear ERK activity, *MYC* gene expression and cell proliferation. These results reveal a non-canonical mechanism for the spatial regulation of ERK through GPCR signalling and identify a functionally important endosomal signalling axis.

Keywords : GPCR, ERK, Biosensor, Signal compartmentation, Live cell imaging

S50-4

An expanded palette of ATP and adenosine sensors for multiplex imaging

S50-5 IBRO AWARDEE

In vivo multiplex imaging of dynamic neurochemical networks with designed far-red dopamine sensors

Yu Zheng[1], Ruyi Cai[2], Kui Wang[3], Junwei Zhang[4], Yizhou Zhuo[2], Hui Dong[2], Yuqi Zhang[2], En Ji[2], Yiwen Cui[1], Jonathan Grimm[5], Kai Johnsson[6], Eric Schreiter[5], Luke Lavis[5], Zhixing Chen[4], Yu Mu[3], Yulong Li[1,2,7]

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[4]Peking University College of Future Technology, Peking University, Shanghai, China
[5]Janelia Research Campus, Howard Hughes Medical Institute, Ashburn, Virginia, USA
[6]Department of Chemical Biology, Max Planck Institute for Medical Research, Heidelberg, Germany
[7]PKU-IDG/McGovern Institute for Brain Research, Peking University, Beijing, China

The human brain consists of billions of neurons that communicate primarily through neurotransmitters. Many brain functions depend on the coordinated regulation of multiple neurotransmitters and integrated control over downstream signaling pathways. To gain a better understanding of their regulation and functional roles, there is an urgent need to monitor multiple neurotransmitters or other neurochemicals simultaneously. One such crucial neurotransmitter is dopamine (DA), which plays a pivotal role in regulating various physiological functions, including learning, motor control and reward. To meet this challenge, we developed a far-red DA sensor based on the G protein-coupled receptor activation (GRAB) strategy, named $GRAB_{haloDA}$ (HaloDA1.0 in short). This sensor leverages the G protein-coupled receptor activation (GRAB) strategy and a cpHaloTag-based chemigenetic approach, offering robust sensitivity, high specificity, rapid sub-second response kinetics, and an expansive spectral range. In combination with existing green and red neuromodulator sensors, Ca^{2+} indicators, cAMP sensors, and optogenetic tools, the HaloDA1.0 sensor exhibits great versatility for multiplex imaging in cultured neurons, acute brain slices, and in behaving animals like zebrafish and mice *in vivo*. Its modular, tunable design can be extended to other GPCRs and protein tags, providing a versatile platform for tracking multiple neurotransmitters and advancing our understanding of neurochemical regulation in health and disease.

Keywords : Neurotransmitter, Dopamine, Sensor, Multiplex imaging
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KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Symposium 51

Day 4 (August 27) **12:30-14:25** **Rm.116-118**

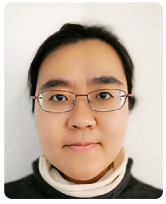
Cognitive and computational neuroscience in nonhuman primate

Organizer : Hansem Sohn (Sungkyunkwan University)
Seng Bum Michael Yoo (Sungkyunkwan University)
Moderator : Hansem Sohn (Sungkyunkwan University)

1. Ensemble Perception in Macaques
   Ning Liu (Chinese Academy of Sciences)
2. Mental programming of spatial sequences in working memory in the macaque frontal cortex
   Liping Wang (Chinese Academy of Sciences)
3. Neuronal representation of counterfactual choice for quick learning in macaque frontopolar cortex
   Kentaro Miyamoto (RIKEN)
4. Allocentric coding in the precuneus: from human psychophysics and fMRI to monkey physiology and vision transformers
   Shigeru Kitazawa (Osaka University)

S51-1

Ensemble Perception in Macaques



Ning Liu

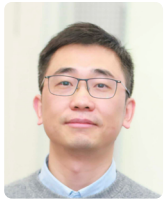
State Key Laboratory of Cognitive Science and Mental Health, Institute of Biophysics, Chinese Academy of Sciences, Beijing, China

Due to the inherent limitations of the visual system, such as constraints on attention and memory, it is unlikely that individuals can simultaneously process each member of a group at a glance. However, the visual system can exploit similarities among objects to rapidly extract statistical summaries of group properties—for example, estimating the average size of oranges on a tree. This phenomenon, known as "ensemble perception" or "ensemble coding," has been extensively documented in humans across a range of visual features—from low-level attributes like orientation and size to high-level properties such as emotional expression. Despite the importance of visual information in the daily lives of non-human primates (NHPs) and their close evolutionary relationship with humans, little is known about whether NHPs also exhibit ensemble perception. In the present study, we conducted behavioral experiments to assess ensemble coding in macaques. Furthermore, we employed functional magnetic resonance imaging (fMRI) and electrophysiological recordings to investigate the underlying neural mechanisms. Our results provide evidence for ensemble coding in macaques and, through fMRI and electrophysiological data, elucidate the relationship between ensemble coding and individual item coding in the primate brain.

Keywords : Ensemble Perception, Macaques, fMRI, Electrophysiological Recording, Vision
Acknowledgements : This work was supported by STI2030-Major Projects (Grant No. 2021ZD0200200) and National Natural Science Foundation of China (Grant No. 32471090).

S51-2

Mental programming of spatial sequences in working memory in the macaque frontal cortex



Liping Wang

Center for Excellence in Brain Science and Intelligence Technology, Chinese Academy of Sciences, Shanghai, China

One of the most intriguing puzzles in cognitive neuroscience is understanding the neural mechanisms behind mental operations. For instance, when you learn a simple algorithmic operation, such as fractions, you not only assign arbitrary shapes “–” or “/” to the operations but also decompose the program into relatively simpler primitives (e.g., numerator and denominator) and their relationships. This mystery of mental programming was first identified by Alan Turing as the basis of all cognition. The main challenge that we face today is understanding how our brain decomposes complex programs into distinct neural steps or primitives in working memory (WM).

Keywords : Cognitive neuroscience, Working memory, Macaque frontal cortex

S51-3

Neural mechanisms of thought experiments in the primate frontopolar cortex

Kentaro Miyamoto

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The mind's ability to conceptualize and reason about what is not present is essential. It allows us to reason counterfactually about what might have happened if we had taken another course of action. It allows us to think about what might happen – to perform 'thought experiments' – even before we try things out for real. This ability is prominent exclusively in primates with a well-developed prefrontal cortex. Thus, we conceived three new experimental paradigms to test the behavioural and neural mechanisms of the thought experiment using psychophysics and whole-brain functional neuroimaging techniques in both humans and macaque monkeys.

Our first fMRI and neuropharmacological studies on memory metacognition ('metamemory') in macaques showed that the frontopolar cortex (FPC) supports introspective evaluation of beliefs about events not directly observed. The FPC was crucial for self-evaluating outcomes of novelty judgments or absence in memory, but not for performing the judgments.

Our second electrophysiological study, recording from the FPC of macaques performing a probabilistic reward task, revealed that FPC neurons were activated when exploration of unknown information was required. Notably, the modulation of the FPC was stronger when the exploration was based solely on one's own memory compared to being guided by external cue feedback. The results suggest the role of the FPC in exploring unknown information guided by metacognition based on intrinsic memory assessments.

Our third functional MRI and transcranial magnetic stimulation study on the transition from metacognitive monitoring to action control in humans revealed that the FPC is essential for adjusting action strategies based on metacognition so as to adapt to the environment.

I will present a model in which the FPC tracks and evaluates alternative choices the self could have taken, enabling adaptive decision-making through thought experiments in primates.

Keywords : Metacognition, Macaque monkeys, Functional MRI, Thought experiments, Frontopolar cortex

S51-4

Allocentric coding in the precuneus: from human psychophysics and fMRI to monkey physiology and vision transformers

Shigeru Kitazawa[1,2]

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[2]Graduate School of Medicine, The University of Osaka, Suita, Osaka, Japan
[3]Center for Information and Neural Networks, National Institute of Information and Communications Technology, Suita, Osaka, Japan

Why does the world appear stable even as we move our eyes? This long-standing question suggests the existence of allocentric (world-centered) representations in the brain. However, it remains unclear whether such representations are fast and robust enough to stabilize visual perception during active viewing.
We hypothesized that the brain instantly extracts the “background” from the wide visual field and encodes object positions relative to it—a background-centered coordinate system. Using fMRI adaptation in humans, we identified the right precuneus as a key cortical region that represents object positions relative to a large background, even when that background is irrelevant to the task. We then confirmed in monkeys that some precuneus neurons exhibit receptive fields anchored to the background, shifting from retinotopic to background-centered coding. Remarkably, this transformation can begin as early as 40 ms after stimulus onset and peaks around 100-150 ms—fast enough to contribute to the stabilization of visual perception across eye movements (Uchimura et al., 2024, *J Neurosci*). Having identified the “where” of this representation, we now turn to the question of “how” it emerges. Recent findings from our lab show that Vision Transformers (ViTs), when trained with the DINO self-supervised method, develop attention heads that mirror human attention patterns (Yamamoto et al., 2025, *Neural Netw*). Notably, some heads spontaneously encode figures in relation to background regions—remarkably similar to background-centered neurons in the precuneus.
These converging lines of evidence—from psychophysics, neuroimaging, and neurophysiology to artificial intelligence—highlight the precuneus as a central hub for allocentric representation. They also raise the intriguing possibility that self-supervised learning may capture essential principles by which the brain constructs world-centered representations.

Keywords : Allocentric coordinates, Precuneus, Vision Transformer
Acknowledgements : This work was supported by KAKENHI 25H01145, 23K17462, 21H04896, 18H0522, and 17H00742 from the Japan Society for the Promotion of Science (JSPS) to SK.

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Special Session 1

Supported By KOREA DEMENTIA RESEARCH CENTER KDRC

Day 1 (August 24) **15:00-16:35** **Rm.206-207**

Cutting-edge approaches to decoding dementia: from genomics to neuropathology

Organizer : Inhee Mook-Jung (Korea Dementia Research Center/Seoul National University)
Moderator : Inhee Mook-Jung (Korea Dementia Research Center/Seoul National University)

1. Decoding Lewy pathology spread: AIMP2-driven α-synuclein transmission and therapeutic rescue
   Yunjong Lee (Sungkyunkwan University)
2. Functional role of somatic mutation in Alzheimer's disease
   Sangwoo Kim (Yonsei University)
3. Multi-omics analysis reveals genes linked to amyloid beta pathology in Alzheimer's disease
   Hong-Hee Won (Sungkyunkwan University)

SS1-1

Decoding Lewy pathology spread: AIMP2-driven α-synuclein transmission and therapeutic rescue

Yunjong Lee, Ji-Hun Kim

Pharmacology, Sungkyunkwan University School of Medicine, Suwon, Gyeonggi-do, Republic of Korea

Lewy body pathology, driven by α-synuclein aggregation and transneuronal transmission, underlies the diverse motor and nonmotor symptoms of Parkinson's disease (PD) and Lewy body dementia (LBD). While multiple factors modulate α-synuclein pathology, the role of aminoacyl-tRNA synthetase interacting multifunctional protein-2 (AIMP2)—a parkin substrate elevated in PD brains—remains poorly defined. AIMP2 can coaggregate with α-synuclein, potentially amplifying its neurotoxic and inflammatory effects. In this talk, I will present recent studies using transgenic mouse models and targeted small molecules to explore how AIMP2 influences the propagation of α-synuclein pathology. These findings identify AIMP2 as a key modulator of Lewy pathology spread and support its potential as a therapeutic target for modifying disease progression in PD and LBD.

Keywords : AIMP2, α-synuclein, Lewy body dementia , Parkinson's disease, Pathology propagation
Acknowledgements : This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center(KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (grant number :RS-2022-KH127042)

SS1-2

The contribution of clonal somatic mosaicism to telomere shortening in Alzheimer's disease

Seungseok Kang[1], Sehoon Jeong[2], Jeong Ho Lee[2], Sangwoo Kim[1]

[1] Department of Biomedical Systems Informatics, Yonsei University College of Medicine, South Korea
[2] Graduate School of Medical Science and Engineering, KAIST, Daejeon,South Korea

Somatic mosaicism has been implicated in various neurological disorders, but its pathogenic role in Alzheimer's disease (AD) remains poorly defined. Although adult hippocampal neurogenesis (AHN), a process essential for maintaining cognitive reserve, is known to decline in AD, the somatic mutation landscape within the subgranular zone (SGZ)—the primary site of neurogenesis—has not been explored. We hypothesized that somatic mosaicism within the SGZ contributes to the risk of AD progression. Here, we applied laser capture microdissection (LCM) and whole-genome sequencing (WGS) to clonal neural stem cell (NSC) niches isolated from the SGZ of 83 AD patients and 23 non-dementia controls. AD patients showed a significant reduction in clonal somatic single-nucleotide variants (sSNVs) compared to controls (p=0.04), primarily due to reduced accumulation of a proliferation-associated mutational signature (p=0.03). Moreover, AD samples harbored fewer low-frequency (0–5%) sSNVs (p=0.01), suggesting impaired NSC proliferation. Although the overall pathogenic sSNV burden was comparable, AD patients exhibited significant enrichment of mutations in telomere maintenance (TM) genes (21.7%). Telomere length quantification via qPCR and visualization assays confirmed markedly shorter telomeres in AD samples with TM gene mutations, regardless of age. Together, our results suggest that TM deficiency may impair NSC proliferation and accelerate telomere attrition in AD, and highlight somatic mosaicism in the SGZ as a novel contributor to AD pathogenesis.

Keywords : Alzheimer's disease, Somatic mutation, Telomere, Adult Hippocampal Neurogenesis, Mosaicism

SS1-3

Multi-omics analysis reveals genes linked to amyloid beta pathology in Alzheimer's disease

Hong-Hee Won

Samsung Advanced Institute for Health Sciences and Technology, Sungkyunkwan University, Samsung Medical Center, Seoul, Republic of Korea

Alzheimer's disease (AD) is a highly heritable neurodegenerative disorder characterized by amyloid-beta (Aβ) accumulation, yet most known genetic risk factors—identified predominantly in European ancestry cohorts—explain only part of its variance. To better understand the molecular mechanisms underlying Aβ pathology, we applied a multi-omics strategy integrating large-scale genome-wide association studies (GWAS) with cell-type–resolved transcriptomic analyses. This approach enables discovery of genetic variants linked to Aβ deposition and functional interpretation through single-nucleus RNA sequencing and microglia-specific eQTL mapping.

We conducted the largest GWAS to date of Aβ deposition in East Asians (EAS, n=3,885), replicated in 753 EAS, and meta-analyzed with 11,816 Europeans. A novel locus on chromosome 11, lead variant rs76490923 in SORL1, showed genome-wide significance (p=2.46e-09 in EAS; p=3.09e-11 meta). This variant is ~10-fold more frequent in EAS (21%) than in Europeans (2%) and reduced Aβ positivity risk by up to 43.5% in APOE4 non-carriers and 55.6% in carriers, with a 91% reduction in non-carrier homozygotes.

Single-nucleus RNA sequencing of Korean brains (n=15) revealed SORL1 is highly expressed in microglia and downregulated in Aβ-positive individuals. eQTL analyses demonstrated that the protective allele increases SORL1 expression specifically in microglia, suggesting enhanced amyloid clearance via lysosomal trafficking of amyloid precursor protein.

Our findings illustrate how combining diverse ancestries, imaging biomarkers, and cell-type–specific functional genomics can uncover novel, biologically plausible targets for AD prevention and therapy. Beyond SORL1, this work underscores the value of multi-omics and multi-ancestry approaches for precision medicine, guiding ethnicity-tailored risk assessment and treatment strategies in dementia.

Keywords : Alzheimer's disease, amyloid beta, genome-wide association study, single-cell transcriptome, SORL1

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Special Session 2

Supported By ICONEUS REVEALING THE BRAIN

Day 2 (August 25) **9:15-10:25** **Rm.104-106**

INSCOPIX 2P miniature microscope seminar

1. Neural circuit mechanisms for episodic memory formation in the entorhinal cortical hippocampal networks
   Takashi Kitamura (University of Texas Southwestern Medical Center)
2. nVista 2P: All-in-One, intuitive, and ready for
   Yu-Ling Lin (Inscopix, a Bruker Company)

SS2-1

Egocentric Coding of Geometric Features in the Anterior Cingulate Cortex

Takashi Kitamura

Department of Psychiatry, University of Texas Southwestern Medical Center, USA

Animals perform action as a motor output in the self-perspective. For this to happen, the allocentric spatial map is transformed into an egocentric spatial map, and is then used by the animals to perform motor action by the secondary motor cortex (M2). Retrosplenial Cortex (RSC) is implicated in the transformation of allocentric to egocentric framework. However, it remains unclear how the information in the egocentric map is transformed for action. Anatomical studies have shown that Anterior Cingulate Cortex (ACC) receives input from RSC and is projected to M2 and is responsive to objects and social cues. These results suggest that ACC could be the site for map to action transformation. Therefore, we hypothesize that ACC could encode a wide variety of geometric features in egocentric fashion. To study the representational schema of the ACC, we expressed GCaMP6f in the ACC neurons using AAV infection and implanted a GRIN lens to monitor calcium activity in the ACC during spatial navigation. We showed that a subset of ACC neurons encode border, convex and concave corners, doors to the compartment, object and social cue. We also observed that a majority of such geometry-encoding cells exhibits egocentric response. Importantly, these representations require multiple exposure to the environment. Our data suggests that the ACC is potentially acting as a gateway to successful motor output by representing geometric features on the environment, social and objects in an egocentric fashion, much like a contour map which provides a 'birds eye view' of the space to the animal.

Keywords : Anterior Cingulate Cortex, Memory, Spatial representation, Social, Object

SS2-2

nVista 2P: All-in-One, Intuitive, and Ready for Discovery

Yu-Ling Lin, Ph.D

Bruker company

The nVista 2P miniscope utilizes two-photon technology to perform neural circuit imaging at higher resolution and greater depths than one-photon techniques during freely-behaving tasks. With over a decade of innovation and expertise in miniature optical design and workflow optimization, Inscopix has developed a high-performance fluorescence imaging system weighing only 2.2 grams that is both user-friendly and reliable. Compatible with a variety of GRIN lens applications and cranial window preparation, nVista 2P allows researchers to target all regions of a rodent's brain using the same techniques as one-photon experiments, but with the additional benefits of two-photon optics.

Keywords : nVista 2P, freely moving

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Special Session 3

Day 2 (August 25) **14:30-16:25** **Rm.116-118**

Parkinson's disease: Unmet needs between clinical practice and basic research

Organizer : Jinyoung Youn (Samsung Medical Center)
Young Eun Kim (Hallym University)
Moderator : Phil Hyu Lee (Yonsei University)
Jun Young Heo (Chungnam National University)

1. Unmet needs and limitations of translational research in Parkinson's disease
   Seong-Beom Koh (Juntendo University)
2. Seed amplification assay (SAA) in Parkinson's disease: clinical significance, limitations, and future directions
   Hatano Taku ()
3. Basal ganglia network dynamics in Parkinson's disease: a perspective on brain modulation
   Jung Hwan Shin (Seoul National University)
4. Drug repurposing for disease-modifying effects in Parkinson's disease
   Seong Ho Jeong (Inje University)

SS3-1

Unmet needs and limitations of translational research in Parkinson's disease

Seong-Beom Koh

Neurology, Korea University Guro Hospital, Seoul, Republic of Korea

Parkinson's disease is highly heterogenic in terms of clinical, pathological, genetic, and imaging findings. In this respect, the diagnostic criteria for Parkinson's disease continue to evolve, and the criteria for the stage of the disease continue to change.For this reason, there are various 'unmet needs' in terms of diagnosis and treatment of patients with Parkinson's disease. Unmet needs can be classified into clinical symptoms such as motor symptoms, gait, axial symptoms, autonomic nerve system symptoms, and neuropsychiatric symptoms. In addition, there are unmet needs for biomarkers and novel therapeutics, including digital therapeutics.

Keywords : Parkinson's disease, Heterogeneity, Unmet needs

SS3-2

Pathological mechanisms and biomarkers of α-synucleinopathies.

Taku Hatano, Yutaka Oji, Ayami Okuzumi

Neurology, Juntendo University, Faculty of Medicine, Tokyo, Japan

Parkinson's disease (PD) and multiple system atrophy (MSA) are neurodegenerative disorders collectively classified as α-synucleinopathies, characterized by the pathological aggregation of α-synuclein (AS). Lewy bodies in PD and glial cytoplasmic inclusions in MSA, which are known as hallmarks of the pathology, are composed of AS aggregates and associated membranous organelles. AS is an amphipathic protein that associates weakly with lipid membranes and plays a role in membrane trafficking. AS preferentially localizes to lipid rafts—membrane domains enriched in sphingolipids and glycosphingolipids—where alterations in glycolipid metabolism influence its aggregation. Actually, glucocerebrosidase, a lysosomal enzyme linked to Gaucher disease, metabolizes glucosylceramide and has been implicated in PD pathogenesis when its function is impaired. Thus, lipid metabolism and membrane composition are critical factors in AS aggregation. Recently, we identified PSAP (encoding prosaposin) as a novel causative gene for autosomal dominant familial PD. iPS cells with pathogenic PSAP mutations exhibited AS aggregation, along with Golgi fragmentation and reduced glucocerebrosidase activity. We also focus on systemically distributed AS oligomers. Amplification assays such as RT-QuIC and PMCA have enabled the detection of AS seeds in various body fluids and tissues by exploiting their seeding activity. Using RT-QuIC combined with immunoprecipitation (IP/RT-QuIC), we successfully detected AS seeds in the serum of patients with α-synucleinopathies, supporting its potential as a diagnostic biomarker. Moreover, the fibrils amplified via IP/RT-QuIC displayed disease-specific aggregation and propagation properties. We have also observed AS aggregation in peripheral organs such as the liver, kidney, thyroid gland, and heart. In this symposium, we will present recent insights into the pathomechanisms and biomarker development in α-synucleinopathies.

Keywords : α-synuclein , α-synucleinopathies, prosaposin, seed amplification assy

SS3-3

Basal Ganglia Network Dynamics in Parkinson's Disease: A Perspective on Brain Modulation

Jung Hwan Shin

Department of Neurology, Seoul National University Hospital, Seoul 03080, Republic of Korea
Department of Neurology, Seoul National University College of Medicine, Seoul, Republic of Korea

Objective: Different subtypes of neurons in the striatum play a significant role in movement and learning by responding to motivational stimuli. In Parkinson's disease (PD), these neurons are linked to immobility and levodopa-induced dyskinesia. However, their activity patterns in the parkinsonian state are not well understood.

Methods: Using genetically modified mice (D1-cre, A2a-cre, ChAT-cre, and PV-cre), we injected AAV-flex-Gcamp8f virus into the right dorsal striatum, followed by an open-field test with in-vivo 1-photon calcium imaging. Parkinsonism was induced with 6-OHDA injections in the medial forebrain bundle.

Results: Recordings from D1, A2a, ChAT, and PV neurons revealed that most neurons encoded motor information. Unlike others, PV neurons were inactive during immobility. In PD-like states, cholinergic neurons showed increased activity at behavior initiation, while they maintained activity in the stop phase, contrasting with a decrease in the baseline state. Cholinergic spatial coactivity was significantly higher than that of D1 or A2a neurons, with decreased ensemble coactivity in the mobile phase. In PD states, this ensemble coactivity decreased during immobility but not during mobility. Notably, pair-wise correlations showed a distance-related decline in the immobile phase for PD states, absent in the baseline state.

Conclusion: Cholinergic ensembles in the striatum encode motor states distinctly in PD, showing heightened activity during immobility and altered spatial organization, suggesting a unique pathophysiological network that could be related to novel treatment strategies.

Keywords : Parkinson disease, Basal ganglia, Neural network, Cell-type specific, neuromodulation

SS3-4

Drug Repurposing for Disease-Modifying Effects in Parkinson's Disease

Seong Ho Jeong

Neurology, Inje University Sanggye Paik Hospital, Seoul, Republic of Korea

Parkinson's disease (PD) is a progressive neurodegenerative disorder for which no disease-modifying therapy (DMT) currently exists. Drug repurposing—applying approved drugs to new indications—offers a promising, time-efficient strategy to address this unmet need. This presentation will provide an overview of repurposed drug candidates for PD, including GLP-1 receptor agonists, ambroxol, calcium channel blockers, iron chelators, and c-Abl inhibitors, emphasizing their mechanisms targeting α-synuclein aggregation, mitochondrial dysfunction, and neuroinflammation. Despite encouraging preclinical data, several phase III trials have failed, highlighting the need for improved trial designs, biomarker-driven outcomes, and patient stratification. In addition to summarizing the current landscape, the talk will introduce our original research on dipeptidyl peptidase-4 (DPP-4) inhibitors. Preclinical studies showed that sitagliptin reduces α-synuclein pathology and neuroinflammation in a gut-brain axis PD model, independent of GLP-1 signaling. Based on these findings, we have launched a phase II multicenter randomized controlled trial evaluating sitagliptin in early PD patients. The trial incorporates clinical, imaging, and inflammatory biomarkers to assess disease-modifying effects. Through a combination of literature-based insights and translational research experience, this lecture will explore how drug repurposing strategies can be refined to better target disease mechanisms and accelerate therapeutic development in PD.

Keywords : Parkinson's disease, Synucleinopathy, Drug repurposing, Drug repositioning, Dipeptidyl peptidase-4 inhibitor

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Special Session 4

Day 2 (August 25) **13:00-17:00** **Rm.107-109**

Meet the Editor

Organizer : Chang Ho Sohn(Korea Advanced Institute of Science and Technology)

Moderator : Chang Ho Sohn(Korea Advanced Institute of Science and Technology), Hyeyoung Shin(Seoul National University), Wuhyun Koh(Institute for Basic Science)

1. Elisa Floriddia, Ph.D., Senior Editor, Nature Neuroscience
2. Yuan Zhao, Ph.D., Associate Editor, Nature Communications
3. Rebecca Wright, Ph.D., Chief Editor, Nature Communications, Neuroscience team
4. Luis Gomes, Ph.D., Scientific Editor, Cell
5. Qingzhong Ren, Ph.D., Scientific Editor, Cell Reports
6. 6. Steffi Sun, Ph.D., Senior Editor, Signal Transduction and Targeted Therapy
7. 7. Thomas McHugh, Editor-in-Chief, Neuroscience Research

SS4-1

Elisa Floriddia, Ph.D., Senior Editor, Nature Neuroscience

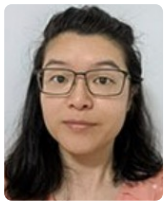
Elisa Floriddia

Senior Editor, Nature Neuroscience

Elisa joined Nature Neuroscience in 2022 after working as Senior Editor at Nature Communications. She received her PhD in cellular and molecular neuroscience from the University of Tuebingen (Germany), where she studied mechanisms of neuroregeneration and repair. During her postdoc at the German Center for Neurodegenerative Disease (DZNE), first, and at the Karolinska Institute (Sweden), later, Elisa primarily investigated cellular and molecular mechanisms of neurodegeneration, neurodevelopment, and glia biology. Her research interests include cellular and molecular neuroscience, functional genomics, and neurodevelopment. Elisa's engagement with the neuroscience community extends beyond her editorial work and, for instance, she volunteers in the SfN Neuroscience Scholar Program selection committee. Elisa is based in the London office.

SS4-2

Yuan Zhao, Ph.D., Associate Editor, Nature Communications



Yuan Zhao

Ph.D., Associate Editor, Nature Communications

Yuan joined Nature Communications in August 2024. She received her PhD in Biomedical Engineering from Huazhong University of Science and Technology, where she studied calcium signaling in astrocytes. She then carried out postdoctoral research on electrical stimulation strategies for cortical visual prostheses at the University of Southern California. After that, she joined the California Institute of Technology, where she did comparative studies on the evolutionary adaptation of ingestive behaviors and the underlying neural basis across species. Yuan handles submissions in neuroscience methods and cellular and circuits neuroscience. She is based in the Shanghai office.

SS4-3

Rebecca Wright, Senior Editor, Nature Neuroscience

Rebecca Wright

Senior Editor, Nature Neuroscience

Rebecca Wright joined Nature Neuroscience in 2016 after having previously worked as an associate editor at Nature Communications. She received her PhD from the University of Oxford, followed by a postdoctoral appointment in Anirvan Ghosh's lab at UCSD, researching neurotransmitter receptor plasticity and trafficking. She then joined Fred Gage's lab at the Salk Institute, where she investigated neural signalling in induced pluripotent stem cell models of neurocognitive disorders. Her research interests include cellular and molecular neuroscience, neurodegeneration, and glial biology. Rebecca is based in the London office.

SS4-4

Luis Gomes, Ph.D., Scientific Editor, Cell

Luis Gomes

Scientific Editor, Cell

Before joining the Cell editorial team, Luis did a Ph.D. at KU Leuven, where he focused on neurodegenerative disorders. Curious by nature, Luis is passionate about science and travel. If he is not learning about new scientific topics, he will probably be exploring new countries and cultures. Based in Barcelona, Luis likes to think about the big picture and engage with the research community and is an advocate of an accessible and fair editorial process. At Cell, he loves the opportunity to read the latest advances across biomedical sciences and contribute to the publication of ground-breaking papers.

SS4-4

Qingzhong Ren, Ph.D., Scientific Editor, Cell Reports

Qingzhong Ren

Scientific Editor, Cell Reports

Dr. Qingzhong Ren, scientific editor at Cell Reports, Cell Press. Dr. Ren received his Ph.D. from the Institute of Neuroscience, Chinese Academy of Sciences, and then conducted postdoctoral research at Janelia Research Campus, Howard Hughes Medical Institute in the United States. In July 2019, he went to the Allen Institute for Brain Science in Seattle as a scientist. He joined Cell Press in 2021 and has long focused on research in neuroscience, immunology, developmental biology, metabolism, single-cell biology and emerging fields.

SS4-6

Steffi Sun, Ph.D., Senior Editor, Signal Transduction and Targeted Therapy

Steffi Sun

Signal Transduction and Targeted Therapy

Yuan joined Nature Communications in August 2024. She received her PhD in Biomedical Engineering from Huazhong University of Science and Technology, where she studied calcium signaling in astrocytes. She then carried out postdoctoral research on electrical stimulation strategies for cortical visual prostheses at the University of Southern California. After that, she joined the California Institute of Technology, where she did comparative studies on the evolutionary adaptation of ingestive behaviors and the underlying neural basis across species. Yuan handles submissions in neuroscience methods and cellular and circuits neuroscience. She is based in the Shanghai office.

SS4-7

Thomas McHugh, Editor-in-Chief, Neuroscience Research

Thomas McHugh

Editor-in-Chief, Neuroscience Research

Thomas (Tom) McHugh is the team leader of the Laboratory for Circuit and Behavioral Physiology at the RIKEN Center for Brain Science in Wako-shi, Japan. He studied molecular and cell biology at the University of California, Berkeley, and then completed a PhD in the Department of Biology at the MIT. In 2009, he moved to Japan to start his laboratory at the RIKEN Brain Science Institute. For the last 14 years, his group has taken a multidisci-plinary approach to studying memory in the mouse, combining genetic tools and the field's deep understanding of hippocampal physiology to investigate how memories are formed, stored, and recalled in the mammalian brain and how damage from factors like stress and disease impair these functions. He was the recipient of the Japan Brain Science Foundation's Tsukahara award in 2019 and currently serves as the editor in chief of Neuroscience Research, the official journal of the Japan Neuroscience Society, and as a member of the Society for Neuroscience Public Education and Communication Committee.

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Special Session 5

Day 3 (August 26) **08:30-10:25** **Grand Ballroom**

Hormonal and neural control of metabolism in obesity and diabetes

Organizer : Sung Hee Choi (Seoul National University)
Hyung Jin Choi (Seoul National University)
Moderator : Min-Seon Kim (Ulsan University)
Hyung Jin Choi (Seoul National University)

1. Central effect of GLP-1 RA
   Julie Broe Honoré (Novo Nordisk)
2. Multifaceted effect of GLP-1 based therapy in obesity and diabetes management
   Jong-Woo Sohn (Korea Advanced Institute of Science and Technology)
3. Regulation of gut glucose absorption and insulin resistance in obesity
   Se Hee Min (University of Ulsan)
4. Targeting GFRAL neuron in the hindbrain for complex metabolic diseases
   Minho Shong (Korea Advanced Institute of Science and Technology)

SS5-1

The central effect of GLP-1 receptor agonists

Julie Broe Honoré

Clinical, Medical & Regulatory Department, Novo Nordisk Pharma Korea Ltd., Seoul 05510, Republic of Korea

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have revolutionized the treatment landscape for obesity and type 2 diabetes, not only through peripheral metabolic effects but also via profound actions within the central nervous system (CNS). This presentation will focus on the central mechanisms by which GLP-1 RAs regulate appetite, satiety, and energy balance. GLP-1 receptors are expressed in key brain regions including the hypothalamus, brainstem, and mesolimbic system, where their activation modulates both homeostatic and hedonic feeding pathways. These central effects are distinct from peripheral insulinotropic actions and are essential for the weight-reducing efficacy of GLP-1 RAs. Moreover, GLP-1 signalling in the CNS has been associated with reduced risk of neurocognitive and psychiatric disorders, suggesting broader neuroprotective roles. Understanding these central pathways provides a foundation for developing next-generation therapies that selectively target CNS GLP-1 receptors to optimize metabolic outcomes while minimizing adverse effects.

Keywords:GLP-1, CNS, Appetite, Neuroprotection, Metabolism

SS5-2

Neural mechanisms for the appetite-promoting effects of orexin

Jeewon Choi[1,4], Seyoung Jin[1,4], Eun-Seon Yoo[1], Daesoo Kim[2], Pann-Ghill Suh[3], Inkyung Jung[1*], Jong-Woo Sohn[1,2*]

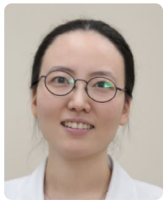
[1]Department of Biological Sciences and [2]Department of Brain & Cognitive Sciences, Korea Advanced Institute of Science and Technology, Daejeon 34141, South Korea. [3]Korea Brain Research Institute, Daegu 41062, South Korea.

Orexin (or hypocretin) is a neuropeptide that plays a key role in maintaining wakefulness and energy balance. While the neurocircuitry underlying orexin-induced wakefulness has been extensively studied, the neuronal circuitry mediating orexin-induced feeding remains poorly understood. Here, we show that orexin A unexpectedly activates a distinct subpopulation of the “appetite-suppressing” pro-opiomelanocortin (POMC) neurons in the arcuate nucleus of the hypothalamus to promote feeding. We demonstrate that the hypocretin receptor 2/phospholipase C β4-dependent closure of the M-type K^+ channels mediate orexin A-induced activation of POMC neurons and appetite. We further delineate the molecular profiles of orexin A-responsive POMC neurons using MERFISH, an advanced spatial transcriptomics technology, and show that *Pcsk1n* is the molecular marker of orexin A-activated POMC neuronal subpopulation. Finally, we show that the central opioid circuitry is activated downstream of orexin A-activated POMC neurons to increase food intake. Together, our work reveals the neural substrate underlying orexin A-induced feeding.

Keywords : Hypothalamus; Mouse genetics; Patch-clamp technique; Spatial transcriptome; Neural circuit

SS5-3

Regulation of gut glucose absorption to counteract insulin resistance by central nervous system



Se Hee Min, Hyo Sun Lim, Hyo Jin Kim, Chae Beom Park, Min-Seon Kim

Division of Endocrinology and Metabolism, Department of Internal Medicine, Asan Medical Center and University of Ulsan College of Medicine, Seoul [05505], South Korea

Hypothalamic neurons that produce proopiomelanocortin (POMC) play a pivotal role in regulating both energy balance and glucose metabolism. We demonstrate that cAMP-dependent protein kinase A (PKA) signaling in these neurons becomes activated following feeding as well as after treatment with glucagon-like peptide-1–based anti-obesity and antidiabetic drugs. To clarify the metabolic function of this pathway, we engineered mice with POMC-specific constitutive PKA activation by deleting the PKA regulatory subunit Prkar1a. These mice developed obesity, attributable to pituitary corticotroph PKA activation and resulting hypercortisolism. Although insulin resistance was aggravated, glucose tolerance was markedly enhanced through reduced intestinal glucose absorption and increased fecal glucose loss. Mechanistically, PKA activation in hypothalamic POMC neurons stimulated vagal motor neurons projecting to the upper gut, which in turn suppressed sodium/glucose cotransporter-1 (SGLT1)-mediated glucose uptake. Collectively, our findings reveal a previously unrecognized POMC–PKA–vagus–gut–SGLT1 signaling axis, highlighting its potential as a therapeutic target for improving glucose tolerance in insulin-resistant states.

Keywords: POMC neurons, PKA signaling, Vagus nerve–gut axis, Sodium glucose cotransporter-1 (SGLT1), Intestinal glucose absorption

SS5-4

Targeting GFRAL neuron in the hindbrain for complex metabolic diseases

Minho Shong

Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), 193, Munjiro, Yuseong-gu, Daejeon 34141, South Korea
Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), 193, Munjiro, Yuseong-gu, Daejeon 34141, South Korea

The hindbrain receptor GFRAL, restricted to the area postrema and nucleus tractus solitarius, is the sole known mediator of growth differentiation factor 15 (GDF15) signaling in the brain. This pathway integrates peripheral stress signals to regulate appetite, energy expenditure, and systemic metabolism. Its functional spectrum spans both physiological adaptation and pathological catabolism. Here, we present parallel evidence from models of mitochondrial stress and cancer-associated cachexia (CAC), each interrogated with Gfral-targeting antisense oligonucleotides (ASOs). In a brown adipose tissue (BAT)-specific Crif1 knockout model, mitochondrial dysfunction elevated circulating and cerebrospinal GDF15, activated GFRAL neurons, increased sympathetic preganglionic neuron firing, enhanced BAT thermogenesis, and induced browning of inguinal white adipose tissue (WAT). Retrograde viral tracing confirmed direct connectivity between GFRAL neurons and sympathetic circuits innervating thermogenic depots. Intracerebroventricular Gfral-ASO administration abolished the rise in energy expenditure and reversed WAT browning, demonstrating GFRAL's necessity in adaptive thermogenic compensation to mitochondrial stress. In murine models of high GDF15–secreting tumors, Gfral-ASOs selectively depleted hindbrain Gfral mRNA, restored body weight, preserved muscle and fat mass, improved grip strength, normalized energy expenditure, and extended survival, without reducing plasma GDF15 levels. No benefits occurred in low-GDF15 tumors, confirming target dependence. Compared with a GDF15-neutralizing antibody, Gfral-ASOs uniquely preserved muscle mass, highlighting receptor-level intervention as a potent anti-cachexia strategy.

Together, these findings identify GFRAL neurons as a central metabolic hub whose modulation can either blunt hypercatabolic states or drive thermogenic adaptation, underscoring the need to tailor therapeutic targeting to disease context.

Keywords : 1. GDF15–GFRAL signaling, 2. Antisense oligonucleotide therapy, 3. Mitochondrial stress response, 4. Cancer-associated cachexia, 5. Thermogenic adaptation

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Special Session 6

Supported By ISTeR Korea Center for Gendered Innovations for Science and Technology Research

Day 3 (August 26) **10:35-12:30** **Rm.204-205**

Spotlight on sexual dimorphism: Analyzing the importance of sex and gender analysis in neuroscience research

Organizer : Frank Kirchhoff (University of Saarland)
Heisook Lee (Korea Center for Gendered innovations for Science and Technology)
Mridula Bhalla (Institute for Basic Science)
Heajin Kim (Korea Center for Gendered innovations for Science and Technology)
Moderator : Frank Kirchhoff (University of Saarland)

1. Astroglial GABAB receptors: Decoding the Gender Puzzle in GHB-triggered Absence Seizures
   Frank Kirchhoff (University of Saarland)
2. Sexual dimorphism in neuroethology revealed by AI-driven behavioral analysis framework.
   Feng Wang (Shenzhen Institute of Advanced Technology)
3. Re-assessing Alzheimer's disease through a sex-specific lens: insights from public and organoid-based transcriptomic data
   Jong-Chan Park (Sungkyungkwan University)
4. Sex difference in neurodevelopment
   Eunha Kim (Korea University)
5. Q&A(15min)

SS6-1

Astroglial $GABA_B$ receptors: Decoding the Gender Puzzle in GHB-triggered Absence Seizures

Frank Kirchhoff

Center for Gender-specific Biology and Medicine (CGBM), University of Saarland, Homburg, Germany

Agonists of the metabotropic GABAB receptor (GABABR), including the endogenous metabolite γ-hydroxybutyric acid (GHB), induce or exacerbate absence seizures, non-convulsive epileptic events characterized by brief loss of consciousness, frequently associated with childhood epileptic syndromes that exhibit a female predominance. Activation of GABABRs has been shown to produce sexually dimorphic effects on functioning and behavioral output of the central nervous system (CNS). As active players in neural excitability and plasticity, astrocytes contribute to epileptic network priming and seizure activity. Here, we investigated the role of astroglial GABABR signaling in the pathological network function of GHB-induced absence seizures in female and male transgenic mice. Female mice displayed higher susceptibility to GHB administration in terms of seizure burden, electroencephalographic spectral alterations, and freezing behavior compared to male mice. Astroglial GABABR-deficient female mice exhibited reduced seizure burden and a shorter and less pronounced increase in δ-band power upon GHB administration. In contrast, the deletion of astroglial GABABRs only partially affected the susceptibility of male mice to GHB. Specifically in female mice, the loss of astroglial GABABRs protected against the emergence of hypersynchronous Ca2+ waves in cortical astroglial networks after GHB administration, as well as the increase in extracellular glutamate levels in the somatosensory cortex. These results show that astroglial GABABRs contribute to the pathological phenotype associated with absence seizures and exacerbate seizure burden. Moreover, these findings suggest that astroglial GABABRs are responsible for the increased GHB susceptibility in female mice. Therefore, astroglial GABABRs and their downstream signaling pathways represent a promising target for future research in epilepsy and potentially for novel pharmacological interventions in absence seizures.

Keywords : Astrocytes, Absence epilepsy, GABAB receptors, Mouse behavior

SS6-2

Sexual dimorphism in neuroethology revealed by AI-driven behavioral analysis framework.

Jialin Ye[1], Jingjing Liu[1], Xue Liu[1,2], Liping Wang[1], Feng Wang[1,2]

[1]The Brain Cognition & Brain Disease Institute , Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, China
[2]Neuroscience, Shenzhen University of Advanced Technology, Shenzhen, China

Understanding how sexually dimorphic neural mechanisms shape distinct neuroethological traits—from molecular pathways to circuit connectivity—remains a fundamental challenge in neuroscience. Species exhibit innate behavioral repertoires with pronounced sexual dimorphism, paralleling sex-biased prevalence and symptomatology in neuropsychiatric disorders. To address this, we integrate machine learning-driven behavioral phenotyping with neural circuit tracing and modulation, pursuing two primary goals: advancing data-driven behavioral genomics and deciphering sex-specific behavioral traits alongside their mechanistic underpinnings. Since behavior comprises modular components governed by inherent logic, its structural deconstruction is essential for mechanistic insight. Here, we establish a Hierarchical Behavioral Analysis Framework (HBAF) that decodes organizational principles of behavioral modules through high-dimensional data analysis. Using a spontaneous behavior paradigm, HBAF enables rapid, accurate behavioral state assessment and bridges theoretical behavioral models with multidimensional data analytics (Ye et al., 2025, *Cell Reports*). Through HBAF, we can accurately characterize the behavioral traits of male and female *Shank 3b* mice across three different genotypes (Liu et al., 2024, *Neuroscience Bulletin*). This approach revealed that male and female mice employ distinct strategies to evade threats, although their evasion abilities remain stable throughout their lifespan (Liu et al., 2022, *BMC Biology*).

Keywords : Neuroethology, Sex differences , Machine learning
Acknowledgements : This work was supported by the National Science and Technology Innovation 2030-Major Project of China (grant 2022ZD0208300 to F.W.), the National Natural Science Foundation of China (grant 32371062 to F.W., 31630031 and 31930047 to L.W.).

SS6-3

Re-assessing Alzheimer's Disease through a Sex-Specific Lens: Insights from Public and Organoid-based Transcriptomic Data

Jong-Chan Park

Department of Biophysics, Sungkyunkwan University, Suwon, Republic of Korea

Sex differences in Alzheimer's disease (AD) are increasingly recognized, yet the molecular basis remains unclear. Building on our previous study (Park *et al., Experimental & Molecular Medicine*, 2023), which identified six sex-associated AD genes, we further investigate their relevance using both public bulk transcriptomic datasets and our own RNA-seq data from AD and control brain organoids. We analyzed the expression patterns of these six genes across datasets and assessed their consistency in our organoid model. In addition, we screened public AD datasets for other reported sex-specific genes and validated selected candidates using our organoid transcriptomes. This combined approach enables cross-validation of sex-related molecular features and highlights organoids as a relevant model to study sex-specific mechanisms in AD. Our findings provide insight into how sex influences AD pathology and may inform future biomarker discovery and therapeutic development.

Keywords : Sex difference, Alzheimer's disease, Brain Organoid, Biomarker, Public database

SS6-4

Sex differences in neurodevelopment

Eunha Kim

Department of Neuroscience, Korea University College of Medicine, Seoul, Republic of Korea

Neurodevelopmental disorders, such as autism spectrum disorder, exhibit a markedly higher prevalence in males than in females. The placenta, a key component of the maternal-fetal interface, plays a crucial role in fetal development. Emerging evidence suggests that the placenta contributes to sex differences in the prevalence of certain developmental disorders, including neurodevelopmental conditions. To investigate fetal sex-specific transcriptional changes within the placenta at a molecular level, we conducted single-cell RNA sequencing. Our analysis revealed that trophoblasts associated with male fetuses exhibited lower expression of interferon (IFN)-stimulated genes (ISGs) compared to those linked to female fetuses. Notably, maternal immune activation (MIA), which induces neurodevelopmental abnormalities predominantly in male offspring, disrupted these sex-specific differences in the placenta. To explore the potential connection between sex-specific ISG expression and neurodevelopmental outcomes in MIA offspring, we selectively deleted IFN alpha and beta receptor subunit 1 (IFNAR1) in trophoblasts. Loss of IFNAR1 in the placenta mitigated MIA-induced behavioral abnormalities in male offspring. These findings highlight the complex nature of sex-specific IFN signaling at the maternal-fetal interface and its contribution to the sex-biased neurodevelopmental effects observed in MIA models.

Keywords : Neurodevelopmental disorders, Sex-bias, Placenta

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Educational Session 1

Supported By JS ENST 진성인스트루먼트(주) JINSUNG INSTRUMENTS, INC

Day 2 (August 25) **10:35-13:00** **Rm.104-106**

Optical techniques in neuroscience

Organizer : Hyeyoung Shin (Seoul National University)
Hyung Jin Choi (Seoul National University)
Min Whan Jung (Korea Advanced Institute of Science and Technology)
Moderator : Hyeyoung Shin (Seoul National University)

1. Probing neural codes with two-photon holographic optogenetics
   Hillel Adesnik (University of California, Berkeley)
2. Applying two-photon imaging and stimulation in mouse cortex
   Ilsong Choi (Korea Advanced Institute of Science and Technology)
3. Optical, molecular, and computational approaches for next-generation holographic optogenetics
   YoungJu Jo (Stanford University)
4. Patterned optogenetic stimulation
   Jongmin Yoon (Seoul National University)
5. Single-cell neural activity imaging in freely moving mice
   Hyung Jin Choi (Seoul National University)
6. Miniature two-photon microscopy for freely moving animals
   Runlong Wu (Beijing Information Science and Technology University)

EDU1-1

Probing neural codes with two-photon holographic optogenetics

Ilsong Choi[1], Ye Jin Kim[2], Seung-Hee Lee[1,2,3]

University of California, Berkeley Department of Neuroscience Berkely, California 94720 USA

I will present advances in the monitoring and manipulation of neural activity with cellular resolution and millisecond precision. I will discuss new methods to massively scale up the addressable volume of two-photon holographic optogenetics, new all-optical techniques for functional connectomics, new approaches for two-color bidirectional optogenetics, and a means to achieve 'super-resolution' optogenetics. These advances help scale up and increase the resolution of the optical control of brain activity and permit the direct longitudinal tracking of synaptic weights for the first time in the mammalian brain.

Keywords:Optogenetics; Two photon imaging; Holography; Neural circuits; Connectomics

EDU1-2

Applying two-photon imaging and stimulation in mouse cortex

Ilsong Choi[1], Ye Jin Kim[2], Seung-Hee Lee[1,2,3]

[1]Center for Synaptic Brain Dysfunctions, IBS, Daejeon, Republic of Korea, [2]Department of Brain and Cognitive Sciences, KAIST, Daejeon, Republic of Korea, [3]Department of Biological Sciences, KAIST, Daejeon, Republic of Korea

Decision-making in animals relies on integrating multisensory information. Previous studies have shown that animals exhibit different behavioral responses to multisensory stimuli depending on the combination of modality-specific stimuli with distinct contingencies. However, it is unclear how learning the contingency of sensory stimuli shapes cortical circuits to induce such specific behavioral responses. Here, we found that learning shapes inhibitory circuits in the posterior parietal cortex (PPC) to exert modality and contingency-specific inhibition. We trained mice with audiovisual Go/No-go discrimination tasks and measured neural activities of layer 2/3 neurons in the PPC and the primary visual cortex (V1) by performing *in vivo* two-photon calcium imaging. In the naïve mice, PPC neurons exhibited broad auditory-to-visual inhibition across all multisensory stimulus pairs. However, in the expert mice, selective auditory-to-visual suppression emerged in the PPC only between incongruent stimulus pairs, not congruent ones. This cross-modal inhibition was absent in the V1. Using targeted optogenetic activation of single neurons during calcium imaging, we found that the auditory-responsive parvalbumin-expressing (PV^+) neurons broadly inhibited visual neurons in naïve mice, but selectively inhibited them in expert mice. Collectively, these results demonstrate that contingency learning across sensory modalities forms a selective cross-modal inhibitory circuit in the PPC, not in the V1, leading to contingency-dependent cross-modal competition in the PPC. Our study highlights the power of combining calcium imaging with single-neuron photostimulation using two-photon microscopy to investigate plasticity in cortical circuits *in vivo*.

Keywords : Learning, multisensory integration, In vivo calcium imaging, single-neuron photostimulation
Acknowledgements : This work has been supported by grants to S.H.L. from the Institute for Basic Science (IBS-R002-A2).

EDU1-3

Optical, molecular, and computational approaches for next-generation holographic optogenetics

YoungJu Jo

Department of Bioengineering, Stanford University, Stanford, California, USA

Holographic optogenetics promises cellular-resolution control of neural population dynamics in behaving animals. However, the technology is still in its early days, which calls for innovations to scale up its capabilities. In this talk, we will present multifaceted approaches to push the limits of holographic optogenetics. First, we engineered a new family of channelrhodopsins through structural and functional characterization of recently discovered potassium-selective channelrhodopsins. Their performance represents the state of the art in both excitatory and inhibitory tools, enhancing the light efficiency and scalability of holographic optogenetics. Next, we devised wavefront engineering methods to improve the effective spatial resolution and field-of-view. Finally, we developed computational tools to design stimulation patterns in both space and time, which are increasingly crucial as we scale up holographic optogenetics. These converging advances pave the way for next-generation optogenetics for probing and controlling neural computations at unprecedented precision.

Keywords : optogenetics, channelrhodopsin, holography, wavefront engineering, computational modeling

EDU1-4

Patterned optogenetic stimulation

Jongmin Yoon[1,2], Myunghwan Choi[1,2]

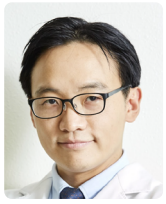
[1]School of Biological Sciences, Seoul National University, Seoul, Republic of Korea
[2]The Institute of Molecular Biology and Genetics, Seoul National University, Seoul, Republic of Korea

By enabling precise control of neuronal activity via light-activated ion channels, optogenetics is a powerful tool for dissecting neural circuits with high temporal resolution. Traditional implementations of optogenetics often rely on wide-field illumination, which lacks spatial specificity and can lead to unintended activation of neighboring neural populations. Patterned optogenetics addresses this critical limitation by selectively projecting light only to desired neural populations, typically with the use of digital micromirror devices (DMDs) that can dynamically shape illumination patterns with microsecond precision. Patterned optogenetics offers several distinct advantages including rapid stimulation rates, large field of view coverage, and straightforward integration with existing optical systems. These capabilities come at the expense of axial precision and limited stimulation depth compared to holographic optogenetics approaches, which utilize spatial light modulators but require more complex optical setups. In this session I will present the fundamental principles and diverse applications of patterned optogenetics, beginning with foundational applications to unveil cellular connectivity in vitro. We will then explore the translation of these techniques to in vivo applications, demonstrating how patterned optogenetics enables investigation of cortex-wide connectivity patterns in behaving animals. Lastly, we will discuss emerging applications including cortex-wide activity replay systems in the primate motor cortex, which demonstrate the potential for recreating complex spatiotemporal neural activity patterns observed during natural behaviors.

Keywords : Patterned optogenetics, Optogenetics, Connectivity
Acknowledgements : This work was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF), funded by the Ministry of Education, Science, and Technology (RS-2024-00334680, RS-2024-00436783, RS-2024-00466703, 2020R1A5A1018081)

EDU1-5

Single-cell neural activity imaging in freely moving mice



Hyung Jin Choi

Department of Brain and Cognitive Sciences, Department of Anatomy and Cell Biology, Seoul National University, Seoul

Understanding how individual neurons contribute to specific behaviors requires precise neural activity imaging aligned with well-designed behavioral paradigms. This talk presents a framework for investigating behavior-time-locked neuronal roles using single-cell-level neural activity imaging in freely moving mice. We emphasize the importance of designing behavioral tasks that directly test neuroscience hypotheses, ensuring precise temporal alignment between neural activity and behavioral events. Understanding how individual neurons contribute to specific behavioral processes, such as food discovery, approach, consumption, reward learning, and extinction memory, requires precise neural activity imaging aligned with well-structured behavioral paradigms. We emphasize the importance of designing behavioral tasks that capture key moments in reward-related behaviors, ensuring precise temporal alignment between neural activity and behavioral transitions. By integrating advanced single-cell-level neural activity imaging techniques with hypothesis-driven behavioral paradigms, we aim to elucidate the neuronal mechanisms underlying reward processing and learning, providing new insights into neural circuit function.

Keywords : Single-cell, Freely-moving, Behavior-time-locked, Hypothesis testing.

EDU1-6

Miniature Two-Photon Microscopy for Freely Moving Animals

Runlong Wu

Beijing Information Science & Technology University, School of Instrument Science and Optoelectronics Engineering, Beijing, China

Here we present the FHIRM-TPM 3.0, a 2.6 g miniature two-photon microscope capable of multicolor deep-brain imaging in freely behaving mice. The system was integrated with a broadband anti-resonant hollow-core fiber featuring low transmission loss, minimal dispersion from 700-1060 nm, and high tolerance of laser power. By correcting chromatic and spherical aberrations and optimizing the fluorescence collection aperture, we achieved cortical neuronal imaging at depths exceeding 820 μm and, using a GRIN lens, hippocampal Ca^{2+} imaging at single dendritic spine resolution. Moreover, we engineered three interchangeable parfocal objectives, allowing for a tenfold scalable field-of-view up to 1×0.8 mm^2, with lateral resolutions ranging from 0.68 to 1.46 μm. By multicolor imaging at excitation wavelengths of 780 nm, 920 nm and 1030 nm, we investigated mitochondrial and cytosolic Ca^{2+} activities relative to the deposition of amyloid plaques in the cortex of awake APP/PS1 transgenic mice. Thus, the FHIRM-TPM 3.0 provides a versatile imaging system suitable for diverse brain imaging scenarios.

Keywords : Two-photon microscopy, Miniature, Freely behaving mice, Neuroimaging, Neuroscience

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Educational Session 2

Day 2 (August 25) **15:30-17:30** **Premier Ballroom C**

History of neuroscience

Organizer : C. Justin Lee (Institute for Basic Science)
Seung-Hee Lee (Korea Advanced Institute of Science and Technology)
Moderator : C. Justin Lee (Institute for Basic Science)

1. The development and milestones in the history of chinese neuroscience
   Yun Wang (Peking University)
2. Fifty happy years of neuroscience in Japan with major milestones of Japan Neuroscience Society
   Keiji Tanaka (RIKEN)
3. Neuroscience in the western world: Historical milestones
   Alexej Verkhratsky (University of Manchester)
4. The role of basic science policy in the history of neuroscience: A Comparative Perspective on the U.S. and South Korea
   Youjung Shin (Jeonbuk National University)

EDU2-1

The Developmental History of Neuroscience in China — A Century in Five Phases

Yun Wang

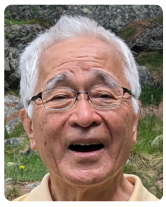
Department of Neuroscience, Peking University, Beijing, 100191, China

This review traces China's neuroscience evolution through five concise phases. Stage 1 (early 20th century–1949): Western anatomy and physiology entered Chinese medical education; returnee physicians and physiologists founded university laboratories, launched neuroanatomy and basic neurophysiology (e.g., electromyography, reflex studies), and seeded clinical neurology services. Stage 2 (1949–1966): The new state prioritized science, expanding universities, research institutes (including CAS units), and hospital neurology departments; animal electrophysiology (EEG, single-unit recording) and early clinical diagnostics were implemented and formal neurology curricula established. Stage 3 (1966–1976): The Cultural Revolution severely disrupted research and training, halted academic exchange, and depleted human and material capital, producing long-term setbacks. Stage 4 (late 1970s–2000s): Reform and Opening Up restored international collaboration and investment; modern electrophysiology, neuroimaging, and molecular methods were introduced, and dedicated neuroscience departments, key laboratories, and journals were founded. Stage 5 (2000s–2010s): Rapid, technology-driven expansion (fMRI, PET, multichannel electrophysiology, optogenetics, single-cell techniques) and major national programs enabled interdisciplinary growth in memory, sensory coding, synaptic plasticity, and disease mechanisms, alongside clinical advances in neurointervention and rehabilitation. Since 2016, the China Brain Project has strategically funded brain atlases, circuit function studies, disease-mechanism research, and brain-inspired computing, accelerating large collaborations, data-sharing platforms, primate models, and translational pipelines. Key challenges remain: strengthening original theoretical innovation, smoothing interdisciplinary-to-clinic translation, resolving ethical and reproducibility issues (notably in primate research), and building robust long-term data governance. Continued focus on foundational discovery, ethical oversight, standardized data infrastructure, and international cooperation will position Chinese neuroscience to make substantial global contributions to understanding brain function and to advancing treatments for brain disease.

Keywords : History of neuroscience; China; brain mapping; China Brain Project; translational neuroscience

EDU2-2

Fifty happy years of neuroscience in Japan with major milestones of Japan Neuroscience Society



Keiji Tanaka

RIKEN Center for Brain Science, Wako, 351-0198, Japan

The Japan Neuroscience Society was founded in 1974 as an interdisciplinary society in neuroscience. It has now ~6,400 members, including those working at the molecular, cellular, and systems levels, those using experimental and theoretical approaches, and those conducting curiosity-driven and applied research. The annual conferences attract 3,000~4,000 participants and ~2,000 presentations.

The most important event in the development of neuroscience in Japan is the public recognition of neuroscience as a strategic basic research field around 2000. Under the slogan of “Understanding the brain”, “Protecting the brain”, and “Creating the brain”, ample research funds were allocated to both basic and applied research, and thereby participation from different fields was promoted, and neuroscience was established as an interdisciplinary research field.

Facing a serious decay of budget several years later, the community of neuroscientists made efforts of outreach to the public and political decision makers, and recovered the budget as the Brain Program (2008~2020) and Brain/MINDS (2014~2023), followed by Brain/MINDS 2.0 (2024~). The Brain Program made clearer load maps to help the society, while Brain/MINDS focused on studying the marmoset brain in a systematic way to link the basic research in rodent models with the clinical research in humans.

Finally, I would like to share my personal views on lessons we can learn from history for the future. First, it is important to continue supporting both basic and applied research. If the support put aside basic research, applied research will also be weakened. Secondly, the pursuit of principles is also important in applied research. Thirdly, it is important to develop research policy through community-wide discussions. Fourthly, the scope of applications should be widened, beyond the fields of medical and engineering to include education, childcare, and development of guidelines for ethics and law.

Keywords:Strategic basic research, Understanding the brain, Protecting the brain, Creating the brain

EDU2-3

Neuroscience in the Western World: Historical Milestones

Alexei Verkhrartsky

The University of Manchester, Oxford Road, Manchester M13 9PT, UK

Neuroscience, like most divisions of natural philosophy, emerged in the classical Hellenistic period following experimental discoveries of the nerves connecting the brain with the body. The ventricular-pneumatic doctrine, introduced by Herophilus and Erasistratus and perfected by Galen, considered a specific substance, pneuma, as a substrate for brain function. The pneuma, responsible for information processing, memory and decision making, was generated in the brain ventricles, and transported through the hollow nerves signalling thus signalled to peripheral organs. In the 17th century, Tomas de Willis and Marcello Malpighi recognised cortical grey matter as the site of higher brain functions, while at the end of 18 century Franz Joseph Gall (father of phrenology) introduced the concept of regional localisation of brain functions. This concept was further developed by Paul Broca, Gustav Theodor Fritsch, Eduard Hitzig, David Ferrier, and Wilder Penfield who produced detailed map of the functional segregation of the brain. The nerve cells and their processes were visualised by Antonie van Levenhoeek, Emanuel Swedenborg, Felice Fontana, Henri Dutrochet, Christian Ehrenberg, and Johann Purkyňe, while the term nerve cell was proposed by Robert Todd in 1845. The neuroglia was invented by Rudolf Virchow in 1850 and the word neuron was coined by Wilhelm von Waldeyer in 1891. Neuronal function, electrical excitability and neurotransmission were developed over two centuries. In 1791 Luigi Galvani introduced animal electricity, and Herman von Helmholtz measured the speed of propagating action potential in 1850. The ionic theory of neuronal excitability was initially considered by Julius Bernstein and was elaborated and perfected by Alan Hodgkin and Andrew Huxley in 1952. The foundation of neurotransmission and synaptic connectivity were laid down by Charles Sherrington, Otto Loewi, Henry Dale, Ulf von Eyler, and Jon Eccles. Technological progress which provides new perspectives marks the 21st century and the century of the brain.

Keywords : Neuroscience, History, ventricular-pneumatic doctrine, neurone, neuroglia

EDU2-4

The Role of Basic Science Policy in the History of Neuroscience: A Comparative Perspective on the U.S. and South Korea.

Youjung Shin

Department of Science Studies, Jeonbuk National University, Jeonju, 54896, South Korea

What was the role of science policy in the history of neuroscience? In conventional accounts, we often hear about how new scientific ideas, laboratory experiments, and discoveries led to the development of the field. However, activities outside laboratories also played an important role in shaping the field's development trajectory. This presentation shows that governmental policy, especially basic science policy, played a crucial role in shaping the initial form of neuroscience in the U.S. in the 1960s, as well as shaping its development in South Korea in the 1980s. From a comparative perspective, this presentation examines first 1) the way the Neurosciences Research Program was shaped at MIT in the U.S. – the moment when the term, neuroscience, was first coined – in the early 1960s, and then analyzes 2) the institutionalization of neuroscience in South Korea in the late 1980s through the establishment of new academic societies and research centers, culminating in the launch of the Korean Society for Neuroscience in 1992. By doing so, this paper highlights how to understand the dynamics between science and policy, which would deepen our understanding on the varieties of the development of neuroscience, and its implications on the future development of neuroscience in East Asia.

Keywords : Science policy, Basic research, Neurosciences Research Program, South Korea, Pluralism

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Educational Session 3

Supported By 라이노바이오(주)

Day 3 (August 26) **10:00-12:30** **Rm.104-106**

Miniature brain models: from generation to application in studying brain development and function

Organizer : Jin-A Lee (Hannam University)
Ki-Jun Yoon (Korea Advanced Institute of Science and Technology)
Jinju Han (Korea Advanced Institute of Science and Technology)
Jinsoo Seo (Yonsei University)
Moderator : Jinsoo Seo (Yonsei University)

1. Modeling human brain development and disease with organoids
   Girogia Quadrato (University of Southern California)
2. Reprogramming techniques for generating induced pluripotent stem cells from human somatic cells
   Haneul Choi (Hannam University)
3. Multiplexed cell-based assays for evaluating the structure and function of excitable cells
   Austin Passaro (Axion Biosystems, Inc.)
4. Generation and application of xenotransplantation rodent models using human embryonic stem cells
   Kiheon Lee (Korea Advanced Institute of Science and Technology)
5. Development and application of a blood-brain barrier organ-on-a-chip model
   Tae-Eun Park (Ulsan National Institute of Science and Technology)
6. Modeling brain-on-a-chip platforms for the study of brain electrophysiological function
   Hong Nam Kim (Korea Institute of Science and Technology)

EDU3-1

Upgrading the physiological relevance of human cerebellar organoids

Giorgia Quadrato[1, 2]

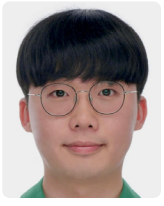
[1]Department of Stem Cell Biology and Regenerative Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA
[2]Eli and Edythe Broad CIRM Center for Regenerative Medicine and Stem Cell Research at the University of Southern California, Los Angeles, CA 90033, USA

The lack of relevant models has constrained human cerebellar development research. We present a novel human cerebellar organoid (hCerO) system that recapitulates the cellular diversity and distinct functional features of the fetal cerebellum. Our hCerOs develop complex cytoarchitecture, including transient laminar organization, and demonstrate functional neuronal connections with coordinated network activity. Long-term culture allows for the maturation of Purkinje cells exhibiting molecular and electrophysiological characteristics of their in vivo counterparts. By integrating these organoids with single-cell -omics techniques and bioengineering methods, our goals are to 1. reconstruct the developmental lineage and dynamic events of individual cells during human cerebellar neurogenesis in both health and disease, and 2. identify disease mechanisms specific to brain regions and cell types. Ultimately, our aim is to provide new insights and tools to understand cerebellar development and disease mechanisms, contributing to foundational knowledge in the field.

Keywords : Brain organoids, Neurodevelopmental disorders, Bioengineering, Cerebellar Organoids, Regional patterning

EDU3-2

Reprogramming techniques for generating induced pluripotent stem cells from human somatic cells



Haneul Choi[1], Semin Park[1], Jin-a Lee[1]

[1]Department of Biological Sciences and Biotechnology, College of Life Sciences and Nanotechnology, Hannam University, Daejeon, [34054], Korea

Induced pluripotent stem cells (iPSCs) are an innovative technology first developed by Shinya Yamanaka in 2007, in which somatic cells are reprogrammed into pluripotent stem cells through the introduction of defined transcription factors. Since the development of iPSC reprogramming, iPSCs have become a pivotal tool in disease modeling, cell therapy, and drug screening. Multiple protocols have been developed for iPSC generation, varying in the choice of somatic cell type and gene delivery system, each affecting reprogramming efficiency, genomic stability, and downstream applications. In this talk, I will overview of current iPSC reprogramming techniques and optimized protocols for generating high-quality iPSC lines. These protocols will include both fibroblast and PBMC based approaches, highlighting their respective workflows, key technical points, and quality control measures. By comparing these strategies, this talk will provide practical guidance for selecting the most suitable method for specific research goals.

Keywords : iPSC, Reprogramming, Fibroblast, PBMC

EDU3-3

Functional characterization of complex neural models: new tools for organoids, spheroids, and organ-on-chip platforms

Austin Passaro

Axion BioSystems, Atlanta, Georgia, USA

Complex human iPSC-derived cell models (e.g., spheroids, organoids, and organ-on-chip devices) are drastically changing neurological disorder research and therapeutic development. These models are more physiologically relevant, providing a closer representation of the human brain compared to traditional methods. To characterize functional activity of these models, live-cell analysis platforms such as high-throughput Maestro MEA and AI-powered Omni imaging are being used. These powerful tools provide deep insights into human biology, across various stages and applications from generating cell lines and 3D models to modeling diseases and screening potential therapeutics. This talk will provide an overview of how these technologies work together through Axion's Connected Lab, as well as new solutions tailored to label-free functional assessment of 3D iPSC-derived models.

Keywords : Microelectrode array, live-cell imaging, stem cell, organoids, spheroids

EDU3-4

Beyond the dish: a new brain somatic mutation model via human neuron transplantation into mouse brain

Ki-Heon Lee[1], Hyoun-Ji Yun[1], Chan-Woo Park[1], Sang-Min Park[2], Young-Hee Joo[2], Eun-Ji Shin[2], Hyunsoo Jang[1], Jiye Han[1], Jeong-Ho Lee[2,3], Ki-Jun Yoon[1]

[1]Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Daejeon, 34141, Republic of Korea
[2]SoVarGen Co., Ltd., Daejeon, 34051, Republic of Korea
[3]Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology, Daejeon, 34051, Republic of Korea

Somatic mosaicism, which arises at the somatic cell level after fertilization, has been increasingly recognized as a potential contributor to various developmental disorders. Such findings have provided valuable insights into brain development and have significantly advanced our understanding of the developmental origins of neurodevelopmental disorders. Nevertheless, the absence of precise models capable of recapitulating somatic mosaicism has limited human-specific studies and the establishment of human-specific characteristics. Here, we aim to establish a human somatic mosaicism model by transplanting human cortical neurons into the mouse brain. By recapitulating the long-term development of human neural cells in an in vivo environment, this approach enables the study of somatic mutation–driven brain diseases in humans. We generate human forebrain organoids (hFBOs) from MTOR mutant human embryonic stem cells, comprehensively characterize their cellular and electrophysiological phenotypes, and identify their specific features in vivo through a transplantation model. Our study highlights the potential of an in vivo transplantation model to reveal the characteristics of human somatic mosaicism.

Keywords : Transplantation, Human forebrain organoid, Neurodevelopmental disorder, Somatic mosaicism, In vivo modeling

EDU3-5

Exploring brain drug delivery with a human blood-brain barrier-on-a-chip model

Tae-Eun Park, Ph.D.

Department of Biomedical Engineering, Ulsan National Institute of Science and Technology (UNIST)

Organ-on-a-chip technology, which accurately replicates the structural and dynamic features of in vivo vasculature, has emerged as a powerful platform for identifying vascular-targeted drug delivery systems (DDS). In this study, a blood–brain barrier (BBB) chip model outperformed conventional transwell systems for nanocarrier screening, owing to its faithful reproduction of the endothelial glycocalyx and physiological shear stress. This enhanced physiological relevance enabled the discovery of BBB shuttles with improved in vivo functionality.

Leveraging this approach, we established a microphysiological system (MPS)-based DDS screening strategy to identify BBB-penetrating aptamers and peptides. Using a dual-channel BBB chip composed of human brain microvascular endothelial cells, astrocytes, and pericytes, we successfully screened and validated novel aptamers and peptides that promote protein transport across the BBB via clathrin-mediated endocytosis. These shuttles exhibited high targeting specificity and efficient brain accumulation both in vitro and in vivo.
Mechanistic studies revealed that the dynamic recapitulation of the brain endothelial glycocalyx under fluidic conditions accounts for the BBB chip's superior performance over traditional static models in DDS screening. Collectively, these findings highlight the potential of MPS not only for DDS screening but also for the functional discovery of BBB-penetrating shuttles under physiologically relevant conditions.

Keywords : Microphysiological system, blood-brain barrier (BBB), endothelial glycocalyx, drug delivery, BBB shuttle

EDU3-6

Brain-on-a-chip technology for modeling aging-associated brain diseases

Minjeong Jang[1], Hae-June Lee[2], Eun U Seo[3], Hong Nam Kim[3]

[1] Division of Radiation Biomedical Research, Korea Institute of Radiological and Medical Sciences, Seoul, 01812, Republic of Korea
[2] College of Veterinary Medicine, Jeju National University, Jeju, 63243, Republic of Korea
[3] Brain Science Institute, Korea Institute of Science and Technology, Seoul, 02792, Republic of Korea

As life expectancy continues to rise, addressing aging and age-related diseases is essential for maintaining a healthy lifestyle. While animal models have been widely used to study brain aging, they fail to fully replicate the aged phenotype of human brain diseases due to differences in lifespan and genetic heterogeneity. To bridge this gap, we present an aged brain model by culturing human brain-originated cells within an aging-mimetic hydrogel matrix. Specifically, we utilized an advanced glycation end-product (AGE)-anchored matrix as a cell culture platform. Cells cultured in this matrix exhibited key aging-related characteristics, including the accumulation of neurotoxic proteins, impaired barrier function, and epigenetic alterations. Notably, these aged phenotypes could be modulated by targeting key regulatory factors. Our model offers an innovative approach for studying human brain aging, providing a more physiologically relevant system for understanding age-related neurodegenerative processes.

Keywords : Brain aging, Brain-on-a-chip, Disease modeling, Extracellular matrix

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Educational Session 4

Supported By INTERNATIONAL BRAIN IBRO RESEARCH ORGANIZATION

Day 3 (August 26) **15:00-17:00** **Rm.104-106**

Advancing neuroscience futures: a career development workshop

Organizer : Jaekyung Kim (Korea Advanced Institute of Science and Technology)
Gunsoo Kim (Korea Brain Research Institute)
Moderator : Jaekyung Kim (Korea Advanced Institute of Science and Technology)

1. Navigating the path to professorship
   Tae-Kyung Kim (Pohang University of Science and Technology)
2. Building a Career without Borders: Embracing the Unexpected
   Sohyon Lee (Korea Advanced Institute of Science and Technology)
3. Pursuing a Biotech and Pharma Career
   Junghuyn Hahn (Boehringer Ingelheim)
4. A Scientist's Journey into Entrepreneurship: Navigating the Transition from Bench to Business
   Eunyoung Park (AinB)
5. Park Jun-seok (Daewoong Pharmaceutical Center)

EDU4-1

Navigating the path to professorship

Tae-Kyung Kim, Ph.D.

Department of Life Sciences, Pohang University of Science and Technology (POSTECH), Pohang, 37673, South Korea

How do you turn years of research training into a thriving academic career? In this workshop, I will share my personal journey—starting as a tenure-track professor in the United States, earning tenure, and later returning to Korea to continue my professorship—highlighting the lessons, challenges, and turning points along the way. Together, we will explore what it truly takes to secure a faculty position, navigate the tenure process, and build a sustainable and impactful career as a scholar. I will offer practical strategies for career planning, mentorship, and competitive grant writing, while also reflecting on the mindset and resilience needed to flourish in academia. Through candid stories and interactive conversations, my goal is to inspire and equip you to take confident steps toward your own academic future—whether in Korea, the U.S., or anywhere your aspirations lead.

Keywords : Professorship, Tenure, Career development, Job interview, Grant writing

EDU4-2

Building a Career without Borders: Embracing the Unexpected

Sohyon Lee, Ph.D.

Department of Biological Sciences, Korea Advanced Institute of Science & Technology (KAIST), Daejeon, 34141, South Korea

Some careers take the straight road, and others take the scenic route across different continents and disciplines. In this workshop, I'll share my own cross-continental journey moving between the United States, South Korea, Switzerland, and back again. Through navigating PhD research, postdoctoral work, and now beginning a professorship, I've found that serendipitous detours, shifting interests, and new environments often lead to the most meaningful opportunities. We'll explore how to balance structure with openness, know when to pivot, and see why success doesn't always require a fixed destination. I will also highlight the importance of finding the right mentor - and the right style of mentorship - for your personal and professional growth. Through candid reflections and practical insights on job applications, scientific communication, and mentoring, this session will encourage you to see your career as a dynamic, evolving journey - one that thrives not despite uncertainty, but because of it.

Keywords : Professorship, Postdoc, Mentoring, Scientific Communication, Career development

EDU4-3

Pursuing a Biotech and Pharma Career

June Hahn, PhD

Business Development and Licensing Korea, Boehringe Ingeheim, Seoul, Korea

In this session, I will provide future innovators with a realistic and encouraging introduction to careers in the biotechnology and pharmaceutical industries. Topics will include an overview of new drug R&D activities, essential skills & qualifications, various career pathways and the mindset needed for success. Together with the following Q&A session, I hope participants will gain a clearer understanding of industry careers and feel more confident in pursuing happiness in science.

Keywords : Biotech, Pharma, Career, Science, Happiness

EDU4-4

A Scientist's Journey into Entrepreneurship: Navigating the Transition from Bench to Business

Eun Young Park, PhD, CEO&Co-founder

AinB Inc., (Artificial Intelligence in Bioscience), 13840. Korea

This session offers an honest and practical perspective on the transition from academic researcher to biotech founder. It details my non-linear career path—from a PhD in cancer research through diverse roles in industry, including regulatory affairs, IND execution, and AI integration—which culminated in the founding of AinB Inc., an AI-powered antibody discovery company. This journey highlights a crucial lesson: the path to entrepreneurship is often not a straight line but an accumulation of diverse skills, providing a holistic view of the biopharmaceutical landscape that is invaluable for a founder.

The talk will explore the fundamental mindset shift required for this transition: moving from a focus on personal technical skills to solving significant, market-defined problems. We will discuss how to leverage the inherent strengths of a scientific background—such as analytical thinking and hypothesis-driven problem-solving—while frankly addressing the common weaknesses. A central theme will be the scientist's typical blind spot: monetization. I will discuss the critical process of translating scientific discovery into a compelling economic value proposition, applying the same rigor used in the lab to the development of a sustainable business model.

Furthermore, the presentation will break down the three pillars of building a sustainable venture: a rock-solid scientific foundation (The 'What'), a vision-aligned, multidisciplinary team (The 'Who'), and a robust strategic plan (The 'How'). Key learnings will be shared on cultivating the non-scientific competencies essential for leadership, including effective communication with stakeholders, strategic decision-making, and building a resilient organizational culture. This talk aims to demystify the entrepreneurial journey for scientists, providing them with a realistic roadmap and the inspiration to translate their research into world-changing impact.

Keywords : Biotech Entrepreneurship, Scientist-Founder, Career Transition, Biotech Startup. Mindset Shift

August 24(Sun)- 27(Wed), 2025

Songdo Convensia, Incheon, Korea

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Educational Session 5

Day 4 (August 27) **12:30-14:25** **Rm.104-106**

How to write "high-impact papers"?

Organizer : Seung-Hee Lee (Korea Advanced Institute of Science and Technology)
Moderator : C. Justin Lee (Institute for Basic Science)

1. In the quest of the neural mechanism of emotion and social behaviors
   Hailan Hu (Zhejiang University)
2. Learning the Hard Way: What lots of failure and a bit of success has taught me about publishing papers
   Thomas McHugh (RIKEN)
3. From Discovery to Presentation: Writing Scientific Papers That People Remember
   Greg Seong-Bae Suh (Korea Advanced Institute of Science and Technology)

EDU5-1

In the quest of the neural mechanism of emotion and social behaviors

Hailan Hu

Zhejiang University

In this talk, I will share personal experience from my lab's published work -- including my first paper as a PI -- on navigating key challenges in scientific writing. I will discuss: How to choose an important problem? How to make a complete logic chain? And, how to handle unexpected results?

EDU5-2

Learning the Hard Way: What lots of failure and a bit of success has taught me about publishing papers

Thomas McHugh

RIKEN

While there is no replacement for the simplest advice, ask a good question and get good data, with age comes the experience of much failure and occasional success. In my talk, I will highlight strategies I have learned and advice I have received that I believe may be useful in writing stronger papers.

EDU5-3

From Discovery to Presentation: Writing Scientific Papers That People Remember

Greg S. B. Suh

Department of Biological Sciences, KAIST, Daejeon, South Korea

This talk will cover why “impact” matters in scientific writing, what are core principles of impactful papers, how to select the right message, how to structure the papers for maximum impact, how to write with “style”, and how to revise the papers. I will end my talk with closing thought – “Good writing does not just report science – it shapes how science is remember.”

In the quest of the neural mechanism of emotion and social behaviors

In this talk, I will share personal experience from my lab’s published work -- including my first paper as a PI -- on navigating key challenges in scientific writing. I will discuss: How to choose an important problem? How to make a complete logic chain? And, how to handle unexpected results?

Learning the Hard Way: What lots of failure and a bit of success has taught me about publishing papers

While there is no replacement for the simplest advice, ask a good question and get good data, with age comes the experience of much failure and occasional success. In my talk, I will highlight strategies I have learned and advice I have received that I believe may be useful in writing stronger papers.

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Luncheon Seminar 1 ~ 5

Day 2 (August 25) **12:30-13:30** **Rm. Premier Ballroom A**

Luncheon Seminar 1

Supported By ZEISS

Organizer : Donghyun Kim (ZEISS Korea)

Lightfield 4D technology: New Fast Volume Imaging Microscope for Neuroscience - Gisu Eom (ZEISS Korea)

Rm. Premier Ballroom B

Luncheon Seminar 2

Supported By Scitech Korea

Organizer : Min-Woo Park (Scitechkorea)

The new era of behavioral research with AI tracking - Tom Pudil (Noldus Information Technology)

Rm. Premier Ballroom C

Luncheon Seminar 3

Supported By CrestOptics

Organizer : Giulia Ballerin (CrestOptics Spa) Moderator : Samantha Xu (CrestOptics Spa)

Advancing Neuroscientific Research with Multimodal and High-Content Imaging using the CrestOptics X-Light V3 and DeepSIM System - Giulia Ballerin (CrestOptics Spa)

Rm. 113-115

Luncheon Seminar 4

Supported By IVIM TECHNOLOGY

Organizer : Jisu Yang (IVIM Technology, Inc.) Moderator : Sujin Park (IVIM Technology, Inc.)

All-in-One Real-time IntraVital Microscopy (IVM): In Vivo Cellular-level Imaging of Internal Organs in a Live Animal
Pilhan Kim (IVIM Technology, Inc.)

Rm. 116-118

Luncheon Seminar 5

Supported By GemPharmatech

Organizer : John Jackson (GemPharmatech) Moderator : SHINAE HWANG (GemPharmatech) Rui Feng)

Unveiling FAD3T: A Groundbreaking Transgenic Mouse Model for Accelerating Alzheimer's Disease Research
Rui Feng (GemPharmatech)

LUNCHEON-1

Lightfield 4D technology: New Fast Volume Imaging Microscope for Neuroscience

Gisu Eom

RMS, ZEISS Korea, Seoul, Republic of Korea

Introducing the latest high-speed volume imaging technology microscope, the Lightfield 4D. Lightfield 4D technology, developed for 3D model organisms that have been extensively studied in the life sciences field, provides a new experience for researchers in the field. Specifically, it offers the best solution for those who have had difficulty with 3D volume live imaging of model organisms, organoids, spheroids, and thick-sectioned brain tissue. Lightfield 4D technology, which can capture up to 80 volumes per second, can obtain 3D information of samples with a thickness of several hundred micrometers with just one capture. There is no longer a need to spend time capturing Z-stacks, and there is no need to worry about phototoxicity.

Keywords : High-speed volume imaging, Model organisms, Organoids, Brain tissue, Live imaging

LUNCHEON-2

The new era of behavioral research with AI tracking

Tom Pudil

Noldus Information Technology

Open-source AI tools like DeepLabCut and others have expanded what we can measure in rodent behavior: markerless pose estimation, multi-animal tracking, and novel, data-driven behavior discovery. Although very flexible, they often require custom pipelines, substantial technical effort, and lack standardized automation and validation needed for routine, publishable experiments. Representing Noldus, I will demonstrate how integrated platforms such as EthoVision XT combine modern deep-learning tracking with turnkey experiment automation, synchronized hardware control, and validated workflows that prioritize reproducibility and scalability. I will argue for a complementary ecosystem in which open innovation fuels novel metrics and algorithms, while validated commercial systems provide effectiveness and robustness for better scientific research.

LUNCHEON-3

Advancing Neuroscientific Research with Multimodal and High-Content Imaging using the CrestOptics X-Light V3 and DeepSIM System

Giulia Ballerin

Sales and Marketing, CrestOptics Spa, Rome, Italy

The intricate complexity of neural systems demands advanced imaging platforms for comprehensive overviews and high-resolution structural details. Key requirements include high spatial resolution, rapid acquisition speeds, large field-of-view coverage, and compatibility with diverse sample types for accurate understanding. The CrestOptics X-Light V3 and DeepSIM system emerges as a powerful, versatile solution, seamlessly integrating spinning disk confocal with lattice-structured illumination microscopy (SIM) into a single, multimodal platform. This system's spinning disk confocal component excels at high-content imaging, offering speed and sensitivity vital for developmental screening. It efficiently captures dynamic processes and large-scale data, crucial for observing neuronal migration or synapse formation over time. Complementing this, the DeepSIM module provides super-resolution capabilities, overcoming the diffraction limit to visualize fine neuronal structures with unprecedented clarity. This enables detailed investigations of dendritic spines, synaptic vesicles, and axonal transport, revealing the nanoscale architecture fundamental to neuronal function. The seamless integration allows researchers to effortlessly switch modalities, leveraging confocal for initial broad overviews and then DeepSIM for detailed, sub-diffraction-limited analysis of specific regions. This multimodal flexibility streamlines workflows, preserves sample integrity, and ensures precise correlation between macroscopic and microscopic observations. Ultimately, the CrestOptics X-Light V3 and DeepSIM system offers transformative capabilities in neuroscience, combining high-content imaging for developmental screening with high-resolution investigations of fine neuronal structures. It's an indispensable tool, accelerating our understanding of the nervous system's complex architecture and dynamic processes in both health and disease.

Keywords : Multimodal Flexibility, DeepSIM Super-Resolution, Neuroscientific Imaging, X-Light V3 Spinning Disc Confocal, High Content Screening

Acknowledgements : We're incredibly grateful to all the researchers who've collaborated with us, leveraging our systems for their vital work. Your projects fuel our progress. A special thanks also goes to our dedicated imaging specialists; your expertise in data acquisition and analysis is invaluable to every study we present. Thank you for your partnership!

LUNCHEON-4

All-in-One Real-time IntraVital Microscopy (IVM): In Vivo Cellular-level Imaging of Internal Organs in a Live Animal

Pilhan Kim

CEO, IVIM Technology, Daejeon, Republic of Korea

In this talk, IVIM Technology's All-in-One real-time intravital two-photon and confocal microscopy system and comprehensive solutions for in vivo cellular-level longitudinal imaging of various internal organs in a live animal model will be introduced. With automatic tissue motion compensation function, it can readily acquire a real-time, multi-color, sub-micron resolution videos and images of complex in vivo microenvironment in various organs including brain, lung, heart, liver, kidney, spleen, pancreas, small intestine, colon, lymph node, and bone marrow will be briefly introduced. Recent intravital imaging studies to investigate cellular pathophysiology in human diseases and to develop novel therapeutics will be introduced.

Keywords : Intravital Microscopy, Two-photon Microscopy, Neurovascular Unit, Glia, Blood Brain Barrier

LUNCHEON-5

Unveiling FAD3T: A Groundbreaking Transgenic Mouse Model for Accelerating Alzheimer's Disease Research

Ziying Lai[1], Bingzhou Han[1], Tao Wang[1,2], Xiang Gao[1,2,3] and Rui Feng[1,2,4]

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[4]Jiangsu Industrial Technology Research Institute, Nanjing, Jiangsu, China

Alzheimer's disease (AD) presents a formidable challenge in contemporary healthcare. Traditional mouse models have a longer disease progression period, thereby slowing down pharmaceutical drug discovery and development. To address this challenge, we generated the FAD^{3T} transgenic mouse model, encompassing three mutations that mirror pivotal genetic factors implicated in AD pathogenesis. Remarkably, this model exhibits phenotypic parallels to AD patients and reveals an early onset of pathogenic markers in FAD^{3T} mice, with elevated levels of phosphorylated Tau (Thr181) detected at 1 month of age. Subsequent observations include Aβ deposition and elevated levels of Phospho-Tau (Thr217, Thr231) at 2 months, followed by elevated levels of Phospho-Tau (Ser396, Ser202, Thr205) at 4 months, all progressively intensifying with age. Notably, cognitive deficits resembling spatial learning and memory impairments manifest at earlier stages in these mice. Our findings underscore the unparalleled fidelity of the FAD^{3T} model in recapitulating the intricate etiology of AD. Crucially, in comparison to traditional AD mouse models, FAD^{3T} exhibits accelerated disease onset and progression, offering a rapid platform conducive to expediting drug testing cycles, particularly for therapies targeting disease progression. In conclusion, this innovative mouse model represents a transformative tool poised to enhance our comprehension of AD pathophysiology and facilitate the expedited development of therapeutic strategies.

Keywords : Mouse model, Alzheimer's disease, amyloid plaque, Tau

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Luncheon Seminar 6 ~ 11

Day 3 (August 26) **12:30-13:30** **Rm. Premier Ballroom A**

Luncheon Seminar 6

Organizer : Jiyoung Kim(Handok) Moderator : Jiyoung Kim(Handok)

Supported By HANDOK

Exelon MoA and Value of BuChEI - JiYoung Kim(Handok)

Rm. Premier Ballroom B

Luncheon Seminar 7-1

Organizer : Kipom Kim(Korea Brain Bank, KBR) Moderator : Kipom Kim(Korea Brain Bank, KBR)

Supported By KBRI 한국뇌연구원 Korea Brain Research Institute

From resource to research: know-how for effective distribution of human brain resources - Kipom Kim(Korea Brain Bank, KBRI)

Rm. Premier Ballroom B

Luncheon Seminar 7-2

Organizer : Dea Hun Kim (MINISTRY Food and Drug)

Moderator : Ji Hoon Kim(Korea Institue Science and Technology)

Supported By 식품의약품안전처 식품의약품안전평가원

Introduction of the MFDS's current policies and R&D initiatives related to narcotics control - Su Jeong Park(Ministry of Food and Drug Safety)

Rm. Premier Ballroom C

Luncheon Seminar 8

Organizer : Su Hyun Lee(Bruker Korea Co ., Ltd) Moderator : Haruhiko Bito(University of Tokyo)

Supported By BRUKER

Multiphoton Imaging the Dynamics of the Nervous System - Jimmy Fong(Bruker Nano Inc.)

Rm. 113-115

Luncheon Seminar 9

Organizer : Hankyung Kim(Bio-Medical Science Co., Ltd.)

Moderator : Jongsoo Woo(STEMCELL Technologies)

Supported By BMS

Enhancing Physiological Complexity In Vitro Neural System - Jongsoo Woo(STEMCELL Technologies)

Rm. 116-118

Luncheon Seminar 10

Exploring N-glycosylation in brain disorders through multi-modal mass spectrometry

Boyoung Lee(Institute for Basic Science)

Supported By BRUKER

Day 4 (August 27) **12:00-13:30** **Rm. Premier Ballroom A**

Luncheon Seminar 11

Supported By Johnson&Johnson

Organizer : Hyunseo, Yang(Johnson&Johnson Innovative medicine)

Moderator : Nuree, Kang(Department of Psychiatry, Gyeongsang National University Hospital)

Clinical benefit of Paliperidone Long-Acting injections : Emphasis on treatment adherence and functional outcomes

Nuree, Kang(Gyeongsang National University Hospital)

LUNCHEON-6

Exelon MoA and Value of BuChEI

The presentation for Luncheon Seminar 6 will be conducted by video.

LUNCHEON-7-1

From resource to research: know-how for effective distribution of human brain resources

Kipom Kim

Korea Brain Bank, Korea Brain Research Institute, Deagu, Republic of Korea

In this session, we will introduce methods to efficiently distribute and utilize human brain tissue resources in neuroscience research. We will cover fundamental aspects of brain tissue management and ethical considerations, along with a detailed explanation of the necessary preparations prior to distribution. The focus will be on integrating brain bank resources into research design and experimental planning. Our goal is to provide practical insights that empower participants to enhance their research capabilities through the effective use of brain resources.

Keywords : Human brain resources, Brain bank

LUNCHEON-7-2

Research and Development on Drug Control at MFDS

Su Jeong Park

Ministry of Food and Drug Safety

The Ministry of Food and Drug Safety (MFDS) is establishing a comprehensive response system for drug control through research and development (R&D) across various fields, including addiction, rehabilitation, detection, synthesis, and epidemiology. The MFDS promptly designates emerging psychoactive substances as controlled drugs based on harm assessments, thereby mitigating potential risks. It also promotes the development of prevention strategies and personalized rehabilitation technologies to support the safe reintegration of individuals with substance use disorders into society.

Moreover, the MFDS synthesizes emerging drugs and certified reference materials (CRMs) for use in evaluation studies, enhances detection and analytical technologies, and supplies reference standards to support drug investigations and testing conducted by agencies such as the Supreme Prosecutors' Office and the National Forensic Service. In parallel, wastewater-based epidemiology and cohort-based studies are utilized to estimate the circulation and consumption of drugs, enabling the MFDS to monitor drug use trends nationwide.

Through these efforts, the MFDS aims to strengthen both proactive and post-market management systems for drugs, contributing to the protection of public health and the realization of a safer society.

Keywords: MFDS, R&D, Drug addiction, Drug control

LUNCHEON-8

Multiphoton Imaging the Dynamics of the Nervous System

Jimmy Fong

Bruker Fluorescence Microscopy, Bruker Corporation, Madison, Wisconsin, USA

Recent technological advances in multiphoton microscopy have dramatically propelled exploration of neural circuits and brain function within the neuroscience community. Developed through collaboration with leading labs, the latest Bruker Ultima 2Pplus multiphoton workstation is enabling many in-vivo imaging and optogenetics experiments that illuminate brain function with resolution and precision at the scale of small networks, single cells, dendrites, and individual spines. This talk will delve into Bruker's newest multiphoton capabilities including the NeuraLight 3D holographic optogenetic activation module, NeuraLeap rapid focusing module, and OptoVolt voltage imaging module. Attendees will gain insights into the transformative impact of these technologies on neural activity imaging and the broader understanding of brain function, while also learning about recent customer successes and future developments in the field.

Keywords : Multiphoton, Optogenetics, Voltage, SLM, In-vivo
Acknowledgements : Bruker collaborators and colleagues

LUNCHEON-9

Enhancing Physiological Complexity In Vitro Neural System

Jongsoo Woo

STEMCELL Technologies

Establishing complex nervous systems in vitro for basic and clinical research poses significant challenges. Although current technologies enable the differentiation of human pluripotent stem cells (hPSCs) into diverse neural cell types and organoids, they have limitations in fully representing and enhancing the physiological complexity of nervous system. Combining the culture of different cell types and/or organoids, along with constructing assembloids, can be a valuable strategy to build complex physiological structures of the nervous system or study intracellular interactions. STEMCELL Technologies has developed various kits and technologies for hPSC-derived differentiation to facilitate nervous system modeling and is sharing these methods to make them easily accessible for researchers.

LUNCHEON-10

SpatialOmx for neuroscience: unveiling brain complexity through molecular imaging

Boyoung Lee

Center for Cognition and Sociality, Institute for Basic Science , Daejeon, Republic of Korea

Glycosylation is a post-translational modification in which carbohydrate chains (glycans) are enzymatically attached to proteins or lipids. This process plays a critical role in protein folding, trafficking, stability, and cell signaling. Recent studies have highlighted glycosylation as a key regulator of brain development and neurological function, with roles in synaptic plasticity, neuronal maturation, and modulation of neural signaling pathways. Aberrant glycosylation has been implicated in various neuropsychiatric and neurodegenerative disorders, including Alzheimer's disease, schizophrenia, and depression, underscoring its importance in brain physiology and pathology. Despite these associations, the mechanisms by which altered glycosylation contributes to disease onset and progression remain poorly understood. In this presentation, I will share our recent findings identifying region-specific N-glycan signatures across the central nervous system—including the spinal cord and brain—using an animal model of neuropathic pain and matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI). Additionally, I will present a more comprehensive study investigating the relationship between altered N-glycosylation patterns and the emergence of specific behavioral symptoms in an animal model of schizophrenia. This includes the identification of differentially expressed glycans and glycoproteins, along with their potential functional relevance to pathophysiology. Together, these studies provide new insights into the role of N-glycosylation in brain disorders and underscore its potential as a target for future therapeutic strategies.

Keywords : Glycosylation, MALDI-MSI, N-glycan, Pain, Schizophrenia
Acknowledgements : This work was supported by the National Research Foundation of Korea funded by the Ministry of Science and ICT,
Republic of Korea (NRF-2022R1A2B5B02001886 to D.W.K.) and also supported by the Institute for Basic Science (IBS), Center for Cognition and Sociality (IBS-R001-D2 to B.L.

LUNCHEON-11

Clinical benefit of Paliperidone Long-Acting injections : Emphasis on treatment adherence and functional outcomes

Nuree, Kang

Gyeongsang National University Hospital

Paliperidone long-acting injections (PLAI) have become an important therapeutic option in the management of schizophrenia, particularly for addressing the challenges of treatment adherence and relapse prevention. While remission can be achieved with adequate antipsychotic therapy, non-adherence to daily oral medication remains a leading cause of relapse and hospitalization. LAIs provide continuous drug delivery and reduce relapse risk, with meta-analyses showing superiority over oral agents in preventing rehospitalization. Paliperidone palmitate 1-monthly (PP1M) and 3-monthly (PP3M) injections have demonstrated improved treatment persistence, lower discontinuation rates, and reduced hospitalization risk compared with oral antipsychotics. In real-world data, PP3M and aripiprazole LAIs showed the lowest risk of discontinuation relative to oral risperidone. Moreover, patients stabilized on PP3M achieved higher continuation rates, with more than 80% remaining on treatment at 18 months, alongside significantly reduced relapse rates. Functional and quality-of-life outcomes were also improved, including better social relationships and daily functioning, while safety profiles were comparable to monthly formulations. These findings emphasize that PLAI, particularly PP3M, not only supports long-term adherence but also enhances patient satisfaction and recovery potential. Incorporating longer-interval PLAI into routine care may provide a clinically meaningful strategy to optimize real-world outcomes in schizophrenia.

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Poster Sessison 1

P1-P282

Day 1(Aug 24, 2025)	13:00-17:40	[Exhibition/Poster Hall]
Day 2(Aug 25, 2025)	8:30-12:30	[Exhibition/Poster Hall]

Mechanisms of Brain Disorders	P-001 ~ P-059
Molecular and Cellular Neuroscience	P-060 ~ P-143
Neuroengineering	P-144 ~ P-161
Others	P-162 ~ P-188
Synapses and Circuits	P-189 ~ P-213
Systems and Computational Neuroscience	P-214 ~ P-262
Translational and Clinical Neuroscience	P-263 ~ P-282

Mechanisms of Brain Disorders P-001~P-059

P-001

Biomarker detection with high-speed single-molecule imaging in neurodegenerative disorder

Sangjun Park[1]

[1]Department of Medical Life Sciences, College of Medicine, The Catholic University of *Korea*, Seoul, Republic of Korea

Alzheimer's disease is a neurodegenerative disorder marked by amyloid beta plaques and tau tangles, causing cognitive decline and neuron death. Diagnosis relies on clinical symptoms, neuropsychological tests, and imaging such as MRI and PET. Early detection is crucial, with FDA-approved treatments like LEQEMBI and KISUNLA available for early-stage patients. Biomarkers in cerebrospinal fluid, blood, and imaging assist in early diagnosis and monitoring. Recent non-invasive blood tests targeting amyloid beta and tau enable personalized treatments, improving outcomes and slowing progression. Researchers use fluorescence and confocal microscopy to study neurodegenerative disorder, but confocal microscopy has limits with thick tissues and organoids. Western blot and ELISA quantify RNA or proteins but lack spatial and interaction data. This study applies single-molecule imaging methods to visualize amyloid beta and tau at high resolution, offering deeper insight into disease mechanisms. DNA-PAINT (DNA Points Accumulation for Imaging in Nanoscale Topography), a type of single-molecule imaging, provides nanometer-scale imaging beyond conventional limits. It uses complementary DNA strands to produce fluorescence signals, enabling multiplexed detection of targets — unlike digital ELISA, which detects only one. DNA-PAINT works at picomolar sensitivity and is enhanced with riboswitches and aptamers for selectivity. Blood-based biomarker detection helps assess risk, monitor progression, and guide tailored treatment. The technique of single-molecule imaging improves sensitivity and accuracy. Sex differences are also notable: women show more memory loss due to hormonal shifts, while men often display behavioral symptoms linked to low testosterone. Key biomarkers include amyloid beta, tau, APOE4, hormones, and inflammation-related proteins, aiding diagnosis, treatment, and understanding of Alzheimer's disease with line-illuminated high-speed single-molecule imaging.

Keywords : Neurodegenerative disorder, Alzheimer's disease, Biomarker, Single-molecule imaging, DNA-PAINT

Acknowledgements : This study is supported by National Research Foundation of Korea (NRF-2022R1A6A3A01085960).

P-002

Transcriptomic evidence of hippocampal hyper-maturity and accelerated aging in mouse models of neuropsychiatric disorders with anxiety-like behavior

Hideo Hagihara[1], Hisatsugu Koshimizu[1,2], Satoko Hattori[1,3], Miho Tanaka[4], Kazutaka Ikeda[4], Tsuyoshi Miyakawa[1]

[1]Division of Systems Medical Science, Center for Medical Science, Fujita Health University, Toyoake, Japan, [2]Office of Research Administration, Fujita Health University, Toyoake, Japan, [3]Research Creation Support Center, Aichi Medical University, Nagakute, Japan, [4]Addictive Substance Project, Tokyo Metropolitan Institute of Medical Science, Setagaya-ku, Japan

Adequate neural maturation and synaptic organization in the hippocampus are essential for ordinary emotional and cognitive functioning. While neuronal immaturity – defined as arrested or reversed development into a pseudo-immature state – has been implicated in various neuropsychiatric disorders, the opposite phenomenon, namely hyper-maturity and accelerated aging remains underexplored. This study presents transcriptomic evidence of hippocampal hyper-maturity and accelerated aging across 16 mouse strains and experimental conditions, identified by screening over 260,000 omics datasets. Model mice whose gene expression patterns (mutant/experimental vs. wild-type/control) showed statistically significant similarity to developmental gene expression patterns (adult vs. infant), as determined by the Running Fisher test, were defined as hyper-maturity models. These included serotonin transporter knockout mice, glucocorticoid receptor overexpression mice, depression/anxiety disorder models, Df(16)A/+ mice, 22q11.2 deletion schizophrenia model, PDE9A inhibitor-treated mice, and senescence accelerated SAMP8 mice. Meta-pathway analysis highlighted synapse-associated genes as key contributors. Based on previously reported behavioral data, mice with hippocampal hyper-maturity tend to show increased anxiety-like behaviors, whereas mice with hippocampal immaturity exhibit the opposite trend. Notably, hippocampal hyper-maturity encompassed two transcriptomic aspects: enhancement of postnatal development and accelerated aging changes (adult vs. aged). For example, SAMP8 mice were more associated with postnatal development, while corticosterone-treated mice and lysosomal storage disorder model mice were more aligned with accelerated aging. These findings suggest that hippocampal hyper-maturity and accelerated aging could represent a neural phenotype underlying anxiety-related behaviors in neuropsychiatric disorders and may provide novel therapeutic or anti-aging targets.

Keywords : Hippocampus, Transcriptome, Hyper-maturity, Aging, Anxiety

P-003

Location of polyglutamine track affects pathogenic threshold of polyglutamine expansion diseases – importance of association with the proteasome

Meewhi Kim[1], Ilya Bezprozvanny[1]

[1]Laboratory of Molecular Neurodegeneration, Peter The Great St. Petersburg State Polytechnical University, St. Petersburg, Russia

The expansion of glutamine residue track (polyQ) within soluble proteins (Q proteins) is responsible for nine autosomal-dominant genetic neurodegenerative disorders. These disorders develop when polyQ expansion exceeds a specific pathogenic threshold (Q_{th}) which is unique for each disease. However, the pathogenic mechanisms associated with the variability of Q_{th} within the family of Q proteins are poorly understood. In the previous publication we proposed that polarity of the regions flanking polyQ track in each protein plays a key role in defining Q_{th} value (Kim, M. *Mol Neurodegener* 9 (2014) 45) and that these effects can be explained as a result of interactions between polyQ-expanded protein and proteasome (Kim, M Bezprozvanny, I (2021). *Biochem Biophys Res Commun* 536:95–99). In the present manuscript we extended our analysis and analyzed effects of location of polyQ-expanded track within the protein sequence. To accomplish this, we divided a family of polyQ-expanded proteins into 3 classes - G1, G2 and G3 groups, which differ by position of polyQ-expanded track in the protein sequence. We determined that polarity of flanking

regions have different effect on $Q_{th.}$ value for each of these classes, and explained these differences by mechanistic analysis of proteasomal function. Our results further support the hypothesis that differences in $Q_{th.}$ values of pathogenic threshold can be explained by different mode of interactions between polyQ-flanking regions and proteasome and these findings provide novel insight in to pathogenic mechanisms of polyQ-expanded disorders

Keywords : Polyglutamine disorders, Ataxin, Proteasome dysfunction, Spinocerebellar ataxia, Ubiquitination

Acknowledgements : This research was funded by the Grant No. 075-15-2024-548 from the Ministry of Science and Higher Education of the Russian Federation (I.B.).

P-004

Dysfunctional S1P/S1PR1 signaling in the dentate gyrus drives vulnerability of chronic pain-related memory impairment

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[1]Department of Anesthesiology, Xuzhou Medical University, Xuzhou, Jiangsu, China

Memory impairment in chronic pain patients is substantial and common, and few therapeutic strategies are available. Chronic pain-related memory impairment has susceptible and unsusceptible features. Therefore, exploring the underlying mechanisms of its vulnerability is essential for developing effective treatments. Here, combining two spatial memory tests (Y-maze test and Morris water maze), we segregated chronic pain mice into memory impairment-susceptible and -unsusceptible subpopulations in a chronic neuropathic pain model induced by chronic constrictive injury of the sciatic nerve. RNA-seq analysis and gain/loss-of-function study revealed that S1P/S1PR1 signaling is a determinant for vulnerability to chronic pain-related memory impairment. Knockdown of the S1PR1 in the DG promoted a susceptible phenotype and led to structural plasticity changes of reduced excitatory synapse formation and abnormal spine morphology as observed in susceptible mice, while overexpression of the S1PR1 and pharmacological administration of S1PR1 agonist in the DG promoted an unsusceptible phenotype and prevented the occurrence of memory impairment, and rescued the morphological abnormality. Finally, GO enrichment analysis and biochemical evidence indicated that down-regulation of S1PR1 in susceptible mice may impair DG structural plasticity via interaction with actin cytoskeleton rearrangement-related signaling pathways including Itga2 and its downstream Rac1/Cdc42 signaling and Arp2/3 cascade. These results reveal a novel mechanism and provide a promising preventive and therapeutic molecular target for vulnerability to chronic pain-related memory impairment.

Keywords : Chronic pain, memory impairment, dentate gyrus, sphingosine 1-phosphate, synaptic plasticity

Acknowledgements : The present study was supported by the National Key Research and Development Program of China Brain Science and Brain-like Intelligence Technology, the National Natural Science Foundation of China, Natural Science Foundation of Jiangsu Province, the Priority Academic Program Development of Jiangsu Higher Education Institutions, China Postdoctoral Science Foundation and Xuzhou Medical University.

P-005

Sleep homeostasis-driving neurons from the hypothalamic paraventricular nucleus regulate glucose metabolism through adipose tissue lipolysis

Abudusalamu Awuti[1], Xiangtong Chen[1], Hong Jiang[1]

[1]Neuroscience Research Institute and Department of Neurobiology, School of Basic Medical Sciences, Peking University, Beijing, China

Sleep abnormalities have markedly increased over recent decades and are frequently associated with metabolic syndrome and type 2 diabetes mellitus (T2DM). However, the mechanisms linking sleep disturbances to glucose metabolism remain poorly understood. In this study, we employed a sleep homeostasis model and metabolic analyses to demonstrate that sleep deprivation-driven disruption of sleep homeostasis impairs glucose metabolism. Using spatial transcriptomics combined with EEG/EMG recordings, we identified a population of sleep homeostasis-regulating neurons in the paraventricular nucleus of the hypothalamus (PVN). Their activation reduces glucose pyruvate tolerance while decreasing insulin sensitivity. Indirect calorimetry revealed that activating these neurons rapidly shifts metabolism toward fatty acid utilization as the primary fuel source. Furthermore, transcriptomic profiling, metabolic flux analysis, and sympathetic fiber morphology studies suggest that enhanced adipose tissue lipolysis in sleep-disordered mice may contribute to systemic glucose dysregulation. Collectively, our findings provide new insights into how sleep abnormalities contribute to metabolic syndrome.

Keywords : Sleep homeostasis, Glucose metabolism, Hypothalamus, Lipolysis

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P-006

Positive allosteric modulators of SERCA pump as potential therapeutics for Alzheimer's disease

Ilya Bezprozvanny[1], Russell Dahl[2]

[1]Laboratory of Molecular Neurodegeneration, Peter the Great St. Petersburg State Polytechnical University, St Petersburg, Russia, [2]Neurodon, Neurodon LLC, Crown Point, Indiana, USA

Alzheimer's disease (AD) is an irreversible neurodegenerative disease that affects millions of people worldwide. AD does not have a cure and most drug development efforts in the AD field have been focused on targeting the amyloid pathway based on the "amyloid cascade hypothesis". However, in addition to the amyloid pathway,substantial evidence also points to dysregulated neuronal calcium (Ca2+) signaling as one of the key pathogenicevents in AD, and it has been proposed that pharmacological agents that stabilize neuronal Ca2+ signaling mayact as disease-modifying agents in AD. In our studies we set out to evaluate the hypothesis that positive allostericregulators (PAMs) of the Sarco/endoplasmic reticulum Ca2+ ATPase (SERCA) pump might act as such Ca2+ stabilizing agents (1). To test this hypothesis we evaluated a number of SERCA PAMs in in vitro and in vivo experiments with 5xFAD, APP/PS1 and APPKI transgenic models

of AD. We demonstrated that SERCA PAMs are able to rescue loss of synaptic spines, prevent hippocampal LTP defects, improve behavioral readouts in cognitve assays, normalize activity of neuronal networks and reduce amyloid load in transgenic models of AD (2,3,4). The results of our studies supported a hypothesis that the SERCA pump is a potential novel therapeutic drug target. for AD and that SERCA PAMs that we invented are promising lead molecules for developing disease-modifying agents in AD and possibly other neurodegenerative disorders. References: 1. Dahl and Bezprozvanny (2024) BBRC, vol 734, 150748; 2. Dahl at al (2023) IJMS, vol 24, 11057; 3. Rakovskaya at al (2023) IJMS, vol 24, 13973; 4. Gerasimov at al (2025). J Neuroscience, in revision

Keywords : calcium, alzheimers, SERCA, drug discovery, miniscope

Acknowledgements : This research was funded by the Russian Science Foundation under grant 22-15-00049 , by the National Institutes of Health under grant R01AG071310 , by the Grant No. 075-15-2024-548 from the Ministry of Science and Higher Education of the Russian Federation, and by the Neurodon Corporation.

P-007

Antioxidant effect of Opuntia Ficus Indica cladode extract in a Wistar rat model of chronic Manganese toxicity induced Parkinson-like disease

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Manganese (Mn) is an essential trace element involved in various physiological processes, particularly in energy metabolism. However, chronic exposure to high levels of Mn leads to neurotoxic effects, especially in dopaminergic brain mechanisms, mimicking Parkinsonian-like symptoms. This study aims to evaluate the neuroprotective effects of *Opuntia ficus-indica* (OFI) cladodes against Mn-induced neurotoxicity in rats. Male Wistar rats received intraperitoneal injections of $MnCl_2$ at a dose of 25 mg/kg for 12 weeks. A second group received a simultaneous treatment with an aqueous extract of OFI cladodes at 4 mg/kg (ip). Body weight was monitored weekly. Behavioral tests were conducted to assess motor function (rotarod test), affective behaviors (forced swim test), and olfactory abilities. Chronic Mn exposure resulted in progressive weight loss, significant reduction in locomotor activity, impaired motor coordination, increased anxiety-like and depressive behaviors. Olfactory dysfunctions were also observed, indicating disruptions in specific brain mechanisms. Conversely, the combined Mn + Cla treatment mitigated these effects: body weight improved, motor performance was restored, anxiety and depressive symptoms were reduced, and olfactory function partially recovered. OFI cladode extract shows significant neuroprotective effects against chronic Mn toxicity, probably via antioxidant and anti-inflammatory mechanisms targeting specific neuronal pathways in the brain.

Keywords : Manganese, Opuntia Ficus indica, Parkinson's disease, Neurotoxicity, Antioxidant

P-008

D2R-specific deletion of NSF Induces ADHD-like behavioral phenotypes in mice

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Dopamine D2 receptor (D2R) dysfunction has been strongly implicated in the pathophysiology of attention deficit hyperactivity disorder (ADHD), which is characterized by inattention, hyperactivity, and impulsivity. However, the molecular mechanisms that regulate proper D2R function remain poorly understood. Previous research has demonstrated that N-ethylmaleimide-sensitive factor (NSF) interacts with D2R and modulates excitotoxicity under experimental conditions. This study investigates the role of NSF in D2R-expressing cells, particularly their contribution to neuronal survival and ADHD-like behaviors. To this end, we generated D2R-specific NSF conditional knockout mice (D2R-NSFcKO) and analyzed their behavioral, neuropathological, and neurochemical phenotypes in vivo. In a behavioral test battery, D2R-NSFcKO mice exhibited ADHD-like behaviors, including hyperactivity and impulsivity. No significant differences were observed between groups in tests of repetitive behavior, social interaction, or pre-pulse inhibition (PPI) at various stimulus intensities. Importantly, co-administration of methylphenidate (MPH) and the D2R agonist quinpirole successfully rescued both hyperactivity and impulsivity in D2R-NSFcKO mice, suggesting a potential synergistic therapeutic strategy. Selective ablation of NSF in D2R-expressing cells led to a pronounced loss of striatal D2R-positive neurons, accompanied by increased apoptosis during postnatal development, reduced striatal volume, and significantly decreased dopamine levels. Further evidence of dopaminergic dysfunction was provided by marked reductions in the expression of dopamine transporter (DAT) and tyrosine hydroxylase (TH). Together, these findings underscore the translational value of the D2R-NSFcKO model for understanding ADHD and suggest that targeting D2R dysfunction represents a promising approach, particularly in treatment-resistant cases.

Keywords : Attention deficit hyperactivity disorder, N-ethylmaleimide-sensitive facto, Dopamine d2 receptor

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P-009

Restoring interbrain prefrontal theta synchronization reverses social deficits

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Social interaction requires the integration of information about oneself, others, and the shared environment. One proposed mechanism for this

coordination is interbrain synchrony—correlated neural activity between interacting individuals—observed in both humans and animals. However, whether this synchrony plays a functional role in orchestrating social behavior remains unclear. Here, we show that theta-band synchronization in the medial prefrontal cortex (mPFC) is essential for naturalistic social interactions in mice. Using genetic models of social dysfunction, we demonstrate that disruptions in mPFC synchrony correlate with impaired social behaviors. We identify a population of social behavior-encoding neurons directly linked to interbrain synchrony, and show that enhancing mPFC theta synchrony restores both interbrain coupling and social behavior, while desynchronization impairs social interaction in wild-type mice. These findings establish prefrontal theta synchrony as a core circuit mechanism for social behavior, with relevance across multiple genetic models of autism spectrum disorder. More broadly, this work provides a framework for understanding how neural circuits across brains dynamically interact to shape behavior.

Keywords : Social behavior, Interbrain synchrony, Autism spectrum disorder , In-vivo electrophysiology

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P-010

Potential of AAV-Based Gene Therapy for the Treatment of Cerebellar Ataxia

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Cerebellar ataxia (CA) is a neurodegenerative disorder characterized by impaired motor coordination and balance, primarily due to progressive loss of cerebellar neurons. Currently, no effective treatments are available. Emerging evidence indicates that mammalian target of rapamycin complex 1 (mTORC1) signaling is downregulated in the cerebellum of spinocerebellar ataxia type 2 (SCA2) mice compared to wild type mice, suggesting its potential involvement in disease pathogenesis. In this study, we investigated whether restoring mTORC1 activity through Ras homolog enriched in brain [Rheb(S16H)], a constitutively active mTORC1 activator, could confer neuroprotection and mitigate motor deficits in a transgenic mouse model of SCA2. Targeted upregulation of Rheb(S16H) via adeno-associated virus serotype 1 (AAV1)-mediated delivery to the cerebellum resulted in robust expression in calbindin-D28K-positive Purkinje cells, leading to enhanced mTORC1 signaling and increased levels of neurotrophic factors. These molecular changes were associated with significant improvements in motor function, reduced abnormal behaviors, and enhanced survival of Purkinje cells compared to untreated SCA2 mice. Collectively, our findings demonstrate that Rheb(S16H)-mediated mTORC1 activation restores cerebellar function and provides neuroprotection, highlighting its potential as a therapeutic strategy for hereditary CA. This study has been published in *Acta Pharmacologica Sinica*.

Keywords : Cerebellar ataxia, Adeno-associated virus, Rheb(S16H), mTORC1, Neuroprotection

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P-011

Neuroinflammatory and histopathological changes in the human olfactory system across the Alzheimer's disease continuum

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Background Olfactory dysfunction is among the earliest clinical manifestations of Alzheimer's disease (AD), yet the underlying neuropathological mechanisms remain poorly defined. The olfactory cortex (OC) and olfactory bulb (OB) are early sites of pathological change, but their roles in neuroinflammation during disease progression remain underexplored. Methods We conducted histological and immunofluorescent analyses on postmortem human brain tissue obtained from the Netherlands Brain Bank, including cognitively normal controls (n = 6), mild cognitive impairment (MCI; n = 6), and AD cases (n = 12). Tissue sections from the OC and OB were examined for Aβ and phosphorylated tau (pTau) accumulation and glial activation using Iba1 (microglia) and GFAP (astrocytes). Results Aβ and pTau pathology progressively increased across clinical stages in both olfactory regions. Glial markers showed parallel increases, with evident microglial morphological changes and astrocytic hypertrophy, consistent with activation. Notably, both the OB and OC exhibited regionally distinct yet converging patterns of glial reactivity, suggesting that inflammatory processes evolve in a structured and anatomically coordinated manner during AD progression. Conclusion Our findings demonstrate that the olfactory system undergoes early and progressive neuroinflammatory and proteinopathic changes during AD progression. The OC and OB exhibit distinct yet converging patterns of glial activation and protein accumulation, underscoring their potential roles in early pathogenesis. These results support the use of the olfactory system as a model for investigating region-specific vulnerability in Alzheimer's disease.

Keywords : Alzheimer's disease, Postmortem human brain tissue, Olfactory system, Neuroinflammation, Aβ and pTau

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P-012

Isopropylphenidate exhibits addictive-like properties via the dopaminergic pathway in mice

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Isopropylphenidate (IPH) is a central nervous system (CNS) stimulant and structural analogue of methylphenidate (MPH). MPH-based analogues,

including IPH, have raised concerns due to their pharmacological similarities to methamphetamine and their potential for abuse. However, the addictive properties of IPH and its underlying mechanisms in the dopaminergic system have not been fully understood. In this study, we evaluated the abuse potential of IPH using the conditioned place preference (CPP) and behavioral sensitization paradigms in mice. To further investigate the involvement of dopaminergic signaling, we administered dopamine receptor antagonists during the CPP procedure, and selectively inhibited dopamine D1 receptors (D1DR)-expressing medium spiny neurons (MSNs) in the nucleus accumbens (NAc) via chemogenetic approach in separate cohorts. Our results demonstrated that IPH administration significantly increased CPP scores in both male and female mice. In the behavioral sensitization test, repeated IPH exposure induced robust behavioral sensitization and exhibited IPH-primed expression of locomotor sensitization. Acute IPH administration also produced marked hyperactivity. Notably, SCH23390, a D1 receptor antagonist, blocked both IPH-induced CPP and the development of behavioral sensitization, whereas raclopride, a D2 receptor antagonist, had no effect. Furthermore, chemogenetic inhibition of D1-MSNs using Gi-coupled designer receptors exclusively activated by designer drugs (DREADDs) activation by clozapine N-oxide (CNO) prevented the expression of IPH-induced CPP. Taken together, these findings suggest that IPH has the abuse potential in mice, primarily by modulating the dopaminergic pathway. These results emphasize the necessity for further research on the molecular mechanisms underlying IPH dependence in the dopaminergic pathway.

Keywords : Isopropylphenidate, Addiction, Dopamine D1 receptor, Nucleus accumbens

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P-013

Black Ginseng mitigates Alzheimer's cognitive decline by activating Nrf2/HO-1 and inhibiting p38 MAPK/NF-κB/STAT3 and NLRP3 via TLR2/4 modulation.

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Background: Korean black ginseng, a specially processed ginseng through repeat steaming and drying, has various pharmacological effects. However, its role on cognitive impairment remains unclear. Purpose and Methods: This study examined whether Korean black ginseng extract (BGE; 50 and 100 mg/kg, orally, 18 weeks) may mitigate cognitive impairment in a 5xFAD mouse model of Alzheimer's disease (AD). Results: BGE significantly improved cognitive performance in 5xFAD mice, associated with reduced Aβ accumulation in the frontal cortex and hippocampus. BGE suppressed microglial and astrocytic activation, alongside the downregulation of pro-inflammatory cytokines (interleukin-6 and tumor necrosis factor-α) and enzymes (cyclooxygenase-2 and inducible nitric oxide synthase). These changes coincided with the inhibition of key inflammatory signaling pathways, such as p38 mitogen-activated protein kinase (MAPK), nuclear factor kappa B (NF-κB)/p65, signal transducer and activator of transcription (STAT) 3, and NOD-like receptor protein 3 (NLRP3) inflammasome. Furthermore, BGE reduced the generation of reactive oxygen species and enhanced the nuclear-E2-related factor 2 (Nrf2)-heme oxygenase 1 (HO-1) signaling pathway in the brains linked to the downregulation of toll-like receptors (TLR)-2 and TLR-4 in the brain. Conclusion: Taken together, BGE could improve AD-related cognitive decline and neurodegeneration by simultaneously regulating anti-inflammatory pathways (p38 MAPK/NF-κB/STAT3 and NLRP3 inflammasome) and an antioxidant pathway (Nrf2/HO-1) via modulation of TLR2/4. J. Ginseng Res. (2025) 294-305. doi:https://doi.org/10.1016/j.jgr.2025.02.002

Keywords : Korean black ginseng, Anti-inflammation, Anti-oxidation, Toll-like receptor 2/4, Alzheimer's disease

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P-014

Febrile seizures induce hippocampal Nav1.1 downregulation and deficits in fear-related cognitive function in a rat model

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Febrile seizures are seizures that occur due to high fever without any infection of the nervous system, and they are one of the most common types of seizures in infants and young children between the ages of 3 months and 5 years. Despite the fact that most children with recurrent or prolonged febrile seizures experience neurological disorders such as depression, sleep disturbances, cognitive impairments, anxiety, attention deficits, autism spectrum disorders, and social deficits, there is very little evidence regarding the correlation between febrile seizures and neuropsychiatric disorders. Therefore, this study evaluated the relationship between neurological changes in the hippocampus due to febrile seizures and cognitive dysfunction induced by fear. The animal model was created by inducing high fever seizures in rats aged 9 to 10 days, and fear conditioning and passive avoidance tests were conducted. The experimental results demonstrated that the febrile seizure rats exhibited impaired hippocampus-dependent memory and amygdala-dependent memory in response to fear. Additionally, immunohistochemical analysis of voltage-gated sodium channel 1.1 (Nav1.1) revealed a reduction of Nav1.1 in the interneurons of the hippocampus in febrile seizure rats. These findings suggest that the cognitive dysfunction and fear-associated memory impairments resulting from febrile seizures may be linked to the decrease of Nav1.1 channels in the hippocampus, indicating a potential target site for treatment. Support: This research was supported by the National Research Foundation of Korea(NRF) funded by the Korea government(NEST) (NRF-2017R1D1A1B05036195 and RS-2023-00245605)

Keywords : febrile seizure, cognitive dysfunction, emotional cognition, sodium voltage-gated channel

P-015

Abnormal O-glycan Sialylation in Depression induced by Chronic Variable Stress

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Depression is a prevalent mental disorder affecting approximately 5 % of the adult population globally. The symptoms range from sadness to fatigue, resulting from a complex interplay of social, psychological, and biological factors. Understanding the molecular mechanisms in the brain is crucial to uncover the biological basis of the disease and develop effective treatments. Post-translational modifications (PTMs) provide critical insights into the molecular processes of various disorders, yet their role in depression remains underexplored. Among these, glycosylation—one of the most complex PTMs—has been particularly difficult to study in neurological contexts due to its heterogeneous nature and analytical challenges, despite its potential to uncover novel disease mechanisms. Here, we demonstrate how chronic variable stress alters brain O-glycosylation across multiple regions. Our unbiased O-glycomics analysis reveals significant alterations in sialylated O-glycosylation patterns across four specific brain regions, including the prefrontal cortex (PFC), a region strongly implicated in depression. Additionally, the knockdown of an O-glycan sialylation-related gene in normal mice induced depressive-like behaviors comparable to those in CVS-exposed mice, even in the absence of stress. Conversely, the gene overexpression in stressed mice alleviated depressive symptoms, highlighting its regulatory role in stress resilience. Using proteomics and O-glycoproteomics analysis, we identify potential glycoprotein targets and downstream regulators in PFC. This study provides novel insights into the molecular basis of depression, suggesting that O-glycosylation could serve as a potential therapeutic target for psychiatric disorders.

Keywords : Depression, Brain glycosylation, O-glycosylation

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P-016

AAV-mediated SCA3 Primate Model Reveals Early Cerebellar Neurochemical and Histopathological Changes

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Spinocerebellar ataxia type 3 (SCA3), or Machado-Joseph disease, is the most common autosomal dominant ataxia. It is caused by a CAG repeat expansion in the *ataxin-3* gene, resulting in polyglutamine-aggregated protein accumulation and progressive cerebellar neurodegeneration. While rodent and transgenic models have facilitated mechanistic insights, they often fail to replicate the complex neuropathological and biochemical features observed in patients. To address this, we developed a novel non-human primate model of SCA3 by stereotaxic cerebellar injection of an adeno-associated virus (AAV) encoding mutant ataxin-3 into cynomolgus monkeys. Eight weeks after injection, magnetic resonance spectroscopy (MRS) revealed a significant reduction in N-acetylaspartate (NAA) in the cerebellar cortex, suggesting early neuronal dysfunction. Histopathological analysis further showed marked Purkinje cell loss, reactive gliosis, and intranuclear inclusions within Purkinje neurons that were immunopositive for mutant ataxin-3—hallmarks consistent with human SCA3 pathology. These findings demonstrate that AAV-mediated mutant ataxin-3 expression induces robust, early-onset cerebellar degeneration in primates. This model represents a valuable translational platform for elucidating SCA3 pathogenesis and for preclinical testing of disease-modifying therapies.

Keywords : Spinocerebellar ataxia, Ataxin-3, AAV-viral vector, Monkey model

P-017

Sex-Specific Salivary Proteomic Profiles as Biomarkers for Suicidal Ideation in Adolescents: A Novel Approach for Early Detection

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Suicidal ideation is a critical public health concern and one of the leading causes of mortality worldwide. Despite advancements in mental health care, early identification of individuals at risk remains a challenge due to the multifactorial and complex nature of suicide. The investigation of specific biomarkers has emerged as a promising approach to enhance early detection and prevention strategies. Saliva has recently gained recognition as a non-invasive and accessible biological matrix for studying biomarkers associated with suicidal ideation. In this study, we employed proteomics to identify adolescent salivary biomarker patterns. Our preliminary findings revealed alterations in molecules related to inflammation, oxidative stress, and mitochondrial function, highlighting their potential as objective indicators of suicide risk. Methodology: This prospective study included three groups: · G1: Patients with mental disorders and suicide risk (19 males, 39 females). · G2: Patients with mental disorders but no suicide risk (10 males, 7 females). · G3: Adolescents without pathology (21 males, 21 females). Participants completed validated questionnaires, including the *Mood and Feelings Questionnaire* and the *Paykel Suicide Scale*. Saliva samples were analyzed using LC-ESI-MS/MS proteomics, with analyses stratified by sex. Results: A total of 2,840 proteins were identified. Among males: · G1 vs. G2: 190 up and 490 downregulated proteins. · G1 vs. G3: 263 up and 234 downregulated proteins. Among females: · G1 vs. G2: 104 up and 948 downregulated proteins. · G1 vs. G3: 204 up and 446 downregulated proteins. Molecular profiles differed by sex. In males, altered pathways were associated with the immune system and nervous system-related proteins, while in females, pathways involved atherosclerosis, intermediate filaments, and the complement

system. These findings underscore the potential of sex-specific salivary biomarkers for suicide risk.

Keywords : biomarker, suicide, adolescents, proteomic, saliva

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P-018

Cancer-associated metabolic reprogramming facilitated by astrocyte glycogenolysis mediates neuropathic pain chronification

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In numerous neuropathological states, astrocytes are involved in modulating neuronal excitability; chronic pain is characterized by aberrant neuronal firing and synaptic plasticity. Although anterior cingulate cortex (ACC) astrocytes have been implicated in neuropathic pain chronification, the underlying intracellular mechanisms remain unclear. Here, we integrated bulk metabolomics with astrocyte-specific RiboTag transcriptomics, where we identified a Warburg–type metabolic reprogramming in ACC astrocytes during the transition from acute to chronic pain. In addition to this, we demonstrated that ACC astrocytes underwent a biphasic glycogen program—an initial synthesis followed by glycogenolysis—and that pharmacological inhibition of glycogen breakdown prevented chronic pain development. Mechanistically, glycogenolysis fueled lactate production and downstream Warburg-type metabolic pathways, driving astrocytic and neuronal hyperactivity; blocking glycogenolysis quenched this reprogramming, restored metabolic homeostasis, and alleviated pain chronification. These findings reveal a novel astrocyte–centric neuropathic pain circuitry and suggest glycogen metabolism as a promising therapeutic target for chronic pain.

Keywords : Astrocyte, Chronic Pain, Glycogenolysis, Metabolic Reprogramming, Warburg Effect

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P-019

Korean Red Ginseng Marc-Derived Gintonin Improves Alzheimer's Cognitive Dysfunction by Upregulating LPAR1

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Ginseng is a representative functional food for brain health. However, its active ingredients have not been well defined yet. Gintonin is a novel material isolated from white/red ginseng. Its lysophosphatidic acid (LPA) is an exogenous G protein-coupled LPA receptor (LPAR) agonist. Korean red ginseng marc (KRGM) is a by-product after KRG extractions. In a previous study, we have demonstrated that KRGM-derived gintonin (KRGM-G) contains LPA C18:2, a major functional component of white and/or red ginseng. To further study molecular mechanisms involved in KRGM-G-mediated anti-Alzheimer's disease (AD) effects. A 5xFAD transgenic mice and SH-SY5Y cells were used to determine molecular mechanisms involved in KRGM-G-mediated anti-Alzheimer's disease (AD) effects. KRGM-G improved cognition impairment in 5xFAD mice associated with alleviation of amyloid-β accumulation in the brain (hippocampus and cortex). KRGM-G inhibited activation of inflammatory cells (Iba-1-positive microglia and GFAP-positive astrocyte) and expression of pro-inflammatory mediators (IL-1β, IL-6, iNOS, or NO) in brains of 5xFAD mice, increased the viability of H2O2-induced SH-SY5Y cells, and down-regulated p38 MAPK, NF-κB p65, and STAT3 signaling pathways. KRGM-G also prevented formation of reactive oxygen species and stimulated Nrf2-HO-1/4-HNE signaling pathway in brains of 5xFAD mice and SY-SY5Y cells. Interestingly, these positive effects of KRGM-G on AD-related symptoms and immunopathology were associated with up-regulation of LPAR1 in brains of 5xFAD mice. These results suggest that KRGM-G might improve AD-related cognitive dysfunction by stimulating anti-oxidant pathway (Nrf2) and inhibiting inflammatory pathways (p38/NF-κB/STAT3) through LPAR1. *Am J Chin Med. 2025;53(1):17-41. doi: 10.1142/S0192415X25500028.*

Keywords : Korean Red Ginseng Marc, Gintonin, Lysophosphatidic Acid Receptor 1, Alzheimer's Disease, Cognition Impairment

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P-020

Initiation of neuronal degeneration by secretory lysosome in Alzheimer's disease

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Neurons are particularly vulnerable to intracellular damage, which contributes to neurodegeneration. One emerging mechanism involves dysfunction in secretory lysosomal pathways, prompting neurons to expel toxic proteins through extracellular vesicles (EVs). While this process is increasingly implicated in Alzheimer's disease (AD)—characterized by extracellular amyloid beta (Aβ) plaques and intracellular tau fibrils—its precise role in disease progression remains unclear. To investigate this, we developed a human brain immune model by co-culturing cerebral organoids with microglia derived from human-induced pluripotent stem cells (hiPSCs) and introduced secretory lysosomal Aβ using an adeno-associated virus (AAV). In this system, secretory lysosomal Aβ induced amyloid plaque formation, axonal dystrophy, and a pronounced microglial response involving synaptic disruption and transcriptomic changes that promoted further amyloid accumulation. Our findings highlight a potential initiating

mechanism in AD pathogenesis: the release of toxic proteins via compromised neuronal lysosomes and their recognition and processing by microglia, which amplifies neuroinflammation and pathological protein spread. Single-cell transcriptomic analysis within this organoid platform reveals previously unrecognized molecular interactions between axons and microglia, offering valuable insight into early disease-triggering events.

Keywords : Alzheimer's disease, Brain organoid, Secretory lysosome, microglia, Amyloid

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P-021

Single-cell Multiomics Integration of Microglia Across Alzheimer's Disease Continuum

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The brain has historically been considered an immune-privileged organ, characterized by a dense network of synaptic connections. Microglia, the resident innate immune cells of the central nervous system, exhibit remarkable heterogeneity and are essential for preserving synaptic integrity and removal of synaptic debris. Recent advancements in single-cell technologies have illuminated a functional continuum of microglial states—ranging from neuroprotective to neurodegenerative—closely linked to individual variability in disease susceptibility and progression, particularly in Alzheimer's disease (AD). In this study, we constructed a comprehensive single-cell multiomics atlas of microglia by integrating single-cell transcriptomics and proteomics, augmented with individualized morphometric parameters. Utilizing our custom-developed single-cell microHOLD proteomic platform, we resolved proteomic alterations at the single-cell level across microglial subsets derived from models spanning the AD continuum. Spatial localization of individual microglial cells was achieved through integration with MERFISH-based transcriptomic data encompassing 2.8 million cells. Additionally, single-cell morphometric profiling was performed to correlate microglial functional states with dynamic morphological transitions along the course of AD pathology. Our integrated single-cell multiomics map reveals disease-associated microglial functional heterogeneity and morphological specialization, offering new insights into region-specific microglial roles in the AD brain and highlighting potential targets for therapeutic intervention.

Keywords : Alzheimer's disease, Multiomics, Single-cell proteomics, Single-cell morphometry, Microglia

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P-022

Asymmetric α-synuclein accumulation and neurodegeneration in a hemiparkinsonian primate model induced by unilateral intracarotid MPTP

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Parkinson's disease (PD) is characterized by dopaminergic neurodegeneration and pathological accumulation of α-synuclein. Hemiparkinsonian nonhuman primate (NHP) models are commonly used to study PD pathophysiology and assess therapeutic strategies. These models are typically generated by unilateral intracarotid injection of MPTP, which induces asymmetric dopaminergic degeneration and enables within-subject comparisons between hemispheres. In this study, three monkeys (C1, C2, and C3) received one or two unilateral MPTP injections via the right internal carotid artery. PET using FP-CIT revealed distinct phenotypes: C1 showed clear hemiparkinsonian features with unilateral striatal dopaminergic loss; C2 exhibited bilateral damage (and unfortunately succumbed during the follow-up period); C3 showed minimal dopaminergic deficit despite two infusions. We histologically analyzed phosphorylated α-synuclein (pS129-α-syn) pathology and dopaminergic neurodegeneration in C1 (hemiparkinsonian) and C3 (undamaged) at 20 months post-injection. A dense reticulated pattern of pS129-α-syn immunoreactivity was asymmetrically increased in C1, particularly in the putamen (119.7 ± 3.7%), substantia nigra (119.9 ± 1.7%), hippocampus (129.0 ± 2.5%), and thalamus (120.4 ± 3.9%), compared to the contralateral side of C1. In contrast, dot-like α-synuclein signals were present in all animals. Lewy body-like inclusions were not detected. Asymmetrical dopaminergic neuron loss was histologically detected in the striatum (37.7 ± 19.7%, optical density) and substantia nigra (20.1 ± 10.6%, cell count) of C1, consistent with PET findings. Although limited in sample size, this study shows that unilateral MPTP models can recapitulate α-synuclein pathology including reticulated and dot-like patterns alongside dopaminergic loss. These models may serve as a useful platform for studying hemiparkinsonian pathology and evaluating candidate therapies.

Keywords : Parkinson's disease, α-synuclein, MPTP, Hemiparkinsonism, Dopaminergic neurodegeneration

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P-023

Hippo signaling pathway is implicated in TSC-associated Intellectual Disability

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Children with Tuberous Sclerosis Complex (TSC) develop intellectual disability (ID) with a prevalence of approximately 40%. Various pathological features associated with TSC, including ID, macrocephaly, and malformations of cortical development, result from loss-of-function mutations in either *TSC1* or *TSC2*. To investigate the pathogenesis of ID in TSC, we examined the role of the *Tsc1* gene in the Hippo signaling pathway, which regulates organ size, cell proliferation, and apoptosis. In *Tsc1*-deficient mice, we observed abnormal brain overgrowth, accompanied by increased activity of YAP, a key effector of the Hippo signaling pathway. Furthermore, in *Tsc1*$^{-/-}$ astrocytes, we found that dysregulation of Hippo signaling pathway induced by *Tsc1* deficiency leads to astrocyte dysfunction, which can be mediated by ICAM-1, a known downstream target of this pathway. Collectively, these findings suggest that *Tsc1* deficiency-induced dysregulation of the Hippo signaling pathway in astrocytes may contribute to the development of ID in TSC.

Keywords : Intellectual disability, Hippo signaling pathway, Astrocyte, Tuberous sclerosis

P-024

Medial amygdala's role in abnormal social behavior in Shank2 haploinsufficiency

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Social familiarity information is essential for maintaining stable and dynamic social networks, influencing behaviors such as keeping proximity, aggression, and mating. The medial amygdala (MeA) is plays a key role in recognizing social cues, such as pheromones and facial expressions. It is involved in distinguishing familiar and unfamiliar conspecifics and modulating social behaviors accordingly. In this study, we identified a specific population of GABAergic, somatostatin-expressing neurons in the posteroventral subdivision of the MeA (MeApv), which are tagging social familiarity information. Based on these findings, we hypothesized that MeApv somatostatin-expressing neurons disinhibit MeApd GABAergic neurons, thereby modulating aggression. To test this hypothesis, we employed Shank2 mutant mice, a well-established ASD model. Shank2 haploinsufficient (Shank2 HT) mice exhibited impaired social recognition and heightened aggression. Additionally, while the population of somatostatin-expressing neurons in the MeA was increased, MeApv somatostatin-expressing neuronal activity was absent, suggesting a potential disruption in the functional connection between social recognition and aggression circuits. Our findings reveal a novel MeA circuit linking social recognition and aggression, providing insights into the neural mechanisms underlying altered social behaviors in ASD.

Keywords : Medial amygdala, Shank2 haploinsufficiency, Social familiarity, Somatostatin

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P-025

Non-saponin experimental autoimmune encephalomyelitis by maintaining blood-brain barrier integrity via NF-κB and p38 MAPK signaling pathway in

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Background: Non-saponin (NS) compounds are the main active components of Panax ginseng, with multifunctional pharmacological activities including neuroprotective, immune regulatory, anti-inflammatory, and antioxidant effects. However, the effects of NS compounds on multiple sclerosis (MS), a chronic and autoimmune disease of the central nervous system, have not yet been demonstrated. Purpose and Methods: The purpose of this study was to investigate the pharmacological effects of NS compounds on movement dysfunctions and the related mechanisms of action using a myelin oligodendrocyte glycoprotein peptide-induced experimental autoimmune encephalomyelitis (EAE) mouse model of MS. Results: NSs (p.o.) alleviated movement dysfunctions in EAE mice related to reduced demyelination in the lumbar spinal cord (LSC). NSs attenuated the recruitment of resident microglia (CD11b+/CD45low) and peripheral macrophages (CD11b+/CD45high) in LSCs from EAE model mice, consistent with the alleviated mRNA expression levels of a representative proinflammatory cytokine (IL-1β), an enzyme (COX-2), and chemokines (MCP-1, MIP-1α, and RANTES). NSs blocked the infiltration of Th17 cells (CD4+/IL17A+) and mRNA expression levels of IL17A (product of Th17 cells) in LSCs from EAE mice. NS compounds inhibited alterations in blood-brain barrier (BBB) components, such as astrocytes and cell adhesion molecules, associated with inhibiting nuclear factor kappa-B (NF-κB) and p38 mitogen-activated protein kinase (MAPK) signaling pathways in LSCs of EAE mice and lipopolysaccharide-induced bEND.3 cells. Conclusion: NS compounds could attenuate movement dysfunctions and related pathological/inflammatory changes by alleviating BBB permeability by inhibiting NF-κB and p38 MAPK pathways in LSCs of EAE model mice. These are the first results suggesting NS compounds as potential therapeutic agents for MS by inhibiting BBB permeability. J. Ginseng Res. 2025 Jan;49(1):53-63. doi: 10.1016/j.jgr.2024.09.005.

Keywords : Non-saponin, Multiple sclerosis, Experimental autoimmune encephalomyelitis, Blood-brain barrier, Ginseng

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P-026

Loss of Cyclin Y modulates autistic-like behaviors in *Shank3*^{InsG3680} mice

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Autism spectrum disorder (ASD) is characterized by elevated repetitive behaviors, impaired social interaction and communication, and decreased cognitive flexibility, which are considered to be the core symptoms of ASD. One of the most prominent genetic risk factors for ASD is the gene that encodes the Src homology 3 (SH3) and multiple ankyrin repeat domain (Shank3) protein, a key postsynaptic scaffolding molecule. We used the *Shank3*^{InsG3680} mouse line, which was generated by the Guoping Feng group at MIT, as an ASD model. This line was created by inserting a single guanine nucleotide (G) at position 3680 of exon 21, corresponding to a variant found in patients with ASD. Our recent findings demonstrated that knockout (KO) of cyclin Y (CCNY), a postsynaptic remodeling protein, enhances long-term potentiation and weakens long-term depression at Schaffer collateral-CA1 synapses in the hippocampus. Furthermore, *Ccny* KO mice exhibited improved spatial learning and cognitive flexibility. Given the association between ASD and impaired cognitive flexibility, we are currently investigating the potential involvement of CCNY in ASD-related synaptic and behavioral abnormalities. Specifically, we assessed whether CCNY deficiency could alleviate ASD-associated behavioral phenotypes, such as increased repetitive behavior and decreased novel social interaction, in *Shank3*^{InsG3680} mice. We also examined whether these CCNY-mediated effects depend on age or sex. The findings of this study will provide insights that will shape future work on mapping a specific ASD-associated behavioral phenotype to the corresponding brain circuits and synaptic changes mediated by CCNY.

Keywords : Autism, Shank3, Repetitive behavior, Social interaction, Cyclin Y

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P-027

Dysregulation of the FGFR1 signaling in hippocampus facilitates depressive disorder

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Major Depressive Disorder (MDD) is a complex psychological disorder with a sophisticated molecular etiology. While the involvement of Fibroblast Growth Factor Receptor 1 (FGFR1) in the hippocampus has been recognized, its precise role in MDD pathophysiology remains poorly understood. In this study, we conducted a detailed molecular analysis of the hippocampus in MDD patients and identified a distinct upregulation of FGFR1 specifically in the dentate gyrus (DG). Using subregional RNA sequencing and immunohistochemistry, we identified a distinct overexpression of FGFR1 specifically within the dentate gyrus (DG) of MDD patients. To explore the functional significance of FGFR1 signaling, we employed in vivo optogenetics and uncovered a sequential FGFR1–Notch–Brain-Derived Neurotrophic Factor (BDNF) signaling pathway within the DG. This pathway was shown to promote adult hippocampal neurogenesis (AHN), a process linked to antidepressant effects. Our results demonstrate that this signaling axis is critical in modulating depressive phenotypes. Importantly, we identified that the protein Numb, which increases with age in individuals with MDD, disrupts this axis. Numb interferes with FGFR1-mediated Notch activation and downstream BDNF expression, leading to impaired AHN and exacerbation of depressive behaviors. Strikingly, therapeutic targeting of Numb restored proper signaling and reversed depressive-like symptoms in the mouse depression model, offering a novel mechanistic insight and potential intervention strategy. Although previous studies have reported growth factor alterations in MDD, our findings provide the first spatiotemporal dissection of the FGFR1 axis and its regulatory mechanisms in the DG, advancing our understanding of MDD's molecular etiology and highlighting a promising target for future therapies.

Keywords : Major Depressive Disorder, FGFR1 signaling, Optogenetics, Senecence, Numb

Acknowledgements : J.S., S.K., and W.D.H. conceived the project and designed experiments. J.S. and H.O. performed mouse experiments. J.H.P. and M.L. performed human tissue sample preparation. H.B., C.M.Y., M.L., and S.K. performed histology of human tissue and quantification. J.S., H.O., S.K., and W.D.H. analyzed and interpreted data. J.S. wrote an initial draft of the paper. This work was supported by NRF of MSIT

P-028

Anxiolytic Effects of Gami-Guibitang in Autism Spectrum Disorder Mouse Model

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by persistent deficits in social interaction and communication, along with restricted and repetitive behaviors. ASD is a multifactorial condition influenced by both genetic and environmental factors, and due to the lack of effective pharmacological treatments, interest in alternative and complementary therapies is increasing. In this study, the behavioral effects and underlying pharmacological mechanisms of Gami-Guibitang (GBT), a traditional herbal prescription, was investigated using a valproic acid-induced ASD mouse model. GBT was orally administered to ASD model mice twice daily at a dose of 150 mg/kg starting from postnatal day 21 for 4 weeks. As a result, the GBT-treated group (AGBT) showed significantly reduced anxiety-like behaviors compared to the ASD

control group, along with trends toward improvement in repetitive behaviors and social deficits. Biochemical analyses revealed elevated serum TNF-α levels in the ASD model. p-CREB expression was significantly increased in the prefrontal cortex and hippocampus of the ASD model, indicating hyperactivation of intracellular signaling. However, in the AGBT group, p-CREB levels were restored to levels comparable to the vehicle control group. Additionally, the expression of synaptic proteins such as synaptophysin, as well as AMPA receptor subunits GluR1 and GluR2, was significantly reduced. These findings suggest that GBT may help restore neural circuit homeostasis by modulating the excitation/inhibition imbalance and synaptic overactivation observed in ASD. Taken together, this study experimentally supports the therapeutic potential of GBT in alleviating core behavioral symptoms of ASD, including anxiety, social deficits, and cognitive impairments. These results provide foundational evidence for the clinical application of traditional herbal medicine in ASD treatment.

Keywords : Autism spectrum disorder, Gami-Guibitang, anxiety, E/I balance, Synaptic homeostasis

P-029

Exacerbation of Alzheimer's Disease Pathology by Brain Insulin Resistance in the 5xFAD Mouse Model

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Alzheimer's disease (AD) is a prevalent neurodegenerative disorder increasingly associated with metabolic dysfunction, particularly insulin resistance. Epidemiological evidence indicates a high prevalence of type 2 diabetes mellitus (T2DM) among AD patients, underscoring a strong association between systemic insulin resistance and AD pathogenesis, with brain insulin resistance proposed as a putative mediator of this relationship. Nevertheless, the mechanistic role of brain insulin resistance in AD progression remains incompletely elucidated. In this study, brain insulin resistance was induced in 5xFAD transgenic mice, an established AD model, via continuous intracerebroventricular administration of the insulin receptor antagonist S961 over a four-week period using osmotic minipumps. Compared to controls, mice subjected to brain insulin resistance exhibited subtle but statistically significant cognitive deficits in behavioral assessments. Histopathological evaluation revealed a significant increase in amyloid-beta (Aβ) deposition in the insulin-resistant group. Alterations in markers reflective of β-secretase activity suggested an upregulation of amyloidogenic processing, while changes in markers associated with Aβ clearance mechanisms likely contributed to its accumulation. Collectively, these findings demonstrate that sustained brain insulin resistance perturbs Aβ metabolism and accelerates AD-related pathology, highlighting the brain insulin signaling pathway as a potential therapeutic target for Alzheimer's disease.

Keywords : Alzheimer's disease, Insulin Resistance, S961, 5xFAD, Insulin Receptor Antagonist

P-030

Effect of chronic corticosterone administration on acute stress-mediated gene expression in the cortex and hippocampus

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The stress-related adrenal glucocorticoid hormones play a pivotal role in the response to environmental and psychological stress stimuli. Although several studies have demonstrated that chronic corticosterone administration induces stress-related behaviors in rodents, it remains unclear whether chronic corticosterone treatment affects gene expression in the brain during the stress response. To investigate whether chronic corticosterone administration has a significant effect on stress-related gene expression in the brain, mice were chronically treated with corticosterone and gene expression was analyzed by quantitative PCR. Moreover, restraint stress was acutely applied as a novel stressor in mice chronically treated with corticosterone in the cortex and hippocampus. In this study, we found that chronic corticosterone administration altered glucocorticoid signaling-mediated gene expression, such as FK506 binding protein 5 (Fkbp5) and glucocorticoid-inducible kinase 1 in the cortex and hippocampus. Next, we found that restraint stress exposure elevated Fkbp5 expression in the vehicle group; however, chronic corticosterone administration occluded further induction of Fkbp5 expression after restraint stress exposure. In addition, pro-inflammatory cytokines tumor necrosis factor α and interleukin-1β mRNA expression in the cortex and hippocampus were remarkably increased by restraint stress in corticosterone-treated mice, but not in the vehicle group. Taken together, our results demonstrated that chronic corticosterone administration modulates glucocorticoid signaling and uncovered the robust induction of pro-inflammatory cytokines after restraint stress exposure in chronically corticosterone-treated mice.

Keywords : Corticosterone, Gene expression, Glucocorticoid signaling, Inflammatory cytokine

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P-031

Interoceptive sensing process against chronic colitis present to anxiety and depressive-like behavior

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Interoception of our body refers to the brain's ability to perceive internal organ defects, which is associated with the development of neuronal

behavior in inflammatory response. Inflammatory bowel disease (IBD), characterized by abdominal pain and diarrhea, is defined by repeated cycles of relapse and remission, which cause chronic intestinal inflammation. Over 30% of patients with IBD have difficulties with mood disorders, such as anxiety and depression. These mood disorders can reduce quality of life and contribute to a vicious cycle of inflammation, further increasing mortality and suicide rates. However, what phase (acute, subacute, chronic) colitis induces mood disorders remain poorly understood. In this study, colitis was induced by administering Dextran sulfate sodium (DSS) for one week, and its symptoms were assessed using the Disease activity index (DAI) score. First of all, with those mice, we assessed the neurobehavioral analysis at 5 days (acute phase) which start to the aggravating DAI score in colitis model. At that time, we can't found any difference of neurobehavioral symptoms compared to vehicle-treated group. Second, one week (subacute phase) after the recovery of colitis symptoms, as assessed by the DAI score, neurobehavioral analyses were conducted. Anxiety-like behaviors were assessed using the Open field test (OFT), Elevated plus maze (EPM), and Light-dark box test (LDT), while depressive-like behaviors were evaluated using the Tail-suspension test (TST) and Forced swim test (FST). Different with acute phase of colitis model, subacute phase of it represents anxiety and depressive-like behaviors even though the DAI score had recovered in during this phase. In conclusion, we found that anxiety and depressive like behaviors act as evoked phenotype of interoceptive sensing process in subacute colitis mouse model. In future studies, we aim to investigate the mechanisms by which colitis induces mood disorders through gut-brain communication.

Keywords : Interoception, IBD, Mood disorder, Anxiety, Depression

P-032

Astrocytic O-GlcNAcylation modulates Social and Affective Behaviors in Mice

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Glycosylation, a post-translational modification, regulates secondary protein processing. Among its forms, O-GlcNAcylation—the addition of a single N-acetylglucosamine residue to serine or threonine residues—plays a crucial role in modulating dynamic protein functions. While O-GlcNAcylation has been extensively studied in neurons, its role in astrocytes remains largely underexplored, despite the high expression of O-GlcNAc transferase (OGT) and O-GlcNAcase (OGA) in these cells. This study investigates the role of astrocytic O-GlcNAcylation in neuropsychiatric behaviors using astrocyte-specific OGT and OGA conditional knockout mouse models. Our findings reveal that astrocyte-specific OGT knockout mice exhibit significantly reduced OGT expression, increased GFAP and GABA levels, and widespread astrocyte reactivity, characterized by a ramified morphology throughout the brain. Behavioral assessments revealed a significant reduction in anxiety-like behavior, impaired sociability, increased repetitive behaviors, and deficits in fear memory retrieval in both male and female mutant mice. To our knowledge, this is the first study to characterize the behavioral consequences of astrocyte-specific OGT loss, particularly in relation to antisocial and autism spectrum disorder–like traits. Given recent findings of de novo missense variants in the human OGT gene among ASD probands, our research suggests that astrocytic OGT may be a potential target for ASD treatment.

Keywords : O-GlcNAcylation, Astrocytes, Social Behaviors, ASD

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P-033

Effect of environmental enrichment on chronic unpredictable mild stress - Focused on microbiota-gut-brain axis

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Major depressive disorder (MDD) is a common mood disorder marked by depressed mood and cognitive impairment. Dysbiosis of gut microbiota can increase intestinal permeability, leading to a leaky gut. This dysbiosis exacerbates inflammatory responses in the gut and contributes to dysfunction in the microbiota-gut-brain axis, which may increase the risk of MDD. Recent studies have suggested that restoring gut microbiota and the microbiota-gut-brain axis could effectively alleviate symptoms of depression. Environmental enrichment (EE) has benefits for depression, though its effects on gut microbiota are unclear. Here we investigated the effects of EE on depressive-like behavior and the gut microbiome using a chronic unpredictable mild stress (CUMS) mouse model. Mice subjected to CUMS were randomly assigned to either a standard environment (SE) or an enriched environment (EE) for four weeks. The tail suspension test (TST) was used to assess depressive-like behavior. The CUMS+EE group exhibited significantly reduced immobility time in the TST compared to the CUMS+SE group, showing results similar to those of the control group. Tryptophan hydroxylase(TPH)-positive cells was significantly higher in both the control group and the CUMS+EE group compared to the CUMS+SE group. Glucocorticoid receptor(GR)-positive cells was notably lower in the control and CUMS+EE groups than in the CUMS+SE group. The composition of gut microbiota was analyzed using 16S rRNA sequencing. The results showed that the bacterial diversity in the CUMS+EE group was comparable to that of the control group, indicating a similar level of alpha diversity. In terms of beta diversity, the bacterial species in the CUMS+EE group were found to be more similar to those in the control group than to those in the CUMS+SE group. In conclusion, our findings suggest EE can serve as a therapeutic approach for depression, contributing to a change in gut microbiota.

Keywords : Chronic unpredictable mild stress, Environmental enrichment, Gut-brain axis, Microbiome

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P-034

Dopaminergic regulation in the synaptic transmission of developing prefrontal cortex and cortisol-mediated disruption.

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Rat pups prenatally exposed to corticosterone (Corti.Pups; 20 mg/kg/day, s.c., for 21 days during gestation) have been reported to exhibit ADHD-like behaviors, cognitive delays, impaired long-term potentiation, and synaptic deficits in hippocampal CA1 neurons. In this study, we investigated alterations in dopaminergic regulation at glutamatergic synapses in the prefrontal cortex (PFC) of Corti.Pups, which may underlie ADHD pathogenesis. ELISA assays conducted from postnatal day 1 to 21 revealed significantly lower levels of BDNF, cAMP, mTOR, PKA, and PSD95 in the PFC of Corti.Pups compared to controls (Nor.Pups), indicating disrupted neurodevelopmental and synaptic signaling. Additionally, D1R expression was slightly increased, while D2R was significantly decreased in Corti.Pups, suggesting an imbalance in dopaminergic signaling. Electrophysiological recordings further showed that dopamine enhanced excitatory postsynaptic currents in Corti.Pup PFC neurons, a response not observed in Nor.Pups, indicating heightened dopamine sensitivity. These findings suggest that prenatal corticosterone exposure disrupts dopaminergic and PKA-mediated pathways in the PFC, contributing to neurodevelopmental impairments and potentially promoting the onset of ADHD-like behaviors.

Keywords : Neurodevelopmental disorder, Corticosterone, Prefrontal cortex, Dopamine, ADHD

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P-035

Transcriptomic analysis of senescence induced in AD patient-derived fibroblasts reveals AD-specific aging signatures

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder in which aging is the greatest risk factor. While most studies have focused on neuronal cells, few have examined aging in peripheral models. Fibroblasts can be directly converted into neurons while retaining age-related molecular features, making them a useful model for studying aging in AD. In this study, we investigated transcriptomic changes during replicative senescence in AD patient-derived fibroblasts to identify AD-specific aging signatures. Fibroblasts from healthy controls and AD patients were serially passaged and harvested at young, mid-old, and old stages. RNA sequencing was performed, and differential expression, functional enrichment, and two-way ANOVA were used to assess the effects of aging, disease condition, and their interaction. To capture aging-associated transcriptomic dynamics, we classified genes by average TPM(Transcripts Per Million) trends across aging stages. Genes with monotonic increase or decrease were grouped as aging-upregulated or -downregulated, respectively. Two-way ANOVA was applied separately to these groups to assess the additional effect of AD and aging–disease interaction. Among aging-upregulated genes with significant interaction ($p < 0.05$), clustering revealed two patterns: one where AD fibroblasts showed delayed increase until old stage, and another where AD showed a flat trajectory while controls increased steadily. In aging-downregulated genes, clusters showed earlier or more rapid decline in AD compared to controls. Functional enrichment of upregulated-interaction genes indicated immune-related processes such as myeloid cell differentiation and MAPK signaling, while downregulated-interaction genes were enriched for pseudogenes and ribosome-associated transcripts. These findings highlight altered aging trajectories in AD and provide a foundation for defining AD-specific mechanisms and identifying characteristic gene signatures.

Keywords : Alzheimer's disease, Patient-derived fibroblasts, Induced cellular senescence, Transcriptomic analysis, AD-specific signatures

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P-036

Dynamic interaction between interneuron and GPR56 expressing cells during the tangential migration of cortical formation

name
address

Dynamic interaction between interneuron and GPR56 expressing cells during the tangential migration of cortical formation The proper development of the neocortex relies on tightly regulated neuronal migration, including the radial migration of excitatory pyramidal neurons and the tangential migration of GABAergic interneurons. Interneurons originating from the medial/lateral ganglionic eminence (MGE/LGE) migrate tangentially to populate approximately 20–30% of cortical neurons, forming critical inhibitory networks that balance cortical excitation. Disruptions in these migratory processes contribute to neurodevelopmental disorders such as intellectual disability, autism, and epilepsy. Interneuron migration is influenced by interactions with the vascular system, microglia, oligodendrocyte precursor cells (OPCs) as well as neural progenitor cells (NPCs). GPR56 (ADGRG1), an adhesion G protein-coupled receptor for the extracellular matrix protein collagen III, plays a crucial role in maintaining radial glial scaffolds and regulating radial migration. While mutations in GPR56 are associated with rare cortical malformations, its broader roles in brain development remain unclear. In this study, we investigate the roles of GPR56-expressing cells in tangential migration during early cortical development using Fragile X syndrome (FXS) mice, which exhibit aberrant neuronal migration. Our findings show that while GPR56 is absent in interneurons itself, it is prominently expressed in pyramidal neuron progenitors and becomes restricted to the subventricular zone after embryonic

day 17.5. Importantly, during the tangential migration of interneurons, GPR56 is predominantly expressed in microglia and OPCs located near GE. These results suggest that disease-specific molecular networks involving GPR56 may contribute to interneuron migration deficits observed in FXS, offering new insights into the cellular mechanisms underlying neurodevelopmental disorders.

Keywords : Interneuron, GPR56 (ADGRG1), Tangential migration, Neurodevelopmental disorders, Fragile X syndrome

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P-037

Translating schizophrenia pathology: The MAM model as a preclinical mirror of human disease

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Schizophrenia is a chronic psychiatric disorder characterized by a range of symptoms, including delusions, hallucinations, disorganized speech, and emotional blunting, often resulting in impaired social functioning. Although the precise etiology of schizophrenia remains unclear, it is believed to involve a complex interplay of biological, genetic, and psychosocial factors. Schizophrenia symptoms are broadly classified into positive, negative, and cognitive domains, and various animal models have been developed to recapitulate these features. However, most existing models are limited by their ability to reproduce only specific symptoms or by a lack of specificity to schizophrenia. In this study, we utilized the neurodevelopmental methylazoxymethanol acetate (MAM) model, which replicates neuroanatomical and neurochemical changes observed in human schizophrenia. MAM was administered to pregnant mice on GD16, inducing schizophrenia-relevant structural, functional, and behavioral deficits in offspring. Behavioral assessments included location/probability-based reversal learning tasks to evaluate cognitive flexibility, novel object recognition (NOR) and Y-maze tests to assess spatial working memory. Social interaction tests were used to quantify negative symptoms, and prepulse inhibition (PPI) tests were conducted to assess sensory processing deficits. To elucidate the underlying neurobiological mechanisms, we performed Golgi staining-based neuronal morphology analyses and parvalbumin interneuron (PV) immunohistochemistry. Our findings demonstrate that MAM-exposed offspring exhibit significant impairments in cognitive flexibility, spatial working memory, social interaction, and sensory processing, which are accompanied by reduced dendritic complexity and decreased PV interneuron density in relevant brain regions. Thus, the MAM model provides a robust platform for comprehensive investigation of the pathophysiology underlying the diverse symptom domains of schizophrenia.

Keywords : Schizophrenia, MAM model

P-038

Elucidating the protective mechanisms of the APOE Christchurch variant (R136S) against Alzheimer's disease via LRP1 interaction

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The APOE Christchurch (R136S, Ch) variant in PSEN1 E280A kindred was reported to have a protective role against Alzheimer's disease (AD), yet the underlying mechanisms remain unclear. While previous studies demonstrated that APOECh attenuates amyloid beta (Aβ) and tau-mediated neurotoxicity in human organoids and mouse models, they focused on phenotypic outcomes without addressing the precise protective mechanisms. Given that the APOECh variant within the receptor-binding domain of the APOE protein, we hypothesized that an altered interaction with the LRP1 receptor mediates the protective effect. To specifically determine how the Ch variant rescues AD pathology, we generated isogenic APOE3, APOE4, and APOE4Ch human-induced pluripotent stem cells (hiPSCs) using the CRISPR-Cas9 system and differentiated them into astrocytes. E4Ch astrocytes restored reduced LRP1 expression and suppressed the enhanced APOE-LRP1 binding affinity observed in E4 astrocytes. Moreover, the impaired LRP1-dependent tau uptake seen in E4 astrocytes was rescued in E4Ch astrocytes. To further explore the interaction between APOE and LRP1 protein, we employed supercomputing-based structural simulations and identified APOE K143A as a potential variant that disrupts the APOE-LRP1 interaction in a manner similar to APOECh. Ongoing studies will validate whether the APOE K143A variant recapitulates the protective effects of APOECh in astrocytes. In addition, transcriptomic and proteomic analyses revealed that the Ch variant rescued the altered transcriptome and proteome profiles caused by APOE4 in astrocytes. We aim to determine whether small molecules that mimic either the structural conformation or the transcriptomic signature of the Ch variant can exhibit resilience in AD. Taken together, our data suggest that the APOE Ch variant has protective effects against AD in an LRP1-dependent manner in human astrocytes.

Keywords : Apolipoprotein E (APOE), APOE Christchurch (R136S), LRP1, receptor binding affinity

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P-039

KINE-PD-28, a cytokine-derived small peptide, improves motor dysfunction through anti-inflammatory-related neuroprotection in PD animal models.

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Parkinson's disease (PD) is a neurodegenerative disorder characterized

by the loss of nigral dopaminergic neurons and their projections into the dorsal striatum, leading to decreased dopamine levels. Emerging evidence highlights the role of neuroinflammation in exacerbating dopaminergic cell loss, defining PD as a multifactorial systemic disease. To achieve dopaminergic neuroprotection, microglia, central regulators of neuroinflammation and homeostasis, have been identified as a potential therapeutic target in PD. In this study, we show the efficacy of candidate PD treatment drugs targeting anti-inflammation by microglia modulation in 6-OHDA-induced PD animal models. KINE-PD-28 is a long-lasting synthetic ultra-small peptide derived from erythroid differentiation regulator 1 (ERDR1), an anti-inflammatory cytokine. In this study, we demonstrate the experimental efficacy of KINE-PD-28 in mitigating neuroinflammation induced in a 6-OHDA PD mouse model. Our results show that treatment with KINE-PD-28 improved motor dysfunction, preserved nigrostriatal dopaminergic neurons, and reduced the activation of astrocytes and microglia. These findings suggest that the anti-inflammatory effects of KINE-PD-28 hold promise for neuroprotection in PD.

Keywords : neuroinflammation, Parkinson's disease, cytokine, anti-inflammatory, microglia

P-040

Alcohol Addiction-like Behaviors in Operant Ethanol Self-Administration Mediated by the mPFC Reward Circuit

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Ethanol is one of the most accessible and commonly used substances associated with substance use disorders. Despite its widespread availability, only a subset of individuals develop alcohol use disorder (AUD), pointing to complex underlying neurobiological mechanisms. Addiction is a chronic brain disorder characterized by persistent, compulsive drug-seeking despite adverse consequences, and distinct neural circuits shape its development and progression. To investigate the neural underpinnings of alcohol addiction, we established an ethanol addictive-like behavioral model using operant oral self-administration in mice. Mice were phenotyped based on behavioral responses in fixed ratio (FR) and progressive ratio (PR) schedules, allowing us to cluster ethanol-seeking behaviors. We found that operant interaction patterns in the PRs are the most highly associated with the alcohol-drinking phenotype. We hypothesize that medial prefrontal cortex (mPFC)-based reward circuits critically modulate these complex ethanol-seeking behaviors in ethanol self-administration. To dissect the contribution of specific mPFC output pathways, we employed inhibitory DREADDs (hM4Di) to selectively target four mPFC-output pathways: mPFC→nucleus accumbens (NAc), mPFC→ventral tegmental area (VTA), mPFC→dorsomedial striatum (DMS), and mPFC→basolateral amygdala (BLA). Immediate early gene analysis following PR sessions revealed region-specific FosB expression. Linear regression analyses showed that FosB expression in the DMS was most strongly correlated with active lever pressing, while FosB in the mPFC was highly correlated with total ethanol intake. These findings suggest that distinct mPFC-output circuits differentially contribute to motivational dimensions of ethanol seeking, with region-specific FosB expression patterns potentially underlying individual differences in alcohol-related behavior. Further research is required to clarify the circuit-specific mechanisms regulating these phenotypes.

Keywords : Alcohol Addiction, Self Administration, Medial Prefrontal Cortex, Reward Circuit

P-041

Inflamed Lung Signals Alert to the brain that present to anxiety like behavior

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More than 35% of patients continue to experience neurobehavioral complications, such as depression, anxiety, and cognitive impairment, even after recovering from COVID-19. Persistent lung inflammation has been suggested to be associated with these neurobehavioral changes through synaptic dysfunction in the brain; However, which phase (acute, subacute, chronic) of lung inflammation is associated with behavioral alterations remains poorly understood. In this study, we established a lung inflammation mouse model by Intratracheal injecting lipopolysaccharide (LPS) at doses of 2 mg/kg and 4 mg/kg. Additionally, to evaluate behavioral changes in an infectious model, we prepared *Mycobacterium abscessus* in bead form and Intratracheal administered it to generate a lung infection mouse model. Behavioral tests, including the Open Field Test (OFT), Elevated Plus Maze (EPM), Light-Dark Box Test (LDT), Forced Swim Test (FST), and Tail Suspension Test (TST), were performed to assess general activity, anxiety-like behaviors, and depression-like behaviors. As a result, on day 3, during the acute phase of lung inflammation, the groups administered LPS showed decreased general activity in the OFT, but no significant changes in mood-related disorders were observed. In the subacute phase (week 2), anxiety-like behaviors were significantly increased in the LPS 4 mg/kg group compared to the LPS 2 mg/kg and saline groups, while no significant changes were observed in depression-like behaviors. However, by week 3, anxiety-like behaviors were no longer observed in any of the groups. These findings suggest in subacute phase that lung inflammation may selectively induce anxiety-related behavioral changes. In future studies, we plan to investigate the underlying molecular mechanisms by analyzing synaptic protein expression in the brain and identifying circulating cytokines that may contribute to brain-lung communication.

Keywords : Anxiety, Depression, Neurobehavioral change, Lung inflammation, Phase

P-042

Mitochondrial Complex I Deficiency Modulates Motor Behavior and Anxiety: Insights into Neurodegenerative Disorders

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Mitochondrial dysfunction is recognized as a common pathological mechanism across various neurodegenerative diseases, with impaired energy metabolism contributing to neuronal damage. However, the impact of long-term, mild mitochondrial dysfunction on behavioral phenotypes in these disorders remains poorly understood. This study investigated behavioral patterns and associated cellular modifications in an transgenic mice with mild impairment of mitochondrial complex I activity. This model recapitulates the mild mitochondrial dysfunction observed in neurodegenerative diseases. Animal behavioral tests revealed that these mice displayed significantly elevated anxiety levels and reduced locomotor activity compared to control. Furthermore, we observed a significant increase in p-tau levels, a hallmark of neurodegeneration in the mice. These findings suggest that even modest impairment of mitochondrial complex I activity disrupt brain homeostasis leading to behavioral abnormalities such as motor deficits and hyper-anxiety. The elevated p-tau levels suggest a potential mechanism by which mitochondrial dysfunction accelerates neurodegenerative pathology. This study highlights the our model as a valuable tool for understanding the role of mitochondrial impairment in the pathological mechanisms of brain disorders, emphasizing the need for further research to elucidate the exact mechanisms. Funding Source : This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center (KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (Grant number: HU23C0199).

Keywords : Neurodegeneration, mitochondrial dysfunction, Complex I activity

P-043

GSK3b activation was modulated the pathology of Alzheimer's disease.

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Alzheimer's disease is one of the most common neurodegenerative diseases. Pathologically, it is characterized by the accumulation of amyloid-beta (Aβ) aggregates in the brain, which is considered as a major cause of cognitive dysfunction. The accumulation of beta-amyloid aggregates leads to the hyperphosphorylation of tau protein and neuronal damage. The main biological function of tau is to stimulate microtubule assembly and stabilize the microtubule network. Tau's dynamic role in microtubule formation is tightly regulated by its phosphorylation status. This phosphorylation is maintained by a complex interplay of various protein kinases and phosphatases. Glycogen synthase kinase-3 beta (GSK-3β) is a proline-directed serine/threonine protein kinase, and its activity is regulated by phosphorylation at Ser9 and Tyr216. Specifically, Ser9 phosphorylation inhibits its activity, and inactivated GSK-3β can reduce tau protein phosphorylation. We performed behavioral analyses and histological examinations in mice. Our findings demonstrated that GSK-3β Ser9 phosphorylation levels correlated with differences in cognitive function, amyloid-beta plaque accumulation, and tau phosphorylation status. Higher levels of Ser9 phosphorylation correlated with improved cognitive function, reduced tau phosphorylation, and decreased amyloid-beta aggregates and glial cells activation. These findings highlight the crucial role of GSK-3β Ser9 phosphorylation in modulating Alzheimer's disease pathology, suggesting a potential therapeutic target for cognitive preservation and disease modification. *Funding Source : This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center (KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (Grant number: HU23C0199).*

Keywords : Alzheimer's disease (AD), Amyloid-beta (Aβ), Tau hyperphosphorylation, GSK-3β Ser9 phosphorylation, Cognitive dysfunction

P-044

The Impact of Chronic Social Isolation on Memory Decline: The Role of Inflammation and Myeloid Receptor Dysregulation in Aging

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Chronic social isolation in aging populations is a significant risk factor for the development and progression of memory decline. This prolonged isolation often leads to a state of chronic, low-grade inflammation, which adversely affects the neurobiological pathways essential for cognitive health. Importantly, emerging evidence suggests that the harmful effects of this chronic inflammation on memory can be significantly exacerbated by reduced myeloid receptor expression, compromising the brain's vital neuroimmune regulatory mechanisms. As a result, the combination of extended social isolation, subsequent chronic inflammation, and diminished myeloid receptor signaling likely creates a synergistic cascade that accelerates memory impairment in the aging brain. To investigate the effect of prolonged social isolation, we used 2-year-old myeloid receptor KO (KO) and WT mice, housed individually for one year. There was no difference in anxiety-like behavior between groups. In contrast to WT mice, social isolation affected KO mice displayed defects in social, fear, and spatial memory. Moreover, deficiencies in myeloid receptor expression resulted in an elevated pro-inflammatory response, including TNF-α and IL-1β levels. These findings support the role of myeloid receptor-mediated microglial dysfunction in the detrimental impacts of social isolation on learning and memory.

Keywords : Social isolation , Myeloid receptor, Memory & Cognition, Inflammation

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P-045

Investigation of Electrophysiological Abnormalities in Local Circuits of Brain Tissue from Drug-Resistant Epileptic Patients

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Epilepsy is a chronic neurological disorder characterized by recurrent seizures caused by sudden, abnormal electrical discharges in the brain. While a significant number of patients become seizure freedom with the anti-epileptic drugs, approximately 30% are diagnosed with drug-resistant epilepsy (DRE). The human brain features a uniquely complex synaptic network compared to other species, making it essential to investigate abnormal structures within local circuits of the human epileptic brain for targeted therapeutic approaches. However, studies examining structural and electrophysiological dysfunctions in human epileptic tissue remain limited. To address this, we performed whole-cell patch-clamp recordings on acute brain slices resected from the epileptic foci of DRE patients. Our study aimed to identify and characterize aberrant synaptic connectivity and intrinsic properties of neurons within epileptic circuits. We focused on pyramidal neurons (PNs) and fast-spiking interneurons (FSINs), which are known to exhibit altered intrinsic properties in epilepsy, as reported by Cho et al., 2024 (Nat. Commun.). Our hypothesis is that Pathological cell-type specific changes in these cell types contribute to local circuit dysfunction, with hyperactivity in recurrent pathological networks triggering epileptic episodes. We performed cell-type-specific whole-cell patch-clamp recordings in both current-clamp and voltage-clamp configurations on acute brain slices to investigate intrinsic properties of PNs and FSINs in epileptic foci. Furthermore, we characterized the functional properties of local pathological circuits by analyzing the activation patterns of abnormal recurrent networks formed by epileptic neurons. This study provides key insights into the cellular and synaptic mechanisms of seizure generation in DRE, aiming to identify therapeutic targets and support the development of more effective treatments.

Keywords : Human brain acute slice, Epilepsy, Patch-clamp electrophysiology, Local circuit dysfunction

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P-046

Ursolic acid ameliorates LPS-induced cognitive impairment by modulating microglial activation and neurotrophic signaling in mice

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Neuroinflammation plays a pivotal role in the pathogenesis of cognitive disorders and neurodegenerative diseases. Microglial activation, driven by pro-inflammatory stimuli such as lipopolysaccharide (LPS), contributes significantly to learning and memory impairments. Ursolic acid (UA), a naturally occurring pentacyclic triterpenoid found in various medicinal plants, is known for its anti-inflammatory properties. However, its neuroprotective effects remain insufficiently explored and poorly understood. This study aimed to evaluate the neuroprotective effects of UA in an LPS-induced mouse model of cognitive impairment, focusing on the modulation of microglial activation and related signaling pathways. Mice were divided into four groups: control, LPS, UA (50 mg/kg) + LPS, and UA (100 mg/kg) + LPS. LPS was administered intracerebroventricularly, and UA was given orally for two weeks. Cognitive function was assessed using the passive avoidance, Y-maze, and Morris water maze tests. Immunofluorescence was performed on hippocampal sections to evaluate microglial activation (Iba-1) and astrocyte reactivity (GFAP). Western blot and ELISA were used to quantify inflammatory mediators, anti-inflammatory cytokines, and neurotrophic signaling pathways. Additionally, transmission electron microscopy (TEM) was performed to observe ultrastructural changes. UA treatment significantly improved behavioral performance, reduced Iba-1 expression, and restored P-CREB, P-TrkB, and P-ERK levels, as confirmed by both immunofluorescence and ultrastructural analysis. UA treatment markedly attenuated these pathological changes, preserving synaptic density and mitochondrial integrity and reducing microglial activation at the ultrastructural level. These results suggest that UA ameliorates LPS-induced cognitive dysfunction by modulating microglial activation and neurotrophic pathways, supporting the therapeutic potential of UA in neuroinflammatory and neurodegenerative conditions.

Keywords : Ursolic acid, Lipopolysaccharide, Microglia, Learning and memory, Synaptic plasticity

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P-047

Exploring FK506 Derivatives as Potential Therapeutic Agents for Alzheimer's Disease.

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Tacrolimus (FK506), an FDA-approved immunosuppressive drug, is widely used to prevent rejection in organ transplant recipients. Previous clinical studies have reported that long-term FK506 treatment in transplant patients is associated with a significantly lower incidence of dementia compared to untreated groups. Additionally, previous preclinical studies showed that FK506 suppresses inflammatory responses by inhibiting microglial enlargement and reducing the expression of inflammatory mediators *in vitro* and that calcineurin inhibition by FK506 reduces astrocyte-mediated neuroinflammation, leading to a neuroprotective effect *in vivo*. FK506, a low-molecular-weight compound with high blood-brain barrier permeability, has emerged as a promising therapeutic candidate for neurodegenerative diseases. Based on previous studies, we developed novel FK506

derivatives that preserve its neuroprotective and neurotrophic properties while eliminating immunosuppressive activity. Currently, we are investigating the therapeutic efficacy of these derivatives in an Alzheimer's disease mouse model by assessing their impact on neuropathology. Our previous study evaluated FK506 derivatives that exhibit no cytotoxicity or immunosuppressive effects *in vitro*, while retaining the ability to promote neurite outgrowth in hippocampal neurons. Here, we investigated the pathological effect on astrocytes and microglia in hippocampal CA1 region using immunohistochemistry to evaluate the therapeutic effects of FK506 derivatives.

Keywords : Alzheimer's disease, FK506, Hippocampus, Neuroinflammation, Neurodegeneration

P-048

Electrophysiological effect of FK506 derivates in Alzheimer's disease mouse model.

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Pathological features of Alzheimer's disease (AD) include the accumulation of amyloid-beta (Aβ) plaques, formation of neurofibrillary tangles composed of hyperphosphorylated tau, and significant synaptic loss. Additionally, recent studies have highlighted the involvement of glial cells, particularly astrocytes and microglia, in the pathogenesis of AD. These glial cells play crucial roles in maintaining and modulating synaptic function. For instance, astrocytes are essential for preserving neurotransmitter homeostasis and ionic balance in the synaptic environment, while microglia actively monitor synaptic activity and contribute to synaptic pruning through phagocytosis, thereby influencing synaptic plasticity. FK506 is an immunosuppressive agent widely used in organ transplantation. Beyond its established role in immunosuppression, recent clinical findings suggest that FK506 may exert beneficial effects in the context of neurodegenerative diseases, including dementia. However, CNS-specific downstream mechanisms of FK506—particularly in glial modulation—remain poorly understood. To investigate the effects of FK506 and its derivatives with reduced calcineurin-binding affinity, we focused on their actions in glial cells and their potential influence on synaptic plasticity through age-dependent electrophysiological assessments in CA1 pyramidal neurons in the hippocampus from 3 to 12 months of age in naïve 5xFAD and wild type mice. Specifically, we found electrophysiological changes in CA1 pyramidal neurons to assess the effects of FK506 and FK506 derivates on synaptic transmission. Furthermore, to elucidate the underlying mechanisms of FK506 action, we conducted immunohistochemistry and quantitative RT-PCR analyses, aiming to identify specific FKBP isoforms expressed in the brain and their associated downstream signaling pathways.

Keywords : Alzheimer's diesase, FK506, FKBP, Neurodegeneration, Hippocampus

P-049

Thalamic cell-specific Alterations in an Alzheimer's Disease Mouse Model

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Alzheimer's disease is a progressive neurodegenerative disorder characterized by brain pathologies, such as the accumulation of amyloid plaques and neurofibrillary tangles, leading to neuronal damage and cognitive decline. Many studies have focused on memory-related brain regions, such as the medial prefrontal cortex and the hippocampus. However, our histological screening of 5xFAD mice, one of the Alzheimer's disease mice models, in 3- to 12-month-old age revealed early and progressive pathophysiological changes in the thalamus, including the accumulation of amyloid plaque and reactive astrogliosis. To investigate the cell type-specific alterations in the thalamus during Alzheimer's disease progression, we conducted single nucleus RNA sequencing using the thalamus of 5xFAD and wild type mice. This analysis identified transcriptionally distinct subpopulations in major brain cell types, including astrocyte and microglia, and revealed disease-associated genes and dysregulated molecular pathways in a cell type-specific manner. Our single nucleus transcriptomic resource previously underexplored thalamic vulnerability in Alzheimer's disease and provides molecular insights into cell-type-specific contributions to disease pathogenesis.

Keywords : Alzheimer's disease, Single nucleus RNA-seq, Thalamus, Cell-type specific alteration, Neurodegeneration

P-050

Ablation of microglial Connexin43 promotes short term and long term recovery from traumatic brain injury.

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Traumatic brain injury (TBI) triggers neuroinflammation and secondary neurodegeneration, with microglia playing dual roles in exacerbating damage and facilitating repair. We have previously shown that Connexin43 (Cx43), a gap junction protein highly expressed in microglia, regulates neuroinflammatory responses inthe context of Alzheimer's disease, a chronic neurodegenerative disease. However, the role of microglial Cx43 in acute nervous system insult such as TBI remain unclear. This study investigates how microglial Cx43 ablation influences acute and chronic outcomes after TBI. Using a tamoxifen-inducible, microglia-specific Cx43 knockout mouse model (Cx43flox/flox;CX3CR1-CreERT2), we subjected mice to controlled cortical impact (CCI) and assessed recovery at short-term (1–7 days) and long-term (28–56 days) timepoints. Longitudinal behavioral assessments demonstrated accelerated motor recovery (Catwalk, beam walk) by day 2~7 and sustained cognitive improvement (Novel object recognition) at 4 weeks post-injury($p<0.05$). Acute-phase analysis revealed that Cx43 ablation reduced pro-inflammatory cytokine release, attenuated microglial hyperactivation and peripheral immune cell infiltration compared to controls. Notably, Cx43-deficient microglia exhibited enhanced

phagocytic clearance of debris and upregulated anti-inflammatory markers during the subacute phase. Chronic histopathology revealed reduced white matter degeneration and increased synaptic density in knockout mice, suggesting preserved neural connectivity. These findings establish that microglial Cx43 ablation mitigates neuroinflammatory cascades, promotes tissue repair, and drives functional recovery post-TBI. Targeting Cx43 in microglia presents a promising therapeutic strategy to improve both short- and long-term outcomes after brain trauma.

Keywords : Microglia, Cx43, Brain injury

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P-051

STIM1-dependent calcium signaling in astrocytes controls glutamate accumulation and ischemic brain injury during acute stroke in mice

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Astrocytes critically influence ischemic stroke outcomes through calcium signaling-dependent mechanisms, which can be both beneficial and detrimental. Stromal interaction molecule 1 (STIM1), a key regulator of store-operated calcium entry, has emerged as an essential mediator of intracellular calcium dynamics in astrocytes, yet its role in acute stroke remains largely unknown. Here, we demonstrate that conditional knockout of astrocytic STIM1 in mice dramatically reduces infarct volume and improves neurological function following ischemic stroke. *In vivo* two-photon imaging revealed that astrocytic STIM1 knockout reduces the amplitude and duration of both spreading depolarization-associated and spontaneous calcium transients during acute ischemia. These transients are highly correlated with improved neurological outcomes. Further, the astrocytic STIM1 knockout mitigated excitotoxic stress by accelerating glutamate clearance and reducing total glutamate burden during ischemic stroke. Our findings establish astrocytic STIM1 as a critical regulator of calcium and glutamate dynamics during ischemic stroke, and therefore, targeting astrocytic STIM1 represents a promising therapeutic avenue for alleviating ischemic brain damage by reducing calcium overload and glutamate excitotoxicity.

Keywords : Stroke, Astrocyte, STIM1, Glutamate, Calcium

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P-052

Cerebellar gliosis and motor impairments in autism-like phenotypes induced by maternal cadmium exposure

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Heavy metal pollution, such as cadmium (Cd), has increased with industrialization and has been implicated in various neurological disorders. Maternal exposure to Cd during pregnancy can disrupt neurodevelopment in offspring, affecting both neuronal and glial functions. Autism spectrum disorder (ASD), a complex neurodevelopmental condition, shows a significantly higher prevalence in males compared to females. Considering the neurodevelopmental impact of maternal Cd exposure and the sex-specific vulnerability observed in ASD, it is important to investigate the sex-dependent effects of such exposure on ASD-like phenotypes. Recent studies have highlighted the critical role of the cerebellum in ASD pathophysiology, particularly in motor coordination, cognitive function, and social behavior. Glial cells in the cerebellum, including astrocytes and microglia, are essential for maintaining homeostasis and regulating immune responses. However, the specific role of cerebellar glia in neurodevelopmental disorders resulting from maternal Cd exposure remains unclear. In this study, we examined the effects of maternal Cd exposure on ASD-like behaviors and cerebellar glial alterations in mouse offspring. Our results demonstrated that only male offspring exhibited increased repetitive behaviors, astrocyte activation, and motor coordination deficits. Moreover, maternal Cd exposure specifically upregulated genes associated with reactive astrocytes in the cerebellum of male offspring. These findings suggest that maternal Cd exposure induces sex-specific changes in cerebellar glial development, with aberrant astrocyte responses potentially contributing to ASD-like behaviors in males. Understanding the role of cerebellar glia may provide novel insights into sex-dependent susceptibility to environmental risk factors in neurodevelopmental disorders and identify potential therapeutic targets for ASD.

Keywords : autism spectrum disorders, maternal exposure, cadmium, glia, behavioral abnormality

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P-053

Prasugrel attenuates dopaminergic neuronal loss in an MPTP-induced model of Parkinson's disease

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The exact etiology of Parkinson's disease (PD) is still not understood and current medications of PD are palliative; therefore, alternative treatments to overcome these hurdles are urgently required. Drug repurposing

offers new therapeutic alternatives for incurable diseases, including PD, and is less costly and time-consuming, in addition to ensuring drug safety compared with traditional drug development strategies. This study aimed to repurpose a novel alternative medication from the U.S. Food and Drug Administration-approved drug library using two *in vitro* PD models, 1-methyl-4-phenylpyridinium-induced primary cortical neurons and lipopolysaccharide-induced BV2 microglial cells. We discovered that prasugrel, an antiplatelet agent used to treat acute coronary syndrome, has neuroprotective and anti-inflammatory effects via inhibition of the mitogen-activated protein kinase signaling pathway. Using integrative pathway analysis results, we found that the expression of various proteins related to apoptotic cell death and neuroinflammation were decreased following prasugrel treatment in *in vitro* PD models. In the protein-protein interaction analysis, caseinolytic peptidase P and leucine-rich pentatricopeptide repeat containing, both of which are involved in neurotoxicity and PD pathogenesis, were core proteins in the interactome of primary cortical neurons. Furthermore, ribosomal protein L35, which is involved in microglial activation, was identified as the core protein-protein interaction protein in the BV2 proteome. Finally, we confirmed the neuroprotective effect of prasugrel in an MPTP-induced PD mice model through behavioral and histological analyses. Therefore, this study demonstrates that prasugrel can potentially be used to treat PD.

Keywords : Parkinson's disease, Proteomics, Prasugrel, Drug repurposing, Neuroprotection

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P-054

Cerebrovascular dysfunction may contribute to cognitive impairment in Down syndrome

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Down syndrome (DS) is the most common genetic cause of intellectual disability and is associated with an increased risk of early-onset Alzheimer's disease (AD). Cerebrovascular abnormalities, including cerebral amyloid angiopathy and microbleeds, are commonly observed in both DS and AD. Moreover, individuals with DS are affected by cerebrovascular diseases such as moyamoya syndrome from early childhood. Given the accumulating evidence of cerebrovascular involvement in AD-related cognitive decline, along with cognitive deficits observed in DS from early childhood, cerebrovascular abnormalities may contribute to cognitive impairment in DS. However, this relationship remains largely unexplored. In a previous study, we employed weighted gene co-expression network analysis and identified the most DS-associated gene module. This module was upregulated in the dorsolateral prefrontal cortex (DFC), and its genes were enriched in microglia, astrocytes, and endothelial cells, and were involved in immune responses and vascular development. To examine the functional role of this module, we overexpressed one of the hub genes, Gene A, in the medial prefrontal cortex (mPFC) of mice and assessed the behavioral phenotypes. Overexpression of Gene A led to reduced social interaction and impaired long-term memory. To elucidate the molecular mechanisms underlying this effect, we performed RNA-sequencing analysis. Most differentially expressed genes (DEGs) were upregulated and enriched in vascular-related cell types. These DEGs were involved in vascular-related functions such as vascular development, cell adhesion, and extracellular matrix organization. Collectively, our results suggest that overexpression of Gene A may contribute to cerebrovascular abnormalities, which in turn could lead to cognitive impairment. These findings indicate that cerebrovascular abnormalities may play a critical role in the development of intellectual disability in DS.

Keywords : Down syndrome, WGCNA, RNA-seq, Cerebrovascular dysfunction, Cognitive dysfunction

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P-055

GATA1-mediated brain-immune interactions in major depressive disorder: a comprehensive analysis of neuroimmune crosstalk in mice

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GATA1, a master transcriptional regulator of hematopoiesis, has emerged as a critical mediator in major depressive disorder (MDD) pathophysiology. Clinical evidence demonstrates GATA1 overexpression in the dorsolateral prefrontal cortex of MDD patients, where it binds to promoters of synapse-related genes and drives microglial activation associated with depressive-like behaviors. However, its role in brain-immune interactions remains incompletely understood. We delivered AAV-GATA1 into the medial prefrontal cortex of mice and performed single-cell RNA sequencing on approximately 250,000 cells from brain tissue and peripheral blood mononuclear cells (n=4 per group). GATA1 overexpression induced significant microglial activation characterized by increased IFN-I-responsive subtypes expressing elevated MHC class I genes, pro-inflammatory cytokines, complement components, and the exosome marker Cd63. Enhanced Cd63 expression and exosome module scores in the IFN-1-responsive microglial subtype indicated microglial exosome-mediated inflammatory signal transmission to the periphery. Within the brain compartment, we observed an increased proportion of effector memory $CD8^+$ T cells, suggesting enhanced $CD8^+$ T cell infiltration following GATA1 activation. In peripheral blood, activated effector $CD8^+$ T cells demonstrated increased motility and brain infiltration capacity, supported by monocyte-derived fibronectin 1 (Fn1) overexpression and concurrent integrin β1 (Itgb1) upregulation in blood effector $CD8^+$ T cells. Plasmacytoid dendritic cells exhibited heightened endocytic activity and increased intercellular interactions. GATA1 orchestrates brain-immune crosstalk through microglial exosome-mediated inflammatory signaling, peripheral immune reprogramming, and facilitated T cell trafficking. These findings establish GATA1 as a central mediator of neuroimmune dysfunction in MDD and identify potential therapeutic targets for modulating brain-immune homeostasis.

Keywords : GATA1, Depression, Single-cell RNAseq, Neuroimmune, Immune cells

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P-056

Pharmacological blockade of TRPA1 modulates morphine withdrawal syndrome and emotion-like behaviors in male and female mice

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Chronic opioid use causes changes in brain reward and affective circuitry. Opioid use cessation leads to development of negative affective states characterized by increased anxiety- and despair-like behaviors. In this study, the potential role of transient receptor ankyrin 1 channel (TRPA1) was examined in morphine-induced dependence and negative emotional behaviors. Male and female C57BL6/J mice were exposed to chronic morphine in escalating doses to induce dependence. To precipitate withdrawal symptoms, naloxone was administered two hours after last morphine dose. Overall attenuation of withdrawal symptoms was shown in both male and female mice through pre-treatment of TRPA1 antagonist, A967079, prior morphine administration. After 5-day abstinence, mice were pre-treated with A967079 before behavioral tests to assess sociability, anxiety-related and despair like behaviors induced by morphine withdrawal. We observed reduction of social deficit in female mice through social interaction test, recovery of anxiety-like behavior in female mice through elevated plus maze test, and improvement of immobility time in both sexes through tail suspension test. These results suggest that TRPA1 may modulate morphine dependence and negative affective states, incorporating the physiological differences of male and female mice.

Keywords : Morphine, Opioid, Withdrawal, Sex difference

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P-057

A RAS family GTPase Rit1 regulates synaptic plasticity and memory in mice

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The long-term potentiation (LTP) , which is a form of synaptic plasticity, is an important mechanism of learning and memory. GTPases such as RAS have been shown to be critically involved in LTP regulation. However, the diversity of GTPase-related LTP mechanism and its behavioral associations are still unclear. Recent clinical studies have shown that mutations in a RAS family GTPase Rit1 induce cognitive impairments in Noonan syndrome patients. We hypothesized GTPase Rit1 might be involved in LTP regulation, which subsequently affect learning and memory. To address our question, we utilized a knock-in mouse expressing a Rit1 gain of function mutation (M90I) in excitatory neurons. We found expressing Rit1 M90I in excitatory neuron impairs spatial learning and memory. Consistently, we found that hippocampal LTP at the Schaffer collateral (SC) pathway is impaired in the mutant mice. Our results suggest that Rit1 is a key regulator of synaptic plasticity and learning and memory.

Keywords : Learning and memory, GTPase, Synaptic plasticity

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P-058

Neuroprotective Effects of *Astragalus mongholicus* via Antioxidant and Anti-Inflammatory Mechanisms in Ischemic Stroke

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Stroke significantly impacts over 12 million individuals each year by contributing to high mortality rates, long disability-adjusted years (DALYs) and high healthcare costs. As existing treatment methods have severe limitations, we sought to find a suitable treatment solution from traditional east Asian medicine. Among these, AM is frequently used for post-stroke treatment. In this study, we aimed to investigate how AM promotes post-stroke functional recovery and survival. With both in-*vitro* and *in-vivo* models, we sought to unearth the mechanisms and potential of AM as a viable therapeutic option for post-stroke treatment. *In-vitro* models using oxygen-glucose deprivation revealed that AM enhances cell viability in neuroblastoma cells, likely by mitigating reactive oxygen species. *In-vivo* analyses utilized photothrombotic (PTB) and transient middle cerebral artery occlusion (tMCAO) models. PTB studies showed AM reduces infarct formation and improves neurological severity scores (mNSS). For both short-term and long-term tMCAO, mice were separated to either the AM administration group, vehicle group and the sham group. Short-term AM treatment for tMCAO mice decreased infarction rates significantly in both magnetic resonance imaging and TTC staining. Magnetic resonance spectroscopy indicated elevated neuroprotective metabolites following AM administration, with no notable differences between ischemic and healthy brain regions. Further analyses revealed AM lowered oxidative stress markers, as assessed with western blotting. AM also lowered gliosis markers as assessed with immunohistochemistry. Long-term AM administration boosted survival rates and enhanced motor (rotarod test) and cognitive functions (novel object recognition test), alongside lowering mNSS scores. To sum up, these findings highlight AM's antioxidant properties and its therapeutic potential for post-stroke recovery. This positions AM as a noteworthy candidate for post-stroke intervention strategies.

Keywords : Stroke, Astragalus mongholicus, Cognitive Impairment, oxygen-glucose deprivation, transient middle cerebral artery occlusion

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P-059

Cerebellar Glial Alterations and Impaired Motor Coordination in a VPA-Induced Mouse Model of Autism Spectrum Disorder

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Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by repetitive behaviors and social deficits. Motor dysfunction is also frequently observed in individuals with ASD, interfering with daily activities, peer interactions, and long-term motor development. These impairments are thought to reflect abnormalities in the cerebellum, a key brain region involved in motor coordination. However, the relationship between cerebellar dysfunction and ASD remains poorly understood. In this study, we investigated the involvement of cerebellar glial cells in ASD pathophysiology, given their emerging role in modulating motor functions. We used a valproic acid (VPA)-induced mouse model of ASD, in which pregnant mice were exposed to VPA. Offspring were analyzed for glial changes in the cerebellum, with male and female mice assessed separately due to the higher prevalence of ASD in males. VPA-exposed mice exhibited ASD-like behaviors, including increased repetitive behavior and impaired motor coordination. We observed elevated expression of glial fibrillary acidic protein (GFAP) in cerebellar astrocytes and increased levels of astrocytic GABA, contributing to tonic inhibition. Monoamine oxidase B (MAOB), an enzyme involved in astrocytic GABA synthesis, was significantly upregulated following VPA exposure. Additionally, we found increased expression of ionized calcium-binding adapter molecule 1 (Iba1), a marker of activated microglia, indicating the presence of neuroinflammatory responses. Our findings suggest that prenatal VPA exposure induces glial dysfunction in the cerebellum, involving both astrocytes and microglia, which may contribute to ASD-like behaviors. These results highlight cerebellar glial pathology as a potential mechanism underlying the motor and behavioral deficits associated with ASD.

Keywords : Autism spectrum disorder (ASD), Cerebellum, Glial cell, Motor coordination, Valproic acid (VPA)

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Molecular and Cellular Neuroscience P-060~P-143

P-060

Inositol 1,4,5-Trisphosphate Receptor 1 Mediated Intracellular Calcium Dyshomeostasis Facilitates Trigeminal Neuropathic Pain

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Trigeminal nerve injury-induced neuropathic pain, arising from damage to the trigeminal nerve, lacks effective treatments due to its complex pathogenesis. Mechanisms driving trigeminal neuropathic pain remain incompletely understood. Here we show that the expression level of endoplasmic reticulum (ER) stress markers in trigeminal ganglia (TG) was increased with the change in micro-structure of ER from trigeminal neuropathic pain(TNP) model mice. Relieving ER stress with a chemical chaperone, 4-phenylbutyric acid (4-PBA), reduced pain hypersensitivity. Meanwhile, ER stress induced the upregulation of Inositol trisphosphate receptor 1 (ITPR1) via the transcription factor Runx2, leading to increased release of Ca^{2+} from the ER in trigeminal ganglion (TG) sensory neurons. Knockdown or pharmacologic intervention of ITPR1 effectively attenuated pIONT-induced mechanical allodynia. Meanwhile, blocking of ITPR1 also inhibited pIONT-induced ERK activation and reduced the expression levels of pro-inflammatory cytokines, including TNF-a, IL-1b, IL-6, and CCL2. Additionally, ITRP1 was found to couple with ANO1 (a calcium-activated chloride channel) in TG neurons, ER released Ca^{2+} through ITPR1 trigger ANO1 activation, resulting in hyperexcitability and pain. Our study demonstrates that ITPR1 plays a crucial role in pIONT-induced neuropathic pain by regulating intracellular calcium signals and ANO1 function in the TG. Targeting ITPR1 emerges as a potential effective strategy for trigeminal neuropathic pain treatment.

Keywords : Trigeminal neuropathic pain, ER stress, ITPR1, Transcription factor, ANO1

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P-061

Distinct Roles of Somatostatin and Parvalbumin Interneurons in tec LEARNING

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Learning involves evaluating multiple dimensions of information and generating appropriate actions, yet how the brain assigns value to this information remains unclear. In this study, we show that two types of interneurons (INs) in the primary somatosensory cortex—somatostatin-expressing (SST-INs) and parvalbumin-expressing (PV-INs) neurons—differentially contribute to information evaluation during trace eyeblink conditioning (TEC). An air puff (unconditioned stimulus, US) delivered after a whisker stimulus (conditioned stimulus, CS) elicited both reflexive eye closure and stress-related locomotion. However, only self-initiated, anticipatory eye closure during the CS window, measured via electromyography (EMG), was directly relevant to learning performance. We found that SST-IN activity changes aligned with the learning induced changes of the anticipatory eye blinks during the CS period, correlated with the EMG changes across learning. In contrast, PV-IN activity was positively correlated with stress-related locomotion following the US and showed no learning related changes, suggesting a role in processing the emotional or aversive component of the task. Furthermore, cholinergic signaling via nicotinic receptors modulated both SST- and PV-IN activities, in a manner consistent with their distinctive roles, linking these interneurons to the regulation of learning-related actions and emotional responses, respectively. These findings demonstrate that distinct interneuron populations evaluate different dimensions of information—SST-INs for predictive, adaptive actions and PV-INs for stress-related emotional responses—to guide learning and behavior.

Keywords : LEARNING, iNTERNEURON, CORTEX, SOMATOSENSORY

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P-062

Poster Award Candidate

A specific association of presynaptic K^+ channels with Ca^{2+} channels underlies K^+ channel-mediated regulation of glutamate release

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Voltage-gated potassium channels (VGKCs) in the presynaptic terminals play a crucial role in the regulation of synaptic transmission. The underlying mechanisms are known to include modulation of action potential (AP) waveforms and membrane potential changes, which are common to the role of most VGKCs. However, the possibility that different VGKC subtypes employ distinct mechanisms to regulate neurotransmitter release remains to be elucidated. Here, we show that different VGKC subtypes, including K_V7, K_V1, and K_V3 channels, differentially modulate glutamate release by modulating specific subtype of voltage-gated calcium channels (VGCCs). Using electrophysiology in hippocampal autaptic neurons, we show that K_V7 inhibition increases glutamate release selectively via L-type VGCCs, whereas K_V1 inhibition increases release selectively via P/Q-type VGCCs. Inhibition of calmodulin and phospholipase C signaling completely abolishes the effects of K_V7 and K_V1 inhibition on glutamate release, respectively, without affecting their effects on membrane potential changes. Immunocytochemistry confirms that K_V7 channels co-localise with L-type VGCCs, and K_V1 channels with P/Q-type VGCCs, supporting the specific coupling between VGKCs and VGCCs. In contrast, K_V3 channels regulate release in proportion to AP duration with no evidence for a specific coupling to VGCC subtype. These findings challenge the traditional view that VGKCs regulate synaptic transmission by modulating membrane potential and highlight subtype-specific interactions between VGKCs and VGCCs as critical mechanisms for synaptic regulation. Collectively, this study advances our understanding of how presynaptic calcium signal, modulated by different VGKCs, precisely controls presynaptic activity and neurotransmitter release.

Keywords : voltage-gated potassium channels, voltage-gated calcium channels, neurotransmitter release

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P-063

Protective effects of polyphenols against oxidative stress and inflammation caused by intracellular zinc deficiency in microglial cells

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Zinc is an essential mineral that plays a vital role in numerous physiological functions. Its deficiency has been implicated in various adverse effects on the central nervous system. Zinc is also known to be involved in the generation of reactive oxygen species (ROS), which contribute to oxidative stress. These ROS, produced during cellular metabolism and in response to various stimuli, can activate the NLRP3 inflammasome, leading to inflammation. In the brain, such ROS-mediated inflammation is a key factor in the onset and progression of neurodegenerative diseases. In this study, we focused on polyphenolic compounds with recognized antioxidant and anti-inflammatory effects as potential agents to suppress reactive oxygen production and inflammation caused by zinc deficiency. When microglia were deprived of zinc with the intracellular zinc chelator TPEN, a significant increase in intracellular ROS production was observed, and this ROS production was completely suppressed by pretreatment with $ZnCl_2$. To further explore potential therapeutic strategies, we selected polyphenolic compounds with potent radical scavenging activity and tested their effects on TPEN-induced ROS production. These compounds exhibited potent inhibitory effects and also inhibited ROS production by hydrogen peroxide, a type of ROS.We then investigated the relationship between intracellular zinc deficiency and NLRP3 inflammasome activation. TPEN-induced intracellular zinc deficiency resulted in upregulation of genes related to the NLRP3 inflammasome in microglia. In particular, polyphenol compounds and ZnCl2 effectively suppressed this gene expression. These findings suggest that intracellular zinc deficiency promotes microglial inflammatory responses through excessive ROS production and NLRP3 inflammasome activation. Furthermore, polyphenolic compounds may have therapeutic potential in preventing or slowing the progression of neurodegenerative diseases by suppressing these pathological processes.

Keywords : zinc deficiency, microglia, reactive oxygen species, NLRP3 inflammasome, polyphenol

P-064

MDGA2 constrains NMDAR functions by targeting EphB2-Ephrin signaling pathway

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Synaptic cell-adhesion molecules (CAMs) orchestrate synapse formation and function by mediating specific trans- and cis-interactions that regulate postsynaptic receptor properties. Among CAMs, MDGA family proteins have been identified as negative regulators of synapse development, but their precise mechanisms remain incompletely understood. Here, we demonstrate that MDGA2 directly interacts with EphB2, a synaptic receptor tyrosine kinase, through high-affinity cis interactions involving the three N-terminal Ig domains of MDGA2 and the ephrin-binding domain of EphB2. In the mouse brain, EphB2 forms complexes with MDGA2 and GluN2B-containing NMDARs, but not with GluN2A-containing NMDARs, AMPARs, or Neuroligin-1. Deletion of MDGA2 increases EphB2/NMDAR complex formation without altering ephrin-B1-induced tyrosine phosphorylation of EphB2 or NMDARs. Functional analyses using an EphB2-binding-defective mutant of MDGA2 reveal that MDGA2 requires its interaction with EphB2 to suppress basal excitatory synaptic transmission and specifically inhibit NMDAR-mediated, but not AMPAR-

mediated, postsynaptic responses. These findings identify a novel mechanism by which MDGA2 modulates excitatory synapse properties through the EphB2-ephrin signaling pathway, distinct from its previously characterized interactions with Neuroligins, and highlight MDGA2 as a key regulator of glutamate receptor-mediated synaptic transmission.

Keywords : Synapse, CAMs, MDGA2, EphB2, NMDAR

P-065

Peripheral Neuronal NPTX2 Exacerbates Chronic Itch in an Atopic Dermatitis Model via Enhancing IL-31/IL-31R Signal Axis

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Atopic dermatitis (AD) is one of the most prevalent chronic inflammatory skin diseases, characterized primarily by intense itching, eczematous rashes, and dry skin. Intense and intolerable itches induce scratching behavior and remain a challenging clinical condition with incompletely understood mechanisms. Neuronal Pentraxin 2 (NPTX2) is associated with neurodevelopment, synaptic plasticity, and neuroinflammation in the central nervous system (CNS). However, its role in mediating chronic itch remains unreported under AD condition. We demonstrated that MC903 application significantly upregulated NPTX2 expression selectively in small- and medium-sized trigeminal ganglion (TG) neurons. Intriguingly, intradermal administration of recombinant NPTX2 alone provoked moderate scratching behavior in mice, suggesting its sufficiency as a pruritogen. Mechanistically, NPTX2 synergizes with interleukin-31 (IL-31), a wellknown pruritic cytokine in AD, to potentiate phosphorylation of extracellular signal-regulated kinase (p-ERK) signaling in primary sensory neurons. PD98059, the inhibitor of ERK, significantly alleviated the scratching induced by the combination of NPTX2 and IL-31. Furthermore, NPTX2 synthesis was restricted to TG neurons under pruritogenic conditions, and transported to peripheral nerve terminals. Additionally, PD98059 also significantly reduced the upregulation of Nptx2 caused by IL-31 stimulation. Our results provides a new understanding of the molecular mechanisms underlying chronic pruritus in the MC903-induced AD model, for targeting NPTX2-dependent signaling as a key therapeutic strategy for refractory itch disorders.

Keywords : Chronic itch, MC903, NPTX2, IL-31, Atopic dermatitis

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P-066

Astragaloside IV improves Muscle Atrophy by modulating UPS and ALP via suppressing Oxidative Stress and Inflammation in denervated mice

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Peripheral nerve injury is common clinically and can lead to neuronal degeneration and atrophy and fibrosis of the target muscle. The molecular mechanisms of muscle atrophy induced by denervation are complex and not fully understood. Inflammation and oxidative stress play an important triggering role in denervated muscle atrophy. Astragaloside IV (ASIV), a monomeric compound purified from astragalus membranaceus, has antioxidant and anti-inflammatory properties. The aim of this study was to investigate the effect of ASIV on denervated muscle atrophy and its molecular mechanism, so as to provide a new potential therapeutic target for the prevention and treatment of denervated muscle atrophy. In this study, an ICR mouse model of muscle atrophy was generated through sciatic nerve dissection. We found that ASIV significantly improved the structural integrity of the neuromuscular junction and muscle fibers in denervated mice, reducing ROS and oxidative stress-related protein levels. Furthermore, ASIV inhibited the increase in inflammation-associated proteins and infiltration of inflammatory cells, protecting the denervated microvessels in skeletal muscle. We also found that ASIV reduced the expression levels of MAFbx, MuRF1 and FoxO3a, while decreasing the expression levels of autophagy-related proteins, it inhibited the activation of ubiquitin-proteasome and autophagy-lysosome hydrolysis systems and the slow-to-fast myofiber shift. Our results show that ASIV inhibits oxidative stress and inflammatory responses in skeletal muscle due to denervation, inhibits mitophagy and proteolysis, improves microvascular circulation and reverses the transition of muscle fiber types. Therefore, the process of skeletal muscle atrophy caused by denervation can be effectively delayed.

Keywords : Denervated muscle atrophy , ASIV, Oxidative stress , Infammatory response, Neuromuscular junction

P-067

The identification of a distinct astrocyte subtype that diminishes in Alzheimer's disease

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Alzheimer's disease (AD) is characterized by the presence of two hallmark pathologies: the accumulation of Amyloid beta (Aβ) and tau proteins in the brain. There is a growing body of evidence suggesting that astrocytes, a type of glial cell in the brain, play crucial roles in clearing Aβ and binding to tau proteins. However, due to the heterogeneity of astrocytes, the specific roles of different astrocyte subpopulations in response to Aβ and tau remain unclear. To enhance the understanding of astrocyte subpopulations in AD, we investigated astrocyte lineage cells based on single-nuclei transcriptomic data obtained from both human and mouse samples. We characterized the diversity of astrocytes and identified global and subpopulation-specific transcriptomic changes between control and AD samples. Our findings revealed the existence of a specific astrocyte subpopulation marked by low levels of *GFAP* and the presence of *AQP4* and *CD63* expression, which showed functional enrichment in Aβ clearance and tau protein binding, and diminished in AD. We verified this type of astrocytes in mouse models and in AD patient brain samples. Furthermore, our research also unveiled significant alterations of the ligand-receptor interactions between astrocytes and other cell types. These changes underscore the complex interplay between astrocytes and neighboring cells in the context of AD. Overall, our work gives insights into astrocyte heterogeneity in the context of AD and reveals a distinct astrocyte subpopulation that holds potential for therapeutic interventions in AD. Targeting specific astrocyte subpopulations may offer new avenues for the development of novel treatments for AD.

Multi-stage spatial transcriptomic analysis for cell-cell communications are underway to further functional characterization.

Keywords : astrocyte subtype, snRNA-seq analysis, Alzheimer's disease progression

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P-068

Celecoxib alleviates denervation-induced muscle atrophy by suppressing inflammation and oxidative stress and improving microcirculation

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The molecular mechanism underlying denervation-induced muscle atrophy is complex and incompletely understood. Our previous results suggested that inflammation may play an important role in the early stages of muscle atrophy. Celecoxib is reported to exert anti-inflammatory effects. Here, we explored the effect of celecoxib on denervation-induced muscle atrophy and sought to identify the mechanism involved. We found that celecoxib treatment significantly increased the wet weight ratio and CSA of the tibialis anterior muscle. Additionally, celecoxib downregulated the levels of COX-2, inflammatory factors and reduced inflammatory cell infiltration. GO and KEGG pathway enrichment analysis indicated that after 3 days of celecoxib treatment *in vivo*, the differentially expressed genes (DEGs) were mainly associated with the regulation of immune responses related to complement activation; after 14 days, the DEGs were mainly involved in the regulation of oxidative stress and inflammation-related responses. Celecoxib administration reduced the levels of ROS and oxidative stress-related proteins. Furthermore, we found that celecoxib treatment inhibited the denervation-induced up-regulation of the ubiquitin–proteasome and autophagy–lysosomal systems related proteins; decreased mitophagy in target muscles; and increased levels of MHC. Finally, celecoxib also attenuated microvascular damage in denervated skeletal muscle. Combined, our findings demonstrated that celecoxib inhibits inflammation and oxidative stress in denervated skeletal muscle, thereby suppressing mitophagy and proteolysis, improving blood flow in target muscles, and, ultimately, alleviating denervation-induced muscle atrophy. Our results confirmed that inflammatory responses play a key role in denervation-induced muscle atrophy and highlight a novel strategy for the prevention and treatment of this condition.

Keywords : Denervation-induced muscle atrophy, Celecoxib, Inflammatory response, Oxidative stress, Microcirculation

P-069

Prion protein-mediated inflammatory responses attenuated by melatonin through calcineurin signal

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Prion diseases are fatal neurodegenerative disorders caused by pathogenic forms of prion proteins (PrPSc) which are actually abnormal or misfolded prion proteins (PrPC). The 106-126 residues of the PrPC functions have similar pathogenic features to the Pathogenic prion proteins (PrPSc) which can lead to neurodegeneration by regulation of calcineurin and autophagy,. Melatonin (Mel), a pivotal hormone, exerts a calcium-dependent neuroprotective effect by preventing neuronal cell death. The present study investigated the effects of Mel on reducing neuroinflammation induced by prion proteins and its potential regulation of calcium and calcineurin. Our results showed that Mel exerted a protective role against PrP (106-126)-induced neuroinflammation. This was due to the restoration of the increased nuclear factor-kappa B (NF-κB) activation by PrP (106-126). Moreover, Mel reduced the inflammatory response that was induced by PrP (106-126). Further investigation revealed that Mel restored the PrP (106-126)-induced calcium and calcineurin activity. Mel achieved this protective effect by inhibiting the autophagy that was accumulated by PrP (106-126). Taken together, our findings revealed that melatonin attenuates PrP (106-126)-induced neuroinflammation by restoring the calcineurin over-activity caused by PrP (1-6-126) which was achieved by inhibition of the lysosomal fusion of autophagy that was induced by the PrP (106-126). This discovery may provide an effective strategy for the treatment of neurodegenerative diseases.

Keywords : Prion, Melatonin, Calcineurin, Autophagy, Neuroinflammation

P-070

Presynaptic CASKIN2 controls postsynaptic NMDA receptor functions via transsynaptic mechanism

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Presynaptic active zones (AZs) perform essential functions in orchestrating speedy and accurateneurotransmission. Despite extensive studies on their molecular constituents, it remains unclear howtranssynaptic signals are organized at AZs. The two members of the CASKIN family of multidomain scaffoldproteins, CASKIN1 and CASKIN2, bind to several AZ proteins and LAR receptor protein tyrosine phosphatases(LAR-RPTPs), and thus likely contribute to presynaptic assembly. Analysis using conditional knockout (cKO)mice deficient for CASKIN1 and/or -2 revealed that CASKIN2, but not CASKIN1, is critical for proper synaptictransmission, synaptic strength, vesicle distribution, and AZ protein arrangement at glutamatergic synapses.CASKIN1/2 deletion recapitulates Caskin2-cKO phenotypes. Strikingly, and in line with the preferentialcolocalization of CASKIN2 with N-methyl-D-aspartate receptors (NMDARs) at excitatory synapses, presynapticCASKIN2 at hippocampal CA3 neurons specifically regulates postsynaptic NMDAR-mediated responses andNMDAR surface expression in CA1 pyramidal neurons. Moreover, PTPσ-mediated tyrosine dephosphorylationand multimerization of CASKIN2 are critical for the ability of CASKIN2 to regulate excitatory synaptictransmission, NMDAR functions, and activity-dependent presynaptic F-actin rearrangement. Lastly, the presence of CASKIN2 and PTPσ at Schaffer collateral circuits is required for proper novel object location memory in mice.Our findings establish crucial roles of CASKIN2 in orchestrating LAR-RPTP-mediated transsynaptic NMDAR-related synaptic functions.

Keywords : CASKIN2, PTPσ, Cell adhesion protein, Synapse, NMDAR

Acknowledgements : We thank Jinha Kim (DGIST, Korea), Younghye Kim (DGIST, Korea) and Woo Chan Jeong (DGIST, Korea) for technical assistance. This study was supported by grants from the National Research Foundation of Korea (NRF), funded by the Ministry of Science and ICT (RS-2022-NR070708 to J.K.; RS-2023-NR076948 to J.W.U.; 2021R1C1C2010767 to K.A.H.), and by Chungnam National University.

P-071

Guanine and isoguanine promote axon regeneration of dorsal root ganglion neurons and survival of retinal ganglion cells after injury

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Neurological injuries usually lead to motor, sensory, or cognitive impairment, which urgently need the development of effective therapeutic strategies. An increasing number of studies have indicated that metabolites can serve as therapeutic drugs for treating diseases or repairing damaged tissues. Among them, purines and their derivatives have shown the neuroprotection effects in the nervous system and garnered significant focus in the field of pharmaceutical development. In the present study, we found that the level of isoguanine in the dorsal root ganglion (DRG) was decreased after sciatic nerve injury. Functional investigations revealed that isoguanine and its isomer, guanine, promote axon growth of primary DRG neurons in vitro and enhance axon regeneration in vivo in the peripheral nervous system (PNS) by activating Akt signaling. Conversely, in the central nervous system (CNS), both guanine and isoguanine could not induce the regeneration of the optic nerve; instead, they enhance the survival of retinal ganglion cells after optic nerve crush injury. Collectively, these data provide experimental evidence supporting guanine and isoguanine as promising therapeutic candidates for the management of neurological injuries within both the PNS and CNS.

Keywords : Neurological injury, Axon regeneration, Retina ganglion cell, Dorsal root ganglion neuron, Guanine/Isoguanine

P-072

H_2O_2-induced astrocytic collagen triggers neuronal death via fucosylation-dependent glial barrier formation upon ischemic stroke

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The cascade of molecular and cellular events leading to neuronal death after a focal ischemic stroke remains enigmatic. Although astrocytes form glial barriers that may protect surrounding tissue, how barriers develop and contribute to neuronal death is unclear. Here, we show that H_2O_2 induces astrocytic type I collagen (COL1)-production via miR-29-mediated post-transcriptional and fucosylation-dependent post-translational regulations, leading to integrin activation and neuronal death. In photothrombosis (PT)-induced cortical stroke model, PT triggered H_2O_2-surge, astrogliosis, glial barrier formation, COL1 expression, fibrotic scarring, altered N-glycosylation, neuronal loss, and neurological deficits. Remarkably, these effects were reversed by astrocyte-specific COL1 or FUT8 gene-silencing or treatment with KDS12025, an H_2O_2-decomposing peroxidase enhancer. KDS12025's neuroprotective effects were also recapitulated in non-human primate stroke model. These findings delineate a previously unrecognized astrocyte-driven mechanism in which oxidative stress induces COL1 production, promoting neuronal death, and position H_2O_2 and astrocytic COL1 and FUT8 as promising therapeutic targets for ischemic stroke.

Keywords : Astrocyte, Stroke, Hydrogen peroxide, type I collagen, fucosylation

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P-073

Mitochondria-associated ER membranes (MAMs) mediate depressive-like behavior and neuronal stress responses via NR3C1 and its proximal protein

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Chronic high levels of glucocorticoids contribute to major depressive disorder. Corticosterone (CORT), a physiological stress hormone, disrupts cellular environments, including reactive oxygen species (ROS) production and calcium homeostasis. However, the intracellular stress response mechanisms remain unclear. Here, we investigate the role of mitochondria-associated endoplasmic reticulum (ER) membranes (MAMs) as dynamic hubs that mediate the early cellular stress responses. We generated two MAM-related transgenic mouse lines: one expressing a BiFC (Bimolecular Fluorescence Complementation) construct to visualize MAMs (MAMs-BiFC Tg), and another expressing a RiBFM (Rapamycin-inducible Bridge Forming Module) to regulate MAM formation (MAMs-RiBFM Tg) in vivo. In MAMs-BiFC Tg, the extent of MAMs increased in the brains of mice exhibiting depressive-like behavior induced by either chronic restraint stress (CRS) or repeated CORT injections. Moreover, MAMs-RiBFM Tg exhibited depressive-like behaviors upon artificially increased MAMs. In primary cultured neurons, CORT exposure increased the extent of MAMs via the glucocorticoid receptor, NR3C1, and disrupted ER-mitochondria calcium homeostasis, leading to mitochondrial fission. We also identified a novel NR3C1-proximal protein that responds to neuronal stress through APEX2-based proximity labeling. Thus, we propose that MAMs function as a stress mediator, with NR3C1 and its proximal protein as key regulators of the CORT-induced neuronal stress responses.

Keywords : Mitochondria-associated ER membranes (MAMs), Depressive-like behavior, Stress response, Corticosterone, protein-protein interaction

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P-074

Heterodimerization and Interaction of the Serotonin-Receptors 5-HT1A and 5-HT2C

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G-Protein coupled receptors (GPCRs) are among the most prominent receptors in the central nervous system. Their malfunction is implicated in various neurological and neuropsychiatric disorders, making them a common target for medical treatment. Thus, it is crucial to gain a comprehensive understanding of GPCR functions and mechanisms to develop more effective and targeted medical treatments with fewer side effects. This study examines the potential interplay between the serotonin receptors 5-HT1A and 5-HT2C, which play a significant role in the pathology of depression. Experiments were performed in transfected HEK-293 cells expressing both receptors. Our findings provide initial evidence of heterodimerization between the 5-HT1A and 5-HT2C receptors, as indicated by FRET in acceptor photobleaching measurements. A significant increase in fluorescence intensity of the CFP-tagged 5-HT2C receptor of approximately 10% was observed after bleaching of the YFP-tagged 5-HT1A receptor. Moreover, phasor analysis of FLIM measurements indicates FRET, as evidenced by a shortened fluorescence lifetime when the 5-HT1A receptor is co-expressed with the 5-HT2C receptor, compared to the expression of the 5-HT2C receptor alone. Further analysis of potential heterodimerization involves Co-Immunoprecipitation/Western-Blot techniques. Additionally, calcium imaging experiments demonstrated significant signals in HEK-293 cells transfected with both receptors and GCaMP8 when exposed to serotonin. The potential interaction between the 5-HT1A and 5-HT2C receptors is further investigated by Patch-Clamp experiments.

Keywords : Heterodimerization, 5-HT1A, 5-HT2C, serotoninreceptor, interaction

P-075

Microglial NLRP3 dysregulation augments repetitive behavior of mice via IL-1R-NMDAR interplay

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Excessive microglial activation and prolonged expression of inflammatory cytokines during chronic neuroinflammation exert detrimental effects on the neural environment, contributing to the development of various neurological disorders. In this context, NLRP3 (NOD-like receptor protein 3), a central immune sensor in microglia, has been implicated in the pathophysiology of several neurodegenerative diseases, including Alzheimer's disease (AD) and Parkinson's disease (PD). However, how NLRP3 dysfunction per se affects brain function in the absence of other overriding pathological conditions remains unclear. Using NLRP3 knock-in (KI) mice expressing a gain-of-function D301N mutation specifically in microglia, we demonstrate that aberrant activation of the NLRP3 inflammasome in response to systemic lipopolysaccharide (LPS) challenge leads to a marked reduction in excitatory postsynaptic structures, accompanied by paradoxical NMDAR (N-methyl-D-aspartate receptor) hyperfunction in the medial prefrontal cortex (mPFC). This profound increase in NMDAR activity appears to be mediated by the interaction between IL-1 receptor (IL-1R) signaling—a key downstream effector of NLRP3 inflammasome activation—and specific NMDAR subunits. In parallel with these synaptic abnormalities, NLRP3 KI mice exhibited aberrant repetitive behaviors. Notably, pharmacological inhibition of either NMDAR or IL-1R signaling efficiently ameliorated these behavioral deficits. Collectively, our findings highlight a critical interplay between cytokine signaling and synaptic receptor function in NLRP3-mediated neuroinflammation and suggest potential therapeutic avenues for inflammation-associated neuropsychiatric symptoms.

Keywords : NLPR3, Repetitive behavior, Neuroinflammation, Excitatory synapse, NMDAR

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P-076

Intrahippocampal delivery of hyperphosphorylated human tau oligomers induces neurodegeneration in non-transgenic wild-type mice

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Hyperphosphorylated tau (p-tau) forms neurofibrillary tangles, a key biomarker for Alzheimer's disease and additional neurodegenerative tauopathies. However, neurofibrillary tangles are not sufficient to cause neuronal dysfunction or death. Intrahippocampal injection of tau isolated from AD patients has limited effects on the cognitive functions of non-transgenic mice, despite the recapitulation of pathological tau deposits in the mouse brain. It therefore remains uncertain as to whether all hyperphosphorylated tau is directly responsible for AD neurodegeneration. We examined this issue by injecting recombinant p-tau oligomers to the hippocampus of non-transgenic, wildtype mice and found progressive cognitive deficits that correlate with neuron death spreading from the ipsilateral hippocampus to the cortex. Apomorphine, which retards p-tau aggregation and cytotoxicity *in vitro*, antagonized p-tau-induced cognitive

deficits and neuron death. These results suggest the pathogenic role of p-tau oligomers and a novel AD model facilitating drug development.

Keywords : tau, hyperphosphorylation, Alzheimer's disease

P-077

The overexpression of TIAM2S alters the macrostructure of the mouse embryonic brain.

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Genetic variants of Human T-cell lymphoma invasion and metastasis 2 (TIAM2) are associated with the pathogenesis of neurodevelopmental behavioral disorders, such as attention deficit hyperactivity disorder and autism spectrum disorders. Overexpression of its short form (TIAM2S) increases brain plasticity in the adult stage; however, how TIAM2S participates in fetal brain development remains unknown. Well-organized neurodevelopment is a complex, dynamic, and sequential cellular process of multiple cell types. This current study aims to determine the effects of TIAM2S on the embryonic brain macrostructure and its regulatory mechanism using the TIAM2S transgenic (TIAM2S-TG) mice with multiple approaches, such as the magnetic resonance imaging (MRI) technique, immunochemistry staining, and single-cell RNA-sequencing. Our data revealed that embryonic-day-14 (E14) TIAM2S-TG embryos had smaller body sizes than E14 WT embryos, as detected by their crown-rump length, but their body weights at 14 days and 10 months old were similar. Furthermore, T2-weighted image analysis revealed that E14 TIAM2S-TG embryos had decreased forebrain parenchyma, especially in the neocortex, and an enlarged lateral ventricle but had no changes in the midbrain, hindbrain, 3rd and 4th ventricles, spinal cord, and heart. Similar to the MRI data, HE and Nissl stains also reveal the thinness of the neocortex and enlargement of the lateral ventricle in E14 TIAM2S-TG embryos. Single-cell RNA-sequencing and immunochemical staining for neural progenitor cells, radial glial cells, and intermediate progenitor cells will be performed to decipher the mechanism by which TIAM2S regulates neurogenesis. In conclusion, our data demonstrate that TIAM2S participates in developing the embryonic neocortex.

Keywords : TIAM2S, Brain development, Magnetic resonance imaging , Neocortex, Neurogenesis

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P-078

Poster Award Candidate

A high-performance fluorescent sensor spatiotemporally reveals cell-type specific regulation of intracellular adenosine in vivo

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Adenosine (Ado), a nucleoside bridging intracellular metabolism with intercellular communication, plays an essential role in regulating processes such as sleep and seizure. While the functions of extracellular Ado ("eAdo") are well documented, our knowledge about the distribution and regulatory functions of intracellular Ado ("iAdo") is limited by a lack of methods for detecting iAdo in vivo. Here, we develop HypnoS, a genetically encoded fluorescent sensor for iAdo characterized by its high sensitivity, specificity, spatiotemporal resolution, and rapid response (sub-seconds). HypnoS enables real-time visualization of iAdo dynamics in live cultures, acute brain slices, flies, and freely moving mice. Using HypnoS for dual-color mesoscopic imaging in mice, we show that seizure-induced iAdo waves propagated across the cortex, following calcium signals. Additionally, two-photon imaging reveals that iAdo decays more rapidly in astrocytes than in neurons during seizures. Moreover, by recording iAdo dynamics in the basal forebrain during the sleep-wake cycle, we observe that iAdo signals are present during wakefulness and rapid eye movement (REM) sleep, regulated by equilibrative nucleoside transporters (ENT1/2). Thus, HypnoS is a versatile and powerful tool for investigating the biological functions of iAdo across a range of physiological and pathological states.

Keywords : adenosine, sleep, seizure, metabolite

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P-079

Properties of tonic inhibition change in age-dependent manner within auditory thalamus

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C57BL/6J mice initially maintain intact auditory function, but begin to exhibit high-frequency hearing loss by approximately two to three months of age. This loss progressively extends to lower frequencies, providing a model for studying age-related hearing loss. In human models, patients with ARHL often exhibit impaired performance in speech processing tasks and the ability to attend to acoustic stimuli. Although previous researches have suggested changes of inhibitory neurotransmission as one of the major causes of such hearing deficit, astrocytic GABA has not been considered as the candidate. We have previously reported that in somatosensory system, tonic GABA released by astrocytic Best1 channels increases temporal fidelity and leads to high discrimination performance in mice. However, the origin and role of tonic inhibition in auditory system, particularly within the lemniscal and nonlemniscal thalamus, has not been elucidated yet. Here, we show that the lemniscal auditory thalamus, MGv, exhibits age-dependent decline of tonic inhibition, which is virtually eliminated by 6months of age. Our findings suggest that such age-dependent reduction of tonic inhibition could contribute to altered tuning curve in 6months mice, as confirmed by *in vivo* neuropixel recordings in MGv. Showing that age-dependent decline of tonic GABA is not due to reduction of extrasynaptic $GABA_AR$s, our findings also reveal that such age-dependent reduction of tonic GABA is due to astrocytic changes in the auditory thalamus.

Keywords : Thalamus, GABA, Astrocyte, Auditory, Aging

P-080

Ligand-independent EPHA2 signaling preserves neocortical progenitor identity by sustaining mitochondrial Complex I

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Embryonic neural stem and progenitor cells (NSPCs) occupy a specialized niche along the lateral ventricles, where receptors on their apical surface mediate extrinsic cues essential for preserving progenitor identity. However, the intracellular mechanisms—particularly those targeting metabolism—that translate these signals into NSPC fate decisions remain poorly elucidated. We identify a previously unrecognized role for ligand-independent EPHA2 receptor signaling, selectively enriched within NSPCs, in maintaining progenitor self-renewal by preventing early cell cycle exit. Mechanistically, this signaling triggers protein phosphatase 2A-mediated dephosphorylation of the mitochondrial Complex I assembly factor ECSIT at Thr179, facilitating its mitochondrial localization. This regulatory event sustains Complex I function and supports NSPC metabolic fitness and proliferative capacity. Notably, maternal NAD^+ supplementation rescues progenitor depletion and mitigates aberrant neurogenesis caused by EPHA2 pathway disruption. These findings delineate an EPHA2-ECSIT-mitochondria axis that bridges membrane receptor activation with intracellular metabolism, addressing a fundamental gap in niche signaling for progenitor maintenance.

Keywords : EPHA2 signaling, ECSIT, mitochondrial Complex I, neocortical development, neural stem and progenitor cells (NSPCs)

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P-081

Research about the cerebrovasculature & BBB distribution and glymphatic system of olfactory bulb as a CSF drainage hub.

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Cerebral blood vessels, along with the blood-brain barrier (BBB), form the perivascular space and play a key role in brain waste clearance via the glymphatic system. Increasing attention has been paid to regional differences in cerebrovascular structure to better understand brain functions and neurological disorders. The olfactory bulb (OB), responsible for odor detection and signal transmission to areas like the amygdala and hippocampus, is uniquely both central and peripheral, making it especially vulnerable to environmental exposure. This structural trait necessitates strong immune and waste-clearance functions. The COVID-19 pandemic highlighted the olfactory route as a viral entry point, with anosmia gaining recognition as a key symptom and sequela. Additionally, olfactory dysfunction is a common early sign of Alzheimer's disease (AD), reinforcing the relevance of olfactory system research. In this study, we analyzed OB vascular area and distribution using tissue clearing techniques, confirming consistent 3D vascular structure results. Aging, a major risk factor for neurodegeneration, was associated with reduced OB vascular area and altered regional patterns. These changes showed strong correlation with amyloid-β accumulation in AD models. Our findings suggest that OB vascular dysfunction may contribute to olfactory deficits or act as an early biomarker of AD pathology. Moreover, the OB may also play a critical role in CSF drainage. Therefore, OB vascular health could represent a novel therapeutic target for preventing or delaying AD progression.

Keywords : Alzheimer's disease, Olfactory bulb, Glymphatic system, Cerebrovasculature, CSF clearance

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P-082

The antipsychotic chlorpromazine reduces neuroinflammation by inhibiting microglial voltage-gated potassium channels

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Neuroinflammation, the result of microglial activation, is associated with the pathogenesis of a wide range of psychiatric and neurological disorders. Recently, chlorpromazine(CPZ), a dopaminergic D2 receptor antagonist and schizophrenia therapy, was proposed to exert anti-inflammatory effects in the central nervous system. Here, we report that the expression of Kv1.3 channel, which is abundant in Tcells, is upregulated in microglia upon infection, and that CPZ specifically inhibits these channels to reduce neuroinflammation. In the mouse medial prefrontal cortex, we show that CPZ lessens Kv1.3 channel activity and reduces proinflammatory cytokine production. In mice treated with LPS, we found that CPZ was capable of alleviating both neuroinflammation and depression-like behavior. Our findings suggest that CPZ acts as a microglial Kv1.3 channel inhibitor and neuroinflammation modulator, thereby exerting therapeutic effects in neuroinflammatory psychiatric/neurological disorders.

Keywords : Microglia, Kv1.3, Chlorpromazine, Neuroinflammation

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P-083

Astrocytic ET-1 System Determines Microglia Phenotype Following Spinal Cord Injury

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Microglia/macrophages accumulate at lesion site by switching towards pro-inflammatory (M1)-dominant phenotype at the acute phase following spinal cord injury (SCI). Such biased polarization shapes the functional

outcomes by expanding tissue damages. In the present study, the astrocytic endothelin-1 (ET-1) system is revealed to be immediately activated after SCI, driving microglia polarization towards M1, but suppressing towards M2 phenotype through activation of transcription coactivator YAP *via* ET_A and ET_B receptors. In addition, the activation of astrocytic ET-1 system results in elevation of blood plasma ET-1 level, suggesting a high diagnostic value. SCI-induced thrombin is pinpointed as a crucial activator of the astrocytic ET-1 system. The serine protease dramatically promotes the astrocytic expression of preproendothelin-1 (ppET-1) through protease-activated receptor-1 (PAR-1)/RhoA/NF-κB and PAR-1/MAPKs/NF-κB signal pathways. Meanwhile, it induces the expression of astrocytic endothelin-converting enzyme 1 (ECE-1) responsible for mature ET-1 processing. Pharmacological inhibitors of PAR-1 and ET-1 are shown to be highly efficient in microglia M1 phenotype reversion and favorable for the recovery of rat locomotor function after SCI. The findings have revealed a novel mechanism of M1 microglia/macrophages swarming at lesion sites at acute phase following SCI, and provide potential therapeutic approaches for neuroinflammation by targeting the astrocytic ET-1 system.

Keywords : spinal cord injury, astrocytes, microglia, endothelin-1, thrombin

P-084

GIRK channel activation modulates circadian membrane excitability in SCN Prokineticin 2 neurons via G protein signaling

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The suprachiasmatic nucleus (SCN) serves as the central circadian pacemaker in mammals, regulating daily rhythms in physiology and behavior. Within the SCN, GABAergic neurons expressing prokineticin 2 (Prok2) have been identified as a candidate output pathway for circadian signals. However, how the daily rhythm of membrane excitability is regulated in Prok2-expressing neurons remains unclear. To address this, we performed patch-clamp recordings from Prok2 neurons expressing GFP in Prok2-tTA mice crossed with Actb-tetO-EGFP reporter mice. The data showed a circadian rhythm in the membrane potential: depolarized during the day and hyperpolarized at night. The membrane resistance showed an opposite rhythm, increasing during the day and decreasing at night. To test the involvement of G protein signaling, we replaced GTP with GDP-β-S in the internal solution. This manipulation caused depolarization and increased the membrane resistance at night, indicating that a tonic G protein-mediated conductance contributes to night time hyperpolarization. We next tested GIRK channels as downstream effectors of G protein signaling. Tertiapin-Q, a selective GIRK blocker, depolarized the membrane during both day and night, with a stronger effect at night, suggesting that GIRK channels mediate night time hyperpolarization. We further examined $GABA_B$ receptor as a potential activator of the GIRK channels. Application of Baclofen, a $GABA_B$ receptor agonist, induced strong hyperpolarization both day and night, showing that $GABA_B$ receptor activation can engage G protein pathways to suppress excitability. However, CGP55845, a $GABA_B$ antagonist, had no significant effect, suggesting that $GABA_B$ receptors are not the primary contributors to the endogenous G protein-mediated rhythm in membrane potential. These findings suggest that G protein-mediated activation of GIRK channels underlies the circadian modulation of membrane excitability in Prok2-expressing SCN neurons.

Keywords : Suprachiasmatic nucleus, Prokineticin 2, G-protein, GIRK channel, Circadian rhythm

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P-085

TRPA1 mediates dimethyl fumarate - induced allergic contact dermatitis and pruritus in mice

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Allergic contact dermatitis (ACD) represents a delayed-type hypersensitivity reaction characterized by persistent pruritus and cutaneous inflammation in sensitized individuals following exposure to specific chemicals or metals. While dimethyl fumarate (DMF) serves as an established oral treatment for multiple sclerosis and psoriasis, it exhibits potent broad-spectrum antimicrobial activity, while also functioning as an effective contact and fumigant insecticide. These properties have led to widespread industrial use in food preservation and furniture protection. In vitro studies demonstrate that DMF exposure triggers ACD development, resulting in chronic pruritus and cutaneous lesions. Despite clinical confirmation of DMF-induced ACD manifestations, the precise molecular mechanisms underlying this pathological process remain unresolved. We successfully established a murine model of ACD using DMF. Transcriptomic sequencing and Western blot analysis of dorsal root ganglion (DRG) tissues from these mice showed elevated transient receptor potential ankyrin 1 (TRPA1) expression. Since TRPA1 mediates itch sensation, we generated *Trpa1*$^{-/-}$ mice and induced ACD with DMF. Behavioral tests confirmed that *Trpa1* deletion reduced scratching in DMF-treated mice. Calcium imaging demonstrated that DMF elevated intracellular calcium levels in both TRPA1-transfected HEK293T cells and wild-type mouse DRG neurons, an effect blocked by the TRPA1 antagonist HC-030031. Primary DRG neurons from *Trpa1*$^{-/-}$ mice failed to respond to DMF stimulation. Molecular docking and dynamics simulations identified C621 as the probable DMF binding site on TRPA1. Mutagenesis studies of C621 and three other reactive cysteine residues verified that C621 is essential for DMF-induced TRPA1 activation. These findings demonstrate that TRPA1 mediates itch signaling in DMF-induced ACD, with DMF likely activating TRPA1 through covalent binding at C621, triggering calcium influx and subsequent itch responses.

Keywords : Allergic contact dermatitis, Itch, TRPA1, DRG, Dimethyl fumarate

P-086

Histo-fMOST: 3D architectonic mapping of intact organs at the mesoscopic scale across diverse animal species/models

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The mesoscopic-scale 3D architectonic mapping of intact organs across diverse animal species and models is critical for elucidating the tissue organization and functional mechanisms that underpin complex

biological activities. However, the conventional histological approaches remain limited to either 2D tissue sections or low-resolution 3D imaging due to technical barriers in both large-scale staining and high-resolution microscopic visualization of extensive tissue volumes. To address these challenges, we developed the Histo-fMOST (histological fluorescence micro-optical sectioning tomography) method, which integrates multicolor fluorescent dyes, ultra-thin real-time surface staining, TDI based wide-field imaging and iterative sectioning-imaging cycles to achieve the uniform labeling and high-resolution 3D histology of entire organs while preserving fine architectonic details. Multicolor fluorescent dyes simultaneously stain diverse subcellular molecules with distinct color and intensity profiles, while ultra-thin staining (~1 μm), facilitated by surfactant solutions and resin embedding, enhances imaging contrast and allows extraction of quantifiable high-dimensional texture features. Performance validation of Histo-fMOST was demonstrated in mouse or macaque brain, skin, kidney, and liver samples at a 0.233 μm × 0.233 μm × 1 μm voxel resolution. Multi-types of anatomical structures such as nerve tracts, vascular networks, and cellular distributions were clearly resolved and revealed richer histological details compared to conventional Hematoxylin and Eosin (H&E) staining. Overall, the pre-staining-free and high-resolution capabilities of Histo-fMOST confer significant value to large-scale 3D histopathological studies and whole-brain architectural mapping in higher model organisms.

Keywords : 3D Histology, fMOST, Mesoscopic-scale, Intact organ, Diverse animal species

P-087

Autophagy activation ameliorates SARM1-dependent axon degeneration in CMT2B sensory neuropathy

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Charcot-Marie-Tooth Disease Type 2 (CMT2) is a disease in which axonal degeneration occurs in peripheral neurons. In particular, CMT2B is caused by mutations in the RAB7A gene, and the main pathophysiology is related to the dysfunction of peripheral sensory nerves. RAB7A is a protein that regulates the formation of late endosomes, lysosomes, and autophagosomes and contributes to autophagy flux. However, how RAB7A mutation processes evoke axon degeneration in peripheral sensory neurons is unclear. Here, we showed that mitochondrial oxidative stress was causative, but autophagy activation was defensive to axon degeneration by $RAB7A^{L129F}$ overexpression in cultured embryonic dorsal root ganglion (DRG) neurons. In addition, $RAB7A^{L129F}$ mutation induced Sterile alpha and TIR motif-containing protein 1 (SARM1)-dependent axon degeneration of the sensory neurons in vitro. Finally, peripheral sensory neuron-specific transduction of adeno-associated virus of $RAB7A^{L129F}$ in Rab7 heterologous mice developed abnormal pain sensation with degeneration of intraepidermal nerve fibers in footpads, and co-transduction of SARM1-dominant negative mutant blocked both axon degeneration and abnormal pain sensation. Our results show that mitochondrial stress-induced and SARM1-dependent axon degeneration are involved in CMT2B-type axonal neuropathy and provide potential therapeutic targets of CMT2B.

Keywords : Peripheral neuropathy, Charcot-Marie Tooth disease, Axon degeneration, Autophagy, SARM1

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P-088

Activation of GLP-1R alleviates macrophage senescence-induced efferocytosis dysfunction via the AMPK/Gas6/Axl pathway following spinal cord injury

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Spinal cord injury (SCI) is a debilitating condition marked by myelin debris (MD) accumulation, chronic inflammation, and limited neural regeneration. Macrophages play a vital role in MD clearing. However, it remains unknown whether excessive MD phagocytosis leads to foam cell formation and macrophage senescence, ultimately impairing efferocytosis and aggravating tissue damage post-SCI. Our previous research showed that exendin-4 (Ex-4), an agonist of the glucagon-like peptide-1 receptor (GLP-1R), effectively suppressed microglia-mediated neuroinflammation following SCI. The present study further investigated the therapeutic potential of Ex-4 in mitigating macrophage senescence, restoring efferocytosis function, and promoting neural repair. A mouse model of SCI combined with *in vitro* experiments was utilized to demonstrate that macrophages engulfing MD exhibited foam-like structure and senescence phenotype characterized by increased β-galactosidase activity and senescence-associated secretory phenotype (SASP) marker expression, causing impaired efferocytosis via Axl receptor expression downregulation. The Ex-4 treatment significantly reduced macrophage senescence, restored efferocytosis, and suppressed pro-inflammatory SASP markers by activating the adenosine monophosphate-activated protein kinase (AMPK)/Gas6/Axl signaling pathway. Furthermore, Ex-4 promoted remyelination, axonal regeneration, and functional recovery in SCI mice while suppressing glial scar formation. These therapeutic effects were abrogated by Gas6 knockdown. In summary, the present study identified macrophage senescence driven by MD phagocytosis as a novel pathological mechanism in SCI and demonstrated that Ex-4 effectively enhanced senescent macrophage efferocytosis, alleviated inflammation, and facilitated neural regeneration via the GLP-1R/AMPK/Gas6/Axl signaling pathway, providing a promising therapeutic strategy for SCI treatment.

Keywords : Spinal cord injury, Macrophage senescence, Efferocytosis, GLP-1R, Gas6

P-089

Application and evaluation of DREADD-mediated neuronal activity suppression in songbirds

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Chemogenetic tools are utilized to study the neural underpinnings of brain function in animal models. Due to their capability of specifically targeting

the activity of specific cell populations within the brain, chemogenetic tools provide valuable insights to understand the mechanisms behind complex behaviors. Within such, the designer receptors exclusively activated by designer drugs (DREADDs) have become the most well-utilized chemogenetic method in rodents and monkeys. However, studies using it in avian species were limited, suggesting a species-specific difference in their action that prevents efficient application in birds. Here, we established a practical application method to use DREADDs in songbirds, based on a systematic evaluation of this effect on songs. We confirmed that the inhibitory DREADD receptor hM4Di was capable of suppressing neuronal activity in vitro by applying it in dissociated neuron culture prepared from zebra finch brains. We also found that DREADD activation by its ligand deschlorroclozapine (DCZ) effectively suppressed song-induced immediate early gene expression in vivo. For further analysis, we evaluated the songs recorded from birds with DREADD-mediated suppression of HVC and Area X. In the HVC-suppressed birds, the number of songs was decreased for approximately 90 minutes after DCZ injection, and the motif duration within songs was shortened. In Area X-suppressed birds, we observed a change in the phonological feature of syllables, with the reduction of winner entropy. These phenotypes indicate that we succeeded in temporal and reversal control of the neural activity in finches. Notably, the observed effect on songs was apparent only when finches were treated with a 10 times higher concentration of DCZ than dose used in mice. Further DREADD study will contribute to elucidating the neural mechanism underlying higher brain functions, such as vocal communication and social interaction, a key area of research in songbirds.

Keywords : Songbird, Chemogenetic, In vitro culture, Zebra finch, Bengalese finch

P-090

Microglial O-GlcNAcylation regulates inhibitory tone in the hippocampus

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Protein O-GlcNAcylation is a post-translational modification critical for multiple cellular functions including transcription, translation, signal transduction, and protein homeostasis. while it has been shown that O-GlcNAcylation modulates neuronal functions through “on-demand” protein modification, it remains to be determined whether O-GlcNAcylation is essential for glial cells such as microglia. In this study, we generated microglia-specific O-GlcNAc transferase (OGT) knockout (KO) mice to reveal the physiological roles of microglial O-GlcNAcylation in the brain. We found that the absence of O-GlcNAcylation in microglia leads to alterations in microglial morphology, lysosomal contents, and innate electrophysiological properties. Notably, the potassium channel Kv1.3 was found to interact with OGT and undergo O-GlcNAcylation. In addition, Kv1.3 exhibited an elevated expression level and channel conductance in the microglia located in the hippocampus of the OGT conditional KO mice. Notably, Kv1.3 abundant microglia specifically modulated hippocampal GABAergic synapses and inhibitory tone, resulting in a shift in E/I balance. Collectively, these data demonstrate that microglia are important for fine-tuning inhibitory tone in the hippocampus through O-GlcNAcylation of the microglial proteins, including the Kv1.3 channel.

Keywords : Microglia, O-GlcNAcylation, Kv1.3, Inhibitory Synapse, Hippocampus

P-091

Poster Award Candidate

GelMA hydrogel loaded with MenSCs-derived exosomes shapes the ecological niche for functional recovery after spinal cord injury

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Spinal cord injury (SCI) remains a significant clinical challenge due to limited endogenous repair capacity and the hostile inflammatory microenvironment. Gelatin methacrylate (GelMA) hydrogels provide structural support for neural regeneration but lack bioactivity to mitigate post-SCI inflammation and glial scarring. Menstrual blood-derived mesenchymal stem cell (MenSCs)-derived exosomes (MenSCs-Exo) exhibit anti-inflammatory and neuroregenerative properties, yet their therapeutic potential in SCI and underlying mechanisms are incompletely understood. We developed a composite Gel-Exo scaffold by encapsulating MenSCs-Exo within GelMA hydrogel. In vitro experiments evaluated biocompatibility, neuronal adhesion, and axonal growth using SH-SY5Y cells. In vivo efficacy was tested in a rat hemisection SCI model via behavioral assessments (Basso-Beattie-Bresnahan scores, CatWalk gait analysis), immunohistochemistry, contrast-enhanced ultrasound (CEUS), and bioinformatics analysis. The cGAS-STING pathway involvement was validated using Western blotting. This study presents a novel Gel-Exo scaffold that integrates biomaterial support with exosome-mediated immunomodulation to enhance SCI repair. The scaffold effectively mitigates inflammation, promotes neuronal regeneration, and modulates the cGAS-STING pathway, offering a promising strategy for translational applications. Further optimization and long-term safety evaluations are warranted to advance clinical translation.

Keywords : axonal growth, spinal cord injury, MenSCs, exosome, biomaterials

P-092

NAD$^+$ supplementation enhances mitochondrial respiration and protects blood-brain barrier integrity in endothelial cells and hemorrhagic stroke model

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Endothelial cells (ECs) in the brain are enriched with mitochondria and tight junctional proteins that are essential for maintaining blood-brain barrier (BBB) integrity as a first line of barrier by restricting toxic substances. Maintenance of BBB is critical to protecting the brain from the pathogen infiltration and acute brain injury by oxidative stress. Currently, treatments such as anticoagulants and thrombolytics are administered only after the onset of stroke. Therefore, effective strategies to maintain BBB integrity or prevent BBB disruption still need to be developed. Our previous work demonstrated that

mitochondrial oxidative phosphorylation (Oxphos) in cerebral ECs is crucial for BBB maintenance. RNA sequencing of isolated cerebral vessels from EC-specific Crif1 knockout mice (TEKCRIF1 KO mice) revealed alterations in multiple signaling pathways, including previously identified alterations in Notch1 signaling. In this study, we focused on the downregulation of the NAD^+ signaling pathway and explored its therapeutic potential. We found that NAD^+ supplementation protects cerebral ECs from mitochondrial dysfunction under oxygen-glucose deprivation (OGD), an in vitro model of ischemia. Pretreatment with NAD^+ preserved mitochondrial respiration and sustained the expression of junctional proteins. Furthermore, systemic administration of NAD^+ in a mouse model of intracerebral hemorrhage (ICH) significantly reduced neurological symptoms and BBB disruption. These findings suggest that enhancing mitochondrial function through NAD^+ supplementation may serve as an effective strategy for preventing BBB breakdown. Targeting mitochondrial metabolism in cerebral endothelial cells represents a promising therapeutic avenue for the treatment of neurovascular disorders.

Keywords : Mitochondria, blood-brain barrier, endothelial cell, NAD+, intracerebral hemorrhage

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P-093

Compartment-specific mitochondrial Ca^{2+} dynamics and molecular composition in neurons

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Neuronal function relies on the distinct polarization of axons and dendrites, which is maintained by compartment-specific regulation of cellular and molecular components. Among these, mitochondria, critical for ATP production and Ca^{2+} homeostasis, exhibit strikingly different morphologies and functions across compartments. While structural differences in mitochondria have been identified, the functional specialization of mitochondria in axons and dendrites and their underlying molecular mechanisms remain poorly understood. In this study, we investigated the compartment-specific mitochondrial Ca^{2+} dynamics and their molecular determinants. We first demonstrated that axonal mitochondria exhibit significantly faster Ca^{2+} clearance than dendritic mitochondria under identical stimulation conditions. Notably, we found that in axons, Ca^{2+} uptake occurs independently of ER-stored Ca^{2+} release, whereas dendritic mitochondria rely on ER-derived Ca^{2+}. To identify the molecular basis of these differences, we employed a porous membrane culture system to physically isolate axonal and whole-cell compartments. Selective enrichment of mitochondrial Ca^{2+} regulatory proteins, MICU1/2 and NCLX, supports ER-independent Ca^{2+} uptake and rapid Ca^{2+} clearance in axons. Importantly, both the molecular composition and compartment-specific mitochondrial Ca^{2+} dynamics were conserved across neuronal types, as confirmed in both cortical and hippocampal neurons. Consistent with the functional significance of this molecular asymmetry, NCLX knockdown, which functionally mimics a mental retardation-associated mutation, led to pronounced axonal branching defects in vivo with minimal effects on dendrites. These findings provide new insights into how subcellular mitochondrial heterogeneity contributes to neuronal polarity and function.

Keywords : Neuron, Polarization, Mitochondrial Ca2+ regulatory proteins

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P-094

Neuron-derived alpha-synuclein triggers aberrant cholesterol accumulation in glial cells

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Parkinson's disease (PD) is characterized by the misfolding and aggregation of alpha-synuclein (α-syn), which propagates between cells and brain regions, thereby driving disease progression. Our previous study demonstrated that cholesterol-lowering agents, such as simvastatin, inhibit both the intracellular accumulation and intercellular transmission of α-syn aggregates, thereby mitigating α-syn pathology and associated behavioral deficits. These findings suggest that cholesterol homeostasis plays a pivotal role in α-syn–associated neurodegeneration. However, the underlying cellular mechanisms, particularly the contribution of neuron-glia interaction, remain poorly understood. In this study, we investigated how α-syn aggregates influence cholesterol metabolism in glial cells, specifically astrocytes and microglia. Conditioned media (CM) containing α-syn aggregates, derived from α-syn–overexpressing neuronal cultures, were applied to cultured glial cells. Interestingly, α-syn CM induced differential cholesterol accumulation in astrocytes and microglia, with astrocytes exhibiting a markedly greater increase in intracellular cholesterol levels. These results indicate that astrocytes serve as key regulators of cholesterol metabolism within the PD microenvironment. Our data highlight the critical role of glial cholesterol regulation in α-syn–mediated pathology and suggest that dysregulated cholesterol metabolism in glial cells may exacerbate PD-associated phenotypes. Targeting cholesterol homeostasis in glial cells may offer a novel therapeutic strategy for slowing the progression of Parkinson's disease.

Keywords : Parkinson's disease, Cholesterol, Alpha-synuclein, Glial cells, Neuron-glia interaction

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P-095

Investigate the underlying mechanism of dendrite degeneration of adult *Drosophila* peripheral sensory neurons during aging

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Dendrite degeneration is a key feature of aging and neurodegeneration, often appearing before clinical symptoms and contributing to the decline of neuronal function. In sensory neurons, such structural changes may underlie the reduced somatosensory perception observed with age. However, the mechanisms driving dendrite degeneration during aging remain poorly understood. To investigate this, we employed an established *Drosophila* model to study age-related structural and molecular changes in skin sensory neurons. Using deep learning-based image analysis, we identified degeneration features in class IV dendritic arborization (c4da) neurons, including beaded dendrites and reductions in dendrite length and tip number. We also observed increased mitochondrial density, suggesting altered cellular homeostasis with age. Bioinformatic analysis of publicly available datasets guided the selection of candidate genes for functional testing. Genetic manipulation of these targets revealed potential regulators of dendrite stability across aging stages. Our findings underscore key cellular and molecular aspects of dendrite aging and highlight the value of this model system for identifying pathways that may contribute to age-related sensory decline.

Keywords : Dendrite degeneration, aging, peripheral sensory neurons, Drosophila melanogaster

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P-096

Motivational Neural Circuitry and Epigenetic Regulation in a VR-Based Decision-Making Task

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Motivation is essential for goal-directed behavior and adaptive decision-making, yet its underlying neural and epigenetic mechanisms remain incompletely understood. To investigate these processes, we employed a virtual reality (VR)-based T-maze task in head-fixed mice, combined with two-photon calcium imaging to capture real-time neural dynamics. Mice were stratified into high- and low-motivation groups based on behavioral performance. The high-motivation group showed significantly elevated neural activity in the anterior cingulate cortex (ACC) during correct trials, a pattern not observed in the low-motivation group. Post-task immunohistochemistry revealed increased c-Fos expression in both the ACC and ventral tegmental area (VTA), indicating task-related activation of these regions. To further dissect the circuit-level underpinnings, we performed two-photon dopamine imaging, achieving single-cell resolution of dopamine signals in the ACC during task performance. Epigenetic profiling revealed a motivation-dependent increase in histone dopaminylation (H3K4me3Q5Dop) within the ACC of high-motivation mice. CUT&RUN assays identified genomic loci enriched with this modification. These findings suggest that motivated behavior engages specific dopaminergic circuits and is associated with distinct epigenetic signatures, offering new insights into the molecular substrates of cognitive engagement.

Keywords : motivation, Vitrual Reality, Dopamine, Histone modification, Epigenetics

P-097

mScarlet Based Calcium and Serotonin Indicators for Improved Compatibility with Optogenetics and Multiplex Imaging

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Fluorescent imaging is important for tracking the activity of cells and analytes both *in vitro* and *in vivo* with great spatial resolution. The combination of multiple fluorescent indicators, in turn, enables exploration of the interaction between multiple components. Red-shifted biosensors are particularly ideal for their lower tissue scattering and low phototoxicity, but come with their own innate limitations. These sensors display dim fluorescence, a low signal-to-noise ratio, and very often experience strong photoswitching when exposed to blue light which complicates their use in multiplex imaging. Here, we introduce two novel sensors based on mScarlet, named PinkyCaMP and sParken, to address these limitations. PinkyCaMP is the brightest existing genetically encoded calcium indicator red calcium indicator and importantly shows no photoswitching, making it highly desirable for multiplex imaging and optogenetics. The developing serotonin sensor sParken is the first red G-protein-coupled receptor-activation-based (GRAB) sensor derived from the $5HT1_A$ serotonin receptor in combination with the fluorescent protein from PinkyCaMP, making it similarly ideal for multiplex imaging.

Keywords : Genetically encoded calcium indicator, Fluorescent imaging, Serotonin sensor, mScarlet, Optogenetics

P-098

Microglial Spatial Proteomics: Unraveling Function in Alzheimer's Disease and the Aging Brain

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Microglia, the resident immune cells of the brain, play a critical and multifaceted role in both brain homeostasis and neurodegenerative diseases like Alzheimer's Disease(AD). We performed microglia-specific spatial transcriptomic analyses in three anatomically distinct brain regions—hippocampal CA3, prefrontal cortex(PFC), and parietal cortex(PC)—using NanoString GeoMx™ Digital Spatial Profiling(DSP) platform. Iba1-positive regions of interest(ROIs) were selected from brain sections of 8-month-old AD mouse and 18-month-old aged mouse to capture region- and condition-specific gene expression change. Setting a ≥2-fold change as significant, we identified upregulated and downregulated genes in CA3, PFC, and PC. Gene ontology(GO) enrichment analysis revealed distinct biological themes per region. In CA3, upregulated genes were enriched in cell communication by chemical coupling, cytoskeletal regulatory protein binding, and postsynaptic intermediate filament cytoskeleton; downregulated genes were enriched in benzene-containing compound metabolic process and hormone activity. In PC, upregulated genes related to trophectodermal cell proliferation and complement C1 complex were noted, whereas downregulated genes were associated with catecholamine secretion regulation and olfactory receptor activity. In PFC, genes upregulated in AD/aged mice were significantly enriched in microglial cell activation involved in immune response, while downregulated genes included those linked to cartilage morphogenesis and stereocilium structure. This study demonstrates the regional heterogeneity of microglial transcriptomic responses in AD and aging, highlighting distinct molecular signatures and immune pathways in CA3, PFC, and PC. The findings from this research are anticipated to pinpoint key protein and pathways that could serve as potential therapeutic targets for AD and age-related cognitive decline.

Keywords : Microglia, Alzheimer's Disease, Aged brain, Spatial transcriptomic analysis

P-099

Perineural nets in anterior cingulate cortex involves sensitive period for social abnormality induced by social isolation

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The social environment during early life influences the development of social behavior in later life. Social isolation (SI) during adolescence is known to cause social deficits, whereas isolation during adulthood does not, suggesting a sensitive period during which the brain is vulnerable to SI. However, the mechanisms underlying this sensitive period are not fully understood. Perineuronal nets (PNNs), extracellular matrix structures, increase in parallel with the closure of sensitive periods for plasticity in the sensory cortex and are known to restrict neural plasticity. Therefore, PNNs may regulate the sensitive period for SI-induced changes in social behavior. In this study, we investigated the role of PNNs in regulating the sensitive period during which SI leads to social deficits. First, we identified the time window during which SI induces social impairment in mice. Consistent with previous findings, SI from 3 to 6 weeks of age reduced social behavior, while SI after 6 weeks had no effect. This indicates that the sensitive period for SI-induced social deficits lies between 3 and 6 weeks of age. We then focused on the anterior cingulate cortex (ACC), a region associated with social behavior, and examined PNN development in this area. PNNs in the ACC increased markedly between 3 and 6 weeks, coinciding with the sensitive period. Finally, to assess the role of ACC PNNs in regulating this period, we injected Chondroitinase ABC (ChABC), an enzyme that degrades chondroitin sulfate proteoglycans which is a major PNN component, into the ACC after the sensitive period, followed by SI. Social deficits emerged only when ChABC treatment was combined with SI, while neither ChABC alone nor SI with vehicle injection produced such effects. These findings suggest that the maturation of PNNs in the ACC contributes to the closure of the sensitive period for SI-induced social deficits.

Keywords : Perineural net, Social isolation, CSPG, Sensitive period, Anterior cingulate cortex

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P-100

Neurodevelopmental function of *Zfp536*

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Znf536 is a transcription factor predominantly expressed in the developing central nervous system. *Znf536* has been reported as a risk gene for various neuropsychiatric disorders such as schizophrenia and autism spectrum disorder. Although a study using a *Znf536*-deficient zebrafish model identified cerebellar volume reduction and behavior deficits, the neurodevelopmental role of *Znf536* remains largely unknown. We investigated neurodevelopmental function of *Zfp536*, the mouse homolog of human *Znf536*, using knockout (KO) mouse model. Single-nucleus RNA sequencing (snRNA-seq) of the developing mouse brain at embryonic day 18.5 revealed that *Zfp536* is highly expressed in medial ganglionic eminence (MGE)-derived cortical interneurons and cerebellar interneurons. Analysis using an interneuron-specific reporter line showed mislocalization of developing MGE-derived interneurons in the cortex of *Zfp536* KO mice, suggesting that *Zfp536* plays a critical role in interneuron development. To determine whether these transcriptional and cellular abnormalities affect postnatal behavior, we conducted behavioral tests. Since *Zfp536* KO mice exhibited neonatal lethality, indicating a critical role in embryonic development, behavioral tests were conducted in heterozygous mice, which exhibited mild sociability deficits and hyperactivity. Ongoing studies aim to understand the underlying mechanisms of altered interneuron development in the Zfp536-deficient mouse. Collectively, our findings provide insights

into understanding the physiological function of *Zfp536* during neurodevelopment.

Keywords : Zfp536, Neurological Disorders, Interneuron development

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P-101

Advancing holotomography for multi-dimensional, high-resolution imaging of mouse brain tissue and organoid structures

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Holotomography (HT) is an advanced label-free imaging technique that leverages refractive index (RI) to achieve high-resolution, four-dimensional (XYZ and time) visualization of biological samples. This study demonstrates the applications of HT diverse applications in brain tissue imaging and organoid analysis. We employed HT to achieve single-axon resolution in mouse brain tissue sections, specifically targeting the hippocampus and cerebral cortex. This method provided clear visualization of neuronal structures and dynamic processes, enabling deeper insights into neuronal development and disease pathology. HT's ability to image fine axonal structures without exogenous labeling presents significant advantages for neuroscience research and clinical applications. Additionally, we applied HT to investigate the morphological and physiological dynamics of mouse hepatic organoids. Using a state-of-the-art HT system, HT-X1 Plus, we successfully obtained depth-resolved, high-resolution 3D images of organoids embedded in Matrigel. This approach allowed for non-invasive observation of structural development and cellular behavior over extended periods. The capability to switch light sources in the HT-X1 Plus system enabled deeper imaging, faster data acquisition, and enhanced visualization of organoid differentiation processes. These findings highlight the versatility of HT in neuroscience and organoid research. HT is an effective tool for both basic research and translational applications because it offers quantitative, label-free imaging that retains sample integrity while increasing experimental efficiency.

Keywords : Holotomography, Tissue imaging, Label-free 3D imaging, Mouse brain, Organoid

P-102

Follistatin regulates voltage-gated sodium channels and potassium channels contributing to neuropathic pain

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Abstract: Neuropathic pain involves voltage-gated ion channel dysfunction in sensory neurons. While Follistatin (FST), a secreted glycoprotein classically known for antagonizing TGF-β superfamily cytokines, its role in neuronal excitability remains unexplored. Here, we demonstrate that FST upregulation in a-fiber dorsal root ganglion (DRG) neurons after spinal nerve ligation (SNL) critically drives neuropathic pain. Inhibition or deletion of *Fst* reduced SNL-induced mechanical allodynia and heat hyperalgesia while normalizing nociceptive neuron hyperexcitability, including increased action potential firing and reduced activation thresholds. Mechanistically, FST bound insulin-like growth factor-1 receptor (IGF1R) through its N-terminal domain, triggering ERK/AKT signaling to enhance neuronal excitability. This pathway increased tetrodotoxin-sensitive sodium currents (Nav1.7) and suppressed A-type (Kv4.3) and delayed rectifier (Kv2.2) potassium currents in DRG neurons. A blocking peptide (PEP4) targeting the FST-IGF1R interaction reversed both ion channel abnormalities and pain behaviors. Our findings establish FST-IGF1R signaling as a central pathway driving neuropathic pain through dual sodium/potassium channel modulation.

Keywords : Neuropathic pain, Dorsal root ganglia, Follistatin, Insulin-like growth factor-1 receptor, Voltage-gated sodium/potassium channels

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P-103

Establishment of an Optimized Protocol for Isolation of Exosomes from Mouse Brain Microvessels

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Exosomes are secreted vesicles that contain intracellular proteins, miRNAs, and mRNAs, functioning as messengers in intercellular communication. To date, several biomarkers of brain injury have been identified through the analysis of brain-derived exosomes, facilitating early diagnosis. Despite extensive efforts to study blood–brain barrier disruption following brain injury, research on the interaction between the brain and microvessels remains limited. To begin with this study, we modified method for isolation of microvessels (MVs) from mouse BBB. First, we identified the exosomes on isolated MV by co-immunostaining with CD63(exosomal membrane) and CD31 (endothelial cell). Next, the isolated microvessels were digested with collagenase type III to facilitate the isolation of exosomes. Following enzymatic digestion, the resulting solution was subjected to a series of sequential centrifugation steps to remove tissue debris, apoptotic bodies, and microvesicles, thereby enhancing the yield of microvessel-derived exosomes (MV-EXOs). To optimize the method for concentrating MV-derived exosomes following sequential centrifugation, we compared ultracentrifugation (UC) and ultrafiltration (UF). Based on three independent experiments isolating MV-EXOs, UC resulted in a 2.8-fold higher exosome yield. Furthermore, exosomal protein quantification revealed that UC samples contained higher levels of the exosomal membrane proteins CD63 and CD81, as well as the internal protein HSP70. In neuroinflammatory conditions,

such as induced by lipopolysaccharide (LPS) treatment, exosome release is increased into the blood and brain. Notably, MV-EXOs from LPS-stimulated mouse exhibited a significantly higher yield following UC isolation. Taken together, our results suggest that UC-based isolation is an optimized method for enriching MV-derived exosomes from mouse brain microvessels, potentially facilitating the development of exosome-based biomarkers for neuroinflammatory conditions.

Keywords : Exosome, Neuroinflammation, Microvessel, Blood brain barrier, Exosome isolation

P-104

In vitro modeling of the crosstalk between neurons and breast cancer cells

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Scientific Context Recent findings in cancer neuroscience indicate that the nervous system plays an active role in tumor progression. In breast cancer, enhanced sensory innervation has been associated with increased aggressiveness and metastasis. However, the underlying mechanisms of neuron–tumor interactions remain poorly understood, partly due to a lack of physiologically relevant human *in vitro* models. Objectives This study aims to characterize the bidirectional communication between human sensory neurons and breast cancer cells, focusing on neuronal responses (axon outgrowth, chemotaxis, electrophysiology) and the influence of neurons on the invasive behavior of cancer cells. Materials & Methods In collaboration with Prof. Ikeuchi's lab (University of Tokyo), we developed custom microfluidic devices to co-culture human iPSC-derived sensory neurons with breast cancer cells. These devices enable spatially controlled interactions and precise analysis of cellular behavior. Results & Discussion Sensory neurons exhibited enhanced axonogenesis and directional growth toward cancer cells overexpressing neurotrophin receptors (NTR+). Electrophysiological recordings revealed a decrease in neuronal activity when co-cultured with wild-type cancer cells, whereas activity was preserved in the presence of NTR+ cells. In turn, neurons significantly increased the 3D invasion potential of NTR+ cancer cells, suggesting a reciprocal influence that promotes both neural remodeling and tumor progression. Conclusion & Perspectives These results support a model in which sensory neurons actively modulate tumor behavior, and breast cancer cells influence neuronal function. This human-based *in vitro* system provides a powerful platform to dissect neuro-cancer crosstalk and could pave the way for novel therapeutic approaches in breast cancer.

Keywords : Neurons, iPSC, Breast cancer, Neurotrophin, Metastasis

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P-105

Presynaptic APP–Contactin complex regulates GABAergic inhibition in hippocampal circuits

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Synaptic cell-adhesion molecules (CAMs) are crucial for organizing inhibitory networks by mediating transsynaptic signaling. Although their role in shaping excitatory synapses has been extensively studied, the molecular mechanisms underlying GABAergic synapse formation remain less well understood. In this study, we examined the role of amyloid precursor protein (APP), a molecule implicated in the pathogenesis of Alzheimer's disease, in controlling inhibitory transmission in the hippocampal CA1 region. We found that APP specifically affects GABAergic, but not glutamatergic, synaptic function, and that this effect depends on its extracellular E1 domain. APP forms cis interactions with contactin-3 and contactin-4, and establishes transsynaptic complexes with postsynaptic proteins including PTPRG, CNTNAP2, and CNTNAP5. These interactions regulate GABA release from somatostatin-expressing interneurons targeting distal dendrites of pyramidal neurons, thereby shaping the inhibitory input pattern. Disrupting APP or its interacting partners diminished inhibitory tone and was linked to heightened anxiety-like behaviors in adult mice. Similarly, overexpression of MDGA1 in pyramidal neurons resulted in comparable effects. Overall, our findings position APP as a structural element essential for the formation of functional inhibitory circuits and the regulation of related behaviors.

Keywords : APP, Contactin, MDGA1, PTPRG, CNTNAP

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P-106

Slitrk3 differentially regulates inhibitory synaptic properties of distinct GABAergic inhibitory neural circuits of medial prefrontal cortex in mice

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Synapses serve as essential units for the transmission of information between neurons. A diverse array of synaptic adhesion molecules localized at the synaptic cleft contribute critically to the establishment, maintenance, and functional regulation of synaptic connections. Synapses are generally categorized into excitatory and inhibitory types; however, in contrast to the extensively characterized excitatory synapses, the molecular and functional mechanisms underlying inhibitory synapses remain relatively underexplored. Here, we focused on Slitrk3 (Slit- and Trk-like protein 3), a postsynaptic adhesion molecule selectively localized to GABAergic inhibitory synapses, to

elucidate its role in synaptic organization and behavioral regulation through neuron-specific loss-of-function in the medial prefrontal cortex (mPFC). Utilizing a conditional knockout (cKO) mouse model with region-specific ablation of Slitrk3 in the mPFC, we observed marked impairments in inhibitory synapse structure and function, as assessed by immunohistochemical labeling and electrophysiological recordings. Notably, cell-type-specific ablation of Slitrk3 within the mPFC yielded distinct outcomes in inhibitory synaptic transmission: deletion in excitatory pyramidal neurons resulted in a significant decrease in inhibitory input, whereas deletion in somatostatin (SOM)-positive interneurons led to an enhancement of inhibitory synaptic transmission. These results suggest that Slitrk3 might exert a cell-type-specific influence on the formation and/or maintenance of different types of GABAergic synapses in the mPFC.

Keywords : Slitrk3, inhibitory synapse, GABAergic synapse, Medial prefrontal cortex, Interneurons

P-107

Compound A attenuates non-cell-autonomous neurotoxicity in multiple preclinical ALS/FTD models

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Fused in sarcoma (FUS) is a DNA/RNA-binding protein that is implicated in various cellular processes, including transcription, RNA splicing, and DNA repair. Mutations in the FUS gene have been linked to several neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). However, treatment strategies for FUS-mediated neurodegeneration remain extremely limited. Here, we identified compound A as a novel modulator of FUS-induced neurotoxicity. Treatment with compound A decreased the cytoplasmic mislocalization of FUS protein and suppressed the activation of inflammatory responses in astrocytes overexpressing FUS. Moreover, compound A ameliorated astrocytic FUS-induced neuronal toxicity and mitochondrial dysfunction. We further demonstrated that the shortened lifespan and impaired locomotor activity observed in *Drosophila* expressing glial FUS were significantly rescued by dietary administration of compound A. TDP-43, another RNA-binding protein associated with ALS and FTD, was also investigated. We found that compound A attenuated TDP-43-induced inflammatory responses and neuronal toxicity in both cellular and *Drosophila* models of TDP-43 proteinopathy. Taken together, these findings suggest that compound A has promise as a potential therapeutic agent for ALS.

Keywords : ALS/FTD, FUS, TDP-43

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P-108

Alleviation of Neuropathic Pain via Intrathecal Administration of ZEB1 siRNA-Loaded PLGA Nanoparticles in a Rat Spinal Nerve Ligation Model

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Neuropathic pain is a pervasive and debilitating chronic condition that significantly diminishes quality of life. The ZEB1 gene has emerged as a critical regulator in neuropathic pain development via the ZEB1–neuroinflammation axis. Here, we investigated the therapeutic potential of ZEB1 siRNA-encapsulated poly(lactic-co-glycolic acid) (PLGA) nanoparticles for attenuating neuropathic pain. In a rat spinal nerve ligation (SNL) model of neuropathic pain, animals received intrathecal injections of PLGA nanoparticles containing either ZEB1 siRNA or scrambled control siRNA on postoperative day 7. We continuously monitored pain behaviors and performed immunohistochemical analysis of spinal cord tissues on day 18. Our findings demonstrate that intrathecal administration of ZEB1 siRNA via PLGA nanoparticles significantly reduced pain behaviors and markedly decreased c-Fos expression in dorsal horn neurons compared to controls. Importantly, we observed ZEB1 expression in spinal astrocytes, and ZEB1 inhibition led to a reduction in inflammatory signals within these astrocytes. These results highlight that PLGA nanoparticle-mediated ZEB1 inhibition effectively attenuates neuropathic pain, suggesting a promising novel therapeutic strategy by specifically modulating astrocytic inflammation.

Keywords : Astrocytes, Neuropathic Pain, Spinal Nerve Ligation (SNL), PLGA Nanoparticles, ZEB1

P-109

Therapeutic Effects of PLGA-Melatonin Nanoparticles in a Murine Model of Ischemic Stroke via Enhanced Microglial Phagocytosis

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Melatonin, a neurohormone primarily known for regulating the sleep-wake cycle, has been shown to exhibit neuroprotective properties by modulating inflammation and promoting cellular repair. In this study, we investigated whether melatonin enhances microglial phagocytic activity in BV2 cells, a murine microglial cell line, and whether its administration improves stroke outcomes in a Rose Bengal-induced photothrombotic ischemia (RB-PI) model. BV2 cells were treated with melatonin, and after 24 hours, we confirmed an upregulation of microglial activation markers. To evaluate the effects of melatonin on microglial phagocytosis, BV2 cells were incubated with pHrodoRed™-conjugated neuronal debris. A significant increase in phagocytic activity was observed in melatonin-treated BV2 cells compared to untreated controls. To selectively deliver melatonin to microglia in the murine

brain, we encapsulated melatonin in poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NP-mel). Mice received intranasal administration of NP-mel once per week for four weeks following RB-PI induction. Neurological function was assessed using behavioral tests, and histological analyses were performed to evaluate infarct volume and microglial activation. Mice treated with NP-mel exhibited improved neurological function and significantly reduced infarct volume compared to untreated mice. Furthermore, NP-mel administration suppressed the expression of pro-inflammatory cytokines (IL-1β, TNF-α, and IL-6) while enhancing anti-inflammatory cytokine expression (IL-4, IL-13, and IL-10). Our findings suggest that melatonin enhances microglial function and may serve as a potential therapeutic strategy for mitigating brain damage and promoting recovery following ischemic stroke.

Keywords : cerebral ischemia, melatonin, microglia, nanoparticles, neuroprotection

P-110

Morphological plasticity of astrocytes in the SCN

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The suprachiasmatic nucleus (SCN) serves as the mammalian central clock, synchronizing rhythms by integrating environmental cues and molecular oscillators. Emerging evidence highlights the key roles of the SCN astrocytes in circadian regulation. While classical tripartite synapse theory emphasizes the astrocyte-synapse interactions through perisynaptic processes (PAPs), here we identified astrocytic lamellar structures enveloping neuronal somata in the SCN, termed perisomatic astrocytic sheets (PASs), using electron microscopy and high-resolution morphological reconstruction. These PASs exhibit distinct ultrastructural features compared to PAPs and demonstrate circadian remodeling patterns. We found that PASs show light-dependent structural plasticity, which was mediated by glutamate receptors.

Keywords : Astrocyte, Circadian rhythm, Suprachiasmatic nucleus, Perisomatic astrocytic sheets, Morphology

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P-111

Gabapentin Attenuates Oxidative Stress–Related Cognitive Dysfunction via Sirt3/MnSOD Signaling in a Tibial Fracture Model

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Perioperative Neurocognitive Disorder (PND) is a common complication following surgery, characterized by deficits in learning and memory. To investigate potential therapeutic strategies, we employed a tibial fracture (TF) mouse model to induce PND. Gabapentin (GBP), commonly used for neuropathic pain, has been shown to exert anti-inflammatory and antioxidant effects in other disease contexts, such as intestinal inflammation and sepsis-induced liver injury. However, its efficacy in surgery-induced cognitive impairment has not been fully explored. In this study, mice subjected to TF surgery exhibited significant impairments in behavioral tasks including the elevated plus maze (EPM), novel object recognition test (NORT), and passive avoidance test (PAT). GBP treatment restored cognitive performance to levels comparable to those of control mice. At the molecular level, GBP markedly reduced hippocampal expression of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) and restored mitochondrial antioxidant capacity, as evidenced by increased expression of MnSOD, a key mitochondrial superoxide scavenger. To explore the underlying mechanism, we examined the Sirt3/MnSOD pathway. Sirtuin 3 (Sirt3) is a mitochondrial deacetylase that regulate acetylation level of MnSOD residues, thereby enhancing its antioxidant function. GBP activated this pathway, and co-administration of the selective Sirt3 inhibitor 3-TYP abolished GBP's protective effects, resulting in worsened cognitive outcomes and increased levels of acetylated MnSOD. These findings suggest that GBP alleviates surgery-induced cognitive dysfunction by suppressing neuroinflammation and enhancing mitochondrial antioxidant defense via activation of the Sirt3/MnSOD pathway. Our results provide mechanistic insight into the potential application of GBP in preventing PND and other oxidative stress-related neurocognitive disorders.

Keywords : Gabapentin, Anti-inflammatory, Antioxidant, Neurocognitive disorders

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P-112

Co-culture of skeletal muscle cells with motor neurons, both differentiated from human iPS cells, leads to NMJ formation and muscle cell maturation

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Human induced pluripotent stem cell (hiPSC) technology can serve as a powerful tool for production of culture models of human diseases. Previous studies reported that overexpression of myogenic differentiation1 (MYOD1) in hiPSCs leads to efficient differentiation of the cells into skeletal muscle cells in a short term, but the muscle cells obtained by this procedure are immature and the culture generated by this method can only be maintained up to 7-10 days at most. Here, we established a co-culture system of muscle cells with motor neurons, both of which are differentiated from hiPSCs, utilizing a compartmentalized culture apparatus. We found that, by using this method, the hiPSC-derived myocytes can be maintained for up to 2 months. Furthermore, we found that neuromuscular junctions are formed between motor axons and myotubes. RT-PCR analysis showed that myotubes express different subunit components of acetylcholine receptors, suggesting that myotubes may show mature phenotype. These results suggest that maturation of hiPSC-derived skeletal muscle cells may be achieved by coculture with motor neurons.

Keywords : Neuromuscular junction, Induced pluripotent stem cells

P-113

Porphyromonas Gingivalis Infection induces the cognitive dysfunction via gut microbiota dysbiosis and IGFBP2 regulation

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Porphyromonas gingivalis (P. gin), a key pathogen in chronic periodontitis, has recently attracted attention for its potential role in Alzheimer's disease (AD). This bacterium can enter the bloodstream and disseminate systemically, with its presence confirmed in the brain tissue and cerebrospinal fluid of AD patients. It is implicated in major AD pathologies such as pTau, amyloid-β (Aβ) accumulation, and neuroinflammation, suggesting a link between *P. gin* infection and cognitive decline. Recent advances in gut microbiome research have identified the gut-brain axis as a critical bidirectional communication pathway, with gut microbiota emerging as a key modulator and promising therapeutic target for CNS. This study aims to investigate the alteration of gut microbiota composition and associated metabolites in AD-like cognitive impairment mice model by *P. gin* infection. Male C57BL/6 mice were orally administered *P. gin* for 12 weeks. Cognitive ability was assessed by neurobehavioral tests. Fecal samples were analyzed via 16S rRNA gene sequencing to examine gut microbiota. To identify target factors influenced by *P. gin*, microglia and astrocytes were isolated from the brain and performed a cytokine array. To assess the vaccine efficacy, mice were vaccinated for 2 weeks, followed by evaluation of changes in cognitive function. *P. gin* infection induced cognitive impairment and increased pTau, Aβ and IGFBP2 expression. The relative abundance of Phylum, the abnormal imbalance between Bacteroidetes and Firmicutes ratio was observed in the *P. gin* group. The vaccine-treated group, cognitive function was significantly restored, accompanied by reduced pTau and IGFBP2 expression and restoration of microbiome balance. Taken together, *P. gin* infection induces cognitive impairment and neuroinflammation via IGFBP2 signaling and microbial dysbiosis. Therefore, targeting IGFBP2 signaling and gut dysbiosis may offer new therapeutic strategies for AD-like cognitive dysfunctions.

Keywords : Porphyromonas gingivalis, Cognitive impairment, microbiome, Neuroinflammation, Hippocampus

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P-114

Temporal Dynamics of Microglial and Macrophage Responses in the MCAO Stroke Model: A single cell RNA sequencing analysis

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Microglia and macrophages are key immune cells that contribute to the inflammatory response, phagocytic clearance, and tissue remodeling in the brain following ischemic stroke. Despite their functional overlap, these cells differ in developmental origin and exhibit distinct temporal roles after injury. In this study, we employed a murine middle cerebral artery occlusion (MCAO) model and observed pronounced phenotypic shifts at days 1 and 7 post-stroke. To elucidate the functional transitions of microglia and macrophages over time, we performed single-cell RNA sequencing. Our results revealed that macrophages play a dominant role in modulating inflammation at day 1, whereas microglia become increasingly involved in debris clearance and repair processes by day 7. We further identified and validated molecular markers that distinguish activated microglia from activated macrophages. Trajectory analysis enabled the classification of activated subpopulations and the identification of gene expression signatures associated with their predicted functional states.

Keywords : MCAO, Stroke, Microglial, Macrophage, bioinformatics

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P-115

UCN1 contributes to the maintenance of trigeminal neuropathic pain in the trigeminal ganglion of mice

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Trigeminal neuropathic pain (TNP) is a common neuropathic pain with severe, stimulus-evoked, short-lasting stabbing pain attacks in the face. Its etiology and pathogenesis are still unclear. Urocortin 1 (UCN1) is a pressure-related peptide containing about 40 amino acids and is also a member of the corticotropin-releasing factor (CRF) family. Here, we show that UCN1 was persistently increased in the trigeminal ganglion (TG) neurons in model of TNP induced by partial infraorbital nerve transection (pIONT). In addition, knockdown of *Ucn1* in the TG attenuated pIONT-induced mechanical allodynia, reduced the activation of MAPKs. Furthermore, UCN1 mediates pIONT-induced mechanical allodynia via corticotropin-releasing hormone receptor 1 (CRHR1), but not CRHR2. Transcriptomic sequencing showed that heat-shock protein family may be potential downstreams of UCN1/CRHR1 signaling. These data indicate that UCN1 contributes to the maintenance of TNP, and targeting UCN1 signaling may be effective for the treatment of TNP.

Keywords : Trigeminal neuropathic pain, Trigeminal ganglion, Urocortin 1, Partial infaorbital nerve transection, Mice

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P-116

Hypothalamic microglial IL-4 signaling mediates cancer-associated cachexia

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Cancer-associated cachexia (CAC) is a debilitating syndrome characterized by adipose tissue and skeletal muscle wasting. The hypothalamus controls whole-body energy metabolism by regulating catabolic programs through the sympathetic nervous system (SNS). However, the detailed mechanism by which the hypothalamus contributes the adipose tissue and skeletal muscle wasting remains unclear. This study investigated the role of interleukin-4 (IL-4) in promoting CAC, particularly through SNS activation. Central IL-4 administration reproduced key features of CAC, including weight loss, anorexia, and adipose and muscle wasting. The mechanisms underlying adipose and muscle wasting differed, involving the hypothalamic-pituitary-adrenal (HPA) axis and autonomic stimulation, respectively. IL-4R is expressed in hypothalamic microglia but not in astrocytes and POMC neurons. Deletion of IL-4R in hypothalamic microglia ameliorated B16F10-induced CAC. Additionally, chemogenetic inactivation of POMC neurons prevented B16F10-induced adipose and muscle wasting. Our findings suggest that targeting hypothalamic microglial IL-4 signaling and POMC neurons could represent a pivotal therapeutic strategy for CAC intervention.

Keywords : Cancer-associated cachexia, Interleukin-4, Hypothalamic microglia, Proopiomelanocortin neurons, Sympathetic nervous system

P-117

Dynamics of hippocampal synaptic landscape underlying associative memory formation

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The hippocampus plays a pivotal role in the formation and storage of memories, with engram synapses, the synapses between engram neurons, serving as key components in this process. Previous studies have revealed that new engram synapses are added to form clusters on engram dendrites. However, engram dendrites have a lower synaptic density and a higher proportion of CA3 engram inputs even before learning, suggesting pre-configured connectivity. Considering the impermanence of hippocampal synapses, how synaptic turnover affects the pre-learning synaptic environment needs further investigation. To address this question, we re-applied the longitudinal two-photon imaging technique on the hippocampus, as reported in Lee et al. (2023). We found that the engram dendrites before contextual fear conditioning (E0) had higher synaptic gain rates than the dendrites of prospective non-engram neurons (N0). Also, Increased contact preference to presynaptic engram was observed after learning. Those results suggest that the rule for synapse formation is regulated by activity-dependent manner.

Keywords : Dual-eGRASP, Synapse, Engram, Two-photon imaging

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P-118

Fine tuning gustatory acuity by glia-like type I cells

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Peripheral taste neurons exhibit concentration-dependent broad tuning, often responding to multiple tastants at higher stimulus concentrations. However, the mechanisms underlying this breadth of tuning remain unclear. While the tuning properties may arise from the intrinsic characteristics of taste receptor cells, the patterns are not uniform across all tastants, suggesting the involvement of taste-specific modulatory processes. Here, we identify a potential mechanism involving localized (1)“ATP spillover” within the taste bud, which may contribute to selective activation of nearby afferent fibers. We find that ATP spillover occurs specifically in response to sweet and amiloride-sensitive low-sodium stimuli, correlating with the emergence of sweet-salty multi-tuned geniculate neurons. Furthermore, ATP released from sweet- and salty-responsive type II cells activates glia-like type I cells via purinergic signaling. These (2) type I cells, in turn, suppress activity in the taste bud, thereby modulating the dynamic range and acuity of peripheral taste responses. Our findings highlight a key role for type I cells in shaping gustatory tuning and maintaining sensory fidelity through ATP-mediated intercellular signaling.

Keywords : Glia-like type I cells, Taste bud, Sensory acuity, Breadth of tuning, Multi-tuned cells

P-119

Cytokine-Mediated Restoration of Social Deficits in Shank2-deficient mice, an animal model of autism

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Autistic Spectrum Disorder (ASD) is a neurodevelopmental disorder shaped by genetic and environmental influences. In recent years, among various pathological mechanisms, neuroimmune modulation has emerged as a promising therapeutic target in ASD. However, the precise mechanisms through which cytokines act within the central nervous system (CNS) are still poorly understood. In this study, we conducted peripheral and central immune profiling of Shank2-deficient

(Shank2 KO) mice, a validated genetic model of ASD, and observed distinct immune dysfunction phenotypes even under non-inflammatory conditions. Based on prior evidence linking immune abnormalities with ASD, we hypothesized that the social deficits in Shank2 KO mice could be ameliorated by restoring specific cytokines whose expression levels were found to diverge significantly from those in wild-type (WT) controls. Using viral vector-mediated cytokine upregulation, behavioral testing, immunohistochemistry and in situ hybridization across various transgenic mice lines, we demonstrated that certain CNS-resident cell types express specific cytokine that regulates sociability in a bidirectional manner. To distinguish central from peripheral immune influences, we also performed bone marrow transplantation from WT CD45 congenic donor mice into Shank2 recipient mice; notably, this peripheral intervention failed to affect social behavior, underscoring the dominant role of CNS immune modulation. This study demonstrates that cytokine signaling within the CNS plays a direct and critical role in regulating social behavior in a mouse model of ASD. Furthermore, our findings also suggest that CNS cytokine functions not merely as passive markers but as active regulators of behavior, offering a novel and precise therapeutic target for ASD.

Keywords : ASD, Shank2-deficient, cytokine, social behavior, CNS

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P-120

Morphological characteristics of Layer 6b neurons in the mouse cortex

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Previous studies have shown that subplate neurons (SPNs) during early development are morphologically diverse, including pyramidal cells, as well as neurons with ovoid somas and bitufted or multipolar dendritic structures. However, it remains unclear whether L6b neurons, the remnants of SPNS, in juvenile and adult rodents show similar heterogeneity. Some studies, using various definitions of layer 6b (L6b), have reported neurons with apical dendrites, inverted pyramidal shapes, and both smooth and spiny multipolar cells. To address this, we investigated the morphological diversity of L6b neurons. We retrogradely labeled deep L6 neurons from layer 1 (L1) and filled them with biocytin to reconstruct their dendritic arbors in primary somatosensory (S1), visual (V1), and motor (M1) cortices. Reconstructed neurons consistently showed multipolar dendritic arbors mostly restricted to infragranular layers. Sholl analysis revealed regional differences in dendritic complexity, with M1 neurons having simpler arbors compared to those in S1 and V1. Despite these differences, the total dendritic length was comparable across regions. We did not observe neurons with apical dendrites extending to L1 or inverted pyramidal morphologies. These findings indicate that L6b neurons labeled from L1 are relatively homogenous population with multipolar dendritic architectures largely restricted in deep layers.

Keywords : Neuroanatomy, Morphology, Layer 6b

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P-121

Cereblon deficiency sensitizes neuroimmune responses and induces affective disturbances

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Cereblon (CRBN) functions as the substrate receptor of the CRL4 E3 ubiquitin ligase complex, regulating neurodevelopment and cognitive processes, and is known to act as the molecular target of lenalidomide, modulating immune responses by suppressing the expression of proinflammatory cytokines such as TNF-α and IL-2. However, its role in central nervous system neuroimmune interactions remains unclear. Here, we investigated whether the deletion of cereblon (CRBN KO) makes the mice more vulnerable to neuroinflammation and furthermore to anxiety and depression. We administered a low dose of lipopolysaccharide (LPS; 0.25 mg/kg, i.p.) to CRBN knockout (KO) mice and quantified levels of proinflammatory cytokines in plasma and the medial prefrontal cortex (mPFC). Anxiety- and depression-like behaviors were assessed using the open field test (OFT), elevated plus maze (EPM), and sucrose preference test (SPT). Compared to wild-type controls, CRBN KO mice exhibited significant increases in inflammatory cytokine levels in both plasma and mPFC, accompanied by heightened anxiety- and depression-like behaviors. Electrophysiological recordings revealed enhanced neuronal excitability and increased sEPSC frequency in mPFC neurons of CRBN KO mice, without the sIPSC reduction observed in controls, and Kv1.3 channel current analysis demonstrated pronounced microglial activation. These findings suggest that CRBN deficiency sensitizes neuroimmune responses, disrupts the excitatory–inhibitory synaptic balance, and may precipitate affective disturbances, highlighting CRBN as a critical regulator of neuroimmune homeostasis and a potential therapeutic target in neuropsychiatric disorders.

Keywords : Cereblon, neuroinflammation, Affective disorder

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P-122

Channel-mediated astrocytic volume transient is required for synaptic plasticity and spatial memory

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Astrocytes are increasingly recognized as active regulators of synaptic plasticity through transient volume changes driven by ion and water fluxes. BEST1 ion channels, as well as the gliotransmitter brain-derived neurotrophic factor (BDNF) are well recognized as key components of these astrocytic volume transients, but their specific contributions to short- and long-term potentiation (STP and LTP) remain unclear. Here, we show that neuronal stimulation induces astrocytic swelling via TREK-1–mediated K^+ uptake and TRPA1-dependent Ca^{2+} influx. This swelling correlates with synaptic potentiation and supports astrocytic BDNF

release, which rescues LTP under conditions of calcium sequestration. While our findings demonstrate that both TRPA1 and astrocytic BDNF are essential for LTP, neither is required for STP, suggesting a distinct mechanism. Building on this, we propose that astrocytic volume transients contribute to STP through mechanical "bumping" of the presynaptic membrane. This hypothesis is supported by our finding that TREK-1 knockdown—known to impair astrocytic volume transients—selectively reduces STP, while astrocytic TREK-1 rescue restores it. These results suggest that astrocytic volume transients may serve dual roles: chemically mediating LTP via calcium and BDNF, and mechanically enhancing STP through direct presynaptic interaction.

Keywords : Astrocytic volume transient, TREK-1, TRPA1, BDNF, Synaptic plasticity

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P-123

Effect of maternal probiotics supplementation on fetal neural development and cognition

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The gut microbiota-brain axis has garnered considerable attention in recent years. The gut microbiota is not only crucial for immune system development but also plays a significant role in shaping the nervous system during development The early postnatal period is a critical time for the establishment of the pioneer microbiota in newborns, significantly influenced by the maternal microbiota. The maintenance of a healthy maternal microbiota is vital for the establishment of a healthy microbiota in the offspring. The use of probiotics supplement during pregnancy is generally considered safe. This study explores how administering the psychobiotics *Lactobacillus plantarum* PS128 (PS128) can improve fetal nervous system development and cognitive function. PS128 has known benefits, including anti-inflammatory and antioxidant properties, and it also increases brain-derived neurotrophic factor (BDNF). We started daily PS128 probiotic supplementation (2×10^9 CFU in 2% sucrose solution) on gestational day 7 and lasted till the pups were weaned on postnatal day 21 (P21). The control dams were supplemented with 2% sucrose solution. After natural delivery, the dams will nurse the pups till they are P21. We started the probiotic or vehicle supplementation to the offspring on P19 when they started to eat solid food. We collected brain samples from one male and one female offspring from each litter at postnatal day 28 (P28) and P60 to examined the hippocampal neurogenesis by immunohistochemical staining. We utilized the cell proliferation marker Ki67 to identify proliferating cells and the young neuronal marker doublecortin to label young neurons. We found that the PS128 male offspring from probiotic supplemented dams has significant higher ratio of young neurons in the dorsal and middle hippocampus. Morris water maze test on P60 offspring also indicated that PS128 supplemented offspring showed better performance. We are currently conducting gut microbiota analysis.

Keywords : Probiotics, Neurogenesis, BDNF, Cognition , Neural development

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P-124

KCC-07, MBD2 inhibitor, expands the therapeutic window of DNA damage inducing reagents in neural tumor cells.

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Neural tumors represent diverse malignancies with distinct molecular profiles and present particular challenges due to the blood-brain barrier, heterogeneous molecular etiology including epigenetic dysregulation, and the affected organ's critical nature. KCC-07, a selective and blood-brain barrier penetrable MBD2 (methyl CpG binding domain protein 2) inhibitor, could suppress tumor development by inducing p53 signaling in medulloblastoma. Here we demonstrate KCC-07 treatment's potential expansion to other neural tumors. KCC-07 treatment reduced proliferation rates of U87 MG (glioma cell line) and SH SY5Y (neuroblastoma cell line). p53 stabilization also occurred in these cell lines without significantly affecting programmed cell death factors under KCC-07 exposure. Furthermore, tumor cell growth inhibition was enhanced when combined with DNA damaging reagents. Both phleomycin (radiomimetic agent inducing DNA strand breaks) and etoposide (topoisomerase II inhibitor inducing DNA strand breaks) treatment activated p53-dependent signaling for apoptosis and cell cycle arrest, consequently suppressing tumor cell growth. Dual treatment with KCC-07 (epigenetic modifier) and DNA damaging reagents augmented tumor cell suppression, suggesting benefits of combinatorial therapy for neural tumors.

Keywords : Neural tumor, DNA damage, p53, KCC-07, MBD2 inhibitor

P-125

Mitochondrial stress protein induced by pancreatic dysfunction mediates increase of anxiety-like behavior

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Over 15% of patients with type 1 diabetes (T1D) have anxiety disorders, despite T1D being caused by the selective destruction of pancreatic beta cells, which involves severe mitochondrial dysfunction. Additionally, puncturing to the floor of the fourth ventricle induces diabetes through hyperglycemia. These findings suggest a connection between the pancreas and the brain though the underlying mechanisms remain unclear. Anxiety-like behaviors in diabetic mice induced by streptozotocin (STZ) were assessed using the open field test (OFT), elevated plus maze (EPM) test, and light-dark transition test (LDT). STZ-treated mice exhibited increased anxiety-like behaviors compared to vehicle-treated mice, as indicated by a higher proportion of movement in the closed arms in the EPM and reduced time spent in the light compartment in the LDT. Given that STZ is known to damage mitochondrial DNA in pancreatic beta cells, the circulating level of one of the mitokines, a

group of mitochondrial stress-induced proteins, was measured using enzyme-linked immunosorbent assay (ELISA). As mitokine level was found to be elevated in the plasma in STZ-treated mice, STZ was injected intraperitoneally into mice with a genetic deletion of the mitokine related gene, and anxiety-like behaviors were subsequently analyzed. Notably, in the EPM, STZ-treated mice with mitokine gene deletion not only showed an increase in total distance moved but also a decrease in the proportion of movement in the closed arms, compared to STZ-treated wild-type mice. Therefore, regulating mitochondrial dysfunction resulting from pancreatic beta cell destruction in diabetes suggests a potential for alleviating anxiety-like behaviors.

Keywords : Type 1 diabetes, Anxiety, Pancreas-brain crosstalk, Mitochondria, Mitokine

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P-126

Restoring aibp expression in the retina provides neuroprotection in glaucoma

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Glaucoma is a neurodegenerative disease manifested by retinal ganglion cell (RGC) death and irreversible blindness. We have identified apolipoprotein A-I binding protein (AIBP) that controls excessive cholesterol accumulation and neuroinflammation in the retina by upregulating the cholesterol transporter ABCA1 and reducing TLR4 signaling and mitochondrial dysfunction. Here, we demonstrated that AIBP and ABCA1 expression were decreased, while TLR4, IL-1β, and the cholesterol content increased in the retina of patients with glaucoma and mouse models of glaucoma. Restoring AIBP deficiency by a single intravitreal injection of AAV protected RGCs and ameliorated visual dysfunction in experimental glaucoma. Conversely, AAV-mediated RGC-specific AIBP knockdown exacerbated RGC loss and visual dysfunction in a mouse model of glaucoma. Mechanistically, AAV-AIBP attenuated TLR4 and IL-1β expression and localization of TLR4 to lipid rafts, reduced cholesterol accumulation, and ameliorated visual dysfunction. Additionally, AAV-AIBP promoted mitochondrial complexity and function in Müller glia *in vivo*. Recombinant AIBP protein inhibited TLR4 and IL-1β activation and alleviated mitochondrial dysfunction in Müller glia in response to elevated pressure *in vitro*. These studies indicate that restoring AIBP expression in the glaucomatous retina reduces neuroinflammation and protects RGCs and Müller glia, suggesting the therapeutic potential of AAV-AIBP in human glaucoma.

Keywords : Glaucoma, Retinal ganglion cells, Neuroinflammation, apolipoprotein A-I binding protein, Mitochondria

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P-127

Screening of novel asymmetric pyridinium-based fluorescent probes with large stokes shifts for imaging live neural stem/progenitor cells

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We report the synthesis of novel asymmetric pyridinium salts via a facile Rh(III) C-H activation, designed to exhibit fluorescence specifically in live cells. Interestingly, a structure–activity relationship (SAR) study revealed a key structural element in pyridinium salts, leading to the identification of the candidate compound KD01, which exhibited fluorescence with a large Stokes shift (excitation/emission = 405/605 nm) only upon exposure to live brain cells. Remarkably, it selectively labels undifferentiated human neural stem/progenitor cells, with limited interaction observed in differentiated neural cells. This work presents a bioactive fluorescent scaffold with distinct photophysical properties and high specificity for neural stem/progenitor cell, offering a promising platform for live-cell imaging and precise identification of these cell populations.

Keywords : Fluorescent molecule, Neural stem/progenitor cell, Large stokes shift, Screening, Imaging

P-128

Divergent Roles of Macrophages and Microglia in Ischemic Stroke: Insight from Multi-omics Analysis

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The brain is one of the most lipid-rich organs in the body, second only to adipose tissue. Following ischemic stroke, the composition of brain lipids undergoes substantial alterations, which are closely associated with the inflammatory response. Notably, microglia and infiltrating macrophages accumulate lipid droplets and actively participate in modulating lipid dynamics during post-stroke inflammation. To investigate the temporal and cellular mechanisms underlying these lipidomic changes, we utilized a mouse model of middle cerebral artery occlusion (MCAO) and conducted both lipidomics and single-cell RNA sequencing at two critical time points: day 1 and day 7 post-stroke, which represent key phases of phenotypic transition. Our lipidomic profiling revealed minimal changes at day 1; however, by day 7, we observed a marked accumulation of triglycerides, cholesterol esters, phospholipids, sphingolipids, and ether lipids. Integration with transcriptomic data demonstrated that microglia and macrophages contribute to these lipid alterations through distinct metabolic programs. Comparative pathway analysis further elucidated the roles of these cell populations in mediating lipid-driven inflammatory responses

and facilitating debris clearance and tissue repair. These findings highlight the divergent yet complementary functions of microglia and macrophages in regulating lipid metabolism during the progression and resolution of post-stroke neuroinflammation.

Keywords : Ischemic stroke, Microglia, Macrophage, Lipidomics, Neuroinflammation

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P-129

Neuroprotective effects of adenosine in models of vincristine-induced peripheral neuropathy

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Peripheral neuropathy induced by anticancer drugs is a common side effect of these medications. Over sixty percent of chemotherapy-treated patients experience chemotherapy-induced peripheral neuropathy (CIPN), and this number is expected to rise further as the survival rate of cancer patients improves due to advancing medical technology. However, there are currently no disease-modifying drugs available to treat CIPN. To develop a treatment for CIPN, it is essential to investigate the mechanisms underlying axon degeneration caused by anticancer drugs and the associated neuropathic pain. Vincristine is an anticancer agent used to treat blood cancers in various age groups that typically induces CIPN. The neuroprotective effect of adenosine has long been recognized, and reports have indicated its ability to slow axon degeneration in damaged peripheral nerves; however, its molecular mechanism of action remains unclear. In this study, we determine the molecular mechanism of vincristine-induced peripheral neuropathy (VIPN) and the neuroprotective effect of adenosine by modeling vincristine-induced axon degeneration using cultured dorsal root ganglia neurons. In addition, a VIPN mouse model was used to assess neuropathic pain and loss of intra-epidermal nerve fibers. We find that adenosine rescues the disruption of mitochondrial membrane potential and NAD+ reduction caused by vincristine treatment in vitro. We suggest that elucidating the neuroprotective mechanism of adenosine will help to pinpoint druggable targets for VIPN treatment.

Keywords : CIPN, Vincristine, Adenosine, Neuroprotection, Axon degeneration

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P-130

The mechanism of oxaliplatin-induced peripheral neuropathy : sensory neuron degeneration and neuronal death

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Chemotherapy-induced peripheral neuropathy (CIPN) is one of the most common side effects of anticancer drug treatment, where peripheral nerve function is damaged by chemotherapeutic agents. Oxaliplatin is a third-generation platinum-based chemotherapeutic agent that exerts its antineoplastic activity by forming DNA adducts, thereby inhibiting DNA replication and transcription through a mechanism analogous to that of cisplatin. It is widely used in the treatment of colorectal cancer. Despite its clinical efficacy, oxaliplatin shows significant neurotoxicity, most notably causing CIPN, which manifests as tremors, hyperesthesia, and allodynia. The pathophysiological mechanism of oxaliplatin-induced peripheral neuropathy (OIPN) is not well understood. Using *in vitro* and *in vivo* assays, we investigated pathways involved in OIPN. When mice were injected with 6 mg/kg oxaliplatin twice a week, we found that the levels of dual leucine zipper kinase (DLK) increased in the sciatic nerves. Inhibiting DLK or the downstream SARM1, both known as major players in axon degeneration pathway, delays the progression of oxaliplatin-induced axon degeneration and mitochondrial damage in cultured dorsal root ganglion neurons. These results suggest that oxaliplatin-treated neurons undergo axon degeneration via activation of the DLK-SARM1 pathway. Furthermore, we found that oxaliplatin-induced cell death can be suppressed by overexpressing Bcl-XL, a key anti-apoptotic protein of the Bcl-2 family. This study suggests potential target mechanisms for the development of a therapeutic agent to treat OIPN.

Keywords : Oxaliplatin-induced peripheral neuropathy (OIPN), Axon degeneration, DLK, SARM1, Bcl-XL

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P-131

The transcriptome analysis for SARM1-dependent axon degeneration-regeneration coupling mechanism.

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Following axon degeneration induced by nerve injury, regenerating axons are observed in the peripheral nervous system (PNS). During this stage, Schwann cell (SC) reprogramming into repair cells occurs and promotes axon regeneration. However, the mechanisms and molecular role of SC reprogramming in axon regeneration remain unclear. In this study, we used a mouse model lacking SARM1—the main executioner of axon degeneration—to investigate the necessity of the SARM1-dependent degeneration signaling pathway in axon regeneration after axonal death. Furthermore, we studied the characteristic gene expression changes resulting from the SARM1-dependent pathway under axonal

injury conditions via RNA sequencing. Sarm1 knockout mice showed significantly delayed axon degeneration and regeneration, consistent with recent reports. The RNA sequencing results from the sciatic nerve suggest that transcripts associated with demyelination and repair cell formation are regulated by SARM1-dependent axon degeneration. In particular, gene ontology analysis seven days after nerve crush revealed that neurotrophic factor secretion and membrane remodeling are important during the axon regeneration stage. On the other hand, regeneration-associated genes showed SARM1-independent expression in dorsal root ganglia (DRG), indicating that the delayed regeneration observed in the SARM1 knockout mice is mediated by a non-neuronal mechanism. Additionally, DRG sequencing data demonstrated that immune activation in the DRG seven days after injury occurs in a SARM1-dependent manner. Taken together, these findings suggest that the reprogramming of SCs and immune cells is induced by SARM1-dependent axon degeneration and contributes to long-term alterations in the immune environment surrounding DRG neurons.

Keywords : SARM1, axon regeneration, Schwann cell, peripheral nervous system

P-132

Mitochondrial Metabolic Reprogramming in Cortical Neurons by Prenatal Corticosterone : A Shift from ATP Synthesis to Membrane Potential Maintenance

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Mitochondrial bioenergetics plays a fundamental role in neuronal development and function. Prenatal exposure to corticosterone in rats (Corti.Pup) has previously been shown to cause delayed neurodevelopment and synaptic plasticity deficits. However, the underlying mitochondrial metabolic adaptations remain unclear. This study investigated mitochondrial function and metabolic remodeling in prefrontal cortex neurons of Corti.Pups, focusing on oxidative phosphorylation, calcium handling, and redox balance. We assessed neuronal viability, reactive oxygen species (ROS) production, oxygen consumption rate (OCR) under both co-culture and neuron-only conditions. Furthermore, we evaluated electron transport chain (ETC) activity, mitochondrial membrane potential (MMP), and mitochondrial calcium uptake in purified isolated mitochondria. In results, Corti.Pup neurons exhibited increased vulnerability to glutamate-induced excitotoxicity in the absence of glial support. Despite reduced ROS production, these neurons showed elevated mitochondrial OCR and proton leak, coupled with decreased non-mitochondrial OCR and ETC complex activity. Surprisingly, MMP remained elevated despite ETC dysfunction, and mitochondrial calcium uptake was suppressed. These features indicate mitochondrial metabolic reprogramming, prioritizing MMP maintenance over ATP synthesis. The observed mitochondrial inefficiency and compensatory adaptations may impair energy production, contributing to delayed neuronal development in Corti.Pups. These findings suggest that mitochondrial dysfunction and metabolic remodeling play central roles in the pathogenesis of neurodevelopmental disorders such as ADHD.

Keywords : Mitochondria, Neurodevelopmental disorders, ROS, ETC, ATP

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P-133

Western diet-induced visceral adipose tissue inflammation promotes Alzheimer's disease pathology via microglial activation in a mouse m

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Western diet (WD)-induced visceral adipose tissue (VAT) inflammation, characterized by adipocyte hypertrophy, hypoxia, and apoptosis, triggers elevated pro-inflammatory cytokines contributing critically to systemic and neuroinflammatory cascades implicated in Alzheimer's disease (AD). Despite accumulating evidence, the precise mechanistic links between WD-driven VAT inflammation and AD pathology remain inadequately defined. In this study, WD-fed mice exhibited significant increases in inflammatory markers within VAT, elevated systemic inflammation, and intensified neuroinflammation, accompanied by augmented levels of key AD biomarkers—including amyloid-beta oligomers, amyloid precursor protein, and phosphorylated tau—in the hippocampus. Additionally, F-18 fluorodeoxyglucose PET imaging revealed decreased glucose metabolism in the thalamus and hippocampus of WD-fed mice compared to controls. RNA sequencing of VAT and cytokine profiling of plasma identified four prominently elevated pro-inflammatory cytokines: CCL8, CCL9, CXCL13, and IL-18. Mechanistic in vitro analyses demonstrated that these VAT-derived cytokines directly activate microglial cells via the IL-6/STAT3 signaling pathway, ultimately promoting hippocampal neuronal cell death. Collectively, these findings elucidate a critical pathway wherein WD-induced VAT inflammation exacerbates AD pathology through a systemic inflammation–neuroinflammation axis, underscoring the therapeutic potential of targeting VAT-derived cytokines to mitigate dietary factor-associated AD progression.

Keywords : Western diet, Visceral adipose tissue, Alzheimer's disease, Neuroinflammation, Cytokine

P-134

Identification and functional characterization of Layer 6b neurons in the neocortex

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To understand neocortical function, it is helpful to first define its constituent cell types. Recent studies indicate that neurons in the deepest cortical layer play roles in mediating thalamocortical interactions, modulating brain state, and are implicated in neuropsychiatric diseases. However, understanding the functions of deep layer 6 (L6b) neurons has been hampered by the lack of a consensus definition for these cell types. In this study, we identified L6b neurons using the molecular markers Complexin 3 (Cplx3) and Connective tissue growth factor (CTGF),

in combination with the retrograde tracer Cholera Toxin Subunit B (CTB). To investigate projection patterns of L6b neurons, we performed retrograde labeling in both hemispheres of the somatosensory, visual, and motor cortex. We found that L6b neurons project axons up to layer 1 in the ipsilateral cortex but do not project to the contralateral cortex. Furthermore, retrograde labeling from the thalamus, combined with CTGF staining, revealed minimal colocalization between corticothalamic neurons and CTGF(+) L6b neurons, suggesting that L6b neurons do not project to the thalamus. Finally, to determine whether L6b neurons are excitatory or inhibitory neurons, we co-stained CTGF with parvalbumin (PV) and somatostatin (SOM), molecular markers of major cortical interneuron populations. The PV(+) and SOM(+) cells did not show any overlap with CTGF positive neurons, suggesting that L6b CTGF neurons are excitatory neurons. Taken together, these findings establish reliable criteria for the identification of L6b neurons and provide a foundation for future studies exploring their functional roles in cortical circuits.

Keywords : Layer 6b, CTGF, Cplx3, cortical circuit

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P-135

Algorithm-Based Identification of Subtype-Specific Therapeutic Targets in the Nervous System

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A strategy that modulates specific cellular subclusters, which drive distinct phenotypes and functions, is critical for achieving both therapeutic efficacy and safety. While these subclusters exhibit unique transcriptomic profiles, converting such specificity into druggable targets remains limited because of challenges at the protein level, such as functional relevance and druggability. To address this, we developed a transcriptome-based approach that quantitatively defines subtype-specific gene expression under physiological and pathological conditions, thereby enabling precision target discovery. We analyzed single-cell RNA sequencing data from the mouse nervous system to identify genes and gene pairs uniquely expressed in specific brain subclusters. Genes exclusively expressed in a single subcluster were designated “single targets,” while gene pairs co-expressed at similar levels only within the same subcluster were termed “dual targets.” Based on these definitions, we constructed an algorithm to identify the target candidates across diverse biological states. Focusing on the dorsal root ganglia (DRG), a key somatosensory tissue, we applied the algorithm to transcriptome from mouse models of neuropathic pain. We identified cluster-specific single and dual targets and evaluated their prioritization by integrating subcellular localization, gene family, and druggability features. This yielded a refined list of clinically relevant candidate genes. Our algorithm offers a scalable precision strategy for the selective modulation of cellular subtypes across various brain cells and conditions. Its integration with deep learning–based prediction models may further improve target identification accuracy and therapeutic applicability.

Keywords : Brain subclusters, Target gene discovery, Dorsal root ganglia, Druggability, Pain

P-136

Intracellular cleavage domain of PROM1 modulates RNA regulatory networks via post-translational control

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Prominin-1 (PROM1/CD133) is a pentaspan transmembrane glycoprotein enriched in membrane protrusions such as microvilli and filopodia, and has been implicated in various physiological processes, including neural regeneration. We previously demonstrated that PROM1 enhances neuronal regenerative capacity via Smad signaling and cholesterol metabolic pathways. However, the downstream regulatory mechanisms remain unclear. In this study, we identified a C-terminal intracellular domain of prominin-1 (PROM1-intracellular cleavage domain, PICD) which is generated through ubiquitin-dependent proteasome degradation. PICD was detected in PROM1-overexpressing cells as well as in various cancer cell lines, and its identity was confirmed by LC-MS analysis. Its stability was regulated by phosphorylation at serine 854, indicating dynamic post-translational control. Furthermore, lysine residues within PICD served as SUMOylation sites that competed with ubiquitination, suggesting that this region may constitute a functionally relevant intrinsically disordered domain (IDR). Transcriptomic analysis revealed that PICD overexpression altered gene expression patterns in a manner similar to PROM1 overexpression, notably enhancing RNA processing pathways including those involving snoRNAs, scaRNAs, and ribosomal protein-coding RNAs. These findings suggest that PICD is a biologically active cleavage product that regulates RNA metabolism and potentially modulates cellular translational capacity. Collectively, our study uncovers PICD as a novel signaling mediator that links PROM1 to RNA regulatory networks, broadening its known role beyond membrane-associated functions.

Keywords : Prominin-1, C-terminal cleavage domain, PTM, IDR, RNA processing

P-137

Neural progenitor cell-like cells in the lateral ventricle of embryonic mouse forebrain

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During early cortical development, neuroepithelial cells adjacent to the ventricles proliferate and differentiate to contribute to the formation of the ventricular wall. Both symmetric and asymmetric divisions are essential for establishing the apical surface of the developing cortex. However, the precise mechanisms that regulate the formation of a smooth apical lining remain unknown. In this study, we report structural irregularities in the apical lining and the presence of novel cell types within the lateral ventricles of mouse embryos at E10.5, a key stage in ventricular lining development. Some cells remained attached to the ventricular wall, whereas others were floating within the lateral ventricle. To characterize these cells, we conducted single-cell RNA sequencing (scRNA-seq) on cells isolated from the lateral ventricles of E10.5 embryos. Analysis of the scRNA-seq data, combined with transcript data from other brain-derived cells, revealed that the cells

within the lateral ventricles are characterized as neural progenitor cells (NPCs). The expression of several genes found in these cells was confirmed using qRT-PCR and immunostaining. Holotomography study showed the presence of a nucleus and mitochondria in these cells, indicating their viability which was confirmed by BrdU incorporation assay. Moreover, these cells potentially differentiate into neurons or astrocytes, suggesting their important role in cortical development. This study suggests that the unknown cells are likely neural progenitor cells that may detach from the ventricular lining and relate to the formation of the apical structure.

Keywords : scRNA sequencing, Brain development, Immunofluorescence, Holotomography

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P-138

HDAC6 Inhibition by Tubastatin A and Vagus Nerve Stimulation Promote Epigenetic Activation of Schwann Cells and Modulate Inflammation

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Previous studies have shown that vagus nerve stimulation (VNS) induces anti-inflammatory reflex responses through neural circuits between the central nervous system and peripheral organs. However, vagus nerve activation and the pathophysiological changes mediated by drug treatment have not been investigated. Based on our recent data demonstrating the involvement of Tubastatin A (TBA), a selective inhibitor of histone deacetylase 6 (HDAC6), in Schwann cell activation in regenerating peripheral nerve, here we investigated the effects of TBA on the vagus nerve activation in association with anti-inflammation in the peripheral target organ. Injection of TBA into the vagus nerve induced mRNA expression of axonal growth-associated protein 43 (GAP-43) in Schwann cells of the vagus nerve and the dorsal vagal complex in the brain stem. TBA treatment also induced the production of phospho-Erk1/2 in the dorsal vagal complex area, thus suggesting TBA-modulation of vagus neurons. We further found that TBA upregulated mRNA expression of α7 nicotinic acetylcholine receptors (α7nAChR) and reduced IL-1β and TNF-α levels in the spleen of LPS-treated mice. To further investigate whether TBA administration into the vagus nerve has an additive effect on cholinergic anti-inflammation in the spleen, TBA was co-applied with VNS in mice. Splenic production of cell survival protein phospho-PI3 kinase and the level of α7 nAChR mRNA were upregulated by TBA in VNS-applied animals. Levels of NF-kB were slightly decreased by TBA in VNS-animals, and the production of inflammatory cytokines such as TNF-α and IL-6 was similar or slightly decreased by TBA treatment in VNS-animals. The present data suggest that TBA may play a supplementary role in modulating the VNS-induced anti-inflammatory pathway.

Keywords : Anti-inflammation, Dorsal vagal complex, Epigenetic , Tubastatin A , Vagus nerve stimulation

P-139

Spatiotemporal control of synapse pruning via enhanced synthetic trogocytosis

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Trogocytosis is a process whereby one cell nibbles membrane patches of another cell through direct cell-cell interaction. In previous study, we developed 'SynTrogo', a synthetic approach to induce trogocytosis by designing synthetic ligands and receptors. Our results demonstrate that the interaction of the ligands and receptors specifically triggers synthetic trogocytosis, which can be applied to various cell types. We observed that following trogocytosis, by applying this approach to neuron-astrocyte interaction, we successfully induced the uptake of neuronal membrane fragments labeled with ligand and synaptic molecules by receptor-expressing astrocytes. We also showed that these SynTrogo can induce in size-dependent synapse elimination and synaptic remodeling. In this study, we achieved chemogenetic temporal control of SynTrogo using the RUSH, an inducible plasma membrane (PM) targeting system. Furthermore, we applied the eGRASP system with synthetic trogocytosis to target specific populations of synapses and found that the specific receptor binds only to intact YFP(1-11) but not split-YFP(1-10). In addition, we found that the addition of signaling domains related to phagocytosis helps to enhance the efficiency of SynTrogo. Therefore, our advanced technique provides a potential means to finely regulate engram synaptic connections in space and time.

Keywords : Trogocytosis, Synaptic remodeling, Temporal regulation, Engram synapse

P-140

Optogenetic inhibition of inflammasome in microglia to relieve neuropathic pain

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Neuropathic pain has a debilitating impact on patients' quality of lite, yet no effective treatments are currently available. A growing body of evidence suggests that excessive neuroinflammation plays a central role in the development and persistence of neuropathic pain. Microglia are activated in response to inflammatory stimuli, leading to the release of inflammatory cytokines, and further amplifying neuroinflammation. One crucial mechanism driving microglial activation is the upregulation of the NLRP3 inflammasome, which facilitates the maturation and secretion of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and interleukin-18 (IL-18). In this study, we introduce an optogenetic tool that enables spatiotemporally precise, reversible, and non-invasive regulation of the NLRP3 inflammasome. We validate the clustering kinetics of NLRP3-CIBN or CIBN-NLRP3 transfected with CRY2(E281A, A9) in microglial cell lines (BV2 and HMC) and, assess whether optogenetically 'trapping' of the NLRP3 inflammasomes reduces pro-inflammatory responses following the addition of inflammatory stimuli. For in vivo application, we encapsulate validated NLRP3-CIBN or CIBN-

NLRP3- and CRY2(E281A, A9)-encoding DNA constructs into PLGA nanoparticles, which are preferentially taken up by microglia, enabling targeted regulation of NLRP3 inflammasomes. In a spared nerve injury (SNI) mouse model, intrathecal injection of PLGA nanoparticles followed by controlled light stimulation leads to significant suppression of microglial activation, reduced pro-inflammatory cytokine production, and sustained alleviation of mechanical allodynia after repeated light stimulation. Thus, the combination of optogenetic and nano-technologies offers an effective strategy for regulating the NLRP3 inflammasomes especially in microglia, establishing a promising framework for translational applications in neuropathic pain therapy.

Keywords : Microglia, Inflammasome, Neuropathic pain, Optogenetics, PLGA nanoparticles

P-141

Effects of psilocybin on immediate early gene expression and electrophysiological properties in the mouse somatosensory cortex

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Psilocybin, a serotonergic psychedelic, has significant psychoactive effects such as auditory and visual hallucinations, perceptual alterations and synesthesia. Similar to other psychedelics like MDMA and LSD, psilocybin is believed to have therapeutic potential for neuropsychiatric disorders, but the underlying mechanisms remain unclear. A recent fMRI study in rats indicated that psilocybin alters the activity of the cortical regions, including motor, visual and somatosensory cortex. In this study, we hypothesize that psilocybin exerts its effects by altering the neuronal activity in the cortex. To investigate the effects of psilocybin on the cortex, we conducted c-Fos analysis in a region- and layer-specific manner across cortical areas after psilocybin treatment. Our results revealed that psilocybin increased c-Fos(+) cell density in the motor, somatosensory and auditory cortex but not in the visual cortex. Based on these findings, we further examined the effects of psilocybin on layer 2/3 somatosensory cortical neurons. Electrophysiological characteristics including RMP, input resistance, and rheobase were investigated using whole-cell patch-clamp recordings following psilocybin administration via either injection or perfusion. This study provides biological evidences how psilocybin modulates cortical activity in a region- and layer-specific manner.

Keywords : Psilocybin, psilocin, somatosensory cortex, psychedelics

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P-142

A K^+ channel in oligodendrocyte precursor cells regulating chronic pain

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Objective: This study aims to determine whether central demyelination occurs in neuropathic pain (NP) conditions, and to establish a causal relationship between central myelin loss and pain hypersensitivity. Methods: NP was induced in mice using the chronic constriction injury (CCI) model. Pain sensitivity was assessed using von Frey and thermal assays. Myelin integrity and oligodendrocyte (OL) lineage cell populations in the spinal cord were evaluated using electron microscopy and immunohistochemistry. RNA-seq, electrophysiology, Ca^{2+} imaging, mouse genetics and AAV-based gene expression were used to identify the molecular targets underlying demyelination in NP. Results: CCI induced demyelination in the spinal dorsal horn, reduced OLs numbers, and impaired OPCs differentiation. A two-pore domain K^+ channel (K2P) was found to be enriched in OPCs but significantly downregulated following CCI. OPC-specific deletion of the K2P exacerbated both demyelination and hyperalgesia, whereas AAV-mediated overexpression in OPCs promoted remyelination and alleviated pain. Furthermore, chronic activation of $Vglut2^+$ excitatory neurons induced persistent pain accompanied by progressive demyelination, with pain onset preceding myelin loss. Conclusion: Neuropathic pain induces myelin loss in the spinal dorsal horn. A K2P, enriched in OPCs, promotes their differentiation and remyelination in the spinal dorsal horn. Its downregulation after nerve injury aggravates demyelination and pain, while restoring K2P expression reverses both. These findings highlight a K+ channel as a critical OPC regulator in pain pathology and suggest it as a promising therapeutic target for remyelination-based treatment of neuropathic pain.

Keywords : Neuropathic pain, Central demyelination, Myelin, K2P, Oligodendrocyte precursor cells

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P-143

Selective roles of astrocytes in the acquisition of spatial representation of place cells in the hippocampus

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Hippocampal place cells are crucial for encoding spatial information and forming the cognitive map. While astrocytes are known to modulate neuronal activity and synaptic transmission, their role in shaping place cell properties remains unclear. We hypothesized that astrocyte activity in the hippocampus plays a key role in modulating place cell function. To test this, we utilized a mouse model with hM3Dq-expressing astrocytes and GCaMP6f-expressing pyramidal neurons to manipulate astrocyte activity and monitor calcium activity in place cells using miniaturized microscopy. During exploration of a novel arena, astrocyte Gq activation induced dramatic effects, significantly decreasing both spatial information and place cell proportion while reducing stability. In contrast, astrocyte Gq activation had minimal effects on spatial coding during familiar arena exploration. Importantly, offline astrocyte Gq activation following spatial exploration also impaired place cell stability in subsequent sessions, indicating astrocyte involvement in spatial representation maintenance. Collectively, our study illuminates the diverse roles of astrocytes in hippocampal place cell function, highlighting their critical contribution to both encoding and stabilizing spatial information.

Keywords : Place cells, Astrocyte, Miniscope, DREADD, Spatial representation

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Neuroengineering P-144~161

P-144

Improvements in primary visual functions in photoreceptor-degenerated mice and macaque monkeys using retinal prosthesis

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Photoreceptor degeneration diseases, including retinitis pigmentosa and age-related macular degeneration, are leading causes of irreversible blindness worldwide. In this study, we evaluated the efficacy of retinal prosthesis based on titanium oxide nanowire arrays in restoring visual function in blind mice and non-human primates with photocoagulation-induced photoreceptor degeneration. Using a combination of electrophysiological recordings and choice-box-based behavioral experiments, we demonstrated that subretinal implantation of titanium oxide nanowires in blind mice restored imaging-forming vision, enabling detection of static, moving, and flashing objects for up to 22 months. Long-term two-photon calcium imaging further revealed that the number of light-responsive neurons in the visual cortex peaked one week post-implantation, with a gradual reduction in light response latency over time, indicating progressive improvement in visual information encoding. Additionally, histological and functional assessments in macaque monkeys showed no significant adverse responses one year post-implantation, highlighting the biocompatibility and safety of the nanowire arrays. These findings provide compelling evidence for the potential of nanomaterial-based retinal prosthesis as a therapeutic strategy for photoreceptor degeneration. Furthermore, the observed recovery of visual function underscores the role of brain plasticity in mediating sensory restoration following implantation.

Keywords : Retinal prosthesis, Photoreceptor degeneration, Photovoltaic materials, Vision restoration

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P-145

Bioresorbable, Self-Deploying Electronics for Minimally Invasive Brain Interfaces

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Advanced brain-computer interface (BCI) systems require large-area neural coverage, but current devices rely on invasive surgical procedures that pose risks of tissue damage, infection, and long-term complications. There remains an unmet need for neural interfaces that can be delivered through minimally invasive methods while maintaining functional performance and patient safety. We present a biodegradable electronic platform that can be compactly packaged into a syringe and automatically unfold into a functional configuration upon implantation. The system is built on shape-memory polymer layers that enable reversible mechanical transformation and complete resorption over time, eliminating the need for surgical removal. Integrated sensors and active electronics—including electrodes, temperature and strain sensors, and wireless components—demonstrate multifunctional capabilities for neural monitoring. The design leverages a radial mesh structure inspired by tent architecture, ensuring uniform deployment and flexibility within confined spaces. This approach paves the way for next-generation brain-computer interfaces that are both clinically safe and functionally robust.

Keywords : brain-computer interface (BCI), electrodes, biodegradable, ECoG

P-146

An ECoG integrated platform for real-time Electrophysiology and Fluorescence imaging

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Simultaneous recording of electrophysiological and optical signals enables complementary observations of neural activity, providing insights into both population-level dynamics and intracellular signaling within the same brain region. Here, we introduce an ECoG integrated platform that simultaneously records electrophysiological and optical signals within a compact and unified system. This platform consists of three core components: 1) a transparent, flexible ECoG electrode array for cortical surface recordings, 2) a miniaturized micro-endoscope for fluorescence imaging, and 3) a custom-designed connection module that physically and functionally integrates the two components. To ensure stable and precise measurements, the connection module was miniaturized and optimized to minimize mechanical interference and maintain alignment between the optical and electrical elements. Additionally, an insertion protocol was developed to facilitate reproducible implantation and support long-term use. We validated the recording capability of this ECoG integrated platform in the visual, somatosensory, and medial prefrontal cortex using appropriate stimulation protocols. The system reliably captured both evoked potentials and calcium signals from the same cortical regions. By integrating complementary recording modalities into a compact and accessible format, this ECoG integrated platform establishes a foundation for future applications in closed-loop neuromodulation, disease modeling, and large-scale functional circuit analysis.

Keywords : Multimodal neural interfaces, Microendoscope, Fluorescence imaging, Electrocorticography (ECoG) electrode array, Mesh electrode

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P-147

Hour-long voltage imaging in behaving mice using a set of photostable genetically encoded indicators

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Genetically encoded voltage indicators (GEVIs) are powerful tools for monitoring neuronal activity, but their application, particularly for long-term recordings in vivo, is often limited by photobleaching under the required high illumination intensities. This constraint restricts the total duration of continuous or trial-based experiments, crucial for studying processes like synaptic plasticity or circuit dynamics during behavior. Here, we introduce ElectraON and ElectraOFF, a pair of green fluorescent eFRET-based GEVIs engineered by incorporating a photostability-enhanced derivative of the bright monomeric fluorescent protein mBaoJin with Ace opsin variants. In cultured mouse neurons, ElectraON shows about 22.8% ΔF/F per action potential, while ElectraOFF shows about -14.5% ΔF/F per AP. Critically, Electras demonstrate over 6-fold improved photostability compared to state-of-the-art eFRET GEVIs, pAce, and Ace-mNeon2, under one-photon illumination, while characterized by bright green fluorescence, millisecond kinetics, and good membrane localization. This enhanced stability translates to a 3- to >10-fold extension in functional recording duration, maintaining reliable spike detection in both cultured neurons in vitro and sparsely labeled neurons in the awake mouse cortex in vivo. We demonstrated sustained in vivo recordings exceeding 60 minutes in several neuronal cell types in the primary visual cortex and the hippocampus. Furthermore, Electras show functionality under scanless two-photon excitation in cultured cells. These highly photostable indicators significantly extend the temporal window for voltage imaging, broadening the scope of accessible biological questions.

Keywords : voltage imaging, genetically encoded voltage indicators

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P-148

MEG-Based Affective BCI for Emotion Recognition and Dynamic Tracking

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Emotion recognition using neurophysiological signals like magnetoencephalography (MEG) is emerging as one of the promising applications for affective computing and brain-computer interfaces (BCIs). MEG, with its high spatio-temporal resolution, offers detailed neurophysiological data well-suited for capturing the complexities of emotional states. Such MEG-based emotion recognition systems have demonstrated potentials in enhancing user experience communication, and mental health treatments by accurately recognizing and responding to user emotions. We developed an MEG-based emotion recognition system to infer emotional states elicited by video stimuli. To induce individuals' emotion effectively, we meticulously constructed a novel video dataset. Stimuli were selected via large-scale online survey (N=500), ensuring well-separated clusters across the arousal-valence space based on Self-Assessment Manikin ratings. Furthermore, subjective measures including PrEmo response and participant-selected highlight scenes were also collected to enrich emotional labeling and support the analysis of temporal dynamics in affective responses. We classified MEG responses to each video stimulus into both binary-class (High vs. Low Arousal/Valence) and four-class (HAHV, HALV, LAHV, LALV) scenarios. Our MEG-based emotion recognition system demonstrated robust performance, with average accuracies consistently exceeding 80% across all scenarios. Notably, this high accuracy was maintained even with the increased complexity of multi-class discrimination, underscoring the system's applicability to diverse affective states. Beyond static classification, the system's design enables the monitoring of emotional dynamics. We further investigated these temporal aspects by analyzing how affective states evolved during video viewing, integrating insights from both MEG signal patterns and subjective responses. Collectively, these findings validate the efficacy of MEG-based emotion recognition system.

Keywords : MEG, Emotion Recognition, Affective BCI

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P-149

Inferring Time Information of Imagined Speech from Human ECoG

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Natural spoken communication includes both periods of speech and silence. Electrocorticography (ECoG) signals have been used to decode an individual's intent to speak, while avoiding decoding during silence. However, previous studies have primarily focused on attempted speech (i.e., silent articulation), with limited attention to purely imagined speech. Given the growing interest in decoding imagined speech directly from neural signals to realize speech brain-computer interfaces (BCIs), there is a corresponding need to detect speech onset for imagined speech. Therefore, this study aims to decode onset information of imagined speech from human brain signals. ECoG of nine patients with epilepsy was recorded while they performed three tasks of speaking words; they either spoke overtly, attempted to speak covertly, or imagined speaking words. We focused on two spectral ECoG features: high gamma activity (HGA; 70-150 Hz) and low-frequency activity (LFA; 1-8 Hz). To infer speech onset, we carried out the following steps. First, we trained a Support Vector Machine (SVM) decoder using features obtained during overt speech. The decoder estimated the probability of speech or silence at each time point. We then applied the decoder to features obtained during attempted or imagined speech. Subsequently, a cumulative sum (CUSUM) algorithm was used to predict speech onset, defined as the time at which the probability of speaking began to increase. During overt and attempted speech, we observed an increase in HGA and a

decrease in LFA. Interestingly, during speech imagined, the decrease in LFA was more prominent than the increase in HGA. Moreover, in attempted speech, the predicted speech onset was close to that of overt speech onset when using either HGA or LFA. In contrast, during imagined speech, predictions based on LFA more closely matched the overt speech onset than those based on HGA. These results suggest that LFA may carry critical temporal information for imagined speech.

Keywords : Speech BCI, Imagined Speech, Electrocorticography (ECoG), Low-Frequency Activity

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P-150

Numerical Study on the Effects of Transducer Design on Trans-Spinal Focused Ultrasound Stimulation

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Low-intensity focused ultrasound stimulation (FUS) is a promising noninvasive neuromodulation technique. Trans-spinal FUS (tsFUS) has modulated spinal reflexes in rodent models; however, translating these findings to humans present challenges due to interspecies anatomical differences. Recent humans studies exploring thermal safety and preliminary effects emphasize the need for systematic evaluation. This study investigates how transducer geometry and positional variation affect the efficacy and safety of tsFUS targeting the human spinal cord using computational modelling. A detailed human anatomical model was used to simulate ultrasound propagation. Beam overlap and peak acoustic intensity were compared across 55 single-element focused transducers (SEFTs) with varied curvature radii and aperture widths. In addition, the effect of vertical misalignment of the transducer by ±10 mm and ±20 mm from the acoustic window center was investigated. Thermal safety was assessed via pulsed sonication (2 s ON, 10 s OFF, 20 cycles over 240 seconds). The optimal SEFT geometry (curvature radius = 80 mm, aperture width = 55 mm) improved beam overlap up to 22% while maintaining acoustic intensity above the neuromodulation threshold (0.77 W/cm²). All tested configurations remained within the 2°C safety limit. Misalignments of ±10 mm led to a 3–6-fold reduction in target intensity, while ±20 mm shifts caused reductions of approximately 10–17-fold. This study demonstrates the importance of transducer design and accurate anatomical alignment as critical to effective spinal cord stimulation using tsFUS. These findings offer foundational insights for clinical protocol in spinal neuromodulation.

Keywords : Focused ultrasound stimulation (FUS), Trans-spinal FUS (tsFUS), Neurostimulation, Spinal cord, Transducer optimization

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P-151

The Role of Mental Fatigue in Modulating Behavioral Responses

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[Background] In recent years, there have been efforts to promote desirable behaviors through interventions utilizing mobile applications and other digital platforms. The effectiveness of these interventions may vary based on individual internal states, such as mental fatigue. This study aims to investigate the impact of mental fatigue on behavioral changes induced by short message interventions. [Methods] Sixty healthy adults (Male = 41, Female = 19, Age = 21.6 ± 4.8 years) participated and were divided into three groups: Fatigue, Video, and Control. All participants completed a fatigue questionnaire and a baseline choice task. The Fatigue Group underwent a 60-minute mental fatigue task, the Video Group watched a non-fatiguing video, and the Control Group proceeded directly to the test trial. All groups performed two trials of the experimental choice task, with short messages presented in the second trial. Finally, participants completed the fatigue questionnaire. [Results] Subjective fatigue significantly increased only in the Fatigue Group after the test trials ($p = 0.002$). In all groups, short messages significantly promoted desirable behaviors ($p < 0.05$). However, the degree of behavior change induced by short messages was significantly lower in the Fatigue Group compared to the Control Group ($p < 0.001$). [Discussion] The results of this study indicate that behavioral change through messaging was suppressed under mental fatigue. In the Fatigue Group, mental fatigue induced by the fatigue task likely led to a temporary decline in executive function, resulting in reduced capacity to process product information. Consequently, participants showed a tendency to avoid new choices. Mental fatigue may have impaired information processing and reduced motivation to respond in the choice task. These findings suggest that mental fatigue could diminish behavioral change.

Keywords : Fatigue, Behavior

Acknowledgements : This study was conducted in collaboration with Oki Electric Industry Co., Ltd.

P-152

Shape Memory Polymer based Cuff Electrode for Chronic Peripheral Nerve Interfacing

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Peripheral nerve interfaces (PNIs) have emerged as essential tools for interfacing with the peripheral nervous system, enabling the monitoring, stimulation, and modulation of neural activity for applications in prosthetics, rehabilitation, and bioelectronic medicine. Among the various interface designs, cuff electrodes are widely adopted due to their circumferential contact with nerves and relatively simple structure. However, conventional cuff electrodes typically require sutures, glues, or mechanical anchoring to remain in place, which complicates implantation procedures and poses risks of nerve compression, inflammation, and long-term instability. To address these limitations, we developed a thermally responsive cuff electrode based on a shape

memory polymer (SMP) that becomes flexible at body temperature, enabling reliable fixation to the nerve. The softening of the SMP allows conformal contact with minimal mechanical irritation, and the device demonstrated excellent performance in long-term evaluations. In vivo implantation in rat sciatic nerves showed that the Auto-Cuff could be secured without sutures or adhesives, maintaining stable positioning and signal acquisition for up to 6 weeks. Upon exposure to body temperature, the device softened to a tissue-like stiffness and gently conformed to the nerve surface. Histological analysis revealed minimal immune response and tissue disruption, with near-complete recovery of the surrounding tissue by 4 weeks post-implantation, supporting its biocompatibility and suitability for long-term monitoring. This self-morphing cuff electrode platform represents a significant step forward in peripheral nerve interfacing technology. It simplifies surgical procedures, reduces iatrogenic injury risks, and improves device stability, potentially opening new possibilities in the development of chronic bioelectronic interfaces for both research and clinical applications.

Keywords : Peripheral Nerve, SMP, Cuff electrode, Bioelectronic interfaces

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P-153

A screw-mounted modular optical window system for long-term, device-compatible optical neurophysiology in non-human primates

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Recent advances in calcium imaging and optical stimulation have enabled the reading and writing of neural activity. Although all-optical techniques have advanced our understanding of brain function, they are mostly confined to rodent models. To investigate more complex cognition, these approaches must be extended to non-human primates (NHPs), which have closer anatomical and functional homology to humans. However, applying rodent-based methods to NHPs is insufficient, as the larger brain volume increases light scattering and requires a large field of view. Therefore, optimized systems capable of observing and manipulating the large-scale brain are required. A key component is the optical window, yet conventional fixed implants poorly control immune responses, allow tissue regrowth, and lack structural flexibility for integration with additional devices. To overcome these limitations, we designed a screw-mounted modular optical window system for NHPs. Unlike previous designs, our system separates the chamber and window ring, joined via threaded coupling. This structure allows: (1) easy window replacement; (2) isolation of the brain from the external environment; (3) modular compatibility with other screw-based devices. We implanted a modular, circular optical window with a diameter of 1 cm over the primate motor cortex, showing biocompatibility with no visible inflammation and stable clarity for two weeks. This platform facilitates the setup of the injection system by integrating with a threaded injection cap, enabling delivery of AAV2.1-A carrying ChRger2-mClover into the motor cortex. We also validated the compatibility of the all-optical neurophysiology (A-ON) system for NHPs, which enables simultaneous visualization and optical stimulation of neural populations, with the modular window platform (Kim et al., 2023). Overall, the screw-mounted modular optical window system enhances the stability, reusability, and scalability of all-optical approaches in NHPs.

Keywords : Optical window, Screw-based, All-optical approach, Non-human primates

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P-154

Implementation of an Eye-Gaze Input System and Evaluation of Physical and Mental Fatigue

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[Background]Eye-gaze input systems are beneficial for industrial environments where hands might be occupied or contaminated, making conventional touch-based interfaces impractical. Despite its advantages, uncertainty remains whether such systems inherently cause physical and mental fatigue. This study aimed to compare physical and mental fatigue between eye-gaze input and touch input interfaces.[Methods]Participants comprised 15 university students with normal vision or corrected-to-normal vision using contact lenses. A web-camera-based eye-tracking system (Tobii Nexsus) and the Unity were utilized, measuring pupil diameter, blink frequency, and subjective fatigue during a task involving origami folding instructions displayed on a screen. Participants performed tasks using both the eye-gaze input method and a conventional touch-based input, with the sequence randomized to minimize learning effects.[Results] Results indicated significant differences in pupil diameter between the two input methods; pupil diameter was notably smaller during eye-gaze input compared to touch input($p=0.05$), and decreased progressively with repeated tasks ($p=0.04$). There was no significant difference in blink frequency between the two methods ($p>0.05$). Although subjective fatigue and perceived task difficulty did not differ significantly between conditions, the eye-gaze input scored significantly lower on UI convenience compared to touch input ($p=0.002$). Additionally, a positive correlation was found between ADHD traits and mental fatigue scores within the eye-gaze input group($p=0.01$). [Discussion]The study concluded that while eye-gaze input systems require some initial adaptation and could induce greater subjective fatigue, they remain viable alternatives to touch interfaces in hygiene-sensitive or hands-free industrial environments. Future research should consider individual characteristics, such as ADHD and ASD traits, to develop more tailored and comfortable eye-gaze interfaces.

Keywords : Eye-movement, Pupil response, Fatigue, Cognitive function

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P-155

Is Modeling of Temporal Interference Valid for Predicting Stimulation?

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Temporal Interference (TI) stimulation is a non-invasive technique using kHz-range currents with slightly different frequencies to generate a low-frequency envelope for neural activation. However, its effectiveness in deep areas remains debated due to limited physiological markers and validation methods. Peripheral nerves offer a more accessible model, allowing higher intensities and direct measurement of responses like muscle activation and pain thresholds. In this study, we investigated the mechanisms of TI by combining electric field simulations with validation via peripheral nerve stimulation. TI stimulation was applied to target the median and ulnar nerves in four male participants (BMI: 19.1–33.4) using 15 montages per nerve. For each configuration, we measured the minimum injection current required to evoke visible finger muscle contractions. An anatomical human forearm model (BMI of 21.7) was used to estimate the electric field strength under the same experimental conditions. However, the efficacy and spatial precision of TI in deep neural targets remain under debate due to the lack of direct physiological markers and limitations in experimental validation in the central nervous system. The results show that the relationship between the measured motor thresholds for the ulnar nerve could be explained by the electric field strength (R^2>0.6) in all participants, except the one with the highest BMI. The lower correlation indicates the difference between the standard anatomical arm and participants with higher BMI, indicating that fat and muscle tissues may hinder the predictability of stimulation efficacy. The computational model showed lower agreement with experimental results for median nerve (R^2<0.36), likely due to its deeper anatomical location, where precise anatomical modelling becomes more critical. In conclusion, these findings highlight the importance of individualized anatomical modeling in achieving accurate predictions of TI stimulation efficacy.

Keywords : Temporal interference stimulation, Electric field, Validation, Nerve, Inter-individual difference

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P-156

A 3D-Printed Microfluidic Platform for Aligned Sensory Neurite Extension and Functional Myelination

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Chronic pain, affecting over 51 million U.S. adults, represents a major global health and economic burden, and preclinical research on pain has traditionally relied on animal models, though these are limited in efficiency and specificity. In response, the FDA now encourages alternative in vitro platforms like organ-on-a-chip technologies for preclinical research. In this regard, we introduce a 3D-printed organ-on-a-chip that enables precise sensory neurite alignment and myelination studies replacing traditional polydimethylsiloxane (PDMS)-based systems which lack scalability and physiological relevance. Our platform integrates open and closed microfluidic principles to ensure stable fluid dynamics. This design creates a controlled co-culture environment that mimics in vivo nerve bundle organization. Finite element modeling and fluid dynamics simulations optimize nutrient distribution and biomechanical forces within the chip. Experimental results demonstrate that neurite alignment significantly enhances neuronal growth, with aligned neurites showing up to 2-fold greater area and length compared to random controls. This structured environment facilitates Schwann cell-mediated myelination, producing compact myelin sheaths with physiologically relevant g-ratios and nodes of Ranvier. Our platform also recapitulates both myelinated and non-myelinated Remak bundles observed in native sensory nerves. This platform is cost-effective, resource-efficient, and has high-throughput, making it a versatile tool for pain research, disease modeling, and regenerative medicine applications.

Keywords : Organ on a chip, Peripheral nervous system, Sensory neuron, Schwann cell, Pain

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P-157

High-frequency focused ultrasound neuromodulation with sonosensitive ion channels in behaving mice

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Ultrasound is a non-invasive neuromodulation technique with high spatiotemporal resolution, yet most studies to date have employed low-frequency stimulation, which affects broad brain regions and lacks spatial precision. To overcome this limitation, we developed a high-frequency focused ultrasound (fUS) approach to target specific brain areas more accurately. This study aims to explore the feasibility of sonogenetic neuromodulation and assess its potential for cognitive enhancement in freely-moving mice. We co-expressed genetically encoded calcium indicators (eg, GCaMP) and ultrasound-sensitive ion channels (eg, TRPV1, TRPA1, or TRAAK) in the striatum and orbitofrontal cortex (OFC). A custom-built miniature transducer was mounted on the skull to deliver low-intensity focused ultrasound (fUS), while neural activity was simultaneously monitored using fiber photometry. In the striatum, we validated the transducer's performance and examined ultrasound-induced changes in calcium activity, locomotor behavior, and c-Fos expression to assess the effectiveness of sonosensitization. In the OFC, we will evaluate calcium signal responses to ultrasound stimulation and investigate its potential to modulate cognitive flexibility. Based on established fronto-striatal circuit

mechanisms, we hypothesize that OFC-targeted sonogenetics may restore dysfunctional cortical-striatal connectivity, thereby ameliorating cognitive deficits associated with OFC hypoactivity. Our findings suggest that high-frequency fUS combined with sonosensitive ion channel expression enables effective and spatially precise neuromodulation in freely-moving animals. This approach not only advances our understanding of ultrasound-based circuit control, but also offers a promising, non-invasive platform for cognitive modulation with potential applications in neuropsychiatric and neurodegenerative disorders.

Keywords : Focused ultrasound, High-frequency stimulation, Sonogenetics, Neuromodulation, Behavior modulation

P-158

A novel biocompatible brain-interfaced electrode using laser-assisted structuring of Graphene film

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Biological electrodes can selectively record neuronal signals, detect biomolecules, and stimulate specific regions to replace or recover damaged sensory or motor neurons. Graphene is a material commonly used in the research of biological electrodes due to its high electrical conductivity, mechanical strength, and biocompatibility. However, obtaining graphene can be time-consuming or require complex methods, making it challenging to produce in large quantities. Recently, laser-induced graphene (LIG) obtained by applying a laser to polyimide has gained significant attention. LIG-based biological electrodes offer the advantage of easily obtaining desired patterns using flexible polymers as substrates. We have developed brain interface biological electrodes by patterning LIG on liquid crystal polymer (LCP), a biocompatible polymer, demonstrating the potential for next-generation biological electrodes. We formed LIG by applying a 2.25 W, 450 nm UV laser to LCP films and manufactured the LIG/LCP biological electrodes for brain interfaces. To evaluate the developed biological electrodes for brain interfaces, we conducted cortical electrical stimulation and recording on anesthetized Sprague-Dawley rats. The LIG/LCP electrodes were placed on the rat's motor cortex, and the current was applied to induce movements in the rat's contralateral hind limb. The displacement of toes and heels relative to the rest positions, as temporally aligned by the onset of stimulation, demonstrates an increasing magnitude of movements induced by stronger stimulation. Additionally, electrodes were placed on the rat's barrel cortex to measure cortical signals induced by whiskers touching. Recorded signals exhibited typical slow-up-down dynamics with oscillations associated with a sleep-like state of rats induced by urethane anesthesia. During the stimulated period of 20-30 seconds, touch-induced activities were observed, accompanied by high-frequency oscillations.

Keywords : biocompatible brain-interfaced electrode , Neural interface, Graphene film, Motor control, Neural recording

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P-159

InGEL Platform for Neural Organoid Culture with Porous Hydrogels Enabling Controlled Network Formation and Cellular Complexity

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Capturing the complexity of human brain development in vitro necessitates a culture system capable of supporting diverse cell lineages and tightly regulated developmental schedules, at scale. However, most current systems fall short in meeting these dual requirements. Here, we introduce the InGEL platform, a porous hydrogel-based culture system specifically engineered to overcome these limitations. The scaffold's interconnected pore structure enhances media exchange, supporting prolonged viability and extended culture duration. By modulating the initial seeding density, we achieved adjustable control over organoid size and number, enabling reproducible, scalable generation. Moreover, the system enables stage-specific introduction of ECM components and additional cell types, allowing precise modulation of inter-organoid connectivity and multicellular architecture. We further demonstrate the platform's utility in guiding the timed formation of inter-organoid neural networks and supporting multi-lineage integration within composite organoids. Altogether, this InGEL system provides a versatile and tunable 3D environment for exploring neural development, network dynamics, and complex cellular interactions.

Keywords : Organoid engineering, Hydrogel scaffold, 3D culture system, Neural network formation, ECM modulation

P-160

A new optokinetic response gain analysis based on mean squared error for accurate and universal visual function assessment in animal study

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Optokinetic response (OKR) is widely analyzed to quantify visual function in animal studies by tracking their pupil movements in response to moving grating stimuli. However, in retinal degeneration models such as retinal degeneration 10 (*rd10*) mice, abnormal eye movements (*i.e.*, nystagmus) often interfere with OKR gain, leading to inaccurate estimation of visual function. To address this, we newly propose an OKR gain analysis based on mean squared error (MSE). Eye-tracking data were collected from both *wt* (C57BL/6J) and *rd10* mice (B6.CXB1-*Pde6b*^{rd10}/J) under OKR stimuli with varying spatial frequencies (*e.g.*, 0.08, 0.16, and 0.32 cpd) with 12 deg/sec velocity. The gain values from both methods were compared. Instead of simply dividing average eye velocity by stimulus velocity, we suggest a new

OKR gain calculation by subtracting the normalized MSE between eye- and stimulus-velocity from 1. Due to the nature of MSE, the gain value decreases sharply as eye movement deviates from the stimulus. Moreover, if the eye movement becomes too rapid, the gain value can become negative, effectively penalizing such abnormal eye movements. For *wt* mice, the conventional OKR gains were 0.33 ± 0.07, 0.39 ± 0.14, and 0.36 ± 0.14 at 0.08, 0.16, and 0.32 cpd, respectively. The new gains were 0.49 ± 0.09, 0.57 ± 0.11, and 0.39 ± 0.14 at the same spatial frequencies. The two gain values show a consistent trend without introducing too much deviation. In sharp contrast, the conventional gains were too high in the *rd10* mice (0.67 ± 0.26, 0.60 ± 0.22, and 0.53 ± 0.19 at 0.08, 0.16, and 0.32 cpd, respectively), primarily due to the nystagmus. However, the new gains were 0.38 ± 0.10, 0.30 ± 0.17, and 0.22 ± 0.11, more precisely reflecting the reduced visual function. The new method better discriminated visual acuity between mouse types. Our MSE-based OKR analysis has the potential for an accurate and universal assessment of vision function in animal studies.

Keywords : Optokinetic Response, Retinal Degeneration, Visual Acuity, Mean Squared Error, Eye-tracking

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P-161

Fully Transparent Neural Interfaces for Simultaneous Recording of Electrophysiology and Cell Photon Imaging

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Simultaneous multiphoton imaging and electrophysiological recordings hold considerable promise for advancing the diagnosis and treatment of neurological disorders. Previous metal-based neural interfaces suffer from photoelectric artifacts due to opacity, while transparent implants use nontransparent interconnects to compensate for poor conductivity. For effective electrical and optical brain recordings, both the interface body and interconnects must be fully transparent with excellent electrochemical impedance. Herein, we developed optically fully transparent poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) based neural electrode array featuring both transparent electrodes and interconnect lines. Our ultra-thin, monolayer pristine PEDOT:PSS array exhibits outstanding electrical performance due to a FPE (formamide–phosphoric acid–ethylene glycol) treatment process which enhances the PEDOT:PSS's conductivity by increasing conductive paths, and removing insulating shells. The FPE-treated PEDOT:PSS electrode array (FPE-PEDOT) shows negligible autofluorescence and imaging interference during cell photon imaging. Moreover, in vivo experiments demonstrate FPE-PEDOT's ability to capture extracellular action potentials and local field potentials with minimal noise even under laser excitation, marking the first-ever use of monolayer transparent electrodes to measure spikes and making them suitable for integrated bioimaging and electrophysiological studies. This work establishes a scalable and biocompatible neural interface platform optimized for high-resolution, artifact-free multimodal brain studies.

Keywords : Transparent Neural Interface, Conductive Polymer, Low Impedance Electrode, Electrophysiology Recording, Two-photon Imaging

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Others P-162~P-188

P-162

A marker-based behavioral analysis system allows for in-depth analysis of the behavior and cognition of songbird

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During natural communication among animals, individuals' reactions continuously affect each other's behavior. The detailed analysis of these behaviors has been a key challenge in behavioral neuroscience. Primarily, the deficiency of sophisticated tools for muti-point body tracking has prevented the understanding of such behavioral aspects, especially in free-moving conditions. In this work, we applied a marker-based motion capture technique—originally for large animals—to analyze small animals' behavior. Employing lightweight color markers and a novel algorithm incorporating silhouette and color feature extraction, this system precisely tracks markers and body locations of freely moving subjects across diverse environments and among different individuals, further enabling the tracking of multiple animals in direct social interactions. With this system, we quantitively analyzed zebra finch (*Taeniopygia guttata*) behaviors in response to various stimulus, including male and female conspecifics in live or virtual formats, auditory stimuli, and assessed differences in social or individual discrimination and learning under conditioning. We thoroughly analyzed the vision use, highlighting the differences in monocular and binocular sight, eye preference (left vs. right), and the visual engagement duration in conspecific recognition. These analyses further enabled us to evaluate the visual attention of songbirds, providing an objective method to infer the recognition of signals . In addition, we examined the behavior of directly interacting subjects, shedding light on more naturalistic aspects of social interactions. Our method presents an efficient and easy-to-use tool to perform advanced behavioral analysis in small animals. Moreover, our system offers an objective approach to evaluate their cognition of communicative signals and to analyze the underlying neural mechanisms through the combination with general methods for neural activity manipulation.

Keywords : Songbird, Cognition, Behavioral neuroscience, Attention, Vision

P-163

Serotonin1A-Receptor-mediated signaling in Astrocytes and its influence on Major Depressive Disorder

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Major depressive disorder (MDD) is one of the most common psychiatric disorders worldwide, affecting more than 200 million people. Despite the long-standing hypothesis that serotonin (5-HT) plays a role in the development and manifestation of depression, the precise mechanisms underlying this condition remain poorly understood. Glial cells, such as astrocytes, are well known for their passive role in the nervous system, protecting neurons and maintaining homeostasis. Recent studies suggest that these cells play a larger role than previously thought. There is considerable evidence for bidirectional communication between astrocytes and neurons, particularly at the synapse. Astrocytes are able to respond to neurotransmitter release from nearby neurons by increasing intracellular calcium and subsequently releasing a neuroactive transmitter. Since astrocytes express different 5-HT receptors, such as the 5-HT1A receptor, which has been implicated in depression, our study focuses on the influence of 5-HT1A receptor-mediated signaling in astrocytes within the medial prefrontal cortex on depressive-like symptoms in mice. We hypothesize that 5-HT1A-mediated calcium elevation in medial prefrontal cortex (mPFC) astrocytes may mediate antidepressant effects. To test this hypothesis, we used our previously published light-activatable 5-HT1A receptor chimera to perform optogenetically manipulated experiments including calcium imaging, behavioral experiments, and brain slice electrophysiology. Our findings suggest that astrocytic 5-HT1A-R signaling regulates neuronal activity and exerts antidepressant effects, highlighting a potential astrocyte-mediated mechanism in MDD pathophysiology.

Keywords : Depression, Astrocyte-Neuron Interaction, Serotonin, Neuromodulation, Tripartite Synapse

P-164

Identifying neural circuitry for exercise-induced growth hormone secretion

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Growth hormone (GH) plays key roles in regulating physical growth and metabolic function. Aerobic exercise is considered a physiological stimulus that promotes GH secretion. However, detailed underlying mechanisms linking exercise to GH release remain unclear. In this study, we focused on the role of the noradrenergic neurons in the locus coeruleus (LC) and the relevant neural circuitry in the regulation of GH secretion. Treadmill exercise (15 m/min, 60 min/day, 2 weeks) in 6-week-old mice significantly increased both body length and plasma concentrations of insulin-like growth factor 1 (IGF-1), indicating enhanced GH secretion. Immunohistochemical analyses using anti-dopamine-β-hydroxylase (DBH) and anti-Fos antibodies revealed a significantly higher proportion of Fos-positive noradrenergic (DBH-positive) neurons in the LC in the exercise group, suggesting exercise-induced activation of noradrenergic neurons. These findings were corroborated by results from electrophysiological cell-attached recordings, which showed increased firing frequencies of LC noradrenergic neurons following exercise. To discover how the noradrenergic system regulates hypothalamic somatostatin (SST)-releasing neurons – inhibitors of GH secretion – we conducted electrophysiological whole-cell recordings. We found that norepinephrine (NE) and adrenergic receptor agonists inhibited the activities of hypothalamic SST-releasing neurons. Therefore, our findings suggest that exercise-induced activation of the noradrenergic system promotes GH secretion, potentially by suppressing hypothalamic SST-releasing neurons.

Keywords : Growth hormone, Exercise, Norepinephrine, Hypothalamus, Brainstem

P-165

Intravital Microscopy Enables Real-Time Visualization of PTZ-Induced Epileptic Calcium Dynamics in Thy1-GCaMP Mice

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Epileptic seizures have traditionally been investigated using electroencephalography (EEG), functional MRI, or ex vivo histological analysis methods that either lack cellular resolution or fail to capture dynamic neuronal activity in vivo. In this study, we first validated the feasibility of detecting baseline neuronal calcium signals in Thy1-GCaMP mice using intravital microscopy (IVM), which allows high-resolution, real-time imaging of Ca^{2+}-dependent GFP expression in live brain tissue. After confirming stable and detectable GFP signals under physiological conditions, we administered pentylenetetrazole (PTZ), a known epileptogenic agent. IVM revealed a marked increase in GFP fluorescence intensity following PTZ injection, reflecting heightened neuronal calcium activity associated with seizure induction. These results demonstrate that IVM not only overcomes the limitations of conventional techniques but also enables reliable, direct visualization of epileptic calcium dynamics in vivo.

Keywords : Intravital microscopy, Epileptic seizures

P-166

Intracalvariosseous administration readily delivers molecular to colloidal drugs to the brain via skull-to-brain route

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Brain drug delivery remains a formidable obstacle in the treatment of central nervous system (CNS) disorders due to the restrictive nature of the blood–brain barrier (BBB). Recent anatomical investigations have revealed direct connections between skull bone marrow, the

meninges, and the brain parenchyma. These direct connections could be exploited for the purpose of brain drug delivery upon drug administration into the skull, namely intracalvariosseous administration (ICO), via BBB-bypassing routes. Here we report that ICO readily delivers small molecules, nucleic acids, and colloidal nanoparticles to the brain in both rabbits and mice. Using a skull-mounted infusion-pump implant with nano-flow rate (nanoIPI), we performed continuous ICO of brain-impermeable paclitaxel (PTX), 20-base-pair antisense oligonucleotides (ASO), and 15 nm gold nanoparticles (AuNP) over a four-week period in both species. Pharmacokinetic analysis revealed that brain concentration reached a steady state within two weeks and remained stable throughout the administration period. Remarkably, ICO led to approximately 30% brain uptake in both rabbits and mice, with no associated biochemical or hematological toxicity. High-resolution imaging demonstrated uniform dispersion of AuNP in the diploic marrow cavities of the skull and adjacent brain parenchyma after ICO. Histological examination further confirmed absence of inflammatory infiltrates at the implant site. ICO serves as a promising approach for brain drug delivery, particularly for emerging therapeutic agents such as macromolecules and colloidal drugs that face challenges in crossing the BBB. This approach holds significant translational potential for clinical interventions targeting neurodegenerative diseases, brain neoplasms, and other CNS pathologies requiring sustained, localized drug exposure.

Keywords : Intracalvariosseous administration, BBB-bypassing route, Brain drug delivery, Skull-to-brain route, CNS diseases

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P-167

Proteomic Characterization of Human Meningeal Fibroblasts Across Neurological Diseases

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The membranous meninges, a protective tissue for the brain and spinal cord, consist of diverse cellular components, including fibroblasts, immune cells, hematopoietic cells, and lymphatic vasculature. These layers are fundamental for neuroprotection and orchestrate brain development during embryogenesis. Within the meninges, meningeal fibroblasts (MFs), originating from mesodermal and neural crest embryonic precursors, constitute the dominant cellular population. MFs contribute critically to neuronal migration and cortical morphogenesis through their production of extracellular matrix components, laminins, and integrins, which functionally interact with neuroepithelial and radial glial cells. Despite recent insights, a thorough understanding of MFs' precise roles in central nervous system homeostasis and their pathogenic contributions to neurodegenerative and neurodevelopmental disorders remains incomplete. This knowledge gap underlines the imperative for comprehensive investigations into human MFs to evaluate their viability as therapeutic targets for neurological pathologies. Our current study established MFs cultures derived from the spinal and cerebral dura mater of patients presenting with 6 distinct neurological conditions. We subsequently conducted a comprehensive, label-free, quantitative mass spectrometry-based proteomic analysis. Proteomic analysis revealed unique protein expression profiles between spinal- and cranial-derived MFs, but a significant proportion of identified proteins overlapped in components of cell projection, microtubule cytoskeleton, focal adhesion, cilium, and centrosome. Functional network analysis, utilizing ClueGO/CluPedia, further elucidated distinct functional protein interactions in each disease-specific context. Collectively, the findings from this exploratory study are anticipated to catalyze subsequent cellular and molecular investigations, thereby advancing our mechanistic understanding of this rare meningeal disorder.

Keywords : Meninges, Meningeal fibroblasts, Dura mater, Proteomic analysis, Functional network analysis

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P-168

Orexin activates a distinct subpopulation of arcuate pro-opiomelanocortin neurons to promote food intake

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Orexin (or hypocretin) is a neuropeptide that plays a key role in maintaining wakefulness and energy balance. While the neurocircuitry underlying orexin-induced wakefulness has been extensively studied, the neuronal circuitry mediating orexin-induced feeding remains poorly understood. Here, we show that orexin A unexpectedly activates a distinct subpopulation of the "appetite-suppressing" pro-opiomelanocortin (POMC) neurons in the arcuate nucleus of the hypothalamus to promote feeding. We demonstrate that the hypocretin receptor 2/phospholipase C β4-dependent closure of the M-type K^+ channels mediate orexin A-induced activation of POMC neurons and appetite. We further delineate the molecular profiles of orexin A-responsive POMC neurons using MERFISH, an advanced spatial transcriptomics technology, and show that *Pcsk1n* is the molecular marker of orexin A-activated POMC neuronal subpopulation. Finally, we show that the central opioid circuitry is activated downstream of orexin A-activated POMC neurons to increase food intake. Together, our work reveals the neural substrate underlying orexin A-induced feeding.

Keywords : Hypothalamus, Hypocretin receptor 2, Phospholipase Cβ, μ-opioid receptor, MERFISH

P-169

Early-life regulatory T cells orchestrate brain immunity to establish proper brain function

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The brain was historically considered an immune-privileged organ, leading to limited exploration of how immune cells regulate brain function. Recent evidence, however, suggests that the brain harbors distinct, tissue-adapted immune populations that contribute to neural development and homeostasis. Among these, the role of brain-resident regulatory T cells (Tregs)—critical for immune tolerance—remains poorly understood, particularly during early life. To address this, we constructed a single-cell atlas of developing mouse brain immune cells and discovered a marked enrichment of Tregs in the infant brain (P8) compared to other developmental stages and peripheral organs. These Tregs exhibited a unique transcriptional identity, with elevated expression of proliferation and tissue-residency markers relative to their peripheral counterparts. To define their function, we selectively depleted Tregs during the neonatal period, which led to robust infiltration of αβ T cells into specific brain regions, notably the retrosplenial cortex. These infiltrating T cells showed inflammatory activation and cytokine production. Microglia in these regions adopted a reactive phenotype with increased MHC expression and enhanced synaptic engulfment, resulting in reduced synaptic density, impaired neuronal activity, and spatial memory deficits. To test the therapeutic potential of brain Tregs, we enhanced their numbers via IL-2 gene delivery in the BTBR autism mouse model. This restored brain immune balance and improved autism-like behaviors. Similarly, ASD patients showed peripheral Treg dysfunction and elevated cytotoxic $CD8^+$ T cells, both of which were reversed by low-dose IL-2 treatment, correlating with clinical improvement. Our findings highlight brain Tregs as key regulators of early-life neuroimmune homeostasis with long-term impacts on brain function and behavior

Keywords : Neuroimmunology, Regulatory T cell, Autism spectrum disorder

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P-170

HYP-101, inhibited OGA, attenuated tauopathy, and improved memory deficits in an acute tauopathy model

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Alzheimer's disease (AD) is the most common cause of dementia which occurs several years before clinical symptoms become evident. The neuropathological hallmarks of AD include extracellular amyloid beta plaque deposition and intracellular accumulation of neurofibrillary tangles (NFTs), which drive neurodegeneration and subsequent cognitive and functional decline. NFTs are composed of hyperphosphorylated tau protein. The phosphorylation of tau is dynamically regulated by tau kinases, phosphatase, and O-GlcNAcylation. Notably, O-GlcNAcylation of tau has been shown to negatively regulate its hyperphosphorylation, thereby reducing tau aggregation and toxicity. Therefore, preventing tau phosphorylation by increasing the level of tau O-GlyNAcylation via OGA inhibitors could be a promising therapeutic approach. Despite its high selectivity and potent inhibitory activity against OGA, Thiamet-G exhibits limited brain penetration in Alzheimer's disease patients due to its relatively low membrane permeability. In this study, a novel OGA inhibitor scaffold was designed based on Thiamet G, its binding mode to OGA, leading to HYP-101, the identification of a lead compound. HYP-101 showed highly effective and specific OGA enzyme inhibition but not β-hexosaminidase. HYP-101 exhibited IC_{50} value of 0.053 μM for OGA enzyme and had barin-blood-barrier permeability with -logPe value of 4.4. It was non-toxic in the hippocampal neuronal cell line, HT22. Furthermore, HYP-101 was shown to attenuate tau phosphorylation by inhibiting OGA in the P301L tau over-expressed cell model. When administered orally every other day, starting two weeks after intracerebroventricular infusion of streptozotocin, HYP-101 restored cognitive function in mice. It also elevated brain O-GlcNAc levels and significantly reduced hyperphosphorylated tau species. These findings highlight the therapeutic potential of OGA inhibition in addressing tau pathology and cognitive deficits in AD.

Keywords : Neurodegenerative disorder, Alzheimer's disease, Tauopathy, OGA inhibitor, OGA

P-171

HYP-102 regulates NLRP3 inflammasome activity in BV-2 cells to confer neuroprotection

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Neuroinflammation is an innate immune response in the central nervous system (CNS) triggered by harmful stimuli such as pathogens or chronic mild stress. It is closely associated with the development of neurodegenerative diseases and is primarily regulated by multiprotein complexes known as inflammasomes. Composed of the NLRP3 receptor, ASC, and procaspase-1, the NLRP3 inflammasome is primarily expressed in microglia cells. Upon stimulation by DAMPs or PAMPs, the inflammasome assembles and activates, promoting the release of IL-1β and IL-18, and inducing pyroptosis through membrane pore formation and rupture. Despite extensive efforts to develop NLRP3 inflammasome inhibitors, few candidates have shown both strong efficacy and low toxicity in the context of CNS disorders. In this study, we aimed to identify a novel inhibitor with favorable pharmacological properties, including low toxicity, high metabolic and plasma stability, effective BBB penetration, and neuroprotective activity. To this end, a compound library comprising 462 small molecules was synthesized and screened for NLRP3 inhibitory activity. Through this process, HYP-102 emerged as a promising lead compound. In THP-1 and BV2 cell models, where inflammasome activation was induced using LPS in combination with nigericin or ATP, HYP-102 effectively reduced the secretion of IL-1β and the activation of caspase-1, without notable cytotoxicity. Additionally, it

suppressed ASC oligomerization and the cleavage of gasdermin-D. In LPS-stimulated BV2 cells, HYP-102 also decreased NO production and the release of proinflammatory cytokines, along with downregulation of iNOS and COX-2 expression. Overall, our data suggests that HYP-102 mitigates NLRP3 inflammasome-mediated inflammatory responses by targeting key components of the pathway, including NLRP3, ASC, caspase-1, and IL-1β. These findings support the therapeutic potential of HYP-102 as a candidate for treating neuroinflammation-driven neurodegenerative diseases.

Keywords : Neuroinflammation, Microglia, NLRP3, Inflammasome, IL-1β

P-172

Acupuncture related therapies for Drug addiction: A systematic review and network meta-analysis

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Background: Drug addiction is a critical global health issue characterized by compulsive drug-seeking behaviors and significant neuropsychiatric challenges. This systematic review and network meta-analysis aimed to evaluate the effectiveness of various acupuncture-related therapies in managing drug addiction. Methods: Ten databases were searched from inception to March 26, 2025, for acupuncture-related therapies for drug addiction. Method quality was assessed using the Cochrane Handbook Risk of Bias 2.0. A pairwise meta-analysis was performed using RevMan 5.4 software. Network meta-analysis was conducted using the R software. Result: A total of 35 randomized controlled trials encompassing 15 intervention types and 2812 participants were included. The most frequently targeted acupoints were PC6, ST36, and SP6, while the commonly used auricular points included TF4 (Shenmen), AH6a (Jiaogan), and CO14 (Lung). The network meta-analysis results indicated that the most effective interventions for withdrawal symptoms were transcutaneous electric acupoint stimulation, manual acupuncture, and auricular acupuncture combined with usual care. For depression, manual acupuncture combined with usual care, electroacupuncture, and usual care alone were the most effective. For anxiety, auricular acupuncture combined with usual care, Western medicine, and usual care ranked the highest. Conclusions: Acupuncture combined with usual care showed superior efficacy in managing the overall symptoms of drug addiction, although the optimal approach may vary according to the specific symptom type. Manual acupuncture combined with usual care was particularly effective for depression, whereas auricular acupuncture combined with usual care was the most effective for anxiety.

Keywords : Acupuncture related therapy, drug addiction, systematic review, network mata-analysis, the complementary and alternative treatment

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P-173

Oral mucosal alterations reflect intestinal barrier dysfunction in a DSS-induced colitis model

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Gastrointestinal diagnosis primarily relies on invasive methods such as endoscopy. Recently, non-invasive diagnostic approaches like tongue diagnosis and blood tests have gained attention, with tongue diagnosis in traditional Korean medicine being widely used clinically due to its minimal patient discomfort. However, fundamental mechanistic research supporting tongue diagnosis is still limited. This study analyzed changes in tight junction proteins and the epithelial cell marker cytokeratin 8 (CK8) in the oral and intestinal mucosa using a dextran sulfate sodium (DSS)-induced acute colitis animal model, and investigated the association between oral mucosal alterations and intestinal barrier dysfunction. Acute colitis was induced in SD rats by administering 5% DSS for 5 days, followed by 2 days of regular water, then 3% DSS for 5 days, and a final 2 days of regular water. Endoscopic examination revealed clear inflammatory lesions in the colonic mucosa of DSS-treated rats. Hematoxylin and Eosin staining showed significant keratin layer loss in the tongue epithelium and reduced colonic mucosal thickness compared to controls. Western blot and immunohistochemical analyses demonstrated a significant decrease in occludin and CK8 expression in the DSS group. Immunohistochemical staining further confirmed the reduced expression of these proteins in both tissues. These findings suggest that oral mucosal changes may reflect intestinal barrier dysfunction and support the potential of traditional tongue diagnosis as a non-invasive tool for assessing intestinal health. This study also highlights the significance of the oral-gut mucosal axis in gastrointestinal diseases.

Keywords : DSS, Ulcerative colitis, Tight junction, Oral-gut axis, Tongue diagnosis

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P-174

Metabolic function of leucine-rich repeat transmembrane neuronal 4 expressed by arcuate AgRP neurons

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It is well known that the agouti-related peptide (AgRP)-expressing neurons of the arcuate nucleus of the hypothalamus regulate energy balance and glucose homeostasis. While it was previously shown that excitatory and inhibitory synaptic input onto the AgRP neurons influence the activity and metabolic function of AgRP neurons, little is known about the role of synaptic adhesion molecules therein. In this study, we focused on a synaptic adhesion molecule, leucine-rich repeat transmembrane neuronal 4 (LRRTM4), which is expressed by the post-

synaptic part of excitatory synapses to be involved in synapse formation and synaptic transmission. We generated conditional knockout mice which lacks LRRTM4 specifically in the AgRP neurons (AgRP$^{LRRTM4\text{-}KO}$ mice). We measured body weight, food intake, and energy metabolism, and tested glucose homeostasis to see physiological functions of LRRTM4 in AgRP neurons. We also measured electrophysiological properties of AgRP$^{LRRTM4\text{-}KO}$ neurons via patch clamp methods. In addition, we generated diet-induced obese mice with high fat diet (over 60% fat) and measured metabolic phenotypes and electrophysiological properties. We confirmed successful deletion of LRRTM4 in the AgRP neurons and found that excitatory postsynaptic current is significantly decreased in AgRP$^{LRRTM4\text{-}KO}$ neurons. We also found that AgRP$^{LRRTM4\text{-}KO}$ neurons has a lower firing frequency compare to normal AgRP neurons in ad libitum state. We found that AgRP$^{LRRTM4\text{-}KO}$ mice show improved insulin sensitivity but normal food intake, body weight, and energy metabolism phenotypes. Our results provide insight how synaptic machinery of hypothalamic AgRP neurons can shape *in vivo* metabolic function.

Keywords : AgRP neuron, LRRTM4, Synaptic adhesion molecules, Glucose metabolism, Arcuate nucleus

P-175

Role of dorsal raphe serotonergic neurons in the regulation of sodium appetite

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An animal with sodium deficiency develops sodium appetite which drives it to consume more sodium. A lot of studies have been performed to understand how sodium depletion may lead to the development of sodium appetite, but there are still unanswered questions. In particular, while the relationship between serotonin receptors and sodium appetite has been identified in previous studies, it is still unclear how serotonergic neurons control sodium appetite in response to sodium depletion (SD). In this study, we focused on serotonergic neurons in the dorsal raphe nucleus (DRN), which is the major source of serotonin in brain. We found that DRN serotonergic neurons are activated in response to SD by patch-clamp technique and immunostaining. Utilizing a chemogentic approach, we found that activation of DRN serotonergic neurons was sufficient to increase sodium consumption in euvolemia, while suppression of these neurons decreased sodium intake in sodium depletion. Moreover, serotonin released from DRN was required to induce sodium appetite via Ang II receptor type 1A. In addition, drug induced-hypotension had no effects on DRN serotonergic neuronal activity and sodium intake. In conclusion, we suggest that serotonergic neurons and serotonin in DRN play a role to evoke sodium appetite via the Ang II system in sodium depletion.

Keywords : Sodium appetite, Fluid homeostasis, Dorsal raphe nucleus, Patch-clamp technique, Immunohistochemistry

P-176

Moxibustion reduces DSS-induced brain stress via gut-brain axis inflammation

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Background: Increasing evidence supports that intestinal inflammation may trigger neuroinflammatory processes via the gut-brain axis, particularly affecting oxidative and endoplasmic reticulum (ER) stress pathways in the brain. This study investigated the region-specific impact of DSS-induced colitis on brain oxidative/ER stress and evaluated the protective effects of moxibustion at Shen-shu (BL23) and Ming-men (GV4). Methods: Colitis was induced by DSS, leading to classic peripheral signs such as shortened colon length, weight loss, and systemic cytokine suppression (CXCL7, VEGF, CINC-1). Hematological abnormalities included increased RBC and decreased platelet count, hemoglobin, and RDW. Brain tissue analysis revealed significantly elevated iNOS expression and reduced SOD2 levels in the cortex, with oxidative DNA damage marker 8-OHdG prominently increased in the prefrontal cortex (PFC). At the molecular level, DSS exposure downregulated mitochondrial biogenesis markers PGC-1α and TFAM, and upregulated the ER stress marker CHOP in cortical tissues. Moxibustion treatment effectively reversed these molecular changes, restoring PGC-1α and TFAM expression and suppressing CHOP upregulation. Histological analysis (Golgi staining) confirmed dendritic simplification in the PFC following DSS treatment, which was mitigated by moxibustion. Behaviorally, open field testing demonstrated that locomotor activity deficits were significantly recovered by moxibustion. Conclusion: DSS-induced colitis contributes to prefrontal cortex dysfunction via enhanced oxidative and ER stress, linking peripheral inflammation to central neuropathology. Moxibustion at BL23 and GV4 demonstrates therapeutic potential in attenuating brain oxidative and ER stress, highlighting its relevance for treating neuroinflammatory complications of gut disorders.

Keywords : Oxidative stress, Endoplasmic reticulum stress, Prefrontal cortex, Moxibustion, Gut-brain axis

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P-177

Odor descriptor profile is influenced by association between color and odor

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Most objects have their own odor and colors, so the objects show the association between odor and color. Previous studies have demonstrated that the association between color and odor influences odor intensity, discrimination, and identification. However, research on

how descriptors of odor change depending on the association with color has not been studied. Therefore, we studied that the degree of change in descriptors would be different depending on the degree of association between color and odor. We conducted a survey with 24 participants (10 male, 14 female), using 146 odor descriptors. First, we conducted a color-odor association test to find high and low color association conditions for cis-3-hexenol and citral. Subsequently, conditions with highly associated colors, low association colors, and no color were established, and the odor descriptor scores were evaluated for each condition. We found significant differences in descriptor scores among color conditions. Additionally, we calculated the Euclidean distance between descriptor scores for each condition and found that the difference in odor descriptor scores due to color association was smaller than that between different odor conditions. In summary, our findings indicate that odor descriptors can be changed according to color associations, with this difference being smaller than differences between other odor conditions. We plan to compare and analyze the results of behavioral experiments and brain signal experiments based on color-odor associations in future studies.

Keywords : Odor and color association, Odor perception, Odor descriptor test, Color, Euclidean distance

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P-178

Associations between categorized odors and color stimuli: Behavioral and EEG experiment

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Olfactory stimuli are primarily processed in brain regions associated with olfaction. Sensory perception is not isolated; rather, it can be influenced by stimuli from other modalities. Previous studies have suggested associations between certain colors and specific odors, for instance, yellow with the odor of lemon and red with the odor of cherry. However, clear empirical evidence on cross-modal interactions between visual (color) and olfactory stimuli remains limited. The present study aimed to explore the associations between specific colors and categorized odors. In the behavioral experiment, participants were first exposed to a color stimulus and then presented with an odor selected from six distinct olfactory categories: Balsamic, Citrus, Floral, Green, Herb, and Mint. Eleven color stimuli were used: Blue, Brown, Gray, Green, Light green, Orange, Pink, Purple, Red, Turquoise, Yellow. The results revealed distinct patterns of association between colors and specific odor categories. Our results showed that floral and mint-type odors were most strongly associated with turquoise, while brown showed the lowest association with these categories. In contrast, balsamic-type odor was most frequently linked to brown and least associated with blue. Citrus odor was predominantly associated with orange, green-type odors were most associated with the color green, and herbal odors showed the highest association with yellow. Based on these behavioral findings, we plan to conduct a follow-up EEG study to investigate the temporal dynamics of color–odor associations. Specifically, we aim to determine at which time windows these cross-modal associations influence brain activity.

Keywords : Odor, Color, Cross-modal, Electroencephalography (EEG)

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P-179

The effects of Repetitive Transcranial Magnetic Stimulation (rTMS) over the left DLPFC on working memory in young adults

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This study aims to investigate the impact of rTMS applied to the left dorsolateral prefrontal cortex (DLPFC) on working memory (WM) performance in young adults. Prior studies have indicated that frontal theta oscillations (θ, 4~7 Hz) are linked to the active maintenance and retrieval of working memory. To explore this causal relationship, the present study employed online TMS at frequencies of 5 Hz and 7 Hz during the retrieval phase of working memory tasks, which included the keep-track task, numeric updating task, spatial updating task, and numeric-spatial updating task, each with three difficulty levels — easy, medium, and challenging. A total of sixty young and healthy participants (mean age: 21.0 years) were recruited and randomly assigned to either the real or the sham TMS group. Results showed that TMS over the left DLPFC affects working memory performance: 7 Hz TMS impaired accuracy in the keep-track task, while 5 Hz TMS negatively impacted the numeric-spatial updating task. No significant effect was observed on reaction times. Furthermore, an analysis of difficulty levels revealed that TMS primarily affected working memory performance at the medium and challenging levels. Specifically, the 7 Hz TMS disrupted both accuracy and reaction times at the medium level of the keep-track task. In contrast, the 5 Hz TMS resulted in decreased accuracy at the challenging level of the numeric-spatial updating task. In conclusion, the study determined that online theta TMS over the left DLPFC does not enhance working memory performance. Contrary to expectations, it demonstrated a detrimental effect on verbal working memory, as indicated by the results of the keep-track task and the numeric-spatial updating task compared to the sham TMS. However, it is noteworthy that spatial working memory remained unaffected, as measured by the spatial updating task.

Keywords : TMS, DLPFC, Working memory, Theta oscillations, Updating

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P-180

Intraventricular baclofen infusion via implantable osmotic pump for mouse model of traumatic brain injury

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Traumatic brain injury (TBI) is a leading cause of mortality and disability worldwide, often leading to cognitive and behavioral deficits. TBI is classified into primary brain injury and secondary brain injury. Primary injuries are uncontrollable, so therapies focus on preventing secondary damage. This study investigates baclofen, a treatment for spasticity, delivered via intracerebroventricular (ICV) injection to prevent secondary brain injury. In this study, C57BL/6 mice (20-25g) were used; Sham, TBI with ICV injection of baclofen via osmotic pump (0.2, 0.6, 4.5μg/kg/day), and intraperitoneal (IP) injection of baclofen (0.2mg/kg/day). Baclofen was given for 4 weeks, and after a 2-week break, the Y-maze test was conducted to evaluate spatial working memory. Neurological impairment was assessed weekly using the modified Neurological Severity Score. After all behavioral tests were completed, animals were sacrificed for immunohistochemistry and Western blot. Our previous studies showed that IP baclofen prevents secondary brain injury by reducing neuroinflammation and that 0.2 mg/kg is the optimal dose in a TBI model. To determine ICV dose, we referred to other published studies showing that the dose ratio between IP and intrathecal administration is approximately 1:300. Despite similar behavioral effects, ICV baclofen more effectively reduced inflammation and brain damage than IP administration. Additionally, higher concentrations of baclofen reduced secondary injury markers and cortical lesion volume. The behavioral results demonstrated a positive correlation between the concentrations and performance except in the baclofen 4.5 μg/kg group. This study indicates that administration of baclofen via ICV routes leads to reduced brain parenchymal tissue loss compared to IP delivery, despite similar results in behaviors. These results suggest the possibility of the usefulness of ICV baclofen administration as a therapeutic strategy to prevent secondary brain injury in TBI.

Keywords : Traumatic brain injury, Secondary injury, Baclofen, Intracerebroventricular, Drug delivery

P-181

PLCb1 regulates observational fear via mediating myelination in ACC-BLA circuits

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Myelination is known to be enhanced by neuronal activities and social experiences. It is involved in regulating brain oscillations which are critical for behavior and cognitive function. We found that phospholipase C beta 1(PLCb1) knockout mice exhibit impaired observational fear, a basic form of emphatic behavior. Furthermore, demyelination was detected in the anterior cingulate cortex (ACC) and corpus callosum of this knockout mouse. Conditional knockout of PLCb1 in the ACC-basolateral amygdala (BLA) circuits decreased observational fear. We detect that the axon of BLA projecting ACC neurons pass through the cingulum and corpus callosum, surrounding the white matter tract of the ACC. In addition, Knockdown of myelin basic protein (MBP) in the ACC disrupted theta oscillation and reduced observational fear. These results suggest that PLCb1 regulates observational fear by modulating theta oscillations through myelination.

Keywords : Empathy, Myelination, Plcb1

P-182

Age-related muscle loss: Tracing its origins to the brain

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Aging-related deterioration of the nigrostriatal dopamine (DA) system, part of the basal ganglia circuitry for motor regulation, leads to reduced motor activity. Currently, there is no evidence linking the long-term preservation of DA neuron activity in the substantia nigra (SN) through anti-aging factors to the prevention of skeletal muscle loss associated with aging. We report that sustained upregulation of sirtuin 3 (SIRT3), a mitochondrial deacetylase that declines with age, using adeno-associated virus serotype 1 (AAV1) encoding *Sirt3* in the SN of mice, significantly mitigates aging-related declines in motor activity and skeletal muscle mass. Our study demonstrates that preserving neural activity in the nigrostriatal DA system by maintaining beneficial anti-aging factors in nigral DA neurons can counteract these declines in skeletal muscle mass and locomotor function. These findings have been published in *Signal Transduction and Targeted Therapy* (IF 52.7).

Keywords : Aging, Nigrostriatal dopamine system, Locomotor function, Skeletal muscle, Sirtuin 3

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P-183

Stress-induced preference for antioxidant by *Drosophila*

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In an ever-changing environment, animals make optimal decisions to ensure their well-being. Faced with limited food sources, they often seek foods that provide the nutrients they require to maintain homeostasis. Under extreme circumstances (e.g., infection), they may exhibit ingestive behaviors, such as seeking out substances (e.g., toxins) that suggest self-medication. Few studies, however, have investigated the mechanisms that ensue self-medication. Here, we report the selective intake of antioxidants by *Drosophila melanogaster* during a period of heat stress or sleep deprivation. This preference

was alleviated by pre-feeding them vitamin C or dehydroascorbic acid (DHA) before exposure to stress. Heat stress led to an increase in reactive oxygen species (ROS) levels in the gut, which was alleviated by the intake of vitamin C. Heat stress reduced vitamin C in hemolymph, whereas the consumption of vitamin C or DHA increased it. Furthermore, the intake of vitamin C ameliorated the intestinal barrier dysfunction and extended the survival of flies that had been exposed to chronic heat stress. The heat-induced preference for vitamin C appears to develop independently of the known peripheral chemosensory receptors for this micronutrient. We propose that fruit flies possess an interoceptive mechanism that mediates the detection of vitamin C to overcome environmental challenges.

Keywords : Stress-induced attraction to antioxidant, Self-medication, Vitamin C, Reactive oxygen species (ROS), Drosophila

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P-184

Comparative analysis and applications of high-resolution multimodal imaging techniques using Correlative Light and Electron Microscopy (CLEM)

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Correlative Light and Electron Microscopy (CLEM) has emerged as a key imaging technique that enables simultaneous acquisition of molecular and ultrastructural information from the same biological specimen. Fluorescence microscopy (FM) offers molecular specificity by visualizing proteins of interest (POIs) in multiple colors, while electron microscopy (EM) provides nanometer-scale resolution of subcellular structures. These complementary features make CLEM a powerful tool for accurately elucidating the structure-function relationship within cells. A variety of CLEM approaches have been developed, and their biological applications continue to expand. In this study, we present a systematic comparison of CLEM methodologies based on scanning electron microscopy (SEM) and transmission electron microscopy (TEM), using real imaging data acquired from biological samples. Our analysis evaluates key aspects of each technique, including imaging depth, spatial resolution, sample preparation complexity, and fluorescence signal preservation. Based on these findings, we propose optimized CLEM strategies tailored for addressing various neurobiological questions. Ultimately, this study offers a novel framework for high-resolution multimodal imaging, enabling more precise and reliable analysis of complex neuronal and brain tissue structures.

Keywords : CLEM, TEM, SEM, Structure

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P-185

Context-dependent engagement of mPFC neurons during active and passive coping in a sex-dependent manner

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Depression exhibits sex-specific prevalence and symptoms, with women at greater risk. The medial prefrontal cortex (mPFC) mediates stress responses, yet it remains unclear how individual mPFC neurons engage during coping behaviors across sexes. We employed a sub-chronic variable stress (SCVS) paradigm, which elicited depressive-like behavior more in female than male mice, and recorded single-cell mPFC activity via a miniscope during home-cage coping behaviors, including social interaction, grooming, digging, and rearing, classified as either active or passive. During active coping, males displayed higher peak calcium signals than females, whereas females showed larger responses during passive coping, especially in social contexts, while males reacted more to grooming, movement, and sniffing. In an open-field test (OFT), center-area activity did not differ by sex, but females exhibited greater peak activity in corners. Tracking neurons across contexts revealed that, in males, similar proportions of cells were active in both home-cage and OFT. In females, however, neurons that engaged only during passive home-cage behaviors were preferentially reactivated in both the center and corner OFT zones. These findings indicate that individual mPFC neurons are recruited in a sex-dependent manner during stress coping, with female neurons tuned toward passive coping reactivation under anxiogenic conditions.

Keywords : Sex difference, mPFC, Depression

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P-186

Gut-brain axis for the maintenance of sodium homeostasis

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Sodium homeostasis is vital for all living organisms, ensuring the maintenance of essential physiological balance. While sodium sensing is mediated by taste-sensing cells in the mouth, our laboratory recently identified a population of enteric neurons in the gastrointestinal (GI) tract that detects and responds to sodium and conveys the information from the gut to the brain of Drosophila (Kim et al., 2024). Notably, these taste-independent sodium-sensing neurons drive a behavioral preference for sodium only after a period of salt deprivation. Whether sodium is detected independently of the taste system in mammals remains poorly understood. We are currently investigating whether the GI tract and gut-brain are important for mediating a response to sodium ions following a period of salt deprivation in mice. This project will provide insights into how sodium homeostasis is accomplished by the taste-independent, gut-brain regulatory mechanism in mammals.

Keywords : sodium homeostasis, gut-brain axis, sodium appetite

P-187

EEG alpha phase synchronization correlates with reaction times during inhibitory control

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Inhibitory control, the ability to suppress distractions in pursuit of goals, is a core aspect of human cognition. While electroencephalogram (EEG) studies have consistently linked alpha phase synchronization to top-down modulation and the frontoparietal network, a key system for cognitive control, its role in inhibitory control remains underexplored. The present study investigated EEG alpha phase synchronization using intersite phase clustering (ISPC) during a color-word Stroop task, focusing on four regions of interest: left/right frontocentral and parietocentral regions. Twenty-four participants identified the color of a word (red or green), regardless of its semantic meaning, across three conditions: congruent (e.g., the word “Red” written in red), incongruent (e.g., “Red” written in green), and neutral (e.g., “XXX” in red or green). Behavioral results showed significantly slower reaction times in the incongruent condition compared to both the congruent (Z = 3.20, p < 0.001) and neutral conditions (Z = 3.57, p < 0.001). Connectivity analyses revealed marginally increased global alpha phase synchronization from the right frontocentral region in the incongruent condition, which showed significantly stronger synchronization with the left parietocentral region than in the congruent (Z = 2.44, p < 0.05) and marginally stronger than in the neutral condition (Z = 2.06, p = 0.059). Notably, the peak latencies of this connectivity positively correlated with reaction times, particularly in the incongruent condition (r = 0.55, p < 0.05). These results suggest that interhemispheric frontoparietal alpha phase synchronization may reflect the neural mechanisms underlying inhibitory control. Specifically, in the incongruent condition, the timing of phase synchronization appears to be crucial for behavioral performance, highlighting the significance of alpha phase clustering in inhibitory control.

Keywords : Inhibitory control, Frontoparietal region, Top-down modulation, Alpha phase synchronization, reaction time

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P-188

Neural mechanisms of uncertainty in intertemporal decision-making: examining the impact of risk and ambiguity on time preferences

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The relationship between risk, ambiguity, and time preferences has been the subject of extensive debate in behavioural and experimental economics. While decision-making theories have long considered the domains of risk, time, and ambiguity separately, real-life decisions often involve these preference dimensions simultaneously. Drawing on economic theories of decision-making under risk, time, and ambiguity, we investigate the behavioural and neural effects of individual preferences for risk and ambiguity in the deliberation of delayed uncertain rewards. Specifically, we show that individuals with a more curved probability weighting function exhibit a steeper hyperbolic discounting for delayed high-risk rewards than those with a more linear weighting function; however, there is no such effect for delayed low-risk rewards. Additionally, we find that ambiguity aversion is associated with steeper hyperbolic discounting of delayed low-ambiguity rewards. We also suggest the idea that rACC may play a central role in the integration of probabilistic and temporal distortions. In contrast, the anterior insula may track probability distortion independently of delay-based valuation. We also suggest that sgACC may integrate ambiguity and time preference, whilst right anterior insula and dlPFC tracks ambiguity preferences independently of delay. Together, we suggest that ACC plays a role in linking preferences for time and uncertainty. We also draw a distinction between two kinds of uncertainty, risk and ambiguity, based on behavioural profile and neural activation patterns. Our findings are consistent with the single process theories that unify preferences for time and uncertainty. By integrating behavioural and functional magnetic resonance imaging (fMRI) data, our study aims to refine existing dual-system models of economic decision-making and clarify the interaction between delay and uncertainty in the human brain.

Keywords : probability weighting, ambiguity aversion, delay discounting, fMRI

Synapses and Circuits P-189~P-213

P-189

Specific and plastic: axo-axonic innervation of pyramidal neurons by GABAergic chandelier cells

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The axon initial segment (AIS) is a highly specialized cellular compartment localized at the proximal axon of the neuron. It serves as a gatekeeper by filtering the somato-dendritic proteins to maintain the neuronal polarity. Additionally, the AIS is instrumental in initiating action potentials (APs) due to its high density of voltage-gated sodium channels, making it the most excitable part of a neuron. Furthermore, the AIS is the only axon subdomain in the mammalian cortex known so far that receives synaptic input, and the cortical PN receives synaptic inputs predominantly from chandelier cells (ChCs). We have been focusing on how axo-axonic synapses are established during developmental stages, and their functions in physiological and pathological conditions. We found that chronic alterations in axo-axonic synaptic input induces homeostatic plasticity of the AIS at structural and functional level. Furthermore, we have established a link between subcellular homeostatic changes and behavioral alterations. Breaking the balance between ChC and AIS connections puts animals in a subthreshold state to develop epileptic seizure. These results suggest that axo-axonic synaptic plasticity is associated with a physiological function in maintaining balanced neuronal activity and normal animal behavior.

Keywords : Axon initial segment, Chandelier cell, Homeostatic plasticity

P-190

Optogenetic modulation of orbitofrontal cortex astrocytes alleviates trigeminal neuropathic pain via restoration of descending pain circuits

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Trigeminal neuropathic pain (TNP) is a persistent condition marked by exaggerated nociceptive responses and neuroinflammatory processes. Although astrocytes are increasingly recognized as key modulators of pain, their contribution to descending pain regulation through the ventrolateral orbitofrontal cortex (vlOFC) remains insufficiently characterized. In this study, we examined how optogenetic modulation of vlOFC astrocytes affects pain behaviors in a chronic constriction injury model targeting the infraorbital nerve (CCI-ION) in adult female Sprague Dawley rats. Naïve and sham-operated animals served as controls. To manipulate astrocytic activity, AAV8 vectors encoding GFAP-driven ChR2, eNpHR3.0, or mCherry were injected into the vlOFC. Behavioral outcomes were evaluated using acetone, von Frey, and elevated plus maze tests. Additionally, we performed in vivo extracellular recordings from the ventrolateral periaqueductal gray (vlPAG) and ventral posteromedial (VPM) thalamus. TNP animals exhibited facial hyperalgesia, reduced vlPAG excitability, and elevated thalamic firing, which coincided with increased astrocytic activity in the vlOFC. Notably, selective inhibition of vlOFC astrocytes restored cortical glutamatergic output, enhanced vlPAG neuronal firing, and attenuated thalamic hyperactivity. This intervention also alleviated pain hypersensitivity and anxiety-like behavior, while reducing expression of neuroinflammatory markers such as P2X3 and Iba-1. Conversely, astrocytic activation and control vectors had no impact on TNP symptoms, emphasizing the functional specificity of astrocytic suppression. These results highlight the critical role of vlOFC astrocytes in modulating pain-related circuits and suggest that their targeted inhibition may represent a promising strategy for treating trigeminal neuropathic pain.

Keywords : Trigeminal neuropathic pain, Ventrolateral orbitofrontal cortex, Astrocytes, Ventrolateral periaqueductal gray, Optogenetics

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P-191

Sleep oscillations induce systems consolidation through astrocytic synapse phagocytosis

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Episodic memories are initially encoded in the hippocampus and subsequently transferred to the medial prefrontal cortex (mPFC), a process known as systems consolidation. During systems consolidation, synapses in the mPFC undergo robust formation and elimination, facilitating the memory transfer to mPFC circuits. Despite the pivotal role of synapse remodeling in the mPFC during systems consolidation, the mechanisms and functional importance of this process remain largely unknown. Here, we demonstrate a crucial role of astrocytes in the mPFC in precise memory transfer through the elimination of specific synapses. Astrocytes actively phagocytose excitatory post-synapses of mPFC neurons within three to six days following memory encoding via MEGF10, a phagocytic receptor of astrocytes. Moreover, astrocytes in the mPFC preferentially phagocytose post-synapses on engram cells, enabling synapse potentiation during systems consolidation. Among the pre-synaptic inputs to the mPFC, astrocytes selectively eliminate pre-synaptic terminals from the retrosplenial cortex, exhibiting circuit-specific remodeling. This process is required for precise memory transfer, as mPFC-specific astrocytic Megf10 knockout mice showed impaired memory discrimination at a remote time point. Remarkably, we found that the activity of hippocampal engram cells during sleep, but not during wakefulness, is essential for astrocytic phagocytosis in the mPFC and behavior. By taking advantage of chronic sleep wave recordings, we found that theta activity during rapid eye movement (REM) sleep in the hippocampus is transiently increased, showing a similar trend of astrocytic phagocytosis following memory encoding. Taken together, this study reveals a novel phagocytic role of astrocytes in long-term memory and provides evidence that synaptic plasticity mediated by astrocytic phagocytosis is indispensable for sleep-dependent systems consolidation.

Keywords : Sleep oscillations, Systems consolidation, Astrocytes, Memory, synapse plasticity

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P-192

Magnetothermal brain stimulation enhances tactile discrimination by modulating synaptic plasticity in the adult mouse barrel cortex

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Magnetothermal brain stimulation (MTS) has garnered significant interest because of its wireless, minimally invasive nature and its ability to precisely regulate the excitability of targeted neurons, leading to motor behaviors in conscious rodents. However, whether MTS reactivates synaptic plasticity in the adult cortex has yet to be elucidated. Here, we investigated whether MTS can reactivate cortical synaptic plasticity in healthy adult mice. Our findings show that a single MTS increased neuronal activity in the barrel cortex, and this effect was mediated by the innate TRPV1 channel. Furthermore, repetitive MTS strengthened thalamocortical (TC) synapses in the layer 4 barrel cortex via a mechanism that depended on increased GluN2B subunit-containing NMDA receptor (GluN2B-NMDAR) function. Moreover, repetitive MTS improved the whisker-mediated tactile discrimination abilities of the mice. These results highlight the potential of MTS to increase cortical

synaptic plasticity and thus enhance tactile discrimination by activating endogenous TRPV1 channels.

Keywords : Magnetothermal brain stimulation, Magnetic nanoparticles, Cortical synaptic plasticity, Critical period, Barrel cortex

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P-193

Distinct modes of dopamine modulation on striatopallidal synaptic transmission

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Dopamine (DA) plays a crucial role in voluntary movement by modulating basal ganglia function. According to the classical model, DA depletion leads to overactivation of the indirect pathway, excessive thalamic inhibition, and ultimately hypokinesia. Although the striatopallidal synapse—linking the striatum to the external globus pallidus (GPe)—is a key node in this pathway, its dopaminergic modulation remains poorly understood due to sparse DA innervation. To address this, we combined projection-specific optogenetics, whole-cell patch-clamp recordings in acute mouse brain slices, and computational modeling. We found that DA exerts region-specific effects through D2 and D4 receptors in the GPe. In dorsolateral (DL) and ventromedial (VM) GPe, D2 receptors mediate presynaptic inhibition by increasing paired-pulse ratio (PPR) and reducing GABA release. In contrast, in dorsomedial (DM) and ventrolateral (VL) GPe, D4 receptors mediate postsynaptic inhibition without affecting PPR. This reveals a spatially organized, pinwheel-like pattern of DA signaling across GPe subregions. Following 6-hydroxydopamine (6-OHDA)-induced DA depletion, this spatial pattern reverses: PPR increases in the VL and DM while diminishing in the DL and VM. Together, our findings demonstrate that striatopallidal synapses are spatially organized and differentially modulated by dopamine across GPe subregions. This structured dopaminergic modulation enables selective gating of indirect pathway signals and may contribute to region-specific dysfunctions in Parkinsonian states. Understanding this spatial logic provides new insight into the functional architecture and pathological vulnerability of basal ganglia circuits.

Keywords : Dopamine, Striatopallidal synapse, External globus pallidus, Indirect pathway, Basal ganglia

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P-194

Flexible fiber–based CaMKIIα-NpHR-mediated optogenetic silencing of dorsal root ganglion glutamatergic neurons attenuates chronic neuropathic pain

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Glutamatergic neurons in the dorsal root ganglion (DRGg) play a critical role in transmitting peripheral nociceptive signals. However, their precise contribution to chronic neuropathic pain (CNP), particularly under neuromodulation, remains poorly understood. In this study, we explored the effect of optogenetic inhibition of DRGg on CNP and related anxiety behaviors in a chronic compression of the DRG (CCD) rat model. The CCD model was induced by inserting an L-shaped rod into the L5 intervertebral foramen, followed by injection of either AAV2-CaMKIIα-eNpHR3.0-mCherry or AAV2-CaMKIIα-mCherry into the L5 DRG. Flexible optical fibers were implanted to deliver yellow light directly to the L5 DRG, enabling targeted optogenetic silencing. Pain sensitivity and anxiety-like behaviors were assessed using mechanical threshold, mechanical and thermal latency, and open field tests. In vivo single-unit extracellular recordings were conducted from both the DRG and the ventral posterolateral (VPL) thalamus. CCD rats exhibited heightened pain and anxiety behaviors, along with increased neuronal activity in both the DRG and VPL thalamus. The DRG and spinal dorsal horn (SDH) also detected elevated expressions of nociception-related molecules. In contrast, optogenetic inhibition of DRGg led to significant attenuation of pain responses and anxiety-like behaviors. Neural hyperactivity in the DRG and VPL thalamus was reduced, and the expression of pain-associated molecular markers in the DRG and SDH was suppressed. These findings suggest that CaMKIIα-NpHR-driven optogenetic silencing of DRG glutamatergic neurons effectively alleviates CNP by modulating peripheral nociceptive input within the spinothalamic pathway during peripheral nerve injury.

Keywords : Optogenetics, Dorsal Root Ganglion (DRG), Chronic Neuropathic Pain, CaMKIIα-NpHR

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P-195

Thalamic reticular circuit refinement via LRRTM3 shapes post-critical period sensory tuning

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Sensory processing enables animals to adaptively engage with dynamic environments by coordinating activity across brain circuits. Within thalamocortical (TC) pathways, the thalamic reticular nucleus (TRN) is a central inhibitory gate, regulating the flow of sensory signals to the cortex. Classical models posit that sensory circuits stabilize after early postnatal critical periods but not whether TRN-mediated inhibition continues to mature in adulthood. Here, we uncover a previously unrecognized phase of post-critical period plasticity, reducing TRN-mediated inhibition onto TC pathways. This plasticity was not driven by the excitability of TRN neurons itself but was driven by a progressive reduction in corticothalamic (CT) excitatory input. We identify LRRTM3, a TRN-enriched synaptic adhesion molecule, as a circuit- and age-specific regulator of CT-TRN synaptic remodeling. TRN-specific deletion of LRRTM3 disrupts this late-stage refinement by altering its extracellular binding interactions and preventing the normal accumulation of extracellular matrix with heparan sulfate, ultimately leading to a marked increase in the inhibition/excitation ratio in TC neurons. This failure in circuit refinement compromises post-critical period sensory tuning, resulting in impaired fine sensory discrimination. These findings revise longstanding models of sensory circuit maturation, positioning LRRTM3 as a molecular switch that sustains circuit adaptability and ensures high-fidelity sensory processing into adulthood.

Keywords : sensory discrimination, thalamic reticular nucleus, synaptic refinement, synaptic adhesion protein, post-critical period plasticity

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P-196

Slitrk paralogs configure excitatory synaptic specificity via different extracellular and intracellular mechanisms

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Synapses are basic elementary units of neural information transfer that connect neurons into specifically wired neural circuits. During development, synapses undergo seemingly distinct stages of biological processes that are shaped by diverse actions of synaptic cell-adhesion molecules (CAMs), which are involved in dictating synapse assembly, specification of synaptic properties, synaptic plasticity, and even synapse elimination. Among these, vertebrate neural circuit properties are shaped by synaptic cell adhesion molecules (CAMs). CAMs often have multiple paralogs but the possible redundancy of such paralogs remains underexplored. Using circuit-specific conditional knockout (cKO) mice deficient for Slitrk1 and Slitrk2, we show that these paralogs lack specific laminar expression in mature hippocampal neurons but divergently guide the specificity of neural circuits in distinct hippocampal subfields. Slitrk1 and Slitrk2 regulate distinct facets of excitatory synaptic properties in a microcircuit-dependent manner through binding to LAR-RPTPs, and additionally in the case of Slitrk2, through binding to PDZ domain-containing proteins and TrkB. Analyses of Slitrk2 V89M knock-in mice revealed that this schizophrenia-associated substitution acts uniquely as a loss-of-function mutation in some microcircuits to impair excitatory synaptic transmission, asynchronous release, and spatial reference memory. These findings demonstrate that even structurally and biochemically similar synaptic CAMs can play completely distinct roles in specifying neural circuit architecture.

Keywords : Slitrks, Synaptic specificity, Leucine-rich repeat, Synaptic adhesion, Hippocampus

P-197

Astrocytic MDGA proteins orchestrate synapse formation and function

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MDGA (MAM domain containing glycosylphosphatidylinositol anchor) family proteins are suppressors of synapse development. However, previous studies solely focused on the role of MDGA proteins that are expressed in neurons. Here, we report that both MDGA family members, MDGA1 and MDGA2, are also expressed in astrocytes. While the majority of *Mdga1* and *Mdga2* mRNAs are expressed in neurons, a significant proportion of *Mdga2* mRNAs is also observed in astrocytes of juvenile and adult mice. Coculturing *Mdga2* conditional knockout (cKO) astrocytes with hippocampal cultured neurons caused a significant increase in synapse number and basal transmission at inhibitory, but not excitatory, synapses in neurons. In contrast there was no significant alteration in either synapse number or transmission when *Mdga1*-cKO astrocytes were cocultured with hippocampal cultured neurons. Strikingly, co-culturing astrocytes lacking both MDGA paralogs with neurons caused a specific decrease in excitatory synapse transmission. Moreover, MDGA2 deletion in astrocytes of mouse hippocampal CA1 enhanced both basal excitatory and basal inhibitory synapse transmission. Together, our data show that astrocytic MDGA proteins might perform distinct roles in regulating synaptic properties, likely via separate mechanisms that operate in neurons, proposing a hypothesis that an identical cell-adhesion molecule can perform different regulatory functions based on its cellular context.

Keywords : Synapse, Astrocyte, Cell adhesion molecule, MDGA

P-198

A top-down insular cortex-parabrachial circuit is crucial for non-nociceptive fear learning

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Understanding how threats drive fear memory formation is crucial to understanding how organisms adapt to environments and treat threat-related disorders such as PTSD. While traditional Pavlovian conditioning studies have provided valuable insights, their near-exclusive use of electric

shock as an unconditioned stimulus (US) has limited our understanding of how diverse, especially non-nociceptive, threats are processed. To address this, we established a visual threat conditioning paradigm using a looming stimulus—a non-nociceptive visual threat—as a US in mice. We found that calcitonin gene-related peptide (CGRP)-expressing neurons in the parabrachial nucleus (PBN) were required for both the acquisition and retrieval of fear memory. Upstream neurons in the posterior insular cortex (pIC) responded selectively to looming stimuli, and their projections to the PBN were crucial for visual threat learning but dispensable for foot-shock conditioning. Furthermore, optogenetic activation of this pathway induced aversive affect and was sufficient to drive fear memory formation. These findings identify a specific top-down cortical pathway that mediates non-nociceptive fear learning, broadening our understanding of how the brain encodes threat beyond traditional nociceptive models.

Keywords : Visual threat conditioning, Non-nociceptive fear learning, Affective pain, Insular cortex, Parabrachial nucleus

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P-199

Synaptic plasticity in mice treated with single-dose psilocybin

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Psilocybin has demonstrated potential to act clinically as an antidepressant. Psilocybin-induced rapid antidepressant effects can last for weeks after a single dose, however, the neurobiological mechanisms that underlie its antidepressant effect are not yet fully investigated. To look for long-lasting forms of synaptic plasticity induced by a single dose of psilocybin, we injected mice intraperitoneally with psilocybin 1 mg/kg or saline and performed ex vivo whole-cell patch clamp recordings 24 h after treatment. We also assessed the acute effect on behavior by recording mice for 90 minutes following injections of different doses of psilocybin and explored the impact of psilocybin on neuronal activity by c-Fos immunostaining of tissue after injections. Psilocybin induced increased miniature excitatory postsynaptic currents (mEPSCs) frequencies in the prelimbic cortex and ventrolateral orbitofrontal cortex, increased mEPSC amplitudes in the infralimbic cortex and hippocampus, measures indicative of synaptic potentiation. Reduced decay time of mEPSCs in the prelimbic cortex and anterior cingulate cortex was also observed, suggesting a change in AMPA receptor subunit composition. Behavioral tests revealed that psilocybin elicited a dose-dependent increase in characteristic head-twitching and the high dose (2 mg/kg) induced hypolocomotion. Psilocybin-treated mice exhibited increased c-Fos-positive cells particularly in cortical areas and the amygdala, suggesting enhanced neuronal activation and engagement of plasticity-related pathways. Ongoing research aims to determine whether these findings underlie psilocybin's antidepressant actions.

Keywords : psychedelic, antidepressant, plasticity

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P-200

Social motivation for effortful reward is reinforced by mesolimbic dopamine via D1R-mediated epigenetic regulation

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Motivation is essential for goal-directed behavior, enabling animals to persist in the face of challenges. In social animals, social interaction serves as a potent motivator. However, how social rewards shape motivational choices to invest effort remains poorly understood. To address this, we developed an effort-based social decision-making (ESDM) task in which mice chose between a neutral and an effortful option. Male mice consistently chose to overcome a barrier to access a female, despite equivalent reward availability. We observed significant upregulation of *Drd1a*, which encodes the D1 dopamine receptor, in the nucleus accumbens (NAc), a key region for dopamine signaling. Consistently, pharmacological blockade of D1 receptors in the NAc reduced effort choice levels. In vivo fiber photometry analysis revealed that NAc dopamine signals during the decision-making period of effortf choice trials from the first to the final day. Notably, effort choice level was further enhanced by optogenetic activation of VTA–NAc projections and abolished by D1 receptor blockade. Finally, we found that increased dopamine activity induced H3Q5dopaminylation at the *Drd1a* promoter in the NAc, reinforcing effortful social choice. These findings suggest that effort-based social decision-making is regulated by dopamine-dependent epigenetic mechanisms within D1R-expressing neurons of the mesolimbic pathway.

Keywords : Social behavior, Decision-making, Motivation, Nucleus accumbens, Dopamine

P-201

Rapid systems consolidation and reshuffling of engram cells in the hippocampal-cortical network by repeated learning

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Our daily life mostly consists of repeated experiences. However, how such experiences are encoded by memory engram cells and consolidated in the brain remains unknown. Here, we combined cFos-based tagging with optogenetics, chemogenetics, spine imaging, and reactivation analyses in the dentate gyrus (DG) and medial prefrontal cortex (mPFC). DG neurons activated during initial encoding were recruited into the engram to support memory. However, following relearning, these DG neurons lost spines, showed reduced reactivation, and became dispensable for memory recall, whereas newly recruited DG neurons during relearning supported the strengthened trace. In parallel, the mPFC neurons tagged during initial encoding were rapidly recruited to form a stable engram in the cortex after relearning, which otherwise mature slowly to be incorporated into the engram through

systems consolidation. These findings uncover dual strategies for multiple-trace formation in the hippocampus and medial prefrontal cortex to support memories established through repeated learning: dynamically reorganizing DG ensembles accompanied by synaptic changes and rapidly engaging stable cortical ensembles, thereby providing insight into how repeated learning transforms memory.

Keywords : Memory engram, Repeated learning, Systems consolidation, Dentate gyrus, Medial prefrontal cortex

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P-202

Sleep-dependent memory consolidation of reward locations under landmark-based and path integration-assisted strategies

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Background: The hippocampus is considered a hub for episodic memory and spatial memory. It has been established that a combination of both environmental cues and self-motion information is used to form a cognitive map of the environment in the hippocampus. Furthermore, recently acquired memories are reactivated during replay events in NREM sleep, a phenomenon believed to contribute to memory consolidation. Yet, it is still unclear how replay events contribute to the formation of cognitive maps and to the integration of information such as rewards. Methods and Results: Mice were trained to run head-fixed on a treadmill apparatus equipped with a 2-meter-long belt enriched with visual-tactile cues. The belt presented a cue-enriched zone and a cue-impoverished zone promoting cue-based and path-integration navigation strategies, respectively. Mice learned to navigate to a pair of reward locations, with each reward location falling within one of the two zones. Within a session, mice first ran for a familiar pair of reward locations and then experienced a new pair of reward locations for a few trials. Then a period of rest/sleep was induced by increasing the resistance of the treadmill belt rotation, following which mice ran again for the same pair of novel reward locations. Hippocampal neural activity was recorded using silicon probes. Place cells and replay events were analyzed. Place cells exhibited various patterns of remapping upon the change in reward locations and following the period of sleep.

Keywords : Hippocampus, Place cell, Sleep

P-203

Septo-entorhinal GABAergic neurons switch memories to enable update

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New experiences are continually integrated with existing knowledge to update memories, a process essential for animals' survival in dynamic environments. Even after updating, the brain can still access previous memories to guide appropriate behavior. However, the neural mechanisms that enable retrieval of updated memory while preserving access to previous memories remain elusive. Here, we identified a novel circuit mechanism that enable flexible memory switching, mediated by medial septum (MS) GABAergic projections to the medial entorhinal cortex (MEC). This MS^{GABA}-MEC projection was selectively recruited during retrieval of updated. Remarkably, silencing these projections not only disrupted but also reversed behavioral performance, indicating a switch to retrieval of previous memories. Simultaneous calcium imaging and optogenetics revealed corresponding shifts in hippocampal CA1 population activity patterns. Finally, we observed online/offline state-dependent memory performance, suggesting brain-state-dependent engagement of MS GABAergic circuits. Together, our findings reveal a neural switch mechanism mediated by the septo-entorhinal GABAergic circuit that organizes memory retrieval to enable updating.

Keywords : memory update, medial septum, medial entorhinal cortex, hippocampus

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P-204

Two-photon optogenetic microcircuit mapping: Insights from V1, M1, and beyond

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The brain operates via interconnected neural circuits arranged in hierarchical networks, where structure determines function. Understanding brain function thus requires connectome mapping, but conventional circuit-mapping methods are slow and technically demanding, hampering progress. To address this, we developed optomapping, a high-throughput connectivity mapping method ~100 times faster than multiple patch clamp. Using optomapping, we compared excitatory microcircuits in primary visual cortex (V1), an input area, and motor cortex (M1), an output area. We injected AAV9-CAG-DIO-STChroME-P2A-mRuby into the cortex of postnatal day (P) 0-2 Emx1-Cre mice for soma-targeted expression of the opsin ChroME in pyramidal cells (PCs). In P18-26 acute slices, we patched PCs, inhibitory basket cells (BCs), or Martinotti cells (MCs) and used 1040-nm Ti:Sa laser spiral scans to sequentially activate hundreds of candidate presynaptic PCs located hundreds of microns away. This revealed how synaptic dynamics, strength, and connectivity depended on cortical layer (L) and target cell type. In both V1 and M1, the L5 PC→L5 BC pathway was strongest, although stronger in V1. Lateral connectivity decayed faster for PC→PC than for PC→BC/MC synapses in both areas. Thus, excitation of inhibition was both stronger and reached farther than excitation of excitation, a feature likely enhancing circuit stability. In both cortices, input strengths onto PCs, BCs, and MCs distributed normally on a log axis, suggesting weight log-normality as a general circuit principle. However, the L4 PC→L2/3 PC pathway was denser ($p<.001$) and stronger ($p<.01$) in V1 than in M1, consistent with thalamic sensory input entering V1 but not M1 via L4. In summary, V1 and M1 microcircuits share fundamental

connectivity principles but differ in specific wiring patterns. We are now extending optomapping to the medial prefrontal cortex, an association area, and investigating altered circuit wiring in a Fragile X model.

Keywords : Two-photon optogenetics, Synaptic connectivity, Cortical microcircuits, High-throughput mapping, Cell-type-specific wiring

P-205

Optogenetic dissection of serotonergic modulation in dCA1: Electrophysiological validation and behavioral correlates

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Precise manipulation of serotonergic signaling is essential for understanding its role in hippocampal processing and behavior. Using optogenetic tools, our lab previously showed that serotonergic input from the median raphe (MR) to the dorsal CA1 (dCA1) influences spatial memory acquisition[1]. We extended this work by validating these tools in vivo and exploring the neural basis of serotonergic modulation during behavior. Specifically, we tested three optogenetic tools targeting dCA1 circuits: Channelrhodopsin-2 (ChR2), expressed in serotonergic axon terminals, and two chimeric tools combining opsins with 5-HT receptors: vertebrate long-wavelength opsin-5-HT_{1B} (vLWO-5-HT_{1B}), expressed in serotonergic axon terminals, and vertebrate short-wavelength opsin-5-HT_{1A} (vSWO-5-HT_{1A}), expressed in pyramidal neurons[2]. To assess their effectiveness and circuit engagement, we combined optogenetic stimulation with in vivo electrophysiology. Using custom multielectrode arrays in freely moving mice, we recorded local field potentials and single-unit activity. To link neural activity with behavior, we employed the Open Field and Elevated Zero Maze as initial assays. Our results confirm the in vivo functionality of all three optogenetic tools and highlight their utility in studying serotonergic modulation in the hippocampus. Preliminary data suggest that serotonergic modulation affects anxiety-related behavior in a context-dependent manner. These findings advance our understanding of how serotonergic signaling tunes hippocampal function during behaviorally relevant states such as learning and memory. [1] Gerdey, Masseck (2023) Linking serotonergic median raphe input to dorsal CA1 with mnemonic functions. *bioRxiv*. https://doi.org/10.1101/2023.09.04.556213 [2] Masseck, Spoida, Dalkara et al. (2014) Vertebrate Cone Opsins Enable Sustained and Highly Sensitive Rapid Control of Gi/o Signaling in Anxiety Circuitry. *Neuron*, 81(6), 1263-1273. https://doi.org/10.1016/j.neuron.2014.01.041

Keywords : Optogenetics, In vivo electrophysiology, Hippocampus, Serotonin

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P-206

A non-hallucinogenic psychedelic reprograms stress resilience

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Cognitive symptoms in depression arise from large-scale network dysfunction, yet the molecular drivers and their sex-specific features remain elusive. Classical psychedelics restore synaptic plasticity but are limited by hallucinogenic effects. Here, we show that harmine, a non-hallucinogenic β-carboline, reverses stress-induced disruption of frontoparietal and default-mode connectivity. Whole-brain manganese-enhanced MRI revealed suppressed activity in these networks in stress-susceptible mice, which was restored by harmine. Transcriptomic profiling of human postmortem cortex showed elevated DYRK1A expression in both sexes with depression. In mice, however, Dyrk1a overexpression induced cognitive and affective deficits exclusively in males, mediated by RNA polymerase II recruitment to the MAO-A promoter and subsequent serotonin degradation. In females, Dyrk1a increased mood-related symptoms without cognitive effects, pointing to divergent circuit outcomes. These findings identify DYRK1A as a sex-specific regulator of depression-related cognition and establish harmine as a non-hallucinogenic psychoplastogen capable of reprogramming stress-vulnerable brain networks.

Keywords : Psychedelic, Epigenetics, Depression, Sex-specific

P-207

Dorsomedial hypothalamic circuit mediates anxiety-induced arousal following psychosocial stress

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Persistent arousal and sleep disturbances in daily life often stem from cognitive processing of anticipated threats or lingering stressful experiences, even in the absence of direct stressors. This underscores the brain's role in mediating sustained arousal through cognitive interpretations of environmental cues, with the medial prefrontal cortex (mPFC) and its downstream targets playing central roles. The dorsomedial hypothalamus (DMH), receiving input from the mPFC, is a key integrative hub for psychological stress, regulating sleep-wake cycles, feeding, and physiological responses. In this study, we newly uncover a previously uncharacterized DMH neuronal population as a novel candidate circuit that links psychosocial stress to arousal, potentially via projections to Hypocretin-expressing neurons in the lateral hypothalamus (LH^{Hcrt}). To investigate this, we assessed sleep-wake states using wireless EEG/EMG recordings and performed behavioral experiments during the light phase (ZT0–3). Psychosocial stress was induced through a 3-day social defeat stress (SDS) paradigm using aggressive CD-1 intruders, followed by re-exposure to the defeat context without an intruder on the test day. We found that SDS-exposed mice exhibited heightened arousal upon re-exposure to the defeat context, despite the absence of an immediate threat. Anatomical and functional analyses revealed that a subset of DMH glutamatergic neurons projects to LH^{Hcrt}. Notably, chemogenetic activation of DMH neurons increased wakefulness, while their inhibition in stress-exposed mice restored sleep to baseline levels. These findings

identify a novel mPFC-DMH–LH^{Hcrt} circuit as a key mediator of sustained arousal following psychosocial stress, offering new insights into the neural mechanisms underlying stress-induced sleep disturbances and suggesting potential therapeutic targets for stress-related insomnia.

Keywords : mPFC, DMH, Hypocretin, Anxiety-induced arousal, Psychosocial stress

P-208

Raphe-driven glutamate co-transmission shapes hippocampal function via modulation of cholecystokinin-expressing inhibitory neurons

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The raphe nuclei consist of heterogeneous neuronal populations, including serotonergic, dopaminergic, glutamatergic, and GABAergic neurons. While most research on the raphe has focused on the modulatory role of serotonergic slow synaptic transmission—given the predominance of serotonergic neurons—growing evidence highlights the significance of fast synaptic transmission mediated by GABA and glutamate. In particular, serotonergic neurons in the raphe nuclei have been shown to co-release glutamate in multiple brain regions, including the hippocampus, amygdala, and ventral tegmental area. Notably, this glutamatergic co-transmission often targets inhibitory interneurons rather than excitatory cells, especially within the amygdala and hippocampus. Such findings suggest that fast excitatory signaling from raphe neurons may preferentially modulate local inhibitory circuits, thereby shaping the activity of downstream networks. In this study, we examined the functional role of raphe-driven fast synaptic transmission in major projection areas of serotonergic neurons. By combining optogenetics, immunohistochemistry, and confocal imaging, we identified that multiple brain regions receive di-synaptic inputs from raphe serotonergic neurons, with the hippocampus showing the most significant functional connection. Within the hippocampus, we discovered that glutamate co-release from raphe serotonergic neurons selectively enhances the excitability of CCK-positive inhibitory interneurons. This modulation of CCK-expressing neurons had a downstream effect on the excitability of CA1 pyramidal neurons and significantly facilitated synaptic plasticity at Schaffer collateral–CA1 synapses. Our findings underscore the functional importance of raphe-mediated glutamate co-transmission and provide new insights into the intricate synaptic modulation exerted by raphe serotonergic neurons in the brain.

Keywords : Serotonin, Co-transmission, Hippocampus

P-209

Top-down and reciprocal synaptic organization between the medial prefrontal cortex, claustrum, sensory cortices, and amygdala

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Anatomical studies have suggested that the claustrum is reciprocally connected with a broad range of the neocortex responsible for multiple different modalities. Medial prefrontal cortex (mPFC) is known as a commanding center in top-down processing of sensory information and emotional responses, and claustum has been suggested as a network hub in the top-down modulation in sensory attention and subsequent behaviors. However, the synaptic connections between mPFC, claustrum, sensory cortices, and brain structures responsible for emotional behaviors (e.g. amygdala) have not been clearly proven yet. We demonstrated these synaptic pathways using two different approaches. First, by combining optogenetics-based whole-cell patch clamp recording with retrograde tracing-based cell type identification, we demonstrated that both visual and somatosensory cortex-projecting claustral neurons receive monosynaptic inputs from the mPFC. Both somatosensory cortex- and visual cortex-projecting claustral neurons receive short latency direct excitatory input from the mPFC as well as longer latency disynaptic inhibitory inputs. Second, using target-specific axonal projection analysis, we demonstrated that claustral neurons projecting to mPFC have axonal collaterals projecting to subcortical structures including the basolateral amygdala. These results suggest that claustral neurons may bidirectionally modulate both top and bottom components of the mPFC-claustro-sensory cortex/amygdala circuit.

Keywords : Claustrum, mPFC, amygdala

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P-210

Stress engages the noradrenergic brainstem-to-hypothalamus circuit to suppress appetite

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Stress triggers adaptive behavioral shifts that override homeostatic drives such as appetite, yet the underlying neural mechanisms remain poorly understood. Here, we identify a noradrenergic brainstem-to-hypothalamus circuit that mediates stress-induced appetite suppression in mice. Using *in vivo* fiber photometry, we found that noradrenergic locus coeruleus (LC^{NA}) neurons exhibit persistent activity extending beyond acute restraint stress, temporally aligned with feeding suppression (n=7). Inhibition of LC^{NA} neurons (n=11) or their projections to the paraventricular hypothalamus (PVH) (n=19) prevents stress-induced appetite suppression, whereas optogenetic activation of LC^{NA} neurons mimics stress effects that suppress feeding (n=7). Real-time norepinephrine recordings in the PVH show sustained elevation after restraint stress, correlating with the duration of feeding suppression (n=8). Pharmacological blockade of α1-adrenergic receptors in the PVH, particularly the α1b subtype, abolishes stress-induced appetite suppression (n=9). Notably, this circuit is also required for feeding suppression after chronic stress (n=5). Collectively, our findings pinpoint the LC^{NA}-PVH^{α1b} noradrenergic circuit as a key driver of sustained appetite suppression following stress, uncovering a direct link between brain stem arousal center and hypothalamic feeding circuits.

Keywords : Stress, appetite, Locus coeruleus, norepinephrine, paraventricular hypothalamus

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P-212

Effect of social relationships during adolescence on the development of vHPC-mPFC pathway

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Adolescence is a socially sensitive developmental period during ego-identity is consolidated and complex social competencies are acquired. A lack of social interaction has been reported to cause irreversible alterations in cognitive function in social animals. In our previous studies, it indicates that social isolation beginning in early adolescence leads to altered sociability, which cannot be rescued by sensory stimulation during adulthood. We hypothesize that deficits in social cognition are caused by permanent dysfunction of neural circuits, particularly the pathway between the medial prefrontal cortex (mPFC) and the ventral hippocampus (vHPC), with a specific emphasis on the inhibitory circuits within the mPFC. To test hypothesis, we measured evoked potentials in the mPFC elicited by optogenetic and electrical stimulation of the vHPC and quantified neural activity using I/O curves to assess the impact of adolescent social isolation. It revealed that social isolation reduced neural activity in the mPFC. We further examined the role of parvalbumin-expressing interneurons (PV INs) in mediating these effects using PV IN specific chemogenetic manipulations. The data showed a diminished contribution of PV INs in socially isolated animals, implying deficits in inhibitory interneuron circuit function. Additionally, we found that long-term potentiation (LTP) induction in the vHPC–mPFC pathway restored EPSP in the socially isolated group. This suggests that although connectivity is disrupted by social isolation, it may be recoverable through LTP-mediated synaptic enhancement. This study show the critical role of social experience during adolescence in the development of the vHPC–mPFC pathway and the associated inhibitory microcircuits in the mPFC. By elucidating the mechanisms underlying social isolation–induced sociability deficits, our findings highlight the role of adolescent social interactions in the maturation of neural circuits necessary for social cognition.

Keywords : Adolescence, Social cognition, Social Isolation, Parvalbumin-expressing Interneurons, vHPC–mPFC Pathway

P-213

Prefrontal inputs to the basolateral amygdala differentially regulate context-dependent fear renewal

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Fear is an adaptive emotion critical for survival, promoting safety through appropriate defensive responses. However, dysregulation of context-dependent fear modulation is a key contributor to anxiety and related disorders. While extinction therapy is effective treatment, its efficacy is limited by its intrinsic context-specificity; extinguished fear often re-emerges when the conditioned stimuli is encountered outside the extinction context, a phenomenon known as fear renewal. Although the mechanisms underlying fear acquisition and extinction have been extensively studied, the precise circuit- and cell type-specific bases of fear renewal poorly understood. In this study, we hypothesized that distinct neuronal populations within the basolateral amygdala (BLA), particularly those receiving projections from the prefrontal cortex regions, differentially modulate fear renewal. Using optogenetics, we found that inhibition of the prelimbic (PL)-to-BLA circuit suppressed fear renewal, whereas inhibition of the infralimbic (IL)-to-BLA circuit promoted renewal responses. Furthermore, fiber photometry revealed increased calcium activity in the PL-BLA circuit specifically during fear acquisition and renewal phases, highlighting its critical involvement in fear memory expression. To examine whether BLA-projecting PFC neurons possess distinct molecular profiles, we employed trans-synaptic labeling using AAV serotype 1 to identify BLA neurons receiving prefrontal input, followed by single-cell RNA sequencing of the labeled cells. This approach revealed circuit-specific transcriptional signatures, offering new insight into the molecular mechanisms underlying projection-defined fear circuits. Together, these findings highlight functionally and molecularly distinct PFC-BLA pathways that mediate fear renewal, advancing our understanding of context-dependent fear modulation.

Keywords : Basolateral amygdala, Fear renewal, Prefrontal cortex, Optogenetics, single cell RNA sequencing,

Systems and Computational Neuroscience P-214~P-262

P-214

Neural mechanisms for regulating impulsive choice via directional visual stimuli in time perception

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Heightened impatience for temporal delays severely impacts decision-making and contributes to impulsivity-related psychiatric disorders. Delay discounting (DD), the diminished subjective value of delayed rewards, is a key behavioral index of this impatience (i.e., impulsive choice). Time perception (TP), the subjective experience of time, is malleable and hypothesized to influence DD. This fMRI study investigated the impact of directional visual motion on TP and subsequent DD. Participants performed a TP task while viewing leftward or rightward moving scenic videos, followed by DD tasks during fMRI. Behavioral results revealed a significant acceleration of subjective TP specifically when viewing rightward (Left-to-Right, LtoR) moving videos, congruent with participants' reading direction. Seed-based connectivity (SBC) analysis, using the left parahippocampal gyrus (involved in temporal processing) as a seed, demonstrated a relationship between these behavioral changes (TP and DD) and left parahippocampal connectivity

specifically during the LtoR condition. Mediation analysis further showed that the functional coupling between the left parahippocampal gyrus and the ventromedial prefrontal cortex (vmPFC), a crucial region for value-based decisions, mediated the link between the subjective acceleration of TP and reduced DD. Specifically, shorter perceived time intervals during LtoR viewing correlated with stronger parahippocampal-vmPFC coupling, which in turn predicted lower impulsivity. Our findings indicate that natural scenic viewing, particularly aligned with native reading direction, can modulate subjective TP and potentially reduce impulsive behavior. The identified parahippocampal-vmPFC pathway suggests a neural mechanism underlying this effect. These results suggest novel visually-based interventions targeting TP to mitigate impulsivity in relevant clinical populations.

Keywords : Delay discounting, Impulsivity, Parahippocampal gyrus, Medial prefrontal cortex, Functional connectivity

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P-215

Testosterone administration slows prosocial learning to avoid harm in healthy men

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Preventing harm to others is a foundational principle of human morality that relies on distinct learning processes when avoiding harm to others compared to oneself. Using a behavioral neuroendocrinology perspective, we investigated computational mechanisms underlying harm-avoidance learning. 120 healthy men randomly received either testosterone or placebo. Three hours later, participants completed a harm-avoidance task, learning over time to choose the option with a lower probability of electric shock to avoid harm either for themselves (Self condition) or for a stranger (Other condition). Behavioral analyses revealed that a quick catch-up of Other to Self existed in both groups, suggesting prosocial learning trends, but this catch-up tended to be delayed after testosterone administration. Computational modeling showed that a reinforcement learning model with separate learning rates for positive and negative prediction errors (PEs) best accounted for individuals' choices. Consistent with the model-independent results, testosterone administration slowed down prosocial learning compared to placebo, particularly when people learned from negative but not from positive PEs. Testosterone also modulated the relationship between trait anxiety and prosocial learning from negative PE, specifying its anxiolytic effects. Together, our findings provide computationally precise insights into how testosterone administration contributes to prosocial learning and thereby affects harm avoidance for others.

Keywords : harm avoidance, aversive learning, altruism, testosterone, hormone

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P-216

An open-source system designed for synchronised neural and behavioural data acquisition

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Studying social behaviour is essential for understanding cognitive processes such as learning, decision-making, and affect. It also plays a key role in modelling disorders like autism and depression. Gaining insights into how the brain generates such behaviour requires the precise temporal correlation of neural and behavioural data. However, existing experimental paradigms often rely on expensive equipment, and synchronising the acquisition of neural and behavioural data remains a major technical hurdle, which is further complicated by proprietary or rigid hardware or software solutions. To address these challenges, we developed a low-cost, open-source framework for social and non-social interaction tasks that is capable of high-fidelity data recording and precise synchronisation of neural and video-based behavioural data. We provide design files for constructing a three-chamber sociability arena as well as user-friendly and modular Python scripts that can be integrated with an affordable microcontroller like LabJack. Further, we propose a workflow that combines neural recordings with video-based pose estimation tools like SLEAP or DeepLabCut and provide a Python-based analysis pipeline for assessing sociability. While the presented framework has been validated in typical social interaction tasks, it is easily adaptable for other experimental paradigms. By providing accurate synchronisation, cost-effective components, and flexible open-source tools, this framework lowers technical and financial barriers, thus making synchronised neural and behavioural research more accessible, reproducible, and scalable across diverse laboratory settings.

Keywords : Social behaviour, Neural recording, Data synchronisation, Open-source, Pose estimation

P-217

In-depth analysis of interbrain correlation with machine learning models

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Interbrain correlation—the temporal similarity of neural activity between socially interacting individuals—has been documented across multiple species, yet the mechanistic underpinnings of this phenomenon remain elusive. In this study, we investigated the neural basis of interbrain correlation in a validated mouse model of autism spectrum disorder (ASD), the Shank2 knockout (KO) mouse, which is characterized by impaired social interactions and repetitive behavior. Utilizing simultaneous in vivo electrophysiological recordings from the medial prefrontal cortex (mPFC) of two freely interacting mice, we identified a marked reduction in theta-band (4–8 Hz) local field potential (LFP) power correlation, measured via the Pearson correlation coefficient (PCC), between Shank2 KO dyads relative to WT controls. To further

elucidate the dynamics of theta-band synchrony and its mechanism, we implemented a suite of machine learning (ML) models, including time-series predictive models and time-matching classification models trained on features derived from temporal characteristics of social interaction. These models effectively captured temporal intersubject synchrony patterns and demonstrated the discriminative relations between theta power LFP and social behavior, which may lead us to the possible candidates of LFP synchrony mechanism.

Keywords : Interbrain correlation, Autism model mouse, Medial prefrontal cortex, time series predictive models, time-matching classification

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P-218

Closed-loop disruption of cortico-cortical communication in NREM impairs skill refinement

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Systems consolidation refers to the gradual integration of newly encoded experiences from the hippocampus into cortical networks for long-term memory storage. Recent studies suggest that the prefrontal cortex (PFC) plays a critical role in the later stages of this process. However, prior investigations have typically relied on short-duration exposure paradigms, limiting insight into the full temporal dynamics of systems consolidation. In this study, we tracked daily changes in motor skill performance, neural representation dynamics, and PFC–M1 slow oscillation (SO) coupling during NREM sleep over a 20-day period in rats trained on a reach-to-grasp task. Employing optogenetic closed-loop stimulation, we selectively disrupted PFC–M1 SO coupling during sleep to test its causal role in long-term motor memory consolidation. Disruption of PFC activity during PFC–M1-coupled SOs delayed the emergence of coordinated PFC–M1 activity and impaired the stabilization of motor performance, particularly in the refinement of reach trajectories. This perturbation also increased neural trajectory variability in M1 and diminished clustered spindle activity, elucidating how sleep contributes to motor memory stabilization. Together, our findings provide causal evidence that PFC–M1 communication during NREM sleep is essential for skill refinement and consolidation of neural manifolds, underscoring the dynamic cortical interactions that support long-term memory stabilization.

Keywords : Memory consolidation, Motor learning, Sleep, Neural manifold, Cortical commounication

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P-219

Distinct roles of regional proximal and distal synaptic weights in neurodevelopmental and neurodegenerative disorders

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Distinct structural and functional properties are observed across different brain regions, which may be attributed to region-specific anatomical wiring and synaptic weight patterns. These patterns can be modeled using large-scale connectivity data through computational biophysical models that reflect heterogeneous proximal synaptic weights between brain regions. However, the distal synaptic weights are represented as a scalar value in existing studies, limiting the ability to investigate the distinct roles contributions of proximal and distal synaptic inputs in shaping neural functions. In this study, we developed a computational model that simulates both proximal and distal synaptic weights while accounting for their heterogeneity across cortical regions. We applied this model to individuals with attention-deficit hyperactivity disorder (ADHD) and Alzheimer's disease (AD). In individuals with ADHD, the proportion of proximal synaptic weights was increased compared to typically developing controls. In contrast, individuals with AD exhibited a monotonically decreasing trend in proximal synaptic weight proportion with increasing disease severity. These findings demonstrate that incorporating heterogeneous synaptic weights across brain regions can reveal mechanistic insights into large-scale circuit dysfunction. Specifically, our results suggest that alterations in the balance between proximal and distal synaptic inputs may reflect distinct neural mechanisms underlying neurodevelopmental and neurodegenerative disorders. Further studies are needed to elucidate biological underpinnings of proximal-distal synaptic weight balance, potentially by targeting gene expression data.

Keywords : Biophysical modeling, Structural-functional coupling, Synaptic modeling, Neurodevelopmental disease, neurodegenerative disease

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P-220

Neural mechanisms of acupuncture stimulation in autism spectrum disorders: Protocol for a randomized, placebo-controlled, fNIRS-EEG neuroimaging study

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Background: Autism spectrum disorder(ASD) is a type of neurodevelopmental disorder that typically appears within the first three years of life. It is characterized by persistent deficits in social communication and interactions, restricted and repetitive patterns of behaviors and problems with sensory integration. Since the causes of ASD have not been clearly identified, fundamental treatments

have not yet been developed. For this reason, there is a demand for complementary and alternative medicine, including acupuncture and herbal medicine in ASD. The effect of acupuncture therapy in neurological diseases has been explored using various neuroimaging methods. In this study, we try to investigate the neural substrates of ASD and neural mechanisms of acupuncture stimulation in ASD using multimodal neuroimaging methods. Method Design: A randomized, placebo-controlled trial (IRB No. 1040782-250213-HR-12-148/Trial regi stration(CRIS):KCT0010437). Participants: Autism spectrum disorders patients and typically developing individuals(35 participants) Intervention and controls: The study group will receive acupuncture stimulation at the genuine acupoints known to be associated with the symptoms of autism spectrum, and the control group will receive acupuncture stimulation at the sham acupoints using superficial needling. Modality: resting state 5-min fNIRS and EEG scan before acupuncture stimulation and after acupuncture stimulation. Clinical indicators: K-CARS2, SRS2 and REVT Outcomes: The alterations of brain activation and connectivity in resting state according to the disease status would be explored. Also, the neural substrates of symptoms in autism spectrum disorders and those of language function would be investigated. Finally, the neural changes according to the acupuncture stimulation and group would be explored. Discussions: In this study, we aim to identify the neural substrates of ASD and mechanisms of acupuncture stimulation in ASD using multimodal neuroimaging methods.

Keywords : Autism spectrum disorder, Multimodal neuroimaging, Acupuncture, Brain Network, Neurodevelopmental disorders

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P-221

Blocking D1 receptors in entorhinal cortex disrupts value-dependent conditioned responses

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A growing body of evidence supports the role of the hippocampus in value-based decision making. Our previous work further showed that neurons in layer II of the medial entorhinal cortex (MEC) robustly encode signals related to reward value. To investigate the role of dopamine in MEC value processing, we examined the distribution of dopamine receptors within the MEC and assessed the behavioral effects of receptor-specific blockade during a probabilistic classical conditioning task. Dopamine D1 and D2 receptors were distributed across layers I, II, and V, with minimal expression in layer III. Selective blockade of D1, but not D2, receptors in the MEC impaired value-dependent anticipatory licking behavior, suggesting a role for D1 receptor-mediated dopaminergic signaling in MEC value processing. Further research is needed to clarify how dopamine influences value-related computations in the MEC and its coordination with hippocampal value processing.

Keywords : D1 receptor, D2 receptor, Entorhinal cortex, Value, Probabilistic classical conditioning

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P-222

High-precision and efficient suppression of pathological brain activity in parkinsonian rats via a closed-loop deep brain stimulation approach

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The increase of high-voltage spindles (HVSs) in the basal ganglia network is a hallmark of dopamine depletion in Parkinsonian rats. Emerging evidence highlights the efficacy of deep brain stimulation (DBS) in suppressing HVSs. It is of significant interest to investigate whether suppressing HVSs can mitigate pathological neuron synchrony in the basal ganglia, particularly in early-stage Parkinson's disease. To effectively suppress HVSs using DBS, we developed a closed-loop stimulator triggered by HVS occurrence. Based on autoregressive modeling at intervals, a predictive model was created with parameters trainable offline using the Kalman filter to detect the onset of HVSs, which is suitable for hardware implementation. This model identified all 1,131 HVS episodes from four Parkinsonian rats using 144 ms of preceding data, achieving a 94% mean precision and a mean latency of 72 ms—well below the average HVS duration of 4.3 s. Additionally, it achieves comparable latency while requiring 95% less computational time than the previous wavelet-based HVS detection model. With the trained model implemented in a microcontroller, we further investigated the effects of closed-loop DBS (cDBS) on HVSs in free-moving Parkinsonian rats with a tethered and wireless system, respectively. In both setups, a stimulation duration as brief as 0.2 s effectively suppressed HVSs. Furthermore, using the wireless system, the inhibition of HVS lasted over 30 minutes post-cDBS application. These findings underscore the potential of cDBS to suppress HVSs, lower stimulation dosages, and reduce side effects, paving the way for its application in early-stage Parkinson's disease treatment through neuromodulation.

Keywords : Parkinson's disease, high-voltage spindles, Kalman filter, smart neuromodulator, closed-loop deep brain stimulation

P-223

Cortical-amygdalar neural dynamics during grooming behavior in rodents

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Rodent self-grooming behavior is increasingly recognized as a useful model for studying internal attention, stress coping, and neuropsychiatric conditions such as autism spectrum disorder (ASD). While cortical and amygdalar involvement in grooming has been suggested, the temporal

dynamics of this functional network remain largely unexplored. In this study, we investigated the oscillatory activity of the prelimbic cortex and basolateral amygdala during stress-induced grooming in mice. Acute stress was induced using a predatory robot paradigm, which reliably increased post-stress grooming behavior. Cortical and amygdalar local field potentials (LFPs) were analyzed during grooming episodes, and we found prolonged theta (~5 Hz) and intermittent long-range gamma (~50 Hz) synchrony were involved during grooming. This study provides novel insights into the neural basis of self-centered behaviors (i.e., internal attention) in rodents, and may inform the development of biologically grounded rodent models of ASD.

Keywords : Grooming, LFP, EEG, Amygdala, Autism

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P-224

Container-based high-performance computing for modeling large-scale biological neural networks

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High-performance computing (HPC) is becoming a crucial tool for computational neuroscience, especially for modeling large-scale neural networks with biophysical details. However, developing these models on modern, distributed, and GPU-accelerated HPC infrastructures is often challenging due to heterogeneity in system software, compilers, and runtime environments across institutions and cloud computing providers. Container technology has emerged as a solution to enable portable and consistent execution environments through virtualization, particularly in shared computing infrastructures without root access to ensure full software compatibility. Yet, its adoption in computational neuroscience studies remains limited, despite its potential advantages. Here we introduce a container-based computational framework that can support diverse simulation and analysis pipelines, particularly for large-scale neural network models. We employed Singularity, an HPC-focused container software, to integrate the traditional message passing interface (MPI)-based distributed computing with modern GPU-accelerated HPC resources. This approach allowed us to simultaneously leverage hardware acceleration and distributed computing while maintaining reproducibility and portability. Using computational models of biologically realistic networks, we compared computing performance across multiple HPC environments, examining how it scales with network size and number of nodes/GPUs used. We demonstrate the practical benefits, including reproducible deployment across different computing environments, minimal performance overhead, and reusable computational workflows. Our work shows that container technology can significantly benefit neuroscientists conducting computationally intensive studies by making it straightforward to share, reproduce, and validate results across diverse HPC environments.

Keywords : Containers, Data science, High-performance computing, Large-scale networks, Singularity

P-225

Place cells in CA3 require more complex visual scenes for spatial firing than in CA1 in VR environment

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It is well known that visual stimuli exert powerful control over the behavior of place cells in the hippocampus. Our lab previously showed individual visual landmarks presented sparsely in a virtual environment were sufficient to trigger spatially localized CA1 place cell spiking (Shin et al., 2022). However, place cells in CA3 weren't easily activated by those sparse landmarks. Instead, they fired more robustly when multiple landmarks formed an ensemble (i.e., visual scene). To further investigate which aspects of visual stimuli effectively drive CA3 place cells, we simultaneously recorded single-unit spiking in CA1 and CA3 while body-fixed male Long-Evans rats (n=8) ran along a 3m linear track in various VR environments. The VR environments were categorized into three types with the visual richness. In "Poor (P)" environment, 2 to 20 individual black-and-white landmarks appeared against a black background in a 1m fixed landmark zone. In "Simple Natural (SN)" environment, more natural-looking landmarks (e.g., trees) appeared against a monotonous green mountain background. In both P and SN, rats ran continuously, unknowingly transported to the start upon reaching the end of the track. In "Complex Natural (CN)" environment, two completely natural visual environments, outdoor mountain and city, with complex and continuous background natural scenes were used. Unlike the P and SN, visual landmarks were provided throughout the track in CN. Our preliminary results indicate that place fields formed robustly across all environments in CA1, with the proportion of place cells highest in the CN. In contrast, significantly less cells showed place-specific activities in CA3 (<10%) in both P and SN. However, the proportion of CA3 place cells jumped to >40% in the CN. Our results suggest that, CA3 cells require more complex visual backgrounds for robust firing in VR environment, whereas CA1 cells are easily activated by sparsely presented individual visual landmarks.

Keywords : Hippocampus, Place cell, Visual landmark, Visual scene, VR environment

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P-226

Differential encoding of value-based contextual behavior in the intermediate and dorsal regions of the hippocampus

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The cognitive map in the hippocampus may represent both spatial and non-spatial information. Prior studies showed that the intermediate hippocampus (iHP) exhibits stronger value-dependent place coding than the dorsal hippocampus (dHP) during value-based navigation (Jin and Lee, 2021; Jin et al., 2024). However, considering that the iHP has

broader firing fields and fewer place cells than the dHP, its function may extend beyond encoding a specific location's value. Instead, the authentic function of the iHP may underlie value-dependent, context-appropriate behavior (e.g., staying quiet in a library while cheering at a concert). To test this, we simultaneously recorded single-unit spiking activities from the dHP and iHP, while body-fixed rats (male, Long-Evans; n=3) performed a contextual memory task in a VR environment. Rats were pseudorandomly placed in one of two contexts (A or B), running along a 2-m linear track. Once arriving at the end of the track, two lick ports (left or right) were extended near the animal's snout. The rat must lick one of the ports providing the higher-value reward (40μl of sugar water) in each context (i.e., left and right ports in context A and B, respectively) and avoid the port associated with a low-value reward (5μl). We also reversed the context-choice value contingencies in the middle of the session. Rats successfully learned the task, including the reversals (≥70% high-value-port licking). Preliminary data showed that after reversal, several iHP neurons exhibited context-dependent firing, even without location selectivity. Importantly, these contextual neurons showed higher firing rates in high-value-port-licking trials compared to the low-value-port-licking trials. In contrast, dHP neurons also showed context-dependent firing, but with location-selective patterns, and they were weakly modulated by the value-based choice behavior. Our preliminary results suggest a potential role of the iHP in value-dependent contextual behavior.

Keywords : Hippocampus, Value, Context, Episodic memory, VR environment

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P-227

A pharynx-to-forebrain circuit for rapid thirst quenching

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Drinking fluids rapidly quenches thirst within seconds, well before fluids are absorbed in the gut and restore homeostatic balance. However, the sensory origin and neural mechanisms underlying this rapid satiation remain elusive. Here, in mice, we identify pharyngeal mucosal mechanosensation that occurs during swallowing reflex as the sensory origin for rapid thirst quenching. Using an integrated approach combining anatomical tracing, nerve transection, neural activity recording and manipulation, we delineate an ascending sensory pathway from the pharynx to the forebrain thirst center. Strikingly, this circuit functions as a high-pass filter, selectively transmitting signals from closely-paced swallows characteristic of fluid intake, while excluding those associated with solid food consumption. Disrupting this signaling prolongs ongoing drinking, establishing its causal role in thirst satiation. Our findings pinpoint the long-sought sensory origin of rapid thirst satiation and demonstrate the comprehensive characterization of the pharynx-to-forebrain circuit, which transforms pharyngeal mechanosensory signals into drinking-specific thirst-quenching signals.

Keywords : Homeostasis, Thirst satiation, Brain-body interaction, Sensory processing, Mechanosensation

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P-228

Dynamic encoding of numbers in the hippocampus

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The ability to estimate and manipulate numerical quantities is essential for flexible, goal-directed behavior, yet how the hippocampus supports such numerical goals beyond simple numerosity encoding remains unclear. Using in vivo calcium imaging and neural decoding in mice, we show that the hippocampus encodes numerical goals through a dynamic, prospective coding scheme. Rather than relying on static labeled-line codes, hippocampal population activity reflects behavioral discriminability of numerical goals in an epoch-specific manner, modulating context-dependent neural representations across task phases. These goal-modulated signals emerge predictively before counting begins and transform as behavior unfolds. Additionally, mice exhibit rudimentary arithmetic-like behaviors, such as combining and decomposing internal counts, suggesting that flexible hippocampal coding supports higher-order numerical manipulation. Our findings reveal how abstract numerical goals dynamically shape hippocampal cognitive maps, enabling adaptable, quantitatively guided behavior.

Keywords : Hippocampus, Cognitive map, Numerical cognition, Arithmetic, Number senses

P-229

A custom imaging-guided intranasal system for brain delivery in a cynomolgus monkey (*Macaca fascicularis*)

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Intranasal drug delivery is a promising non-invasive route for accessing the central nervous system (CNS). However, anatomical complexity in nonhuman primates (NHPs)—such as intricate nasal structures and increased nose-to-brain distance—presents significant challenges compared to both rodents and humans. To address these limitations, we developed an optimized intranasal delivery system for a cynomolgus monkey (*Macaca fascicularis*), incorporating CT imaging for guided administration and post-delivery evaluation. A custom-designed injection frame enabled stable, accurate, and reproducible delivery while minimizing agent loss and preventing off-target diffusion. Real-time CT imaging verified precise injection into the upper region of the ethmoturbinate (EMT), which contains olfactory epithelium and serves as an optimal anatomical target for brain access. Notably, the CT contrast agent reached the olfactory bulb within 1 hour post-administration and remained localized in

the EMT region for up to 3 hours. These findings highlight the feasibility of non-invasive intranasal delivery in NHPs. Future studies incorporating nanoparticle-based carriers—such as gold nanoparticles (AuNPs) and lipid nanoparticles (LNPs)—are expected to further enhance nose-to-brain delivery efficiency and therapeutic potential.

Keywords : Intranasal delivery, Brain, CT, Nonhuman primate

P-230

Altered spine architecture and epileptogenesis : A simulation study in human dysplastic neocortex

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Focal cortical dysplasia (FCD) is a primary cause of drug-resistant epilepsy in children, characterized by structural and functional abnormalities in the brain. This study investigates how alterations in dendritic spine structure might contribute to hyperexcitability associated with epileptogenesis in FCD. We conducted morphological analyses on postsynaptic spines in the temporal cortical layer III of a patient with FCD using 3D scanning electron microscopy. Using the NEURON simulation environment, we examined how changes in spine density and morphology affect the integration and amplification of excitatory signals in dysplastic cortical neurons. Our results suggest that aberrant dendritic spine morphology enhances local hyperexcitability by amplifying excitatory postsynaptic potentials, which may contribute to epileptic activity and signal propagation at the cellular level. Future research will extend these simulations to include inhibitory synapse modifications, offering a more comprehensive understanding of network-level effects in FCD.

Keywords : Dendritic spine, Focal Cortical Dysplasia, Epilepsy, Modeling, Simulation

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P-231

Regularization of high-dimensional cerebellar representations by sparse parallel fiber inputs: A virtual sample-based L2 regularization perspective

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The cerebellum dramatically expands input signals into high-dimensional spaces via parallel fibers (PF) from granule cells, enabling precise motor learning and predictive control. However, this excessive dimensionality risks overfitting by exceeding the intrinsic dimensionality of the input data. Here, we propose that sparse, spontaneous PF inputs act as internal L2 regularization, analogous to multiple linear regression. Specifically, these sparse PF inputs function as virtual samples, each with a single nonzero feature (λ) and target output y=0. Improper Purkinje cell (PC) activation by such inputs triggers climbing fiber (CF) error signals, inducing long-term depression (LTD) at PF-PC synapses, thereby pruning synaptic weights.Traditional adaptive filter models explain cerebellar learning via the delta rule, adjusting synaptic weights based on CF-mediated errors. Yet, the explicit functional role of PF inputs has remained unclear. We reinterpret sparse PF activation as implementing regularization, preventing overfitting in the cerebellum's high-dimensional representations. Biologically based estimates put spontaneous PF firing at ~0.28 Hz per fiber, leaving < 0.03 % active at any moment—consistent with the virtual-sample hypothesis. We propose experimental validations using optogenetics to manipulate PF activation frequency and electrophysiology to record PC and CF responses. By systematically varying PF sparsity, we can observe long-term structural and functional synaptic changes, directly testing our theoretical predictions.Our framework integrates with recent ideas on spontaneous activity-driven pruning in generative models and developmental synaptic refinement, offering a unified view of how the cerebellum maintains functional efficiency and robustness. These insights have implications not only for understanding cerebellar computation but also for advancing artificial intelligence models inspired by biological systems.

Keywords : Cerebellum, Expansion recoding, Parallel fiber, Purkinje cell, Regularization

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P-232

Move All Together (MovAI): A new framework for multi-animal identity tracking and pose estimation

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Recent advances in machine learning–based animal pose estimation and spatial tracking have enabled novel approaches for the quantitative analysis of complex animal behaviors in neuroscience research. While pose estimation for individual animals has achieved high accuracy, current methodologies for multi-animal tracking in freely behaving settings remain constrained by several critical limitations. These include substantial computational overhead stemming from prolonged training and inference durations, reduced tracking fidelity due to occlusions and phenotypic similarities among animals, and the absence of robust post-processing frameworks to resolve identity ambiguity and maintain trajectory continuity. Consequently, existing systems are generally inadequate for supporting real-time behavioral analysis in experimental contexts. To overcome these limitations, we introduce MovAI, a novel behavioral analysis pipeline optimized for efficient and accurate tracking of multiple freely moving animals. MovAI significantly reduces computational demands by minimizing both training and inference time, while concurrently enhancing detection precision. Importantly, our method markedly decreases identity-switching errors, a persistent challenge in multi-animal tracking scenarios. This system represents a scalable and reliable solution for experimental neuroscience, facilitating real-time monitoring and analysis of social behaviors, and potentially establishing a new paradigm for AI-driven behavioral phenotyping.

Keywords : Instance segmentation, Contour, Pose estimation, Social behavior, Real-time

P-233

Distinct neural coding of sensory and mnemonic representations in the human early visual cortex

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Studies on working memory (WM) in the early visual cortex (EVC) traditionally assume shared neural codes for sensory perception and memory representations, leveraging specialized structures such as orientation columns and retinotopic organization. However, WM generally stores only task-relevant features, raising questions about the optimality of sensory structures for mnemonic representation. Here, we investigated whether sensory and WM representations in EVC share neural codes, using fMRI data from 50 participants who encoded and later recalled orientations after a long delay (16.5s). We maximally separated sensory (4-8s) and mnemonic (16-20s) phases. Results indicated significant distinctions: (1) sensory and mnemonic representations occupied orthogonal planes in low-dimensional state space, (2) decoding orientation via inverted encoding models showed the different roles between codes: Sensory code represents external stimulus and mnemonic code represents internal memorized information, (3) voxel-level analysis showed distinct distributions of orientation preferences, and (4) retinotopic analysis found correlations between orientation preferences and radial positions during perception but not WM. These findings suggest that the EVC employs distinct neural codes for sensory perception and WM. However, we found the shared trial-to-trial variability between sensory and mnemonic decoding, implying orthogonal but linked structure between codes. Lastly, we found the behavioral correlates of mnemonic codes are better than sensory code. The differentiation of codes may enhance cognitive performance by reducing external interference, underscoring specialized role of EVC for cognitive demands of working memory.

Keywords : Neural Code, Working Memory, Perception, Visual Cortex, fMRI

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P-234

Temporally dynamic prefrontal processing during goal-dependent memory retrieval

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Retrieving goal-relevant information from memory is essential for adaptive functioning in everyday life. During this process, the dorsolateral prefrontal cortex (dlPFC) is known to support behavior by manipulating goal-dependent retrieval processes. However, it remains unclear what types of information the prefrontal cortex encodes during these retrieval processes, and whether this processing is temporally dynamic. In this study, we conducted an event-related functional magnetic resonance imaging (fMRI) experiment to investigate the nature of information processed in the prefrontal cortex during goal-dependent retrieval. Participants performed a selective retrieval task, in which they retrieved a cued object from previously learned real-world scenes containing multiple objects. This retrieval task was followed by separate object and scene perception tasks. A direct comparison of neural response patterns during selective retrieval and those elicited during perception revealed transient representation of the targeted object in the dlPFC during the early retrieval phase. During the later phase, although significant overlap between retrieval and perception was not observed, retrieval cue-specific representations were consistently maintained. Furthermore, pattern similarity analysis across adjacent time points during retrieval revealed dynamic changes in neural representations during the early phase, followed by stable, temporally consistent representations in the later phase, indicating distinct neural processes between the early and later phases of retrieval in the dlPFC. Taken together, these findings suggest that goal-dependent memory retrieval engages temporally dynamic information processing in the dlPFC.

Keywords : dorsolateral prefrontal cortex, goal-dependent memory retrieval, dynamic information processing, temporal dynamics, distinct neural processes

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P-235

Ventral medial prefrontal and motor cortex interaction mediates cost-benefit tradeoffs

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Decision-making is challenging because the most rewarding option often involves costs, such as a delay in receiving the reward, requiring careful deliberation. For example, when receiving income, we might choose between investing in a long-term option with higher returns or taking cash immediately with no growth. The decision-maker must weigh potential rewards against associated time costs to guide an optimal choice. While frontal cortical areas are implicated in value-based decision-making, how distinct regions within the frontal cortex represent conflicting decision variables, and integrate them into a single choice remains poorly understood. To address this, we developed a delay discounting task in which mice chose between a large, delayed reward and a small, immediate reward. Using large-scale electrophysiology, we observed persistent activity bridging past and upcoming actions across frontal cortical areas, with encoded task variables varying across regions. The motor cortex strongly encoded upcoming choices, and its optogenetic inhibition randomized choices, indicating its critical role in choice execution. In contrast, the representation of reward magnitude was broadly distributed across frontal cortical areas, whereas time cost representation was concentrated in the motor cortex and ventromedial prefrontal cortex (vmPFC). Optogenetic inhibition of the vmPFC disrupted delay representation in the motor cortex, causing mice to disregard time costs in their choices. To probe circuit interactions, we recorded MOp/s activity while silencing vmPFC and found that vmPFC specifically modulates MOp/s along the neural dimension encoding delay, which is integrated into a choice representation in MOp/s. These findings suggest that the vmPFC plays a critical role in representing

costs and relaying this information to the motor cortex to guide action, highlighting a coordinated frontal circuit mechanism for integrating reward and cost during decision-making.

Keywords : Decision-making, Temporal-discounting, Motor and prefrontal cortex, Multi-region recording, Multi-brain region interaction

P-236

Common neural processes engaged during memory retrieval under self-distancing

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While autobiographical memories are often recalled from a first-person viewpoint, they can also be retrieved from a third-person, observer-like perspective—a cognitive process known as self-distancing, which contrasts with self-immersion, the typical fist-person mode of recall. Prior research has shown that self-distancing alters the content of recalled memories, suggesting distinct underlying neural process. To investigate this, we conducted a functional magnetic resonance imaging (fMRI) study consisting of a pre-scan interview session and retrieval session. In the pre-scan interview session, we collected vivid autobiographical memories of each participant, which were later recalled inside MRI scanner during the retrieval session under both self-distancing and self-immersion conditions. Our results revealed increased mean activation in the middle frontal gyrus (MFG), inferior frontal sulcus (IFS), angular gyrus (AG) and precuneus during self-distanced retrieval, compared to those during self-immersed retrieval. Focusing on these regions, we next examined whether self-distancing engages shared neural processing, by comparing pattern similarity in neural responses across self-distancing, both within and across participants. Notably, we found significantly greater shared neural representations across trials involving different memory contents during the self-distancing condition, compared to the self-immersion condition, within individual participants. This effect was more prominent in the left hemisphere than[MOU1] the right hemisphere. Moreover, shared representations in the MFG, IFS and precuneus were observed even across participants during self-distancing. Collectively, these findings suggest that adopting a self-distanced perspective during memory retrieval engages common neural processes across varied memories and individuals, particularly within prefrontal and parietal areas.

Keywords : self-distancing, autobiographical memory, fMRI

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P-237

Disruption of social experience during early adolescence induces long-term behavioral and neural alterations

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The role of social interaction during adolescence is crucial for shaping adult social behaviors and other cognitive abilities. Despite evident neuronal and behavioral changes in adulthood reported in previous literature, the developmental progression of neuronal alterations induced by adolescent social interactions remains poorly understood. In this study, we analyzed progressive social behavioral changes in adolescent mice using machine learning-based behavioral analysis across various social settings, including littermate interactions, the sociability task, and the social recognition memory task. Home cage behavior tracking revealed a sharp decrease in herding behavior at 5 weeks of age. In the socially isolated (SI) mouse group, we observed a significant increase in prosocial behaviors, such as allogrooming and mounting, during early adolescence in the sociability task. To mitigate the effects of social isolation, we provided tactile or olfactory social stimuli. Although sensory interventions yielded modest improvements during early adolescence, their efficacy diminished in adulthood. We further investigated whether chronic oxytocin infusion into the medial prefrontal cortex (mPFC) during early adolescence in SI mice could rescue behavioral deficits. As hypothesized, oxytocin-infused mice exhibited reduced levels of attentive and prosocial behaviors compared to controls. Finally, we analyzed cFos and parvalbumin (PV) expression in the infralimbic area (ILA), hippocampus (HPC), and lateral amygdala (LA). While social interaction enhanced cFos expression in the ILA, HPC, and LA in both SI and group-housed (GH) mice, cFos-PV co-expression was significantly increased in the dorsal HPC and LA only in the SI group. Notably, LA showed reduced cFos-PV co-expression when SI animals received tactile stimulation. Together, these findings highlight the dynamic changes in adolescent social behaviors and their potential role in shaping long-term social outcomes.

Keywords : Adolescence, Social interaction, Hippocampus, Medial prefrontal cortex, Oxytocin

P-238

Exploring more efficient methods for habit formation through count based and time based learning

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Humans are constantly learning. Even seemingly simple actions, such as walking or eating, cannot be performed without prior learning. These behaviors, now executed effortlessly, are the result of repeated learning processes. Thus, learning is a process through which individuals acquire knowledge and experience, enabling personal development. Through repetition, learning can become habitual. Once a habit is formed, behavior can be executed with minimal conscious effort, and this process is considered a form of learning. Habits are typically formed through four stages: cue, craving, response, and reward. In the process of habit formation, the corpus striatum is critical in facilitating behavioral automation and reward prediction. While the prefrontal cortex is involved in the early stages of learning, the striatum becomes more dominant as the behavior becomes habitual. In this study, we conducted an experiment using the Single-Pellet Reaching Task to compare which method—count-based (Count group) or time-based (Time group) learning—more effectively contributes to habit

formation. To ensure equal learning opportunities, the Count group was trained first by performing 50 repetitions, and the time it took for the Count group to reach a 60% success rate was used to determine an equivalent 5-minute training period for the Time group. We then compared the average period required for each group to reach a 60% success rate. Initially, both groups demonstrated similar performance; however, as the experiment progressed, the Count group showed a gradually increasing or stable success rate, whereas the Time group exhibited more irregular and fluctuating patterns. These findings suggest that count-based training may facilitate more effective habit formation.

Keywords : Learning, Habitual, Repetition, Behavior, Corpus Striatum

P-239

Harmonizing cerebellar uniformity and diversity: A transformer-inspired hierarchical algorithm perspective for neuroscience and machine intelligence

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The cerebellum has long been considered a paradoxical brain region, exhibiting remarkable structural uniformity despite its vast functional diversity. This characteristic has fueled a long-standing debate regarding cerebellar function, particularly between the Universal Cerebellar Transform (UCT) hypothesis and various arguments emphasizing observed functional heterogeneity and diversity at the implementational level. This study proposes a novel perspective to integratively understand this enduring debate through an analogy with the Transformer architecture from artificial intelligence (AI). Transformers, while constructed by repeatedly stacking relatively uniform basic blocks (layers), can effectively perform a wide array of diverse tasks. This is conceptually similar to the core idea of the UCT hypothesis, where the cerebellum's uniform microcircuitry might be universally applied across different functional domains. Concurrently, Transformers exhibit qualitatively different behaviors and performance profiles depending on training objectives, information flow, and conditional computation mechanisms (e.g., Mixture-of-Experts), which can be interpreted as functioning through various sub-algorithms specialized for specific contexts. This duality observed in Transformers—the potential for universal processing capability and functional diversity at the observational level—suggests the necessity of a hierarchical algorithm framework that distinguishes between a 'meta-algorithm' representing core computational principles and context-dependent 'sub-algorithms'. This framework refines David Marr's 'algorithmic level' of analysis by subdividing it into these two layers. From this hierarchical viewpoint, UCT can be reinterpreted as the cerebellum's conserved meta-algorithm level, while the observed functional diversity is a result of this meta-algorithm being implemented as various sub-algorithms.

Keywords : Universal cerebellar transform, Transformer, Cerebellum, Computational neuroscience, Deep learning

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P-240

Dopamine signaling in the retrosplenial cortex during goal-directed navigation

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Egocentric cognitive map is believed to play a crucial role in goal-directed navigation. Neurons in the retrosplenial cortex (RSC) have been shown to encode environmental geometry in the egocentric coordinates. Previous anatomical studies suggested the existence of dopaminergic projections from the ventral tegmental area (VTA) to the RSC, which may convey reward-related dopaminergic information. However, it remains unknown whether and how dopaminergic input dynamically modulates RSC activity to integrate reward signals into the egocentric cognitive map. To address this, we first confirmed the presence of VTA-to-RSC dopaminergic projections using fluorescence-based histological methods. We then expressed GRAB-DA, a genetically encoded dopamine sensor, in RSC neurons and conducted fiber photometry recordings during a goal- or reward-directed navigation task. Our preliminary data suggest that dopamine signals in RSC ramp up toward reward location during goal-directed navigation. These findings indicate that dopaminergic signaling in the RSC may modulate egocentric spatial representations in a reward-dependent manner.

Keywords : Retrosplenial cortex, Ventral tegmental area, Goal-directed navigation, Dopamine, Egocentric cognitive map

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P-241

Intralayer disinhibitory circuit regulates feed-forward circuit of somatosensory cortex

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Withdrawn

Thalamocortical (TC) circuit has been extensively studied in wide area of neuroscience. Especially, barrel cortex has been the subject of extensive research due to its ability to provide a precise anatomical definition of cortical columns and their correlation with microcircuits. Somatosensory cortex has been reported that the L4 cortical circuit in barrel precisely endoces tactile sensory inputs using thalamic recruitment of feed-forward inhibition(FFI) regime starting from homologous barreloid of the VPM thalamus. FFI regime imposes restricted integration time window during transfer information. However, the exact effects of disinhibition around FFI are still unknown despite extensive research. Previous computational model neglects disinhibition assuming low connectivity of L4 barrel cortex, which limits to explain why actual brain slices cannot transfer spikes. Although previous research has reported that TC circuits allow highly flexible adaptive sensory processing within the same hard wired neuronal networks, the computational model in the barrel cortex has yet to explain this phenomenon. Furthermore, amount of disinhibitory circuit regimes have been reported before, computational approach to examine the circuit has been still limited. In this study, our aim was

investigating dynamics between TC and intralayer disinhibitory regime. First, we present a computational model to show disinhibitory circuit makes the thalamocortical circuit stable under strong connectivity. Based on simulation, our study inferring L5 somatostatin cell as the primary component of gating somatosensation through disinhibiting L4 Pyr and L4 PV cell. Our study might provides keys into the functional organization between somatosensory circuit and higher-order thalamus.

Keywords : Thalamocortical Circuit, Disinhibition, L5 Somatostatin

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P-242

Prefrontal representational changes during learning predict long-term associative memory

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The persistence of memories has long been thought to depend on consolidation processes involving interactions between the hippocampus and prefrontal cortex. Our previous research showed that the dynamic reorganization of memory traces in the hippocampus during learning is critically associated with subsequent memory retention. However, it remains unclear whether such reorganization within the prefrontal cortex during learning contributes to long-term memory persistence. To address this question, we conducted functional magnetic resonance imaging (fMRI) to track neural representational changes during learning and examined whether these changes predicted memory retention after delays of one day and four weeks. We found that neural patterns became increasingly assimilated for associated stimulus pairs that were remembered after four weeks, but not for those that were forgotten, as learning progressed in prefrontal regions including the ventromedial prefrontal cortex (vmPFC), lateral orbitofrontal cortex (lOFC), dorsolateral prefrontal cortex (dlPFC), anterior superior frontal gyrus (aSFG), and inferior frontal gyrus (IFG). This effect was not observed for pairs that were retained after one day but forgotten after the four-week delay. Furthermore, classification analyses revealed that while representational changes in the hippocampus selectively predicted memories retained after one day, changes in the lOFC predicted long-term memory retention over four weeks. Collectively, these findings suggest that reorganization of memory traces in the prefrontal cortex during learning specifically predicts the retention of long-lasting associative memories that persist beyond four weeks.

Keywords : fMRI, Associative memory, Long-term memory, Learning, Lateral orbitofrontal cortex

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P-243

Auditory alarm modulates hippocampal theta phase resetting and hippocampal theta-cortical gamma coupling to enhance associative memory encoding

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In our previous research, an auditory alarm delivered when hippocampal theta power dropped below a threshold increased theta power and improved associative memory encoding. Since hippocampal theta phase organizes phase-specific spiking and network synchrony, its modulation by alarms warrants further study. We hypothesized that alarms delivered precisely at theta power troughs selectively reset or modulate hippocampal theta phase, creating a neural state optimal for associative memory encoding. We analyzed intracranial EEG from seven subjects performing an associative memory task under three conditions: no alarm, random alarm, and theta-based alarm. Hippocampal theta phase resetting was significantly stronger for successful versus failed trials in the no alarm condition. Moreover, random and theta-based alarms significantly increased phase resetting in alarm-triggered trials compared to trials without alarms. Successful encoding was also associated with increased phase-amplitude coupling (PAC) between hippocampal theta phase and cortical gamma power. Random alarms selectively enhanced PAC in the primary auditory and right parietal cortices. In contrast, theta-based alarms enhanced PAC more broadly, including left parietal and fusiform regions. This extensive PAC effect of the theta-based alarms provides supports greater improvement in associative memory encoding observed under the theta-based alarm condition compared to the random alarm condition. Our findings support that auditory alarms can causally enhance hippocampal theta phase resetting and hippocampo-cortical theta-gamma coupling. Especially, theta-based alarms boosted PAC across memory-relevant regions, including those involved in visual word processing. These results suggest that auditory alarms can modulate hippocampo-cortical dynamics to improve memory and highlight the potential of theta-based auditory stimulation as a closed-loop neuromodulation strategy for memory enhancement.

Keywords : Associative memory encoding, Theta rhythm, Hippocampal theta phase resetting, hippocampal theta-cortical gamma coupling, Human iEEG

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P-244

Phonetic vs. phonemic representation in neural activity during speech production: evidence from denasalized [n] Sounds resembling [t] in Ko

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Speech-decoding from intracranial EEG (iEEG) has advanced rapidly,

with most systems targeting phoneme-level outputs. However, they rarely discriminate between phonetic and phonological process: phonetics deals with concrete acoustic realizations, whereas phonology abstracts over them. Consequently, identical phonemes can manifest in divergent sound patterns. In Korean, for instance, nasals in word-initial position are frequently denasalized, exhibiting spectral pattern that is like those of plosives. To determine whether neural activity around articulation tracks abstract phonemic categories or fine-grained phonetic detail, we recorded iEEG from one native Korean speaker. We specifically asked whether denasalized word-initial /n/ is encoded more like a nasal or a plosive. For every word initial alveolar /n/, /t/, /th/, /t*/ phonemes in 33 various sentence utterances, band-limited power (theta to high gamma) were extracted and used to train decoders discriminating [t, th, t*] from [n]. The six top-performing decoders (72–85 % balanced accuracy) were then probed with five held-out denasalized [n] tokens. All six decoders consistently labeled these tokens as plosives. Except for one decoder that classified two tokens as [n], the other 5 top decoders all categorized denasalized /n/ to [t, th, t*] group. Although our data are drawn from a single subject, the consistency of our findings points unequivocally to a phonetic—as opposed to phonemic—neural encoding. We therefore contend that future speech-decoding research should explicitly distinguish between phonetic and phonemic levels of analysis.

Keywords : Phonetics, Phoneme, Neurolingusitics, iEEG

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P-245

Neural representations of the clarity of subjective emotion

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Subjective feeling, the consciously accessible component of internal emotional experience, is a core constituent of emotion, alongside physiological and behavioral responses. However, individuals do not always perceive these feelings with high clarity—some emotions are vividly experienced, whereas others are vague or mixed. This study investigated whether the brain differentially processes emotional experiences depending on how clearly they are internally experienced. We conducted a functional magnetic resonance imaging (fMRI) experiment in which participants viewed images from the International Affective Picture System (IAPS) and rated the intensity of their subjective experience of happiness, sadness, and fear for each image. Whole-brain univariate analysis revealed that cortical regions, including the ventral frontal cortex, fusiform gyrus, and anterior temporal areas, were commonly engaged during emotion recognition, regardless of whether the emotion was experienced clearly or vaguely. We next conducted multivariate pattern analysis to examine differences in neural processing between clearly and vaguely experienced emotions, and found that clear emotional experiences were associated with greater pattern similarity in the right middle and posterior superior temporal sulcus (STS) compared to vague emotional experiences. This effect was not observed in the anterior STS. To further assess whether the effect of emotional clarity varies by emotion category, we compared clearly experienced trials of happiness, sadness, and fear. These analyses revealed no significant differences in pattern similarity across emotion types, suggesting that the observed effect in the right middle and posterior STS is more likely driven by emotional clarity rather than by emotion category. Together, these findings identify neural correlates of emotional clarity and suggest the right middle and posterior STS as key regions representing the subjective clarity of emotional experience.

Keywords : Emotion recognition, Superior Temporal Sulcus, Emotional clarity, Human fMRI

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P-246

Differential integration of visual value and feature information in basal ganglia regions

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For primates, evaluating visual value information and translating it into actions is critical for survival. Visual value signals are known to be processed in the basal ganglia circuit, which modulates eye movements accordingly. However, visual stimuli also contain non-value features that interact with value signals to influence behavior. Despite this, most prior basal ganglia research has focused solely on value, offering limited insight into how diverse visual features are integrated with value and propagated through the basal ganglia. In this study, we recorded neuronal activity from the caudate nucleus (CD), putamen (Put), ventral striatum (VS), and substantia nigra pars reticulata (SNr) in monkeys performing a visual value-based saccade task. Consistent with previous works, all striatal regions robustly encoded value information. However, other visual features were differentially represented across regions: Put and CD encoded spatial location strongly, while VS preferentially encoded perceptual salience. Population decoding further revealed that all striatal regions discriminated interaction effects between value and other visual features, indicating that the striatum engages in integrative processing. In the SNr, which is thought to control final motor output, value signals emerged more slowly than in the striatum, consistent with known anatomical pathways. In contrast, perceptual salience was encoded more rapidly and strongly in the SNr than in the striatum. This suggests that visual features like salience may be conveyed to the SNr via distinct anatomical inputs, separate from those involved in value processing. This suggests that, unlike value information, visual features may be conveyed through distinct anatomical inputs. These findings highlight functional specialization within the basal ganglia regions for integrating multiple types of visual features with value, in a region-specific and feature-dependent manner.

Keywords : Primate electrophysiology, Basal ganglia, Visual information

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P-247

Differences in modality-selective value neurons of the primate striatum underlie functional dissociation of tactile and visual value-guided behavior

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Primates rely on tactile and visual information to recognize object shape and evaluate them, an ability critical for survival. These sensory inputs are relayed from distinct cortical areas to the striatum, which includes the putamen (PUT), caudate (CD), and ventral striatum (VS). Our previous study (Hwang et al., 2024) showed that PUT encodes both tactile and visual values, likely supported by converging tactile, visual, and dopamine inputs. CD and VS also receive these inputs, but differ in the cortical origins: PUT from sensorimotor cortex, CD from associative/visual regions, and VS from limbic areas. These similarities and differences in anatomical connectivity raise the question of how CD and VS neurons encode tactile and visual value information, relative to those in PUT. Monkeys were trained to discriminate the values of tactile (braille) and visual (fractal) stimuli while single-neuron recordings were conducted. We found bimodal, tactile-selective, visual-selective value neurons in all regions. Regional differences were prominent among modality-selective neurons in decoding: tactile value is encoded most prominently by tactile-selective value neurons in PUT, whereas visual value is more strongly represented by visual-selective value neurons in CD and VS, suggesting that the regions contribute differentially to value-guided behavior based on modality. To test behavioral effects, we selectively inactivated PUT, CD, or VS as the monkeys made value-based choices. Interestingly, PUT inactivation selectively impaired tactile value-guided choices, CD inactivation impaired visual value-guided choices, and VS inactivation disrupted both. These deficits across the three striatal regions reflect impairments in exploiting learned values, rather than in value learning, as predicted by the Rescorla-Wagner model. Our results demonstrate that each striatum guides modality-specific, value-based behavior through distinct populations of modality-selective value neurons.

Keywords : Tactile, Visual, Value, Primate, Striatum

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P-248

Parallel processing of tactile and visual value information in the globus pallidus externa

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The cortico-basal ganglia circuit exhibits an anatomical funneling structure: information flows from the cortex to the striatum and then to downstream nuclei, with substantial reduction in neuron number. This raises the question of how diverse information is processed with progressively fewer neurons. There are three possible information processing strategies: convergent, parallel, or divergent. Interestingly, a recent study of the putamen (PUT) identified bimodal neurons encoding both tactile and visual value, suggesting convergence of modality and value information. We ask how such convergence is transformed along the funneling architecture, focusing on the downstream target of striatum, globus pallidus externa (GPe). We recorded GPe neural activity while monkeys performed tactile and visual value discrimination tasks. Two monkeys consistently responded faster to high-valued stimuli in both tasks, confirming their ability to recognize tactile and visual values. Among 54 task-related neurons, 45 (83%) encoded value information, including 8 tactile-selective, 21 visual-selective, and 16 bimodal neurons. Among them, 35 showed positive value-coding (5 tactile, 16 visual, 14 bimodal), and 10 showed negative value-coding (3 tactile, 5 visual, 2 bimodal). This suggests that value and modality information is neither fully converged nor strictly segregated in the GPe. The proportion of these neurons is comparable to that in the PUT, suggesting that two structures similarly process tactile and visual values. The GPe serves as a hub in the indirect pathway and, despite being a downstream structure, appears to retain all information in parallel form. Our results suggest that the brain requires identical tactile and visual values to be processed through both the indirect (GPe) and direct (PUT) pathways, ensuring proper relay to downstream motor structures like GPi and SNr. How such information is further processed in output nuclei will be a subject of our future investigation.

Keywords : Primate, GPe, Value information

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P-249

The role of the primate caudal subthalamic nucleus in processing long-term value memory for habitual behavior

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Deep brain stimulation (DBS) of the subthalamic nucleus (STN) alleviates motor impairments in Parkinson's disease (PD). Accordingly, the STN has been regarded as a key structure for motor function. However, recent clinical studies have reported that STN-DBS worsens value-based decision-making deficits in PD patients (Saint-Cyr et al., 2000, Brain). Furthermore, anatomical studies have shown that the STN receives inputs from value-processing structures involved in goal-directed and habitual behaviors, including the substantia nigra pars compacta and the globus pallidus externa (Kim & Hikosaka, 2015, Cell; Kim et al, 2017, Neuron). These findings suggest a potential role for the STN in value-guided behaviors. However, it remains unclear how the STN processes object values for goal-directed and habitual behaviors. To examine this, we recorded STN neuronal activity in monkeys performing a reversal learning task with visual objects to assess flexible value for goal-directed behavior, and a passive-viewing task to assess stable value for habit. In

both tasks, monkeys more frequently gazed at good objects, confirming value-based behaviors. Among 149 object-responsive neurons, 73 neurons (49%) encoded flexible value, and 48 neurons (32%) encoded stable value. Notably, flexible value neurons were distributed throughout the STN, whereas stable value neurons were concentrated in the caudal STN (cSTN) and responded more strongly to bad objects, suggesting a mechanism for suppressing habitual gaze toward bad objects. To test whether the cSTN plays a crucial role in visual habit, we inactivated the cSTN by Muscimol injection. Interestingly, cSTN inactivation led to automatic saccades toward bad objects, indicating impaired habit. Overall, our findings suggest that excitatory responses of cSTN neurons to bad objects enhance activity in the substantia nigra pars reticulata, thereby suppressing automatic gazes toward bad objects during habitual behavior.

Keywords : Primate, Subthalamic nucleus, Value, Memory, Basal ganglia

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P-250

Learned value and spatial preference, but not visual salience, shape value-based habitual hand choice in primates

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Value-based visual habits are well documented, with primates showing persistent gaze biases toward previously rewarded objects even without reinforcement (Kang et al., 2021; Hwang et al., 2022). In contrast, it remained unclear whether similar long-term habits can form in hand choice behavior. We previously showed that habitual hand choices can emerge through long-term object–value learning, even without immediate feedback. Building on this, we asked whether value-driven habits differ across eye and hand effector systems. These effectors serve distinct functions: gaze is typically object-centered, driven by visual recognition, while hand movements are spatially directed and constrained by biomechanical demands (Yamamoto et al., 2012; Johansson & Flanagan, 2009). Based on these differences, we hypothesized that the key drivers of value-based habits would differ across these systems. To induce habits, two monkeys learned object–value associations in a two-choice discrimination task. Habit formation was later assessed in a separate choice task without feedback. In this task, previously learned objects appeared on a touchscreen, and monkeys erased them by touching in a self-selected order. Monkeys showed choice biases toward high-valued objects, confirming value-based hand choice habits. To identify the underlying drivers, we performed trial-level regression with visual salience, spatial preference, object preference, and value as predictors. Visual salience had no significant influence on behavior either before or after learning (95% CI: -0.19, 0.21), whereas spatial preference remained a strong predictor. Notably, object preference, which was predictive prior to learning, lost significance after learning (95% CI: -0.19, 0.34), suggesting that learned value suppresses innate object biases but not spatial bias. These results demonstrate that value-based hand habits are shaped primarily by stable spatial preferences and learned value, rather than visual features.

Keywords : Value-based habit, Non-human primate, Hand choice habit, Spatial preference, Visual salience

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P-251

Comparison of advanced augmentation methods for predicting postoperative delirium in older adults undergoing spine surgery

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Background: Postoperative delirium is a common neuropsychiatric complication among older adults undergoing spine surgery, leading to adverse clinical outcomes. Current predictive models typically overlook temporal dynamics, clinical subtypes, and class imbalance. Methods: This study compared the performances of advanced time series data augmentation methods, including dynamic time warping simple synthetic minority oversampling techniques (DTW-SMOTE), time-series generative adversarial networks (TimeGAN), and a hybrid method. Statistical validation was conducted on augmented datasets created from real-world data. Dynamic multi-output long short-term memory models were trained on original and augmented datasets, and their performances were evaluated for predicting delirium occurrence, clinical subtype, and severity, using metrics such as accuracy, recall, precision, F1-score, and area under the receiver operating characteristic curve (AUC). Results: Models trained on augmented datasets consistently outperformed those trained on original data. TimeGAN showed the highest predictive accuracy (overall accuracy = 0.95, AUC = 0.98). DTW-SMOTE demonstrated superior temporal coherence (mean minimum DTW distance = 885.423) and strong performance in severity prediction (AUC = 0.96). The hybrid method effectively balanced baseline characteristics while achieving intermediate predictive performance (overall accuracy = 0.84, AUC = 0.91). Conclusions: No single augmentation method universally outperformed the others, and statistical alignment alone did not guarantee superior predictive performance. Researchers and clinicians should therefore select augmentation methods tailored to specific clinical contexts, data characteristics, and research objectives.

Keywords : Postoperative Delirium, Time-Series Data Augmentation, Dynamic Prediction, DTW-SMOTE, TimeGAN

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P-252

Topographic cortico-basal ganglia computational model reveals motor and non-motor symptom comorbidity in Parkinson's disease

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The basal ganglia (BG) processes diverse inputs from motor and non-motor regions of the cerebral cortex via topographically organized cortico-striatal projections. While previous research has focused primarily on fragmentary aspects of the BG feedback loop to the cortex via the thalamus, it has often overlooked the wide-range topographical organization within the BG and its direct influence on downstream targets. Considering that Parkinson's disease (PD) often accompanies non-motor symptoms such as executive dysfunction, in addition to the canonical motor symptoms, topographical organization of neuronal arrangements within each subnucleus in BG and connectivity between cortex and BG could underlie the comorbidity of distinct symptoms. To examine this hypothesis, we developed a computational spiking neural network (SNN) models of the cortico–basal ganglia circuit that explicitly incorporates topographic connectivity as well as the biologically plausible neuronal population ratio between subnuclei, dopaminergic projections, and other vital aspects of neuronal and synaptic model. We utilized various integrate-and-fire models that have been adapted to fit the firing characteristics of each neuronal type. First, we could successfully reconstruct the firing patterns and their changes by dopamine depletion in accord with the classical model explaining motor symptoms, referred as imbalance hypothesis between direct and indirect pathways. With the model incorporating topographic organization, we observed the emergence and propagation of pathological firing from the motor-related cortex-BG loop to other modality-specific loops. To this end, we seek to suggest the potential mechanism and the requisite of comorbidity of symptoms in PD using our SNN in silico model of cortex-BG.

Keywords : Basal ganglia, Parkinson's disease, Topographic connectivity, Spiking neural network, Motor and non-motor symptoms

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P-253

A computational modeling approach to the role of Serotonin in cued fear learning and extinction

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Although serotonin has long been implicated in mood and anxiety regulation, its mechanism remains insufficiently understood. Cued-fear conditioning (CFC), a well-controlled framework for examining how organisms learn to associate neutral cues with aversive outcomes, has been widely used. While several computational approaches have explored circuit dynamics involving neuromodulators such as serotonin, the specific mechanisms by which serotonin modulates threat learning and memory in CFC have yet to be fully characterized. This study aims to understand how serotonin modulates aversive learning to uncover the neurocomputational basis of fear-related classical conditioning. We present a computational framework that specifically investigates serotonergic modulation in CFC. We first developed a behavioral-level model of punishment-based reinforcement learning to simulate how the acquisition and extinction of cued fear responses are influenced by two distinct dynamics of serotonin release. The hypothesis that phasic and tonic release of serotonin correspond to risk discounting factor and learning rate, respectively, could successfully explain the prior experimental results. As a deeper investigation of the circuit mechanisms, we incorporated rate-based neural circuit model to examine how the temporal dynamics of serotonin can be linked to the reinforcement learning variables by modulatingmemory encoding and retrieval processes across key brain regions, such as amygdala, prefrontal cortex, and hippocampus. This framework provides a novel account of the role of serotonin for learning and forgetting in response to discrete threats, offering insights into the neural computations underlying affective disorders such as PTSD.

Keywords : Serotonin, Fear Conditioning, Punishment-base Reinforcement Learning, Extinction

P-254

Memory trace of a virtual butterfly encounter

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Episodic memory is necessary for animals to adapt to the dynamically changing world. A substantial body of research has described how the hippocampus updates its representation of the external world in response to novel cues. However, the mechanism that enable the parallel processing and integration of familiar spatial information and novel transient information is still unclear. In this study, we developed a novel paradigm in which head-fixed mice run on a cue-enriched treadmill and occasionally encounter a butterfly dummy controlled by 3-motor axes, and we recorded neuronal responses in hippocampal CA1 and CA3 regions using silicon probes. We found that the f irst encounter with the butterfly rapidly remodeled the activity patterns of place cells. While the prior encoding of treadmill belt locations could still be observed in the population code of gamma-scale time windows, new population activity patterns emerged and recurred during the butterfly encounters, multiplexing with spatial information. Furthermore, a neural network model of competitive learning effectively replicated the range of place cell responses and revealed a parallel development of engrams for both spatial environments and butterfly encounters. These results demonstrate the existence of hippocampal memory traces for single encounter events and provide insights into the neural network mechanisms that support the 'one-shot' encoding of experiences

Keywords : Hippocampus, Engram, Competitive Learning

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P-255

The role of retrosplenial cortex input to nucleus accumbens in modulating behavior

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The retrosplenial cortex (RSC) is a key cortical region involved in encoding egocentric spatial representations, particularly through landmark and object-based coding. It is also known to support contextual memory and guide navigation. While its contribution to spatial cognition is well established, its downstream influence on brain regions responsible for translating spatial information into behavior remains unclear. One potential target is the nucleus accumbens (NAc), a region involved in integrating spatial and motivational signals to guide motor output. Given these roles, the RSC is well positioned to influence behavior via its projections to the NAc, but the anatomical and functional significance of this pathway has not been fully explored. To address this question, we first injected AAVrg-Ef1α-mCherry-IRES-Cre into the NAc and AAV-DIO-eYFP into the RSC to retrogradedly verify projections from RSC to NAc. We then used in vivo optogenetic inhibition to selectively silence NAc-projecting RSC neurons during two behavioral tasks: the object location task (OLT), which tests spatial novelty preference, and contextual fear conditioning (CFC), which assesses contextual fear memory. We selectively inhibited these projections by expressing AAVrg-Ef1α-mCherry-IRES-Cre into the NAc and AAV-DIO-eNpHR into the RSC and delivering yellow light (565 nm, 2 mW) via an optic fiber implanted above the NAc. In the OLT, control mice showed a robust preference for the displaced object, whereas mice with inhibited RSC-NAc projections showed significantly reduced discrimination indices. In the CFC, inhibiting RSC-NAc projections during retrieval reduced the freezing behavior. These results suggest that the RSC-NAc pathway contributes to transforming egocentric spatial representations into behaviorally relevant output across exploratory and defensive behavioral contexts.

Keywords : Retrosplenial cortex, Nucleus accumbens, Object location task, Contextual fear conditioning, Optogenetic modulation

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P-256

Structured semantic information is reflected in cerebral cortical activity during single-word production

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While speech brain-computer interfaces have made strides in decoding articulatory and phonetic features, capturing the intended meaning of language remains a major challenge. Mapping semantic representations of language enables higher-level, more flexible communication. Recent work suggests that natural language processing-derived embeddings can be used as proxies for human semantic spaces. Here, we ask whether structured semantic information is reflected in neural activity during single-word production. We analyzed intracranial electroencephalography data from 3 epilepsy patients during a visual word reading task of 108 words. Each 4-second trial began with 1s fixation before stimulus onset. High-gamma (70–170 Hz) amplitudes were baseline-corrected and used to compute neural representational dissimilarity matrices (RDM) per electrode in 200 ms windows with 25 ms frameshift. Sentence Transformer embeddings for each word were reduced to 20 dimensions, and hierarchical density-based spatial clustered into 10 semantic groups. Semantic RDMs were constructed from cosine distances between embeddings in each cluster pair. Representational similarity analysis (RSA) compared neural and semantic RDMs per electrode, time window, and cluster pair. Significance was determined through 3,000 permutations with false discovery rate correction. Our results revealed significant semantic structure in neural activity across all participants. Peak representational similarity for each participant reached r = 0.77 in the left middle temporal gyrus, 0.69 in the right superior temporal gyrus, and 0.65 in the left anterior prefrontal cortex, at latencies from 0.25 to 1.35 s, time-locked to stimulus presentation. These intervals correspond to pre-speech through early speech production. Average RSA values across time and channels ranged from 0.33 to 0.39 per participant. Our results suggest that spatial semantic relationships defined by word embeddings are preserved in cortical neural activity.

Keywords : Speech BCI, Semantic Space, Intracranial EEG, Representational Similarity Analysis

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P-257

Multidimensional dynamics of the cerebellar output neurons encoding saccadic eye movement

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The cerebellum is one of the critical brain regions for coordinating saccadic eye movements, and studies have focused on understanding how it precisely controls various kinematic parameters. Previous work revealed the neural manifold-like activity patterns in key cerebellar units, mossy fibers (MF) and Purkinje cells (PC), encoding specific kinematic parameters [1]. However, the role of the deep cerebellar nuclei (DCN), the final output gateway of the cerebellum, remains poorly understood. Here we show how neurons in the fastigial nucleus (FN), the part of the DCN relevant for saccades, encode these movements by using a pool of FN neurons (FNN) from three rhesus monkeys (*M. Mulatta*) performing saccade tasks [2]. Through dimensionality reduction, we identified a low-dimensional manifold in FNN population activity that, similarly to the PC manifold, comprised four movement direction (θ)-independent temporal patterns and their θ-dependent linear transformations. The θ-dependence became significantly more organized when we analyzed the data with θ-θ_L, where θ_L is the movement direction for the maximal bursting latency of individual FNNs, an approach inspired by previous work [2]. This mirrors a similar phenomenon observed in PCs, known as "potent vectors," which provide intrinsic references for movement direction coding of individual PCs [3]. We also found that the MF and PC population data from [1] can predict the activity of individual FNNs

accurately (R^2=0.991±0.011). Notably, using the PC data alone achieved similar accuracy (R^2=0.971±0.034), while the MF data alone performed significantly more poorly (R^2=0.781±0.213). Overall, our findings demonstrate the predominant influence of PCs on FNNs, suggesting that FN primarily serves as a gateway to transmit computational outcomes of the cerebellar cortex. References 1. Markanday et al. (2023) Nat Commun *14*, 2548. 2. Sun et al. (2016) Eur J Neurosci *44*, 2531. 3. Fakharian et al. (2025) Science *388*, 869.

Keywords : Cerebellum, Deep cerebellar nuclei, Neural manifold, Eye movement, Saccades

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P-258

Higher-order connectivity, jointly determined by distance, net synaptic inputs and outputs, influences recurrent dynamics in mouse V1 layer 2/3

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Understanding the logic of recurrent connectivity in neocortex and linking it to neural activity has been a long-standing goal of neuroscience. The functional connectomics data spanning multiple areas of mouse visual cortex provides an unprecedented opportunity to address these questions (The MICrONS Consortium, 2025 *Nature*). Using this dataset, we sought to determine the rules underlying higher-order connectivity in primary visual cortex (V1) layer 2/3. Connection probability between a pair of neurons depends on the inter-soma distance. While this 'distance rule' is widely accepted for first-order connectivity, it is not sufficient to recapitulate higher-order connectivity. We found that scaling the distance-based connection probability by the total number of input and output synapses for each neuron succeeded in recapitulating second-order connectivity with remarkable accuracy. Next, we sought to identify neural activity metrics that are indicative of connectivity measures. Prior literature suggested that population coupling, defined as correlation between a neuron's activity and the population net activity, is indicative of net synaptic inputs (Okun et al., 2015 *Nature*). We verified this relationship among proofread V1 layer 2/3 neurons in the MICrONS data, and in the in-silico simulation of this network. The correlation between population coupling and net synaptic input was non-existent in random networks drawn from uniform connection probability (Erdős–Rényi network). Factoring in distance, net synaptic output, and net synaptic input progressively increased this correlation, in that order of importance. In sum, higher-order connectivity is determined by net synaptic inputs and outputs in addition to inter-soma distance, and higher-order connectivity influences the relationship between population coupling and net synaptic inputs.

Keywords : Higher-order connectivity, Population coupling, MICrONS, In-silico simulation, Primary visual cortex

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P-259

Value-related activity of interneuron subtypes in hippocampus

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Beyond its well-established role in spatial navigation and episodic memory, the hippocampus has increasingly been implicated in processing value-related information. However, the circuit-level mechanisms by which value signals are represented within hippocampal networks remain incompletely understood. To dissect these microcircuit dynamics, we used one-photon calcium imaging to monitor the activity of parvalbumin (PV)-, somatostatin (SST)-, and vasoactive intestinal peptide (VIP)-expressing interneurons in dorsal CA1 while mice performed a probabilistic classical conditioning task. In this task, three distinct odor cues predicted water delivery with 75%, 25%, or 0% probability. We found that all three interneuron subtypes exhibited value-related activity, yet with distinct temporal and quantitative characteristics. SST neurons encoded cue-related value signals more rapidly and strongly compared to PV and VIP neurons. In contrast, PV neurons displayed greater across-trial consistency in their encoding of value, indicating their potential role in maintaining value information over time. During the outcome phase, all interneuron subtypes showed negative responses to rewards but increased activity with higher expected value, consistent with a role in computing reward prediction error. These findings suggest that distinct CA1 interneuron subtypes differentially contribute to hippocampal value computations. Ongoing work is examining how subtype-specific modulation alters pyramidal cell encoding and behavioral outcomes.

Keywords : Classical conditioning, Hippocampus, Interneuron, Value processing

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P-260

Dissecting temporal dynamics and cross-area information integration during online goal correction

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Flexible adaptation to unexpected changes in behavioral goals requires the dynamic coordination of multiple cortical regions. Here, we investigated how the dorsolateral prefrontal cortex (DLPFC), primary motor cortex (M1), and posterior parietal cortex (PPC) jointly and individually encode and integrate information during online goal correction in non-human primates performing a center-out reaching task with unpredictable target changes. We simultaneously recorded single-unit population activity from DLPFC, M1, and PPC. We applied the Joint and Individual Variance Explained (JIVE) framework to decompose neural population activity into joint (shared across regions) and individual (region-specific) components. This approach allowed us to quantify the extent and timing of information integration and segregation across cortical areas during different phases of online goal correction. Our results reveal a clear temporal sequence in the emergence of goal-related information: joint components associated

with updated goal representation appear earliest in the DLPFC, followed by PPC and then M1. Furthermore, JIVE analysis demonstrated that joint variance accounted for a substantial proportion of the population activity during periods of target updating and movement correction, suggesting active information exchange and integration among these areas. In contrast, individual components captured region-specific dynamics, such as sustained goal maintenance in the DLPFC, spatial processing in the PPC, and motor execution in the M1. These findings offer new insights into the neural mechanisms by which prefrontal, parietal, and motor circuits coordinate to flexibly update and execute goal-directed actions in the face of environmental uncertainty.

Keywords : motor adaptation, joint and individual variance explained, dorsolateral prefrontal cortex, primary motor cortex, posterior parietal cortex

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P-261

Thalamocortical circuit mapping in macaque monkeys using combined stimulation-fMRI

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Higher-order thalamic nuclei—such as the mediodorsal (MD), central lateral (CL), and pulvinar—are increasingly recognized as dynamic controllers that modulate activity across distributed cortical areas. These thalamocortical circuits support a wide range of cognitive functions, including working memory, arousal regulation, and attention. Yet, a large-scale, detailed directional mapping of thalamocortical connectivity is still lacking in primates, despite well-established anatomical maps between specific thalamocortical regions. Here, we mapped whole-brain directional connectivity from higher-order thalamic nuclei, using combined electrical microstimulation (EM) with ultrahigh-field 7 Tesla (7T) fMRI in anesthetized monkeys. EM-fMRI allows us to assess how activity generated in a stimulated thalamic nucleus causally influences distributed brain regions through direct perturbation. Moreover, ultrahigh-field MRI facilitates *in vivo* whole-brain imaging with high resolution and sensitivity. To validate our approach, we first demonstrated that stimulation of the ventral posterolateral (VPL) nucleus reliably evoked activation in the primary somatosensory cortex (S1), consistent with the well-characterized VPL-S1 pathway. We then applied the same protocol to map the network-level effects of stimulating higher-order thalamic nuclei. Notably, stimulation of the CL evoked activation in the frontoparietal network, involved in arousal regulation, along with concurrent activation in the striatum. This activation was clearly distinct from the sensorimotor network responses elicited by stimulation of the adjacent ventrolateral nucleus. Additionally, stimulation of CL elicited responses in MD regions, suggesting functional interactions among thalamic nuclei potentially via thalamo-cortico-thalamic loops. Together, these findings provide a detailed functional map of how distinct higher-order thalamic nuclei differentially influence widespread brain networks in primates.

Keywords : fMRI, Thalamocortical connectivity, Non-human primates, Microstimulation

P-262

Place fields as probabilistic cognitive maps induced by predictive learning

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While hippocampal place fields are believed to represent the allocentric (world-centered) location of an animal, how such representations are learned from egocentric (self-centered) sensory inputs remain unclear. This learning is nontrivial, because egocentric inputs often give noisy (e.g., a step's length can vary) and ambiguous (e.g., different places can look similar), i.e., due to perceptual uncertainty. However, such perceptual uncertainty has rarely been considered in prominent models of the place fields, including the successor representation (SR). Here we show that place fields are better explained by considering perceptual uncertainty. We compared the SR to a Bayesian ideal observer of navigation (BION) inspired by robotics, which optimally considers perceptual uncertainty to update probabilistic beliefs about its location. Unlike the SR, BION could explain how place field size and shape depend on the size and shape of familiar and unfamiliar environments. Notably, this required considering the animal's false beliefs (of being in a familiar environment while it is in fact in an unfamiliar one), underscoring the role of perceptual uncertainty in explaining place fields. We further asked how such probabilistic allocentric representations can be learned from egocentric inputs. We trained recurrent neural networks to predict upcoming egocentric visual input from current visual and self-motion inputs, and found that this leads to internal states that encode the probabilistic beliefs about the location as in BION. These internal states resembled place fields, both in familiar and unfamiliar environments, even though the network was never trained in the latter. Our results suggest that the brain is capable of probabilistic inference, robust against perceptual uncertainty, similar to models in robotics. Furthermore, our results provide a mechanism to learn such a representation: by predicting upcoming egocentric sensory inputs, inspiring research in AI.

Keywords : Bayesian model, Probabilistic representation, Navigation, Cognitive map, Deep learning

Translational and Clinical Neuroscience P-263~P-282

P-263

A novel therapeutic strategy and drug candidate for treating Spinal Cord Injury

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The limited ability of the central nervous system (CNS) to regenerate damaged axons strongly restricts recovery from spinal cord injury (SCI) and other CNS trauma. Regeneration is suppressed by the lack of neuron-intrinsic regenerative capacity and by the neuron-extrinsic

inhibitory environment of the injured CNS. To address this problem, we developed a therapeutic strategy that co-targets kinases in both extrinsic and intrinsic signaling pathways. We identified a kinase inhibitor (RO48) with advantageous polypharmacology (co-inhibits multiple intended targets and avoids detrimental off-targets). RO48 strongly promoted neurite outgrowth in cultured primary neurons in vitro and axon sprouting in a pyramidotomy model of spinal cord injury (SCI) in vivo. We then showed that RO48 promotes corticospinal tract (CST) sprouting and/or regeneration in multiple mouse models of SCI. Notably, these in vivo effects were seen in several independent experimental series performed in distinct laboratories at different times. Finally, in a cervical dorsal hemisection model, RO48 not only promoted growth of CST axons beyond the lesion, but also improved behavioral recovery in the rotarod, gridwalk, and pellet retrieval tasks. Hit-to-lead studies of RO48 revealed a clear structure-activity relationship (SAR), underscored the importance of its polypharmacology profile, and identified a lead candidate, TMP-316, that is currently in preclinical development. Our results suggest that co-targeting protein kinases is a promising therapeutic strategy for SCI and related disorders.

Keywords : Kinase inhibitor, Phenotypic screening, Machine learning, Axon regeneration, Polypharmacology

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P-264

Cross-species transcriptome profiling of mesial temporal lobe epilepsy and corresponding rodent models

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Mesial temporal lobe epilepsy (MTLE) is a common form of drug-resistant epilepsy, underscoring the need for appropriate rodent models to support translational research. In this study, we performed a meta-analysis of transcriptomic data from human MTLE and assessed rodent epilepsy models by comparing their gene expression profiles to those of human MTLE. Analyzing 24 bulk RNA-seq datasets comprising 1,020 samples, MTLE showed upregulation of genes involved in neuroinflammation, gliogenesis, and neuronal death. Additionally, we identified novel genes differentially expressed in chronic drug-resistant MTLE including ADRA1A, PTGS2, and CCL2. Cross-species correlation analysis showed that the kainate intrahippocampal injection model with bilateral sampling most closely resembled MTLE with hippocampal sclerosis (HS), characterized by enriched neuroinflammatory, neurodegenerative, and gliogenic pathways. Conversely, the perforant path stimulation model correlated more strongly with MTLE without HS and with seizure-related initial precipitating events, reflecting transcriptomic signatures involving synaptic plasticity and ion channel dysfunction. These results enhance our understanding of MTLE pathogenesis and drug resistance, while providing a transcriptomic framework for selecting suitable rodent models aligned with specific research goals.

Keywords : Temporal lobe epilepsy, Animal model, Kainate, Neurologic kindling

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P-265

Development of a serum-based miRNA panel for Alzheimer's disease diagnosis

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BACKGROUND: MicroRNAs (miRNAs) are emerging as promising blood-based biomarkers for Alzheimer's disease (AD) because of their stability and regulatory roles in disease-related pathways. This study aimed to develop a serum-based miRNA panel for AD diagnosis. METHODS: Serum samples from 550 participants were categorized into discovery (85 AD, 65 healthy controls [HC]), training (73 AD, 53 HC), and validation (99 AD, 99HC, 36 vascular cognitive impairment [VCI], 40 dementia with Lewy bodies [DLB]) cohorts. We identified a 7-miRNA panel via small RNA sequencing and qPCR and validated it via machine learning. RESULTS: The 7-miRNA panel achieved area under the curve values of 0.970 and 0.928 in the training and validation cohorts, respectively. The risk score derived from the 7-miRNA panel was significantly associated with cognitive impairment (MMSE score, r = -0.72) and plasma amyloid pathology biomarkers (Aβ42/40 ratio, r = -0.25; *p*-tau217, r = 0.36). CONCLUSIONS: A serum-based 7-miRNA panel, which offers a minimally invasive and accessible approach, has strong diagnostic potential for AD.

Keywords : Alzheimer's disease, biomarker, diagnosis, microRNAs, serum

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P-266

Early activity rhythm disruption and behavioral changes in a long-term non-human primate model of Alzheimer's disease

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This study aimed to investigate activity-related and behavioral changes associated with the early progression of Alzheimer's disease (AD) using a long-term non-human primate (NHP) model. To establish the model, amyloid beta 1-42 (Aβ1-42) oligomers were repeatedly administered into the cisterna magna (CM) of NHPs. Behavioral and cognitive monitoring was conducted using a touchscreen-based testing system, allowing for sensitive, longitudinal assessment of psychological and cognitive functions. In parallel, an accelerometer embedded in a wearable necklace continuously tracked daily activity patterns to capture circadian

and behavioral fluctuations. Following Aβ oligomer injections, significant alterations in activity rhythms were observed. Notably, both nocturnal and daytime activity levels increased, suggesting a disruption in normal rest-activity cycles. Additionally, the typical peak in activity shifted, indicating a disturbance in circadian timing, which may reflect early sleep-wake cycle disruptions often seen in patients with Alzheimer's disease. These activity changes were most prominent around one month post-injection and showed partial normalization over time. Alongside these physiological alterations, behavioral testing revealed signs of psychological change, including increased stubbornness and reduced motivation, which mirror affective symptoms observed in early AD. Despite these disturbances, cognitive performance remained stable with no significant deficits detected up to nine months after the injections. These findings demonstrate that the long-term NHP model successfully captures early behavioral and circadian disruptions linked to Alzheimer's pathology, even in the absence of overt cognitive decline. This model provides a valuable platform for studying the prodromal stages of AD, with future work involving neuroimaging and fluid biomarker analyses to further understand disease progression and evaluate potential interventions.

Keywords : Alzheimer's disease, Non-human primate, Behavioral assessment, Circadian rhythm, Amyloid beta oligomer

P-267

Cerebellum and self-esteem in children and adolescents: The moderating effect of depression

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Self-esteem, a critical determinant of psychological well-being, develops concurrently with brain maturation during childhood and adolescence. Emerging evidence has identified the involvement of the cerebellum in self-related processing and its structural links to self-esteem. Depression, which is highly prevalent in this developmental period, affects both self-esteem and cerebellar functions, but their interaction remains understudied in pediatric populations. A community sample of 103 children and adolescents (mean age = 12.23 years) underwent structural magnetic resonance imaging (MRI) to assess the cerebellar gray matter volume (GMV) using voxel-based morphometry. Self-esteem and depressive symptoms were measured using the Rosenberg Self-Esteem Scale and Children's Depression Inventory, respectively. Moderation analyses were performed to determine how depression influences the relationship between the cerebellar GMV and self-esteem. Moderation analyses revealed different cerebellar GMV–self-esteem relationships across cerebellar regions, with depression altering the strength and direction of these associations. In most regions, including crus I and II; lobules VI, VIIb, VIII, IX, and X; and vermis regions VIII and IX, GMV was positively associated with self-esteem at low levels of depression, but this relationship weakened or became nonsignificant as depression severity increased. Conversely, left lobule III and vermis regions I–III exhibited the inverse pattern, with GMV being negatively associated with self-esteem at low depression levels. The distinct relationship patterns across the cerebellar regions underscore the multifaceted role of the cerebellum in self-esteem during critical developmental periods, and depression moderates its functional contribution. Given the neuroplasticity of the brain during childhood and adolescence, understanding these neural–psychological interactions opens new avenues for promoting well-being in the pediatric population.

Keywords : cerebellar volume, self-worth, mental health, childhood, neuroimaging

P-268

Novel microRNA biomarker in human blood and convergence diagnostic medical device for early Alzheimer's disease

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Alzheimer's disease (AD), an intractable disorder responsible for about 80 % of dementia, is detectable by MRI or PET only after it reaches a moderate or severe stage; hence blood-based biomarkers are urgently needed. Here, we discovered novel 18 nt microRNAs (miRNAs) with diagnostic value. EDTA blood from cognitively normal, mild cognitive impairment (MCI) and AD subjects was processed to plasma, stored at –70 °C, and total RNA was isolated with the QIAGEN miRNeasy Serum/Plasma kit. Small-RNA libraries were prepared with the SMARTer smRNA-Seq kit and proceed NGS(Next generation sequencing) on an Illumina NovaSeq 6000. Adapter, quality and length trimming preceded miRDeep2* analysis. A new miRNA having a miRDep2* score of -10 to 10 is derived. Among them, miRNAs having a miRDep2* score of 1 or more, RNAfold of "yes" and a number of feature reads of 10 or more are selected. Target genes were ranked with miRDB, and AD-related high-score hits were filtered, identifying MAP1A, a microtubule-associated protein critical for neuronal homeostasis and synaptic plasticity. SH-SY5Y neuroblastoma cells were transfected with a miRNA mimic, a miRNA inhibitor, or a negative control; western blotting and immunofluorescence showed that over-expression of miRNA markedly reduced MAP1A protein, whereas inhibition restored it, confirming 3′-UTR-dependent regulation. In addition, target sequencing to analyze the expression level of new miRNA in plasma of patients classified as normal, MCI, and AD confirmed the significant difference in the expression level of miRNA in each group. Thus, we have isolated a circulating miRNA that exhibits high specificity and sensitivity, modulates an AD-relevant target, and discriminates clinical stages, underscoring its potential as a minimally invasive biomarker for early AD diagnosis. And It is also possible to develop a convergence diagnostic medical device including a new miRNA detectable dedicated PCR cartridge.

Keywords : microRNA, biomarker, Alzheimer's disease(AD), In vitro diagnostics, convergence diagnostic medical device

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P-269

Sustainability of the effect of taste recall training on taste sensitivity in healthy adults

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The prevalence of taste disorders has approximately doubled over the past three decades in Japan, increasing from an estimated 140,000 cases in 1990 to around 280,000 cases in 2019. This trend is attributed to factors such as zinc deficiency, drug side effects, aging, and COVID-19. Currently, zinc supplementation is the primary therapeutic approach; however, its effectiveness is largely limited to zinc-deficient cases, and effective interventions for other etiologies remain insufficient. To address this unmet need, the present study developed taste recall training, intended to enhance taste discrimination. The training aimed to improve the recognition of four basic tastes (sweet, salty, sour, and bitter) through repeated exposure to sub-threshold taste stimuli, followed by tasks requiring recall and identification of the perceived taste. In a previous study, healthy subjects were assigned to either a training or a control group. After a three-day intervention, the training group demonstrated significant improvements in recognition thresholds for all four basic tastes compared to the control group. The current study further examined the durability of these effects and the influence of training duration by comparing outcomes from three-day and five-day training protocols. Taste assessments were conducted weekly for eight weeks following the intervention. Sustained improvements in taste sensitivity were observed in both groups, with the five-day training group exhibiting greater effect sizes and more robust statistical significance. Importantly, the enhancement in taste sensitivity induced by the training was consistently maintained over the entire eight-week follow-up period. These findings indicate that mental taste recall training may serve as a non-pharmacological strategy for taste rehabilitation. Clinical trials in patients with taste disorders are underway to validate this approach as an accessible alternative to current therapies.

Keywords : Taste disorder, Taste recall training, Non-pharmacological intervention, Non-pharmacological intervention, Sensory plasticity

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P-270

Leveraging inflammatory plasma protein ratios for enhanced parkinson's disease diagnosis

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Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms. Accurate and early diagnosis remains challenging due to symptom overlap with other disorders and the lack of blood-based biomarkers. Inflammation is increasingly recognized as a central mechanism in PD pathogenesis, motivating the search for inflammatory biomarkers. To identify plasma-based inflammatory protein biomarkers and evaluate the diagnostic and prognostic potential of individual proteins and their ratios using Olink Proximity Extension Assay (PEA) and absolute quantification platforms. We analyzed plasma samples from Dopa PET-confirmed PD patients and healthy controls using the Olink Target 96 Inflammation panel. Diagnostic performance was assessed via logistic regression models, including protein ratios computed as NPX value differences. Targeted proteins were further validated using Luminex and Olink Flex platforms in a separate cohort. Correlations with PD severity (UPDRS, Hoehn & Yahr) were assessed using Pearson's correlation. Our findings support the use of inflammatory protein ratios as promising blood-based biomarkers for PD diagnosis. Additionally, absolute concentrations may serve as a potential prognostic marker. Further research is warranted to validate these findings in larger longitudinal studies and to explore their clinical utility in improving PD management.

Keywords : Biomarkers, Diagnosis, Parkinson's disease, Protein ratios

P-271

Risk factors for postoperative cognitive dysfunction in older adults undergoing elective spine surgery: a prospective cohort study

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Background: Postoperative cognitive dysfunction (POCD) is a frequent complication in older adults following spine surgery, associated with prolonged hospitalization and diminished functional recovery. This study aimed to identify modifiable risk factors for POCD by developing a comprehensive risk model that combined structured patient-reported outcomes and traditional clinical markers. Methods: A total of 600 patients aged ≥70 years who underwent elective spine surgery were screened, and after completing all assessments, 374 of them were included in the final analysis. POCD was defined as a decline of ≥3 points on the MMSE from baseline to one week postoperatively. Using hierarchical logistic regression, independent risk factors were identified, including sociodemographic variables in Model 1, clinical variables in Model 2, and preoperative Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) symptom scores in Model 3. Results: POCD occurred in 50 patients (13%). Bivariate analysis showed the POCD group had a significantly higher proportion of females, lower education level (<7 years), poorer preoperative nutritional status (MNA-SF), increased frailty level (K-FRAIL), higher depressive symptom level (GDSSF-K), and increased rates of diabetes mellitus (DM) and postoperative delirium (POD). They also experienced a longer hospital stay. In the final model (Model 3), independent predictors were female sex (OR 3.07, 95% CI 1.16–8.10), education level ≥7 years (OR 0.44, 95% CI 0.21–0.91), preoperative nutritional status (MNA-SF) (OR 0.83, 95% CI 0.70–0.99), DM (OR 2.28, 95% CI 1.15–4.53), POD (OR 5.31, 95% CI 2.55–11.09), and physical function (PROMIS-29) (OR 0.92, 95% CI 0.86–1.00; p = 0.049). Conclusions: Modifiable factors, such as nutritional

optimization, glycemic control, delirium prevention, and preoperative physical function, may help reduce the risk of POCD in older adults undergoing spine surgery.

Keywords : Postoperative cognitive dysfunction, Spine surgery, Older adults

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P-272

A synthetic RNA enhances functional restoration following CNS injury through neuroepigenetic modulation

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Protein synthesis is essential for neural regeneration in the injured central nervous system (CNS). Unlike the peripheral nervous system (PNS), which exhibits inherent regenerative capacity, the CNS is hindered by a non-permissive environment that impedes endogenous repair mechanisms. Thus, restoring translational activity in damaged neurons has emerged as a promising strategy for CNS recovery. In this study, we introduce a synthetic RNA element engineered from the 5′ untranslated region (5′UTR) of *Gpr151* mRNA. This RNA construct (e5′UTR) enhances protein synthesis through its interaction with the RNA-binding protein CSDE1. In mouse models of spinal cord and peripheral nerve injury, administration of e5′UTR significantly improved motor function recovery, accompanied by increased axonal growth. These findings underscore the therapeutic potential of modulating RNA–protein interactions to activate translational control mechanisms in injured neurons. Our work establishes a non-genomic RNA-based platform for promoting functional recovery after CNS injury via neuroepigenetic modulation.

Keywords : Functional recovery, Synthetic RNA (e5'UTR), Spinal cord injury, Protein synthesis, Neuroepigenetic modulation

P-273

Chlorpromazine increases the frequency of EPSC by non-canonical Ca^{2+} elevation of astrocytes

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Chlorpromazine, a widely used antipsychotic for schizophrenia, exerts its effects primarily via dopamine D2 receptor antagonism. However, the precise mechanism by which chlorpromazine acts in the brain is not fully understand. In this study, we investigated the effects and mechanisms of chlorpromazine on synaptic transmission. To investigate the effect of chlorpromazine on the glutamatergic synaptic transmission, we performed spontaneous excitatory postsynaptic currents (sEPSC) in rat primary cortical neurons and miniature EPSCs (mEPSC) in hippocampal CA1 pyramidal neurons. Chlorpromazine increases the frequency of sEPSC and mEPSC. The increase in mEPSC frequency is closely associated with astrocyte. We utilized fura-2 imaging to determine that astrocytic Ca^{2+} is respond to chlorpromazine. Chlorpromazine showed Ca^{2+} elevation by concentration. SKF96365, a TRPC channel inhibitor, and HC030031, a TPRA1 antagonist, were used, and Ca^{2+} levels increased in astrocytes. Additionally, chlorpromazine increased astrocytic Ca^{2+} in external 0 mM Ca^{2+}, suggesting that chlorpromazine increases intracellular Ca^{2+} level of extracellular Ca^{2+}. We utilized store-operated calcium entry (SOCE) to see whether chlorpromazine relates to SOCE. Chlorpromazine showed the additional Ca^{2+} elevation on SOCE, suggesting that chlorpromazine-increased Ca^{2+} is irrelevant to ER Ca^{2+}. After ER Ca^{2+} depletion, Ca^{2+} entry by chlorpromazine was increased when external 0 mM Ca^{2+}, demonstrating that chlorpromazine-increased Ca^{2+} elevation does not require extracellular Ca^{2+}. Chlorpromazine did not change the frequency with NPS2390, group I mGluR1/5 antagonist. These findings suggest that astrocytic glutamate releases by chlorpromazine-mediated non-ER Ca^{2+} elevation enhance the presynaptic glutamate release through the activation of group I mGluR1/5. Our results provide the strategy for reduction of side effect of chlorpromazine.

Keywords : Chlorpromazine, Ca^{2+} elevation, mGluR1/5, Ca^{2+}, tripartite synapse

Acknowledgements : This research was supported by the National Research Council of Science & Technology(NST) grant by the Korea government (MSIT) (No. GTL24021-400) to D.H.W.

P-274

Cell-Type specific contributions of PRX isoforms to Alzheimer's pathology and their therapeutic implications With PRX mimetic

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2-Cys peroxiredoxins (PRX1/2) play critical but distinct roles in Alzheimer's pathogenesis through redox regulation. Our studies reveal PRX1 primarily modulates astrocyte function, while PRX2 protects neurons. Immunohistochemical analysis showed significant accumulation of hyperoxidized PRX (PRX-SO2/3) in both 5xFAD mice and AD patient brains, indicating disrupted redox balance. Genetic deletion studies demonstrated PRX1 knockout exacerbates AD pathology by increasing amyloid burden and reactive astrogliosis. Mechanistically, PRX1 regulates STAT3 phosphorylation in astrocytes, controlling neuroinflammatory responses. In contrast, PRX2 deficiency led to selective neuronal vulnerability without affecting glial activation, demonstrating its neuron-specific protective role against oxidative stress. These findings establish that PRX isoforms maintain cellular homeostasis through cell-type-specific mechanisms. A PRX-mimetic compound targeting these pathways demonstrated therapeutic potential by restoring redox balance and attenuating AD pathology.

Keywords : Peroxiredoxin, Alzheimer's disease, Amyloid, Astrocyte, Neuron

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P-275

Electrophysiological signatures of network remodeling in the retinal detachment mouse model

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Purpose: Retinal detachment (RD) is a major cause of visual impairment requiring prompt surgical reattachment. However, metamorphopsia and blurring often persist after successful surgery, suggesting that RD may induce alterations in the retinal network besides photoreceptor deterioration. To explore this possibility, we investigated retinal network changes related to RD. Methods: RD was induced in mice (C57BL/6J) by trans-scleral subretinal injection of sodium hyaluronate. At post-detachment 24, 72 hours, and 1, 2 weeks, retinal ganglion cell (RGC) spikes were recorded using an 8×8 MEA. With full-field flash stimulation, RGC subtypes (ON or OFF) were classified. To evaluate network alterations, the cross-correlation index (CCI), power spectral density (PSD) of local field potentials (LFPs), and inter-spike intervals (ISI) were analyzed and compared between control and RD mice. The CCI quantified correlated firing strength between RGC pairs, PSD analysis identified LFP frequency components, and ISI analysis assessed the RGC spike frequency. Results: ON-RGC pairs in RD mice exhibited elevated CCI at all post-detachment time points ($p < 0.05$; control *vs.* RD), peaking at 1 week ($p < 0.001$). PSD analysis revealed that the number of RGCs exhibiting abnormal 5–10 Hz oscillations increased after RD induction, peaking at 2 weeks ($p < 0.05$ *vs.* control). In the 2-week RD group, ISI analysis also showed a significant increase in RGCs displaying multiple peaks ($p < 0.05$ *vs.* control). Conclusion: Enhanced CCIs in RD retinas suggest an abnormally clustered firing of RGC, indicating the presence of retinal network remodeling. This observation is further supported by the detection of oscillatory rhythms in LFPs and the increased presence of multiple peaks in ISI histograms—both recognized features of retinal network remodeling. Our findings suggest that the retinal network remodeling in RD may contribute to poor visual recovery even after successful retinal reattachment surgery.

Keywords : Retinal detachment, Retinal remodeling, Multielectrode array, Cross correlation, Oscillatory rhythm

Acknowledgements : This research was funded by a grant from the National Research Foundation (NRF) of the Ministry of Science and ICT (MSIP) of Korea (RS-2024-00340391).

P-276

Dynamic patterns of relative phase in ADHD brain activity: A resting-state EEG study

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Introduction Attention-Deficit/Hyperactivity Disorder (ADHD) is marked by persistent attentional and regulatory difficulties, yet accessible and precise diagnostic tools remain scarce (Brandeis et al., 2018, DOI:10.1093/med/9780198739258.003.0010). Cognitive theories propose that ADHD involves diminished top-down control and impaired coordination with bottom-up processing. To examine this imbalance and support biomarker development, we applied Relative Phase Analysis to resting-state EEG data from children with inattentive-type ADHD and controls. Method We analyzed eyes-open and eyes-closed EEG data from 30 children with inattentive-type ADHD and 30 age-matched controls under age 10. RPA was performed by (i) extracting the phase of each signal using the Hilbert transform and (ii) subtracting the global mean phase to assess relative phase lead/lag patterns (Park et al., 2025, DOI:10.1101/2025.03.12.642768).Phase-leading regions were interpreted as sources, and lagging regions as sinks of directional activity flow. Result Both groups exhibited alternating phase dynamics between anterior-to-posterior (higher order cognitive anterior area phase leading posterior area interpreted as top-down information flow) and parietal-to-anterior (parietal area phase-leading anterior area interpreted as bottom-up information flow) modes. However, the ADHD group showed a significantly higher occurring frequency of bottom-up mode, with more self-transitions within this mode under both eyes-open and eyes-closed conditions. These results support the hypothesis that reduced top-down modulation facilitates excessive bottom-up processing in ADHD. Conclusion Our findings indicate dominant bottom-up dynamics in inattentive-type ADHD, reflecting impaired top-down regulation. Group differences in phase dynamics suggest RPA-derived features hold promise as physiological biomarkers for ADHD diagnosis. Future work will investigate task-related dynamics and expand to additional ADHD subtypes.

Keywords : Relative Phase Analysis, EEG Phase Dynamics, Top-down – bottom-up, ADHD Diagnoses, Psychological diagnostic marker

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P-277

Altered muscle synergies during gait in posterior cord syndrome

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Posterior cord syndrome (PCS) is a rare incomplete spinal cord injury characterized by damage to the dorsal columns, resulting in proprioceptive deficits while motor function remains relatively preserved. Loss of proprioception often leads to gait disturbance due to impaired balance and coordination. This study aimed to investigate the neuromuscular control mechanism and muscle synergy patterns during walking in PCS patients. Ten PCS patients (mean age 57 ± 13.8 years) and nine age-matched healthy controls (mean age 60.9 ± 7.4 years) walked 8 m at a self-selected speed while lower-limb muscle activation was recorded using motion capture and a wireless electromyography system. Seven gait cycles per participant were analyzed; EMG signals were peak-normalized, time-interpolated to 700 points, and normalized to the window maximum. To identify common muscle synergies across all participants, k-means clustering was applied. Functional ability was assessed with the Berg Balance Scale and the modified Barthel Index.

The mean number of muscle synergies was 3.82 ± 0.18 in controls and 3.55 ± 0.34 in the PCS group (U = 67.5, p = 0.065). Clustering arranged synergies into eight clusters with a mean intraclass correlation coefficient of 0.63 ± 0.06 (range 0.51–0.73). Of these, one cluster was specific to PCS, four to controls, and three were non-specific. Notably, PCS patients in the primary PCS-specific cluster were absent from all control-specific clusters. These findings suggest that posterior cord damage alters the structure of muscle synergies without reducing neural complexity.

Keywords : Posterior cord syndrome, Motion capture, Electromyography, Muscle synergy, K-means clustering

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P-278

Generating 3D whole-brain neurovascular coupling maps using resting-state fMRI and ASL: a preliminary study

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Neurovascular coupling (NVC) refers to the mechanism by which cerebral blood flow (CBF) is regulated in response to neural activity. Previous studies have generated NVC maps on the cortical surface in a vertex-wise manner. While surface-based NVC mapping has provided valuable insights, it is limited in capturing whole-brain interactions and lacks depth information. In this study, we aimed to construct 3D whole-brain voxel-wise NVC maps to enable comprehensive assessment of neurovascular dynamics with preserved cortical depth and subcortical coverage. This study used de-identified data from a longitudinal neuroimaging study funded by NIH (NIH R01NS065980; PI: Junghoon J. Kim, PhD, CUNY School of Medicine). Resting-state blood oxygen level–dependent (BOLD) and arterial spin labeling (ASL) images were acquired to generate fractional amplitude of low-frequency fluctuations (fALFF) and cerebral blood flow (CBF) maps, respectively. The CBF maps were co-registered to the fALFF maps for NVC calculation. To reduce interpolation artifacts at the brain boundary, voxels with cerebrospinal fluid (CSF) signal intensity lower than the mean minus one standard deviation were excluded from fALFF and the registered CBF maps. Voxel-wise locally weighted linear regression was then performed using fALFF as the dependent variable and CBF as the independent variable within each patch (9×9×9 voxels). The resulting t-statistic of the regression slope was used as the voxel-wise NVC index. Compared to uncorrected NVC maps, corrected maps demonstrated reduced signal irregularities at the outer brain boundaries, suppression of abnormally high values in peripheral voxels (see red arrows in Figure 1), and improved visual homogeneity within cortical regions. The present study proposed a new approach for generating a 3D whole-brain NVC map that captures local NVC patterns while minimizing boundary-related artifacts. Further research is warranted to validate its utility in clinical applications.

Keywords : Neurovascular coupling, Cerebral blood flow, Arterial spin labeling, Fractional amplitude low-frequency fluctuations, Blood-oxygen-level-dependent

P-279

Prediction of acute postoperative pain intensity using EEG phase characteristics in patients under propofol anesthesia

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Background: Moderate-to-severe postoperative pain is common (20–80% prevalence) and can increase healthcare burdens and chronic pain risk. Thus, accurate pain assessment in anesthetized patients is challenging. Autonomic responses (e.g., heart rate, blood pressure) are often used as indicators but lack clinical reliability. Prior EEG-based approaches using spectral power have not yielded significant results in distinguishing between pain groups (mild vs. severe). This study examines whether electrocortical dynamics—particularly phase-based EEG features between prefrontal and frontal regions—can predict the intensity of acute postoperative pain under propofol anesthesia, as phase dynamics may reflect directionality of information flow (Park et al., 2025). Methods: We recorded 4-channel prefrontal EEG (Fp1, F7, Fp2, F8) from 64 patients at Kangbuk Samsung Hospital. Patients were divided into mild (NRS<4, n=32) and moderate-to-severe (NRS>4, n=32) pain groups. EEG was analyzed at baseline, induction, unconscious, and emergence stages using power spectrograms, relative phase (RP), and connectivity metrics (PLE, PLI, wPLI, dwPLI, coherence) across 0.5–50 Hz. Results: RP-based phase dynamics analysis revealed distinct directionality and phase relationships between prefrontal and frontal regions in the beta–gamma bands (14–50 Hz) during deep anesthesia and emergence. The prefrontal region consistently led the frontal region in both groups, but the severe-pain group showed a greater RP difference, suggesting stronger directional coupling. This was most pronounced between the right prefrontal (Fp2) and left frontal (F7) regions. Conclusion: Phase dynamics between prefrontal-frontal regions during deep anesthesia and emergence, especially in the 14–50 Hz range, may serve as reliable indicators of postoperative pain under propofol. The Fp2–F7 combination is especially meaningful, capturing prefrontal–frontal and interhemispheric dynamics, and may improve pain assessment accuracy.

Keywords : Prefrontal EEG, Power dynamics, Phase dynamics, Functional connectivity, Propofol-induced postoperative pain

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P-280

Enhancing the efficacy of low-dose doxorubicin using focused ultrasound: A strategy to reduce toxicity

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Introduction Doxorubicin is a first-generation cytotoxic anticancer agent that exhibits strong therapeutic efficacy but also induces significant toxicity by damaging normal cells in addition to tumor cells. Therefore, this study aims to reduce the dose of Doxorubicin below the standard

clinical level (5.67 mg/kg) and combine it with Focused Ultrasound (FUS), with the goal of maintaining the anticancer efficacy of the standard dose while minimizing adverse effects such as systemic toxicity. Materials and Methods Before initiating in vivo experiments, the cytotoxicity of Doxorubicin was first evaluated in vitro. Cell viability at various concentrations was assessed using the Cell Counting Kit-8 (CCK-8). Subsequently, a glioblastoma model was established by implanting C6 cells into the frontal cortex of rats. The animals were divided into three groups: control, Doxorubicin-only, and Doxorubicin combined with Focused Ultrasound (FUS). In vivo drug delivery and distribution of Doxorubicin were monitored using magnetic resonance imaging (MRI). Results Based on the IC50, the concentration range of Doxorubicin was further refined in vitro. Apoptosis level shifts were used to determine the timing of repeated ultrasound application in the in vivo experiments. In vivo, co-administration of Focused Ultrasound (FUS) with a reduced dose of Doxorubicin resulted in lower toxicity to normal cells compared to Doxorubicin monotherapy, while effectively reducing tumor volume. Conclusions This study demonstrated that using Focused Ultrasound (FUS) allows for a reduced dose of Doxorubicin while maintaining anticancer efficacy comparable to the standard clinical dose and minimizing toxicity to normal cells. These findings suggest that FUS-assisted combination therapy has the potential to maximize therapeutic outcomes while minimizing side effects. Furthermore, this approach may be applicable to a wider range of treatment scenarios beyond conventional protocols.

Keywords : Drug deilvery, Doxorubicin, Focused Ultrasound, Glioblastoma

P-281

Developed a novel peptide targeting the high-affinity EPOR site activated in ischemic stroke and verified receptor-level changes in silico

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Ischemic stroke divides the affected brain into two zones: the core and the penumbra. The penumbra is hypoperfused tissue that surrounds the infarct core; although it has lost its electrical activity and its metabolism is suppressed, it is not yet irreversibly damaged and therefore remains salvageable. Thanks to collateral blood flow, cells in the penumbra can survive for several hours. Clinically, the larger the penumbra that can be preserved, the better the neurological recovery—a correlation demonstrated in numerous studies. Accordingly, acute stroke therapies such as intravenous thrombolysis and mechanical thrombectomy aim to reperfuse the penumbra as rapidly as possible, rescuing this tissue at risk, limiting neuronal death, and improving outcomes. One critical point, however, is that the penumbra undergoes programmed cell death over the course of hours. If treatment is delayed, penumbral cells progressively die, expanding the permanent infarct. Importantly, this injury mechanism affects not only neurons and glia but also endogenous neural stem cells in the brain, underscoring the need to boost stem-cell–driven repair in the ischemic milieu. The novel peptide we propose binds to the strong binidng site of Erythropoietin receptor, stimulates stem-cell proliferation in the subventricular zone (SVZ), and is expected to promote neuronal survival and neuroregeneration. Beyond the protective effects of existing Erythropoietin-derived peptides, our compound is designed to actively enhance proliferation, thereby contributing to cell regeneration after stroke.

Keywords : Ischemic brain, Peptide drug, Protein structure prediction, Molecular Dynamics

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P-282

Effects of a biofeedback-based sleep aid smartphone application on post-stroke sleep disorders: Case report

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Post-stroke sleep disorders (PSSD), especially insomnia, significantly hinder stroke recovery, yet standardized treatments are lacking. Current pharmacologic and cognitive-behavioral therapies often show limited efficacy, safety, or practicality, particularly in acute stroke settings. This preliminary study explored the feasibility of a smartphone-based biofeedback application as an alternative intervention for insomnia in PSSD patients. The app collects respiratory data, calculates an optimal breathing rate, and provides immediate feedback to regulate the autonomic nervous system (ANS). It features dynamically generated auditory feedback (music based on user input) and visual guidance to help users maintain the calculated breathing rate. An on-off study design evaluated intervention efficacy, with sleep quality assessed via the K-RCSQ, ISI, and PSQI. Three male patients with subacute PSSD, unresponsive to pharmacotherapy, participated. All showed improved subjective sleep quality during intervention. K-RCSQ scores increased in all cases, with two patients reaching higher sleep quality categories. ISI scores exceeded the MCID of 6 points for all, and two achieved remission (ISI < 8). PSQI scores showed meaningful improvements (dPSQI >3 points), though full remission (PSQI <5) wasn't reached. The intervention was well-tolerated, with no adverse effects. Its accessibility, usability, and safety were notable. These findings suggest this biofeedback application, with its audiovisual stimuli and user-input-driven music, is a non-invasive, cost-effective, and scalable alternative for PSSD. Its rapid action, strong safety profile, and ease of use highlight its potential as both an adjunctive and standalone therapy. However, larger, randomized controlled trials with long-term follow-up are needed to validate these results and explore sustained benefits.

Keywords : Post-stroke insomnia, Biofeedback application, Autonomic nervous system (ANS), Sleep quality, Digital Therapeutics

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Poster Session 2

P283-P564

Day 2(Aug 25, 2025)	13:30-18:00	[Exhibition/Poster Hall]
Day 3(Aug 26, 2025)	8:30-12:30	[Exhibition/Poster Hall]

Mechanisms of Brain Disorders P-283~P-341

P-283

Poster Award Candidate

Neurodevelopmental disease-associated WWP1 gain-of-function drives developmental anoikis through TGFβ pathway

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The E3 ubiquitin ligase WWP1 orchestrates multiple cellular functions, yet the neurodevelopmental role and pathological implications of its dysregulation remain poorly defined, in contrast to its established oncogenic effects. Here, we demonstrate that hyperactive WWP1 induces neurodevelopmental abnormalities characterized by impaired neuronal migration and caspase-dependent cell death in the developing mouse brain and human neural progenitor cell models. Mechanistically, WWP1 gain-of-function (GOF) mutation disrupts cell adhesion, leading to detachment-induced cell death. Pathway-level screening identifies TGFβ1 ligand treatment to restore cell survival in both neural progenitor cultures and embryonic mouse brains. Conversely, TGFβ pathway inhibition phenocopies WWP1-induced apoptosis, establishing that WWP1 hyperactivity promotes cell death via TGFβ pathway downregulation. Transcriptomic profiling of the WWP1 GOF cellular models confirms the downregulation of cell adhesion and TGFβ signaling pathway signatures, highlighting the necessity of balanced WWP1 activity during neurodevelopment. In addition, we clinically identified a novel WWP1 variant in a patient with an undiagnosed neurodevelopmental disease presenting with epileptic encephalopathy. Biochemical and *in vivo* functional analysis characterizes the novel variant as GOF, supporting the clinical relevance of WWP1 dysregulation in neurodevelopmental disorders.

Keywords : WWP1, E3 ligase, Neurodevelopment, Anoikis, TGFβ signaling

Acknowledgements : This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (RS-2023-00265883, RS-2024-00350610).

P-284

Neuregulin-1 mitigates autism-like behaviors in adolescent rats prenatally exposed to valproic acid

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Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder marked by impaired social interaction and repetitive behaviors, with prenatal valproic acid (VPA) exposure as a known risk factor. This study investigates the effects of Neuregulin 1 (NRG1) on autism-like behaviors in a rat model induced by prenatal valproic acid (VPA) exposure. NRG1 administration improved social deficits and repetitive behaviors, suggesting its potential to restore ASD-like behavioral impairments. NRG1 administration restored the VPA-induced alterations in ErbB4 pathway-related protein levels in the hippocampus, suggesting its role in rescuing disrupted signaling. We also observed decreased levels of synaptic markers and mature form spine number in ventral hippocampus (vHPC), which were ameliorated by NRG1. Our results offer novel insights into the therapeutic potential of NRG1 in alleviating ASD-like symptoms, emphasizing its ability to restore the neuronal signaling pathway and synaptic plasticity affected by prenatal VPA exposure.

Keywords : Autism Spectrum Disorder, Neuregulin1, ErbB4, Synaptic plasticity, Valproic acid

P-285

Poster Award Candidate

Effect of transcutaneous vagus nerve stimulation on ketamine reinstatement

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Despite growing concerns over ketamine addiction, the underlying mechanisms of relapse and effective therapeutic interventions remain poorly understood, especially in comparison to opioids and psychostimulants. Previous studies have demonstrated that vagus nerve stimulation (VNS) reduces relapse-like behaviors in animal models of cocaine and heroin addiction, and VNS is already used clinically to treat depression and epilepsy. In this study, we established a cue-induced reinstatement model of ketamine addiction in mice and evaluated the effects of transcutaneous VNS (tVNS) on relapse-related behaviors and neural activity across addiction-related brain regions. Using a self-administration paradigm followed by extinction and cue-induced reinstatement, behavioral analysis revealed a rapid decrease in active lever pressing during extinction, and a significant increase in drug-seeking behavior during reinstatement. c-Fos immunostaining revealed increased neuronal activity in the hippocampus, medial prefrontal cortex (mPFC), and central amygdala (CeA), suggesting their involvement in ketamine-induced relapse. Notably, tVNS-treated mice exhibited lower level of drug-seeking behavior compared to controls. These findings suggest that tVNS may attenuate ketamine craving and relapse by modulating neural excitability within key addiction-relevant circuits.

Keywords : Social behavior, Decision-making, Motivation, Nucleus accumbens, Dopamine

P-286

Poster Award Candidate

Cognitive reserve and its genetic basis modulate transsynaptic tau propagation in Alzheimer's disease

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Cognitive reserve (CR) refers to the phenomenon by which certain individuals maintain better-than-expected cognitive performance despite significant Alzheimer's disease (AD) pathology. This study aimed to characterize the biological underpinnings of CR and its

impact on cognitive outcome, tau pathology dynamics and brain network vulnerability. CR was operationalized as the residual from a regression model predicting cognition based on global amyloid-ß and tau PET burden, age, sex, Mini-Mental State Examination (MMSE) results and intracranial volume in 589 subjects from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database to capture resilience unexplained by pathology or demographics. To investigate the basis of this phenomenon, we conducted a genome-wide association study (GWAS) using CR residuals and identified several nominally significant SNPs mapped to genes involved in synaptic metabolism and transcriptional regulation. Notably, many of these genes are implicated in mechanisms relevant to transsynaptic communication, adding biological plausibility to the hypothesis that tau propagation follows transneuronal spread along functional and structural pathways. We then modeled tau propagation using the epidemic spreading model (ESM) and examined how CR levels and CR-associated genotypes influenced patterns of tau spread. Individuals with higher CR or protective genotypes showed attenuated or spatially altered tau diffusion patterns, particularly in heteromodal association cortices such as lateral temporal and inferior parietal lobes. These findings extend prior works which demonstrated that regional Aß-tau interactions and network architecture drive the onset and acceleration of tau spread. By contrast, our study highlights why some individuals are less susceptible to these network-based mechanisms, suggesting that the genetic correlates of CR serve as biologically grounded moderators of transsynaptic tau propagation in AD.

Keywords : Alzheimer's disease, Cognitive reserve, PET

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P-287

Astrocyte priming enhances microglial Aβ clearance and is compromised by APOE4

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Innate immune priming, which enables heightened responses upon secondary challenge, has been primarily characterized in peripheral immune cells and, more recently, in microglia under disease-associated conditions. Here, we show that human iPSC-derived astrocytes, but not microglia, acquire a primed state following transient immune stimulation under non-disease conditions. Upon subsequent exposure to amyloid-β(Aβ), primed astrocytes increased the release of cytokines in the media that enhanced microglial Aβ phagocytosis. In contrast, astrocytes carrying the *APOE4* allele exhibited reduced priming capacity and failed to promote microglial Aβ clearance. Transcriptomic analyses revealed that Aβ-treated primed astrocytes showed gene expression patterns inversely correlated with early-stage Alzheimer's disease (AD) brains, suggesting a potential protective role. These effects were confirmed in co-culture of astrocyte and microglia, cerebral organoids, and APOE knock-in mouse models, where astrocyte priming induced microglial activation and Aβ clearance which is deminished in the presence of APOE4. Our findings identify astrocyte immune memory as a modulator of microglial phagocytic activity and Aβ pathology, providing insight into early protective mechanisms disrupted by genetic risk factors in AD.

Keywords : hiPSC-derived models, Astrocyte priming, Amyloid-β, Microglial phagocytosis, APOE4

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P-288

Longitudinal characterization of seizure evolution in *CYFIP2* p.Arg87Cys mouse model of West syndrome

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West syndrome is a severe early-onset epileptic encephalopathy characterized by infantile spasms. However, many patients subsequently develop other types of seizures, a progression known as seizure evolution, which is significantly linked to poor long-term outcomes. Despite clear clinical recognition, the underlying neurobiological mechanisms remain poorly understood. Recent genetic studies have identified a recurrent *CYFIP2* p.Arg87Cys variant in West syndrome patients, and the *Cyfip2*$^{+/R87C}$ mouse model carrying this mutation has been shown to recapitulate key symptoms of the disorder, including infantile spasms. To investigate the underlying mechanisms of seizure evolution, we conducted a longitudinal, in-depth characterization of *Cyfip2*$^{+/R87C}$ mouse model from the neonatal stage to seven months of age. Using long-term video-EEG monitoring, we observed a progression from neonatal spasms to a latent seizure-free phase,

followed by spontaneous recurrent seizures in adulthood, ultimately leading to premature death. During disease progression, we observed progressive neuronal loss, synaptic remodeling, sequential activation of different glial cell types, lipid droplet accumulation in astrocytes, and significant proteomic and lipidomic changes in the brain. Overall, these findings suggest that seizure evolution in West syndrome is mediated by dynamic, temporal cellular and molecular changes in neurons and glial cells and dysregulation of lipid metabolism. Our study deepens the understanding of seizure evolution and suggests that targeting these changes could offer novel therapeutic strategies.

Keywords : West syndrome, Seizure evolution, CYFIP2 p.Arg87Cys, Neuronal-glial interaction, Lipid metabolism

P-289

Investigating the effects of thalamic reactive astrocytes on Alzheimer's disease progression

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Alzheimer's disease (AD) is the leading cause of dementia, accounting for 60-80% of dementia cases, and is characterized by progressive cognitive decline caused by synaptic dysfunction and subsequent irreversible neuronal loss. Most pathological studies have focused on the abnormal intracellular accumulation of neurofibrillary tangles and extracellular accumulation of amyloid-beta plaques as a cause for this impairment, yet no effective treatment for AD has been discovered. Thus, having a clear understanding of the mechanisms of the disease is crucial for therapeutic advancements. Recent studies using PET imaging, plasma, and CSF biomarkers suggest reactive astrogliosis—a state in which astrocytes become hypertrophic and highly immunoreactive in response to CNS injury or inflammation—may emerge before classical AD hallmarks such as amyloid beta plaque deposition and tau tangle accumulation. This raises the possibility that reactive astrocytes represent early biomarkers or modulators of AD pathogenesis. However, the contribution of reactive astrocytes in brain regions beyond the cortex and hippocampus remains underexplored. To investigate the effects of reactive astrogliosis on AD progression, we performed histopathological analysis of 5xFAD mouse brains at 3, 6, 9, and 12 months of age, followed by morphological analysis of individual astrocytes and electrophysiological recordings of thalamocortical neurons in healthy and disease model mice. Our findings suggest that early-onset thalamic astrogliosis is a prominent and underrecognized feature of AD progression in the 5xFAD model. These results support the notion that the thalamus may serve as an early site of pathological change and that reactive astrocytes may offer insight into novel diagnostic or therapeutic approaches.

Keywords : Alzheimer's disease, Reactive astrocytes, Thalamus, Early-onset, Neurodegeneration

P-290

Discriminative stimulus properties of psilocybin and substituted tryptamines on mesolimbic area

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Substance Use Disorder (SUD) remains a critical and increasingly prevalent global health issue, shaped by complex interactions among biological, psychological, and environmental factors. Tryptamines, a class of hallucinogenic compounds structurally related to serotonin, have gained increasing attention due to their psychoactive properties and increasing presence in illicit drug markets. Although compounds such as psilocybin are generally regarded as having low addictive potential, repeated use may still result in compulsive, reward-driven behaviors. Despite their rising use, the precise impact of tryptamines on the brain's reward circuitry remains inadequately understood. To explore the behavioral and neurobiological effects of psilocybin and its synthetic analogs, we examined the discriminative stimulus properties of psilocybin in mice and evaluated the substitution potential of synthetic tryptamines, including 4-OH-MET, 5-MeO-2-TMT, and 4-Aco-DALT. We further assessed their influence on neural activity and neurotransmitter release in the nucleus accumbens (NAc), with a focus on the underlying neuronal and astrocytic mechanisms. The psilocybin cue fully or partially generalized to the tested synthetic tryptamines. Systemic administration of psilocybin and its analogs significantly decreased GABA release while increasing neuronal firing rates in the NAc. Immunocytochemical analyses further revealed that psilocybin modulates GABA release primarily through astrocytic, rather than neuronal, mechanisms. Taken together, these findings suggest that psilocybin and its synthetic analogs alter NAc activity by decreasing GABAergic transmission and promoting neuronal excitability, predominantly via astrocyte-mediated mechanisms.

Keywords : Psilocybin, Synthetic tryptamines, Substance Use Disorder(SUD), Nucleus accumbens(NAc), GABA release

Acknowledgements :

P-291

Neurovascular restoration through treadmill exercise mitigates age-related cognitive impairment

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Aging is associated with various physiological changes, including microvascular dysfunction, which impairs cerebral blood flow and neuronal health, leading to cognitive impairment. While exercise has demonstrated positive effects on aging process, its specific impact on

age-related microvascular dysfunction and blood-brain barrier (BBB) disruption requires further investigation. This study aimed to evaluate whether an 8-week treadmill exercise regimen in aged mice could improve cognitive impairment by alleviating microvascular and BBB damage, as well as reducing neuroinflammation. In this study, twenty-month-old C57BL/6J male mice were subjected to a treadmill exercise program, consisting of 60 minutes of daily exercise over 8 weeks. The results showed that treadmill exercise increased microvessel length and decreased fragmentation, indicating improved microvascular integrity. The exercise regimen led to a reduction in the activation of these cells, suggesting a decrease in neuroinflammatory responses. BBB integrity was evaluated by examining the expression levels of tight junction proteins, including ZO-1, Occludin, and Claudin-9, as well as PDGFRβ in the cortex, through immunostaining and Western blotting. Treadmill exercise preserved BBB integrity by maintaining the expression of these proteins, counteracting the age-related decline typically observed. Overall, the findings of this study suggest that regular treadmill exercise effectively mitigates cognitive impairment and vascular dysfunction associated with aging by enhancing microvascular health and maintaining BBB integrity. These results highlight the potential of exercise as a non-pharmacological strategy for treating age-related neurodegenerative diseases, primarily through the preservation of vascular and BBB structures and the reduction of neuroinflammation. This study underscores the importance of physical activity in promoting brain health and resilience against age-related cognitive impairment.

Keywords : Aging, Cognitive impairment, Treadmill exercise, BBB, Neuroinflammation

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P-292

Adenine base editing of *BEST1* for modeling best disease

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The *BEST1*, located on chromosome GRCh38 11q12.3, encodes a transmembrane pentameric protein consisting of 585 amino acids. *BEST1* functions as a Ca^{2+}-activated Cl^- channel in the RPE (Retinal Pigment Epithelium) cells of the retina. When Ca^{2+} binds to the channel, Cl^- enters the RPE, maintaining ion homeostasis and fluid balance, which helps preserve retinal structure. Over 250 pathogenic *BEST1* mutations can cause retinal diseases. Among these, Best disease is a macular degeneration caused by *BEST1* mutations. Unlike other macular degenerations, it originates in the RPE, making it suitable for RPE-specific research. It is the most common hereditary macular dystrophy, appearing from adolescence to early adulthood, with an egg-yolk-like fundus change in both maculae. Loss of *BEST1* function leads to ion imbalance and lipid-protein aggregate accumulation between the RPE and photoreceptors, causing vision loss and central visual field defects. To create a gene editing based disease model and explore therapies, we used ABE to substitute A-to-G in *BEST1* and studied editing efficiency and off-target effects. Five candidate sites related to Best disease were selected. HEK293T cells were transfected with ABE and sgRNAs by lipofection, and Deep sequencing was performed. Three sgRNA target sites (Candidates 2, 3, 4) showed the highest editing efficiency(~27%). To assess correlation with tumor suppressor genes, we aligned the five *BEST1* target sequences with tumor suppressor genes and analyzed a graph showing total matches of 23 nucleotides and seed matches of 8 nucleotides. We aim to investigate the efficiency and off-target effects of various ABE and sgRNA delivery methods for RPE cells. Additionally, we plan to generate a humanized best disease mouse model to assess efficiency of A-to-G substitution and off-target effects in vivo. Furthermore, we aim to understand sgRNA impact on tumor suppressor genes, providing guidance on minimizing side effects in gene editing applications.

Keywords : BEST1, RPE, Best disease, Adenine base editor, gene editing

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P-293

SGLT2 inhibition by Enavogliflozin significantly reduces Aβ pathology and restores cognitive function via upregulation of microglial AMPK signaling

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline. Metabolic dysfunctions, particularly type 2 diabetes mellitus (T2DM), have been implicated in AD pathogenesis, highlighting the potential for novel therapeutic approaches targeting shared underlying mechanisms. Here, we investigate sodium-glucose cotransporter 2 (SGLT2) inhibition as a therapeutic strategy for AD using Enavogliflozin, a potent SGLT2 inhibitor, in the 5XFAD mouse model. Five-month-old 5XFAD mice were treated with Enavogliflozin (0.1 mg/kg or 1 mg/kg) or vehicle for 8 weeks. The higher dose significantly improved cognitive performance in Y-maze and Morris Water Maze tests, which correlated with enhanced synaptic plasticity and increased acetylcholine levels. Moreover, Enavogliflozin treatment reduced Aβ pathology and plaque burden, particularly affecting larger plaques. Mechanistically, SGLT2 inhibition attenuated neuroinflammation by suppressing NF-κB signaling and proinflammatory cytokine production while promoting microglial recruitment to plaques. In vitro and ex vivo analyses further revealed that Enavogliflozin enhances microglial phagocytic capacity via AMPK-mediated mitochondrial biogenesis and function. These findings highlight the multifaceted neuroprotective effects of SGLT2 inhibition in AD, demonstrating its potential to mitigate pathology and improve cognitive function. By uncovering its impact on neuroinflammation and microglial function, this study establishes SGLT2 inhibition as a promising therapeutic avenue for AD and other neurodegenerative disorders.

Keywords : Alzheimer's disease, SGLT2 inhibition, Anti-diabetic drugs, amyloid-beta, cognitive function

P-294

Neuroprotective effect of pimobendan in amyloid-beta treated primary neurons and 5xFAD Alzheimer's disease mice model

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Alzheimer's disease (AD) is the most common neurodegenerative disorder, characterized by the accumulation of amyloid-β (Aβ), for which no curative treatment is available and the etiology remains poorly understood. In this study, we explored the potential of PDE3 inhibitors—previously reported to have antioxidant and anti-inflammatory effects—as part of a drug repurposing approach to discover new therapeutic agents for AD. Through cell-based screening using an FDA-approved drug library, we identified pimobendan, a selective PDE3 inhibitor, as a potential candidate with beneficial effects for AD. In Aβ-induced *in vitro* AD model, pimobendan significantly attenuated Aβ-induced apoptosis in a dose-dependent manner. In addition, pimobendan dramatically inhibited MAPK-induced reactive oxygen species production and mitochondrial dysfunction. Neuroprotective effect of pimobendan also validated in 5xFAD *in vivo* AD model. Mice were administered pimobendan (10 or 100 mg/kg, intraperitoneally) for two weeks. Interestingly, administration of pimobendan at a dose of 100 mg/kg showed a tendency to improve learning and memory performance in the passive avoidance test. These findings suggest that pimobendan may enhance cognitive function by modulating oxidative stress and promoting mitochondrial recovery, rather than by reducing Aβ accumulation. Further investigation is required to elucidate its underlying mechanisms and assess its potential as a repurposed therapeutic candidate for AD.

Keywords : Alzheimer's disease, Drug repurposing, PDE3 inhibitor, Pimobendan, Proteomics

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P-295

Impact of SSRI exposure during development on Autism Spectrum Disorder (ASD)

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Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by restricted, repetitive behaviors and deficits in social communication. Serotonin (5-HT) plays a critical role in brain development, including synaptogenesis and plasticity, and is implicated in ASD pathogenesis. Elevated blood serotonin levels and genetic variations in serotonin-related genes have been associated with ASD. Selective serotonin reuptake inhibitors (SSRIs), which increase synaptic serotonin, are commonly prescribed to manage mood and anxiety symptoms in ASD. However, growing evidence suggests that prenatal SSRI exposure may affect fetal brain development and increase ASD risk. This study examined the behavioral and neurobiological effects of prenatal fluoxetine (FLX) exposure in mice. Pregnant mice received FLX from embryonic day (E) 12 to birth. Offspring were tested in the open-field (locomotion, anxiety), repetitive behavior (grooming, rearing, digging), and social interaction tests (three-chamber, direct interaction). Hippocampal expression of C-Fos (neuronal activity marker) and 5-HT7 receptor (5-HT7R) was analyzed using immunohistochemistry. FLX-exposed offspring showed reduced locomotion and fewer center zone entries in the open field, indicating increased anxiety-like behavior. Grooming and rearing were elevated, while social interaction remained unaffected. C-Fos expression in the hippocampus was decreased, suggesting lower neuronal activity, whereas 5-HT7R expression was increased, indicating altered serotonergic signaling. These results suggest that prenatal FLX exposure induces anxiety-like and repetitive behaviors and alters hippocampal function. This model may help clarify how early SSRI exposure contributes to ASD-related phenotypes and inform safer therapeutic approaches during pregnancy.

Keywords : SSRI, Autism, Development

P-296

Effects of *Humulus japonicus* water extract on the cholinergic system and neuroplasticity in age-related cognitive decline

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Aging is often accompanied by a decline in cognitive functions such as learning and memory, which has been associated with decreased hippocampal neurogenesis and dysfunction of the cholinergic system. *Humulus japonicus* (HJ), a plant belonging to the Cannabaceae family, has shown potential neuroprotective properties in models of neurodegenerative diseases including Alzheimer's and Parkinson's disease. However, its effects on cognitive decline associated with normal aging have not been thoroughly investigated. In this study, we aimed to explore the potential of *Humulus japonicus* water extract (HJW) to modulate cognitive function in aged mice and in a scopolamine-induced amnesia model. Behavioral assessments such as the novel object recognition and Morris water maze tests were employed to evaluate learning and memory functions. In addition, we examined acetylcholinesterase (AChE) activity and associated intracellular signaling pathways, such as CaMKIIα/CREB and AKT/GSK3β, along with neurogenesis in the hippocampus of mouse brain. This research aims to determine whether HJW can influence age-related cognitive decline through modulation of cholinergic signaling and neuroplasticity-related mechanisms.

Keywords : aging, acetylcholine, Humulus japonicus, cognitive function, scopolamine-induced model

P-297

Optogenetic induction of TDP-43 proteinopathy drives neuronal vulnerability and behavioral deficits in *C. elegans*

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TDP-43 proteinopathy is a pathological hallmark of several neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD). To investigate how TDP-43 aggregation contributes to neurodegeneration, we established an optogenetic *C. elegans* model that enables precise spatiotemporal control of TDP-43 phase transitions and aggregation using the optoDroplet system. Upon blue-light illumination, human TDP-43 mislocalized from the nucleus to the cytoplasm and neurites, where it formed insoluble aggregates that recapitulate key features of ALS/FTLD pathology. These aggregates preferentially induced degeneration of GABAergic motor neurons, resulting in severe locomotor impairments. Aggregation also disrupted sensory functions, including mechanosensation and chemotaxis. To identify modulators of TDP-43 toxicity, we conducted a genetic suppressor screen and isolated multiple suppressors that alleviated aggregation-induced phenotypes. Ongoing work focuses on elucidating the molecular mechanisms by which these suppressors modulate TDP-43 pathology. This light-controllable model provides a powerful platform for dissecting the cellular consequences of TDP-43 aggregation and for screening therapeutic targets relevant to ALS and related disorders.

Keywords : Neurodegenerative diseases, TDP-43 proteinopathy, OptoDroplet, C. elegans, Amyotrophic lateral sclerosis (ALS)

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P-298

Synergistic enhancement of structural plasticity and functional recovery via combined PTEN deletion and activity modulation after ischemic stroke

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Motor deficits are a major consequence of ischemic stroke, primarily due to the disruption of neural connections. Spontaneous recovery occurs to a limited extent through brain plasticity, which supports the functional and structural remodeling of neural circuits. Enhancing the capacity of post-ischemic plasticity through targeted therapeutic interventions can further improve motor function. In this study, we conditionally deleted the phosphatase and tensin homolog (PTEN) gene in the rostral forelimb area (RFA) following a stroke in the caudal forelimb area (CFA) to facilitate intracortical axon plasticity. Machine learning-supported measure of axonal plasticity demonstrated that PTEN deletion markedly increased axonal sprouting of RFA projections to the peri-infarct region, accompanied by improved motor function. In addition, activity-dependent rehabilitation was induced by injecting botulinum toxin-A into the non-paretic forelimb muscles, thereby encouraging use of the impaired limb. Although rehabilitation did not significantly enhance axonal growth compared to stroke alone, its combination with PTEN deletion resulted in a greater functional recovery. Retrograde tracing using pseudorabies virus (PRV) from the forelimb muscles revealed increased recruitment of corticospinal neurons following activity-dependent rehabilitation. Moreover, PTEN-deleted axons projecting to the peri-infarct region formed close contacts and synaptic connections with PRV-labeled neurons. These findings suggest that combining genetic manipulation with activity-dependent rehabilitation synergistically promotes structural reorganization of intracortical neural circuits and enhances motor recovery after stroke.

Keywords : Ischemic stroke, PTEN, Rehabilitation, Motor recovery, Neuronal tracing

P-299

Role of DRG2 in the regulation of dopamine release and changes in energy metabolism

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Developmentally Regulated GTP-binding protein 2 (DRG2) is expressed in all cells, with the highest concentrations found in the brain such as dopamine neuron. We demonstrated that DRG2 associated with physical developmental delay, motor coordination, motor deficit, dopamine dependent neurological function. Especially, DRG2 regulates nigrostriatal dopamine release and when a dopamine precursor (L-DOPA) was externally injected to the striatum of DRG2 knockout (KO) mice, behavioral motor deficiency was rescued. However, the physiological role of DRG2 in regulating dopamine release is still poorly understood. Interestingly, DRG2 KO mice lose weight, become hyperactive, and have higher respiratory energy expenditure despite no significant change in food intake. To identify the regulatory mechanism, we found that the levels of the hypothalamic diet genes AgRp, POMC, and SOCS3 were not significantly changed, but UCP1, which increases energy expenditure in brown adipose tissue (BAT), was significantly increased. DRG2 KO mice exhibit sleep disturbances, increased anxiety, and obsessive-compulsive behavior, suggesting that these changes are related th the regulation of energy metabolism and various neurobehavioral symptoms such as ADHD through the regulation of dopamine secretion.

Keywords : Developmentally Regulated GTP-binding protein 2 (DRG2), Developmental delay, Motor defect

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P-300

Nonlinear dynamics of microRNAs in alzheimer's disease: biomarker mining and clinical validation

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Alzheimer's disease (AD) is the most common form of dementia and is characterized by the accumulation of amyloid-beta plaques and tau tangles. These pathological changes gradually lead to cognitive decline, and to date, early intervention remains the only viable strategy to slow or halt disease progression. Consequently, extensive research has been dedicated to identifying reliable biomarkers for early detection. However, omics-based approaches such as proteomics and transcriptomics, as well as the gold-standard diagnostic methods involving amyloid-beta detection via MRI or CT imaging, are typically effective only after significant disease progression, highlighting a major limitation in current diagnostic strategies. In contrast, microRNAs (miRNAs) have emerged as promising early diagnostic biomarkers due to their detectable changes in the early stages of the disease—even before clinical symptoms appear—and their stable presence in minimally invasive samples such as serum and plasma. Nevertheless, the inherently nonlinear expression patterns of miRNAs and their high biological heterogeneity have resulted in poor consistency across studies, posing challenges for clinical application. In this study, we utilized an explainable machine learning approach to identify key miRNA biomarkers associated with AD-related cognitive decline using the GSE110743 mouse dataset, and validated their predictive performance in humans using the GSE120584 dataset. Furthermore, we quantitatively interpreted the nonlinear expression patterns of miRNAs through SHAP analysis, aiming to uncover predictive contributions that may be overlooked by traditional linear approaches. These findings enhance the clinical utility of miRNAs as early diagnostic tools and provide foundational data for the development of precision diagnostic technologies and a deeper understanding of AD pathophysiology.

Keywords : Alzheimer's disease, Cognitive impairment, microRNA, Machine learning, Shap

P-301

Nanoplastics-induce NLRP-3 activation via labile iron in proteinopathy and neurodegeneration

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Emerging evidence shows that nanoplastics accumulate in the human brain, with elevated levels linked to neurodegenerative diseases. However, the precise mechanisms underlying NP-induced neurotoxicity remain poorly understood, as most current studies rely on animal models or simplified systems that overlook complex human-specific interactions. To address this gap, we utilized a nanoplastic-exposed human brain model to investigate how nanoplastics disrupt neuron–glia communication and contribute to neurodegenerative pathology. NP exposure in glial cells rapidly drives v-ATPase–mediated lysosomal acidification and labile iron buildup, which together ignite mitochondrial dysfunction and activate the NLRP3 inflammasome. This inflammasome signaling cascade fuels reactive glial responses and provokes the release of proinflammatory cytokines, including IL-1β, IL-6, TNF-α, and IFN-γ. NP-activated microglia emerge as potent drivers of neuronal injury, triggering tau phosphorylation, phosphorylated α-synuclein aggregation, and synaptic deterioration. Collectively, these findings reveal that iron-mediated NLRP3 inflammasome activation serves as a critical molecular axis linking nanoplastic exposure to glial-driven neuroinflammation, neuronal injury, and heightened vulnerability to neurodegenerative disease.

Keywords : NLRP-3 inflammasome, Labile iron, Glial activation, Neuroproteinopathy, Nanoplastic

P-302

Spatial and temporal dynamics of progenitor cell activation in the neonatal brain after ischemic stroke

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Neonatal ischemic stroke, defined as a focal brain infarction occurring between birth and 28 days of age, is a major cause of severe developmental delays, spastic cerebral palsy, and cognitive impairment. Unlike the adult brain, the neonatal brain harbors a rich population of progenitor cells and exhibits intrinsic plasticity and self-repair capacity. However, it remains to be elucidated the cellular responses during the early post-stroke period and, consequently, the optimal time and location for treatment in the neonatal brain. In this study, we aimed to investigate the temporal dynamics of inflammation and endogenous progenitor cell activation following neonatal stroke. We established a neonatal stroke model by performing transient middle cerebral artery occlusion (tMCAO) in postnatal day 7 mice. Brains were collected at 30 minutes and 4 hours post-occlusion to evaluate acute responses. Stroke induction was confirmed in the neocortex, striatum, and hypothalamus using cresyl violet staining. By immunostaining, we obtained an expression profile of several cell markers in the ischemic core, penumbral, and intact areas. Noticeably, we observed an early inflammatory response at 30 minutes post-stroke, followed by activation of endogenous progenitor cells in the penumbral region by 4 hours. Progenitor cell marker expression was significantly higher in the penumbra compared to both the ischemic core and intact brain areas. Our findings reveal that inflammatory responses occur rapidly at the early stage, followed by activation of progenitor cells in the penumbral region after neonatal stroke. These pathophysiological mechanisms differ from those observed in the adult brain and provide valuable insights for developing targeted therapies for neonatal stroke.

Keywords : Neonatal stroke, MCAo, Penumbra, Progenitor cells

P-303

Social defeat stress induces alterations in the glutamatergic system during adolescence

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Background Adolescence is a developmental stage with a higher sensitivity to stress compared to adulthood. Representative social stressors during this period include school-related experiences such as bullying, which can negatively affect brain development. Nevertheless, studies investigating functional changes in neuronal circuits induced by social stress during adolescence remain limited, especially compared with adulthood. This study aimed to identify differences in stress responses between adolescent and adult brains using a social defeat stress (SDS) model. Methods Male Wistar rats (n=7 per group) were subjected to SDS either during adolescence (postnatal day 35) or adulthood (postnatal day 63). Physiological and behavioral changes were evaluated by measuring body weight, serum corticosterone levels, and various behavioral tests. PET scans using multiple PET tracers were conducted in the same animals. Finally, Western blotting was performed. Results SDS exposure led to reduced body weight, elevated corticosterone levels, decreased social interaction, impaired cognitive function, and depressive-like behaviors, with all effects being more pronounced in adolescents than in adults. PET imaging revealed a 33.7% increase in uptake of the PET tracer for mGluR5 in the hippocampus of adolescent SDS rats ($p < 0.05$), with no significant changes in glucose metabolism, GABAergic and serotonergic systems. Western blot analysis also demonstrated increased mGluR5 expression in the amygdala, hippocampus, mPFC, and striatum of adolescent rats. In contrast, adult rats exhibited increased mGluR5 expression only in the hippocampus and decreased expression in the mPFC. Conclusion Adolescence represents a period of increased susceptibility to social stress, during which the glutamatergic system appears particularly vulnerable. These findings provide insight into age-dependent stress responses and suggest that mGluR5 may represent a potential therapeutic target for adolescent social stress.

Keywords : Adolescence, Social defeat stress, PET, Glutamate, mGluR5

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P-304

Electroacupuncture at GB34 and BL60 enhances subventricular zone neurogenesis via BDNF-ERK signaling in a mouse model of Parkinson's disease&

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It has been reported that acupuncture at GB34 enhances neurogenesis in the subventricular zone (SVZ) of mice treated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). However, the signaling mechanisms underlying this effect remain unclear. In this study, we investigated the neurogenesis-promoting effects of electroacupuncture (EA), focusing on the extracellular signal-regulated kinase (ERK) signaling pathway. Male C57BL/6 mice (10 weeks old) were intraperitoneally injected with MPTP (30 mg/kg) once daily for 5 consecutive days to induce a Parkinsonian phenotype. EA was applied at acupoints GB34 and BL60 for 3 weeks. To assess cell proliferation, mice were also intraperitoneally injected with bromodeoxyuridine (BrdU, 50 mg/kg). We evaluated dopaminergic neuron survival in the nigrostriatal pathway, BrdU-positive and BrdU/doublecortin (DCX)-double-positive cells in the SVZ, and protein expression levels of brain-derived neurotrophic factor (BDNF) and phosphorylated ERK (pERK) in the striatum. MPTP administration resulted in dopaminergic neuronal loss in the nigrostriatal pathway and a significant reduction in BrdU-positive and BrdU/DCX-double-positive cells in the SVZ. These effects were markedly reversed by EA. In addition, EA restored striatal levels of BDNF and pERK, which had been decreased by MPTP treatment. These findings suggest that EA at GB34 and BL60 promotes neurogenesis in the SVZ and protects dopaminergic neurons, potentially through activation of the BDNF-ERK signaling pathway.

Keywords : acupuncture, electroacupuncture, Parkinson's disease, neurogenesis, ERK

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P-305

Modulation of creatine energy metabolism mediates mitochondrial hormesis enhancement in intracerebral hemorrhage

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Intracerebral hemorrhage (ICH) characterized by bleeding into the brain tissue, and ICH patients have been reported to have reduced energy metabolism due to decreased mitochondrial respiration. Creatine, the fastest energy supply system in our body, transfers phosphate to ADP and phosphorylated creatine stimulates the mitochondrial respiratory chain. Moreover, the administration of creatine analogue to the mouse increased mitochondrial biogenesis in brain cortex and induces behavioral change. However, there is lack of investigation into the underlying mechanism of enhancement mitochondrial function by the treatment of creatine analogue and how this contributes to attenuation in intracerebral hemorrhage. Since creatine transporter is primarily localized in brain endothelial cells, we analyzed the mitochondrial OXPHOS system and mitochondrial hormesis-related

proteins incerebral endothelial cells. As we expected, creatine analogue treatment increased mitochondrial respiration in cerebral endothelial cells of creatine analogue-treated group compared to vehicle-treated groups. Furthermore, creatine analogue treatment altered the levels of mitochondrial UPR-associated protein expression which are regulator of mitochondrial hormesis in cerebral endothelial cells. To investigate changes in mitochondrial respiration in vivo, we measured the mitochondrial oxygen consumption rate in an ICH mouse model after inhibition of creatine transporter by intraperitoneal injection of a creatine analogue. Interestingly, mitochondrial respiration was increased in the perihematomal area of the creatine analogue-treated mice compared to the vehicle-treated group. Additionally, we identified elevated levels of mitochondrial UPR-related proteins in mice brain tissue. These results suggest that creatine analogue mediate through the enhancement of mitochondrial hormesis in the ICH mouse model and could be therapeutic agents for brain-related diseases such as intracerebral hemorrhage.

Keywords : creatine analogue, creatine transporter, mitochondria, Intracerebral hemorrhage

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P-306

Vitamin D improves cognitive function through neurovascular remodeling in an aging mouse model

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As life expectancy increases, the global population is rapidly aging. Even during normal aging, cognitive abilities gradually declines, leading to decline in quality of life and the ability to live independently. Accumulated oxidative stress and chronic inflammation in the aging process are considered major contributors to brain aging and neurovascular damage. Vitamin D, known for its anti-inflammatory and antioxidant properties, has demonstrated neuroprotective effects and may prevent or delay neurodegenerative processes. However, as skin synthesis of vitamin D decreases with age, making vitamin D supplementation particularly important for older adults. In this study, we investigated the effects of vitamin D administration on cerebrovascular integrity and cognitive function in aging mouse models. We used the male C57BL/6J(n=28). C57BL/6J mice 64 weeks (n=21) were divided into 3 groups including aging(n=7), aging+corn oil and aging+vitamin D(25μg/kg, n=7). C57BL/6J mice 9 weeks (n=7) were used as the young group. Vitamin D was administered orally once every 3 days for 8 weeks. Vitamin D significantly improved cognitive functions in the Y-maze test and passive avoidance test, compared to the young group. Vitamin D alleviated age -related neuronal loss in the hippocampus and attenuated microglial and astrocytic activation. Neurovascular damage in the aging group was evidenced by a decreased density and length density of PECAM-1-positive vessels and degeneration of BBB markers in neurovascular units. Vitamin D administration effectively reversed these age-related neurovascular changes. Vitamin D administration ameliorates cognitive impairment by reducing neuroinflammation in hippocampus and promoting neuronal survival. Additionally, Vitamin D enhances cerebrovascular health by increasing the density and length of cerebral microvessels. These findings suggest that Vitamin D has potential as a therapeutic agent for brain aging and preserving cerebrovascular integrity.

Keywords : Vitamin D, Aging, Neurovascular unit, Cognitive

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P-307

The role of sleep stages and cyclic rhythms in seizure dynamics of temporal lobe epilepsy rat model

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Sleep and epilepsy exhibit a complex, bidirectional relationship. Epilepsy disrupts sleep, while sleep stages modulate epileptic activity. In addition, emerging evidence showcases cyclic temporal patterns as key modulators of seizure dynamics. This study aims to assess the impact of epilepsy on sleep architecture, explore how each sleep stage affects seizures and interictal epileptiform activity, and analyze circadian and multidien rhythmicity in epileptiform activity in a temporal lobe epilepsy (TLE) rat model. Electroencephalographic (EEG) and electromyographic (EMG) recordings were obtained using chronically implanted electrodes in chronic TLE rat models that developed spontaneous recurrent seizures after status epilepticus via injection of kainic acid or pilocarpine into the right hippocampal region. The control group received saline injections in the same region. Sleep stages and seizures were manually scored, while interictal spikes were annotated semi-automatically. Continuous wavelet transforms were applied to multi-day spike count time series to assess rhythmic modulation. Circular statistics assessed the seizure-phase relationship in both circadian and multidien cycles. TLE rats exhibited reduced rapid eye movement (REM) sleep compared to control animals. Seizures and spikes occurred predominantly during non-rapid eye movement (NREM) sleep and were significantly suppressed during REM sleep. All animals displayed circadian rhythmicity in spike activity, and multidien cycles of ~5.5, 8~10, and 16~17 days were identified. Seizures demonstrated significant phase-locking to both circadian and multidien spike rhythms. These findings confirm that sleep stages strongly regulate epileptic activity, and that both circadian and multidien rhythms influence seizure risk in a TLE rat model. Understanding these dynamics may benefit chronotherapy and individualized seizure forecasting, which may have future clinical implications with further verification in TLE patients.

Keywords : Epilepsy, Sleep, Electroencephalography, Seizures, Circadian rhythm

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P-308

Neuroprotective effect of Korean red ginseng extract in the hippocampus of mice acutely exposed to polystyrene nanoparticles

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Background: Polystyrene nanoparticles (PS-NPs) are emerging pollutants detected in the environment and organisms and can pose a threat to living organisms. PS-NPs have been reported to cross the blood-brain barrier and interfere with the function of the central nervous system. However, the molecular mechanism of the pathogenesis is still unclear. Korean red ginseng has been used as a herbal medicine to treat various diseases for a long time, but the neuroprotective effect of Koran red ginseng extract (KRGE) has not been studied much. Therefore, in this study, we investigated the pathological mechanism of mice acutely exposed to PS-NPs and the therapeutic efficacy and molecular mechanism of KRGE. Methods: KRGE (100, 200, and 400 mg/kg) was orally administered 3 days before exposure to PS-NPs in mice. Results: In the hippocampus (CA3) of mice acutely exposed to PS-NPs, reactive oxygen species were increased along with neurodegeneration/necroptosis, but microglia and astrocyte activation and TNF-α secretion were not induced. KRGE reduced necroptosis in the hippocampus of mice exposed to PS-NPs, which was related to the action of Nrf2. HT-22 hippocampal cells were pretreated with KRGE (1, 10, and 100 μg/ml) and then exposed to PS-NPs. As a result, KRGE increased the expression of NeuN protein and inhibited the expression of necroptosis proteins. Conclusion: KRGE exhibits neuroprotective effects in the hippocampus of mice acutely exposed with PS-NPs by inhibiting the generation of reactive oxygen species induced by PS-NPs through antioxidant action. These results suggest that KRGE may be a potential therapeutic strategy for PS-NPs-induced toxicity.

Keywords : Korean red ginseng extract, Polystyrene nanoparticles, antioxidant action, neuroprotective effects, hippocampus

P-309

CHO001 inhibits experimental autoimmune encephalomyelitis by downregulating microglial NF-κB/NLRP3 inflammasome signaling pathways

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Background: CHO001 is a synthetic compound belonging to the ceramide family. In particular, CHO001 has been shown to exert neuroprotective effects on neurological diseases such as Alzheimer's disease and ischemic brain damage. However, the effect of CHO001 on multiple sclerosis (MS), a representative autoimmune disease of the central nervous system, has not yet been elucidated. Purpose and Methods: The purpose of this study was to investigate the pharmacological effects and related molecular mechanisms of CHO001 in experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis. Results: Oral administration of CHO001 at the time of disease onset improved motor function and alleviated spinal cord demyelination in EAE mice. In addition, CHO001 administration inhibited the infiltration and activation of resident microglia and monocyte-derived macrophages, and reduced the expression of major pro-inflammatory cytokines (IL-6 and TNF-α) and chemokines (MCP-1, MIP-1α and RANTES). CHO001 not only suppressed NF-κB/NLRP3 signaling pathways in the spinal cord and activated BV2 microglial cells of EAE mice, but also reduced astrocyte reactivity and vascular leakage, thereby maintaining blood-brain barrier (BBB) integrity. Transcriptomic profiling supported the broad inhibition of neuroinflammation and immune activation pathways. Conclusions: CHO001 may alleviate motor dysfunction and neuroinflammation in EAE and prevent BBB destruction by downregulating NF-κB/NLRP3 signaling pathways. These results suggest that CHO001 may be a promising therapeutic agent for MS and other neuroinflammatory diseases.

Keywords : CHO001, Multiple sclerosis, Experimental autoimmune encephalomyelitis, Neuroinflammation, blood-brain barrier

P-310

Populus tomentiglandulosa exerts neuroprotective effects in an MPTP-induced parkinson's disease model by growing antioxidant and inh<

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Background: Parkinson's disease (PD) is a representative neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc). Despite extensive research, no definitive cure for PD currently exists. *Populus tomentiglandulosa* (PT), an endemic Korean plant, has demonstrated anti-inflammatory properties; however, its neuroprotective potential in neurodegenerative diseases remains unexplored. Purpose and Methods: This study investigated the neuroprotective effects of ethanol extract of PT in a murine model of PD induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Mice were orally administered PT (50, 100, or 200 mg/kg/day) for three consecutive days prior to intraperitoneal MPTP injection. Results: PT administration significantly alleviated MPTP-induced motor deficits, as evidenced by improved performance in behavioral tests. These functional improvements were accompanied by preservation of dopaminergic neurons in the SNpc, indicated by sustained tyrosine hydroxylase expression. At the molecular level, PT suppressed neuroinflammation and apoptosis by inhibiting glial fibrillary acidic protein activation, downregulating caspase activity, and upregulating the anti-apoptotic protein Bcl-2. Moreover, PT enhanced antioxidant defenses through the activation of the nuclear factor erythroid 2–related factor 2 signaling pathway. Conclusion: PT ameliorated dopaminergic neurodegeneration in MPTP-induced PD model mice via anti-inflammatory, antioxidant, and anti-apoptotic mechanisms, leading to functional motor improvement. These findings suggest that PT holds promise as a potential therapeutic agent for PD-like symptoms and associated neuropathologies.

Keywords : Populus tomentiglandulosa, MPTP, Parkinson's disease, Antioxidant, Apoptosis

P-311

Overexpressing TFEB in microglia attenuates Aβ pathology by enhancing the autophagy lysosomal pathway

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Alzheimer's disease (AD) is characterized by the accumulation of amyloid plaques and neurofibrillary tangles. The autophagy–lysosomal pathway (ALP) plays a central role in cellular homeostasis, with transcription factor EB (TFEB) serving as a key regulator of autophagy and lysosomal biogenesis. Increasing evidence indicates that ALP dysfunction and altered microglial activity in AD impair amyloid-β (Aβ) clearance, contributing to plaque formation. This study investigated whether microglia-targeted expression of TFEB could enhance Aβ phagocytosis and lysosomal degradation, thereby mitigating Aβ pathology. We first confirmed ALP impairment in 6-month-old 5xFAD mice, as evidenced by reduced nuclear TFEB levels and elevated LC3-II and p62 expression. TFEB mRNA levels were also significantly decreased in microglia from 5xFAD mice compared to WT controls. To assess the impact of microglial TFEB, we used TFEB-CA transgenic mice, which selectively express constitutively active TFEB in microglia. Adult microglia were isolated from TFEB-CA mice using MACS and exposed to oligomeric Aβ (oAβ) in vitro. Additionally, TFEB-CA mice were crossed with 5xFAD mice to generate 5xTFEB mice, enabling in vivo evaluation of microglia-specific TFEB expression in AD. Behavior tests and molecular analyses were performed to assess cognitive function, Aβ burden, neuroinflammation, and ALP activity. Microglial TFEB expression enhanced oAβ clearance, reduced intracellular ROS, and alleviated oAβ-induced cytotoxicity via ALP activation in the microglia of TFEB-CA mice. In 5xTFEB mice, microglial TFEB expression significantly improved cognitive performance and reduced Aβ deposition compared to 5xFAD mice. Furthermore, TFEB expression attenuated neuroinflammation and restored ALP function in 5xTFEB mice. These findings suggest that microglial TFEB activation may be a promising strategy to promote Aβ clearance and reduce pathology in AD.

Keywords : Alzheimer's disease, Amyloid plaque, Microglia, Autophagy lysosomal pathway

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P-312

Bestrophin1 drives glioblastoma progression and suppresses apoptosis via Ca^{2+}-dependent glutamate release

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Glioblastoma (GBM) is a highly aggressive primary brain tumor with poor prognosis, largely due to its infiltrative nature that limits the effectiveness of conventional treatments such as surgical resection, radiotherapy, and chemotherapy. GBM cells actively modulate the tumor microenvironment through the release of gliotransmitters, a process closely linked to intracellular calcium (Ca^{2+}) signaling. In this study, we demonstrate that Bestrophin1 (Best1), a Ca^{2+}-activated Cl^- channel that also functions as a glutamate release channel, facilitates Ca^{2+}-dependent glutamate release from GBM cells. This glutamate promotes both tumor proliferation and invasion by shaping a microenvironment favorable for GBM progression. Best1-mediated functions were also found to be critical for GBM cell survival; downregulation of Best1 led to reduced cell viability, increased apoptosis, and disruption of glioblastoma organoid (GBO) spheroid formation. Furthermore, Best1 expression was enriched at the invasive front and infiltrating regions of GBM, with significantly higher levels observed in high-grade gliomas compared to low-grade gliomas. These findings suggest that Best1 plays a multifaceted role in glioblastoma by promoting tumor proliferation, invasion, and survival, and may serve as a promising therapeutic target to limit tumor progression and enhance apoptosis.

Keywords : Glioblastoma, Glutamate, Best1, Calcium, Viability

P-313

Cooperative regulation of compulsive-like eating behavior by dopamine D2 and insulin receptors

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Dopamine plays a pivotal role in motivated behavior and reward processing, with the dopamine D2 receptor (D2R) serving as a key regulator in these mechanisms. Compulsive eating is defined by persistent consumption of palatable food (PF) despite adverse consequences. The central amygdala (CeA) is critically involved in both appetite regulation and reward processing. In this study, we identify a critical neuromodulatory mechanism wherein D2Rs modulate insulin receptor (InsR) signaling in the CeA to regulate compulsive-like eating behavior. We assessed compulsive-like eating behavior by performing PF self-acquisition task. Increased active lever presses in the presence of footshock punishment were used as an indicator of compulsive eating. Conditional deletion of D2R in the CeA enhanced compulsive-like eating behavior under aversive conditions, suggesting that D2Rs in the CeA critically contribute to the compulsive-like perseverance of PF-seeking behavior. We observed substantial colocalization of D2Rs and InsRs in CeA neurons, and genetic disruption of D2R signaling impaired InsR expression and downstream signaling. Conversely, pharmacological activation of D2Rs facilitated InsR phosphorylation and subsequent insulin signaling, representing a previously unrecognized mechanism by which D2R activity promotes InsR signaling. Real-time calcium imaging demonstrated that CeA D2R-expressing neurons were suppressed during PF consumption, while their activity was restored by D2R and InsR co-activation, which

concurrently reduced PF intake. Consistently, optogenetic activation significantly suppressed PF consumption, and pharmacological inhibition of InsR signaling via S961 completely blocked this regulation, demonstrating that InsR signaling is necessary for regulating compulsive eating. These findings uncover a novel dopamine–insulin signaling axis in the CeA that integrates reward and metabolic cues to constrain maladaptive eating behavior.

Keywords : dopamine D2 receptor, central amygdala, compulsive eating behavior, insulin receptor, food rewards

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P-314

ORP1L deficiency disrupts endolysosomal function in neurons and exacerbates amyloid pathology in a mouse model of Alzheimer's disease

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Membrane contact sites (MCSs) between the endoplasmic reticulum (ER) and endosomes orchestrate lipid transfer, endosome positioning, and lysosomal homeostasis. Emerging evidence implicates disruption of these contacts in neurodegenerative diseases such as Alzheimer's disease (AD), yet their precise roles in AD pathogenesis remain unclear. We identified oxysterol-binding protein-related protein 1L (ORP1L) to be a strong candidate mediator of neuronal MCS. In mouse primary hippocampal cultures, ORP1L knockdown (KD) induced lipid droplet accumulation, late endosome mislocalization, and lysosomal dysfunction. ORP1L KD also decreased dendritic complexity and reduced miniature excitatory postsynaptic currents (mEPSCs) frequency. In vivo, AAV-mediated ORP1L silencing in the CA1 region of 5XFAD mice doubled amyloid-β deposition and impaired performance in novel object recognition and contextual fear conditioning. Collectively, our data identify ORP1L as a critical regulator of ER–endosome contact site integrity in neurons and demonstrate that its loss exacerbates both cellular and behavioral AD phenotypes. Targeting ORP1L-mediated MCSs may therefore offer a novel therapeutic strategy to preserve neuronal function in neurodegenerative disorders.

Keywords : Membrane contact sites, ORP1L, Late endosome, 5XFAD, Alzheimer's disease

P-315

The circuit and molecular mechanisms underlying hypothalamic and oxytocin neuronal abnormalities in 15q11-13 duplication mice

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Autism spectrum disorder (ASD), is an inheritable and heterogeneous neurodevelopment disorder. Its core clinical phenotypes are social deficits and repetitive behaviors. The hypothalamus and the oxytocin system are essential to regulate social behaviors. Some autistic patients also showed abnormal hypothalamus structure and oxytocin secretion. However, the relationship among the genetic causes of autism, the abnormal hypothalamus and oxytocin system and autistic phenotypes are unclear. Here we used a mouse model of human ASD, named human 15q11-13 chromosome duplication mice (*15qDp/+*), to explore the hypothalamus and oxytocin system abnormalities in autism and its molecular mechanism. We used bulk RNA-seq to detect the hypothalamic transcription differences at postnatal 18 and 35 days (P18 and P35) and found reduced expression of various neuropeptides (oxytocin, vasopressin, etc.). The expression of oxytocin from birth to adolescence was consistently decreased in *15qDp/+* mice. At the level of neuronal activity, spontaneous firing rates of oxytocin neurons were significantly reduced in *15qDp/+* mice. To further investigate the molecular mechanism of oxytocin neuronal deficits, we isolated the fluorescence-labeled oxytocin neurons by FACS at P18 and did RNA-seq and ATAC-seq. The sequencing data indicated that down-regulated genes in the expression or chromatin accessibility level played important roles in neuronal projection and synaptic transmission. Among the co-regulated genes, some possible candidates stood out, which may cause oxytocin neuronal deficits in *15qDp/+* mice. According to the oxytocin system abnormalities, we gave *15qDp/+* mice a long-term oxytocin i.p. injection and this intervention rescued deficits in oxytocin expression and neuronal excitability. All these data indicated that defects in oxytocin system may induce autistic phenotypes and oxytocin system can be a good target for clinical intervention.

Keywords : Autism spectrum disorder, Hypothalamus development, Oxytocin neuronal activity, Oxytocin administration

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P-316

Identifying disease-associated neuronal differences using neurons directly converted from Alzheimer's disease patient-derived fibroblasts

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Alzheimer's disease (AD) is the most common cause of dementia, characterized by progressive cognitive decline and neuronal loss. While a small proportion of cases are familial, most AD cases are sporadic. Sporadic AD is a complex, late-onset neurodegenerative disorder whose pathogenesis is influenced by genetic risk factors and age-associated biological processes. Neurons, as long-lived post-mitotic cells generated during early development, are rarely replaced and thus particularly vulnerable to cumulative age-related damage.

This intrinsic susceptibility contributes to irreversible declines in neuroplasticity and cognition over time, ultimately increasing the risk of neurodegeneration. However, many existing in vitro models rely on induced pluripotent stem cells (iPSCs), which undergo rejuvenation during reprogramming and lose critical aging-associated features. To overcome this limitation, we avoided iPSC-based differentiation and instead adopted a direct conversion approach, enabling the generation of neurons while preserving age-related molecular signatures. Using fibroblasts derived from AD patients and control participants, we performed direct conversion into induced neurons by overexpressing Ascl1 and Ngn2 in combination with small molecule treatment, followed by neuronal marker-based sorting. The resulting cells expressed key neuronal markers such as NEUN and TUBB3, confirming successful reprogramming to neuron. In future studies, we plan to perform RNA sequencing to investigate transcriptomic differences between AD and control neurons under age-maintained conditions. Furthermore, we aim to assess senescence-associated phenotypes to explore whether AD neurons show enhanced susceptibility to aging-related stress. This strategy may offer new insights into the molecular interplay between aging and AD pathogenesis in human neurons.

Keywords : Direct conversion, Patient-derived fibroblasts, Neurons, Alzheimer's disease, Aging

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P-317

Orally Active Tau-ATTEC demonstrates in vivo efficacy in P301S tauopathy model: Novel breakthrough therapeutic modality for tauopathies

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Tau, a microtubule-associated protein that plays a critical role in stabilizing axonal microtubules, becomes neurotoxic upon misfolding and hyperphosphorylation, leading to the formation of insoluble aggregates that contribute to neuronal dysfunction and cell death. Due to its intrinsically disordered structure and lack of active binding pockets, tau—like many non-enzymatic proteins—presents a significant challenge for conventional small-molecule drug development. While genetic knockdown strategies offer sustained suppression, their clinical translation is hindered by issues related to delivery, stability, and safety. Targeted protein degradation (TPD) has emerged as a promising approach to selectively eliminate pathogenic proteins. This strategy employs bifunctional molecules that recruit intracellular quality-control machinery to degrade target proteins via the proteasome or autophagy pathways. Although proteasome-based degraders have shown efficacy against soluble targets, autophagic degradation provides a more suitable and efficient route for clearing aggregated tau species, which are a pathological hallmark of tauopathies. Autophagosome-tethering chimeras (ATTECs) represent a novel TPD modality that facilitates autophagic clearance by linking a tau-targeting ligand to an LC3-binding motif, thereby directing pathological tau to the autophagosome for lysosomal degradation. In this study, we developed and characterized orally bioavailable Tau-ATTECs that selectively degrade tau, reduce phosphorylated tau (p-tau) levels, and confer neuroprotective effects in cell-based models. Notably, systemic administration of Tau-ATTECs led to efficient blood–brain barrier penetration and significantly reduced pathological tau accumulation in the P301S tau transgenic mouse model. These findings establish Tau-ATTECs as a novel and clinically translatable therapeutic strategy for the treatment of tauopathies.

Keywords : Tau, Tauopathy, Targeted protein degradation, Autophagy, Autophagosome-tethering chimera

P-318

Gut-derived pathologic α-synuclein and its transmission through neural circuits

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Parkinson's disease (PD), which is the second most common type of neurodegenerative disease, is mainly caused by formation of intracellular aggregates containing α-synuclein (α-syn), resulting in neuronal loss (e.g. dopaminergic neuron). In the early stages of PD, α-syn inclusion bodies are observed in the relatively lower brain regions such as the olfactory bulb or the medulla, but in later stages, they are also found in the relatively central brain region such as midbrain substantia nigra. Based on the analysis of PD pathology, the Braak hypothesis has been proposed that pathological α-syn aggregates can be transmitted through neural circuits. Vagus nerve, which connects the brain and body (especially the gut), has been intensively investigated as a transmission route of pathologic α-syn implied by the Braak hypothesis. Interestingly, there are two relevant studies supporting the vagus nerve and Braak hypothesis: 1) statistical cohort analysis from Northern Europe and 2) gut-to-brain α-syn transmission mouse model. However, it is still elusive how α-syn fibrils or aggregates initially form in the intestine and begin to spread through the neural circuit. Also, the splanchnic nerves, which connect the spinal cord and gut, may be another candidate route in which pathologic α-syn spreads. Therefore, in this study, we investigated the characteristics of pathological α-syn originating in the gut and the possibility of transmission along the gut-brain axis neural circuit.

Keywords : α-synuclein, Parkinson's disease, Gut-brain axis, Autonomic nervous system, Aggregate transmission

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P-319

Effects of sitagliptin on L-dopa induced dyskinesia in 6-OHDA-induced mouse model of Parkinson's disease

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Parkinson's disease (PD) is characterised by movement disorders associated with progressive dopaminergic neurodegeneration of the midbrain. L-dopa-induced dyskinesia (LID) is a form of involuntary movement that emerges following long-term treatment of L-dopa, the most commonly used pharmacological therapy for PD. Glucose dysregulation has been reported in patients with PD, while higher glucose levels are related to longer disease duration and more sever dysautonomia. There is growing evidence for an association between PD and type 2 diabetes mellitus (T2DM). The T2DM drug sitagliptin, selective inhibitor of dipeptidyl peptidase 4 (DPP4), is often used as monotherapy, initial combination therapy, or add-on therapy. Diabetic patients with PD treated with DPP4 inhibitors show increased dopamine transporter, and a slower longitudinal increase in the L-dopa-equivalent dose than those without. In this study, we evaluated whether sitagliptin has a potential therapeutic effect on LID. PD mouse models were induced by unilateral injection of 6-hydroxydopamine (6-OHDA) into the substantia nigra pars compacta area. After then, L-dopa was administered alone or in combination with sitagliptin, and sitagliptin was used at two dose: 10 and 30 mg/kg. The effect of sitagliptin on LID was monitored by scoring abnormal involuntary movements (AIMs), an indicator of dyskinesia, on days 5 and 10 of L-dopa administration. To investigate the effects of sitagliptin on proteomic changes, quantitative proteomic analysis using tandem mass tag (TMT) labelling was performed on 6-OHDA-lesioned striata of L-dopa-treated mice with or without sitagliptin. In addition, based on the results analyzed in the proteomic analysis, the expression patterns of proteins in which changes were confirmed by western blot and RT-PCR. Through this study, we aimed to determine whether co-administration of sitagliptin with longterm treatment of L-dopa can reduce LID in PD patient.

Keywords : Proteomics, Abnormal involuntary movement, L-dopa induced diskinesia, Striatum, Parkinson's disease

P-320

From Acupoint to Biomarker: Metabolomic Insights into the Therapeutic Effects of Invasive Laser Acupuncture in Parkinson's Disease

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Parkinson's disease (PD) affects 1–2% of the global population and presents significant therapeutic challenges. In search of novel approaches, this study investigated invasive laser acupuncture (ILA), a technique integrating traditional acupuncture with photobiomodulation by inserting optical fibers into the muscle layers of the acupoint to enhance therapeutic outcomes. We applied ILA at 830 nm and 650 nm in MPTP-induced PD mice, assessing motor performance, nigrostriatal TH-positive immunoreactivity, neuroinflammation, and muscle metabolomics. ILA at 830 nm significantly improved motor functions, protected dopaminergic neurons, and reduced brain inflammation. Metabolomic analysis revealed increased glucose and galactose linked to behavioral recovery. ILA outperformed noninvasive laser, and lidocaine pretreatment did not diminish its effects, suggesting mechanisms beyond local nerve activation. Our results highlight ILA as a promising PD therapy that induces systemic metabolic changes detectable in peripheral tissues. These metabolic shifts may serve as future biomarkers, offering new possibilities for diagnosis and treatment monitoring.

Keywords : Parkinson's disease, Acupuncture, Photobiomodulation

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P-321

Synergistic effects of environmental enrichment and Aptamin C on amyloid-beta clearance via enhanced autophagy in the 5xFAD Mice

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Background : Alzheimer's disease (AD) is a progressive neurodegenerative disease characterized by the pathological accumulation of amyloid-beta (Aβ) protein, leading to cognitive decline. Although AD accounts for approximately 50–60% of all dementia cases, no definitive cure is currently available. Environmental enrichment (EE) is a therapeutic strategy, has shown promise in mitigating the progression of neurodegenerative disorders. Aptamin C (AptC), a novel compound composed of vitamin C conjugated with a DNA aptamer, enhances the stability and bioavailability of conventional vitamin C. This study aimed to investigate the synergistic effects of EE and AptC on autophagy induction and Aβ clearance in the 5xFAD mice model. Methods : wild-type(WT) as control; Alzheimer's disease (Tg) as untreated transgenic control; Tg+AptC group, tg mice treated with AptaminC; Tg+EE group, tg mice exposed to environmental enrichment (EE); and Tg+AptC+EE group, transgenic mice receiving combined AptC treatment and EE exposure. Cognitive performance was assessed using behavioral testing. Neuroinflammation, Aβ plaque deposition, and autophagy-related protein expression were analyzed via immunohistochemistry and Western blotting. Results : As a result, it was confirmed that Aβ deposition were reduced in all intervention groups compared to the Tg group. Enhanced autophagy was confirmed through upregualtion of autophagy initiation marker(Beclin-1). In addition, glial responses were

modulated, as shown by decreased expression of Iba-1 (microglial activation), indicating attenuated neuroinflammation. Conclusion : The present study demonstrates that both EE and AptC independently promote Aβ clearance, enhance autophagic activity, and suppress neuroinflammatory responses in the hippocampus of 5xFAD mice. Importantly, the combination of EE and AptC resulted in superior therapeutic efficacy, highlighting their potential as a complementary strategy for the treatment of AD.

Keywords : Alzheimer's disease, AptaminC, Environmental enrichment, Autophagy, Neuroinflammation

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P-322

Regional tau resistance mediates genetic contributions to cognitive reserve in alzheimer's disease

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Cognitive reserve (CR) refers to the brain's ability to maintain cognitive function despite Alzheimer's disease (AD) pathology. While previous studies have linked CR to amyloid-beta (Aβ), tau pathology, and genetic variants, the direct relationship between CR and AD pathological mechanisms remains unclear. This study aimed to construct a CR model explained by AD pathology and to identify genetic factors contributing to CR. Using the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset (n=586), we defined tau modulation as the deviation between observed and predicted tau levels based on Aβ burden and covariates. CR was operationalized as the residual of Alzheimer's Disease Assessment Scale (ADAS) cognitive scores after adjusting for Aβ and tau pathology. Regions of interest (ROIs), including the prefrontal cortex (PFC), orbitofrontal cortex (OFC), parietal cortex (PC), and others, were delineated using the Desikan-Killiany atlas. Our analysis revealed that tau modulation in the PFC, OFC, anterior cingulate cortex (ACC), and amygdala was positively associated with CR. This suggests that reduced regional tau accumulation, beyond what is expected based on Aβ levels, contributes to enhanced CR in areas responsible for higher-order cognitive functions. Genome-wide association studies (GWAS) identified 34 significant SNPs linked to genes such as STK25, FABP12, UVSSA, and ASB15, which are involved in cell signaling and epigenetic regulation. Mediation analysis further demonstrated that genes such as ABCC1 and EFCAB8 indirectly promote CR by influencing tau modulation in specific brain regions. In conclusion, our study demonstrates that certain genes promote cognitive reserve by modulating tau accumulation in the PFC, OFC, ACC, and amygdala, resulting in lower-than-expected tau deposition relative to Aβ burden. These findings advance.

Keywords : Cognitive reserve, Tau resistance, GWAS, Tau modulation

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P-323

DTI-ALPS reveals glymphatic mediation of choroid plexus and ventricular enlargement in MCI patients

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Objective: The choroid plexus(CP) and cerebral ventricles are major structures in cerebrospinal fluid(CSF) circulation and are known to be enlarged in Alzheimer's disease (AD)[1][2]. These enlargements may be related to glymphatic outflow dysfunction. Ventricular volume is negatively correlated with glymphatic function measured by the Diffusion Tensor Image Analysis Along the Perivascular Space(DTI-ALPS) index[3]. CP volume has also been shown to predict DTI-ALPS change, suggesting its role in glymphatic regulation[4]. This study aimed to examine the relationship between ventricular volume and glymphatic outflow function in mild cognitive impairment(MCI), and whether glymphatic outflow function mediates the association between CP and ventricular volumes. Methods: T1-weighted and diffusion tensor images from 398 MCI patients were analyzed. DTI-ALPS was used to assess glymphatic outflow. Volumes were calculated from T1 images and normalized by total intracranial volume(TIV). Covariates(age, sex, education, TIV, cortical gray matter, cerebral white matter, and subcortical gray matter volumes) were adjusted in the analyses. Results: Multiple linear regression showed that the volumes of the lateral, inferior lateral, and third ventricles were significantly associated with both DTI-ALPS and CP volume. The fourth ventricle was significantly associated only with CP volume. Mediation analysis showed that DTI-ALPS partially mediated the association between CP and ventricular volumes (lateral: 6.9%, inferior lateral: 11.7%, third: 6.6%). Conclusion: CP enlargement may affect ventricular volume directly and indirectly via glymphatic dysfunction in MCI. However, DTI-ALPS does not reflect whole-brain glymphatic flow, and CSF-glymphatic relationships may be more complex than our model. As this is a cross-sectional study, causality cannot be inferred. Careful interpretation and further studies are needed.

Keywords : Glymphatic system, Ventricle, Choroid plexus, Mild cognitive impairment

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P-324

Ultrastructural analysis of scar-forming PDGFR-β^{+} fibroblasts after photothrombotic stroke

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The morphological dynamics of fibroblasts during fibrotic scar formation in the central nervous system remain elusive. We previously demonstrated that platelet-derived growth factor receptor-β (PDGFR-β)

is a shared marker of leptomeningeal and perivascular fibroblasts in healthy rats, with the former displaying an activated phenotype and the latter remaining quiescent. Here, we induced focal cortical and meningeal injury by photothrombotic stroke and delineated the spatiotemporal dynamics of PDGFR-β-positive (PDGFR-β$^+$) fibroblast subsets. Multi-label immunohistochemistry revealed that perivascular as well as leptomeningeal fibroblasts co-expressed extracellular matrix protein in the acute and chronic phases. Immuno-electron microscopy showed that both fibroblasts had euchromatic nuclei with dilated endoplasmic reticulum, corroborating immunohistochemical findings. At 7days post-stroke, three-dimensional electron-microscopy reconstructions demonstrated PDGFR-β$^+$ fibroblast processes surrounding vessels and collagen fibers and interdigitating with neighboring cells. PDGFR-β expression levels varied among activated fibroblasts, underscoring heterogeneity in activation status. By 14days, the cells exhibited sheet-like, highly branched extensions that formed a web-like network in the extravascular space and closely associated with macrophages. In addition, lysosome-like electron-dense organelles were observed in fibroblasts from 7days to 14days post-injury. Finally, quantitative analysis revealed a loss of activation-related characteristics in late fibroblasts compared to early fibroblasts. Collectively, our data provides new insights into key cellular players in the tissue repair response by spatiotemporally investigating the dynamic morphological characteristics of post-stroke fibroblasts.

Keywords : PDGFR-β, Perivascular & leptomeningeal fibroblast, Fibrotic scar, 3D reconstruction, Electron microscopy

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P-325

Antioxidant microglial subtypes mitigate ischemic injury in a photothrombotic stroke model via Prdx1-dependent mechanisms

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Ischemic stroke triggers not only neuronal loss but also complex neuroimmune responses. Microglia, as the brain's intrinsic immune cells, are central to post-stroke inflammation and repair. A unique subpopulation known as stroke-associated microglia (SAM) displays antioxidant activity through Prdx1 and is proposed to play a neuroprotective role. However, their relevance beyond the MCAO model remains unexplored. We aimed to assess the presence and functional significance of SAM in the photothrombotic (PT) cortical stroke model. Photothrombotic stroke was induced in wild-type (WT) and Prdx1 knockout mice. Western blot and immunohistochemistry were used to examine expression and localization of SAM markers (Fth1, Spp1, Prdx1) in defined brain regions (contralateral, infarct, peri-infarct). Infarct volumes were evaluated using TTC staining to assess stroke severity. Due to the relatively small infarct size characteristic of the PT stroke model, no significant difference in SAM marker protein levels was observed when comparing the contralateral and ipsilateral hemispheres. Therefore, the brain was subdivided into three distinct regions: contralateral, infarct, and peri-infarct (non-infarct), for more precise analysis. Three days post-stroke, protein levels of SAM markers—including Fth1, Spp1, and Prdx1—were notably elevated in the peri-infarct cortex. Immunohistochemistry revealed that microglial cells co-expressing CD63 and Iba1 were predominantly localized to this region, suggesting active microglial remodeling. Furthermore, Prdx1 knockout mice showed a significant increase in infarct volume compared to wild-type controls, supporting the role of Prdx1-expressing microglia in mitigating ischemic damage. Our data highlight the emergence of a neuroprotective microglial phenotype in the PT model, driven by Prdx1. These findings suggest that modulation of microglial antioxidant responses may serve as a therapeutic avenue to preserve neuronal integrity after cortical ischemia.

Keywords : Microglia, Ischemic stroke, Peroxiredoxin 1, Photothrombotic stroke

P-326

Patient-derived iPSC-based modeling of microglial function in alzheimer's disease

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by memory loss, cognitive decline, and behavioral changes. As the most common form of dementia, accounting for 60–80% of all cases, it currently lacks effective treatment, with existing therapies offering only symptomatic relief. Microglia, the brain's resident immune cells, are essential for maintaining neural homeostasis through immune surveillance, synaptic pruning, and clearance of cellular debris. In AD, microglia become chronically activated in response to amyloid-beta (Aβ) plaques, leading to persistent neuroinflammation and neuronal damage. Apolipoprotein E (APOE), a lipid-transport protein critical for cholesterol and phospholipid metabolism in the CNS, plays a key role in AD pathology. The APOE4 variant increases the risk of AD by stabilizing toxic Aβ oligomers and promoting plaque formation. Additionally, APOE4 activates the TREM2 pathway, driving microglia into a disease-associated microglia (DAM) state that enhances inflammation and neurodegeneration. Oxidative stress, which increases with aging, results from an imbalance in redox homeostasis, often due to elevated reactive oxygen species (ROS) or impaired antioxidant defenses. ROS play a significant role in AD by exacerbating inflammation and cell damage. Microglia are particularly sensitive to oxidative stress. In AD, NOX2-derived ROS production is linked to DAM activation, inflammation, and Aβ accumulation. Both mitochondrial and NOX-derived ROS act as signaling molecules that amplify immune responses, contributing to disease progression. We hypothesize that the APOE genotype (ε2, ε3, ε4) differentially influences microglial ROS production and activation. Specifically, APOE ε4 is expected to increase oxidative stress and promote a stronger pro-inflammatory microglial response compared to ε2 and ε3 genotypes.

Keywords : iPSC, Microglia, Alzheimer's disease, APOE, patient derived microglia

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P-327

Acute stress impairs subregion-specific dopamine signaling in the nucleus accumbens shell

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The nucleus accumbens (NAc) integrates rewarding and aversive stimuli through dopaminergic input from the ventral tegmental area (VTA). We investigated how acute learned helplessness (aLH) alters dopamine dynamics in two NAc subregions: the lateral shell (NAcLsh) and medial shell (NAcMsh). Ex vivo patch-clamp recordings showed increased neuronal excitability selectively in NAcMsh neurons after aLH, and this increase was abolished by a D1 receptor antagonist, suggesting dopamine-dependent plasticity. To examine subregion-specific dopamine dynamics *in vivo*, we recorded dopamine release in the NAcLsh and NAcMsh using $GRAB_{DA}$ sensors, during social interaction, chocolate consumption, and foot shock, before and after aLH induction. Behaviorally, aLH reduced social interaction and decreased mobility during foot shock. Social interaction triggers dopamine release in the NAcLsh, and this dopamine release was significantly attenuated following aLH. In contrast, dopamine release in the NAcMsh was selectively evoked by foot shock and also diminished by aLH. Retrograde tracing revealed distinct populations of VTA neurons projecting to NAcLsh and NAcMsh, supporting subregion-specific dopaminergic modulation. These findings demonstrate that aLH disrupts dopaminergic signaling in the NAc shell in a subregion-specific manner, affecting both social and aversive processing. Such disruptions may underlie broad motivational deficits observed in stress-related disorders.

Keywords : Nucleus accumbens shell, Dopamine, Stress, Social behavior

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P-328

Age-dependent behavioral and synaptic changes in 3xTg-AD mice: Insights into alzheimer's disease progression

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Alzheimer's disease (AD) is an age-associated neurodegenerative disorder characterized by progressive cognitive decline and synaptic dysfunction. Synaptic impairment is widely recognized as a critical early event in AD pathogenesis and directly correlates with the severity of cognitive and memory deficits observed in patients. As the disease advances, the gradual loss of synapses in key brain regions such as the hippocampus and cortex undermine neural circuit integrity essential for learning and memory formation. This study aimed to comprehensively investigate the age-dependent progression of behavioral impairments in 3xTg-AD mice across different stages of their lifespan, as well as the underlying alterations in synaptic protein expression at a later disease stage. Cognitive and general behavioral phenotypes were assessed using behavior tests, including the open field test (OFT), novel object recognition test (NORT), Y-maze, cross-maze, and fear conditioning test at 2–3, 4–5, and 9 months of age. Following these assessments, brain tissues from 9-month-old mice were collected to analyze the expression levels of key synaptic proteins, postsynaptic density protein 95 (PSD-95) and synaptophysin. Our results refine the characterization of behavioral phenotypes in this AD mouse model and may contribute to a better understanding of the development and progression of both behavioral deficits and synaptic pathology in AD.

Keywords : Alzheimer's Disease, Synapse, Behavioral test

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P-329

NRA-specific role for autophagy disruption-based pathogenesis of Alzheimer's disease

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Aging-related autophagy is considered a significant risk factor for Alzheimer's disease (AD); however, the mechanisms are unknown. Therefore, its clinical application as a therapeutic strategy is limited. Here, we show that a negative regulator of autophagy, NRA, is involved in AD pathology. NRA expression is upregulated in the postmortem human brain with AD and is localized in the neuropathological lesions of AD. In the AD mouse model, NRA increased with aging and during Aβ generation. We found that Aβ increased the level of the NRA complex, which is responsible for age-related autophagy disruption. NRA overexpression enhanced extracellular Aβ concentration and tau phosphorylation, whereas NRA depletion reversed these concentrations. NRA can be secreted extracellularly and control neuronal chemokine CCL2 secretion. Depletion of NRA blocked microglial inflammation following Aβ treatment. Our findings demonstrate that neuronal NRA regulates CCL2 secretion, extracellular Aβ accumulation, and tau phosphorylation, indicating that it plays a crucial role in the pathogenesis of AD.

Keywords : AD, Autophagy, pTau, Ab

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P-330

Distinct behavioral phenotypes in multi-gene transgenic mouse models of alzheimer's disease

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Animal models are essential for elucidating the mechanisms underlying neurodegenerative diseases. While individual genetic risk factors for Alzheimer's disease (AD) have been extensively modeled, the combinatorial effects of these factors remain incompletely understood. In this study, we investigated the behavioral phenotypes of transgenic mice harboring APP/PSEN1 and tau mutations, along with knockout of a

myeloid receptor gene. These combined genetic modifications resulted in pronounced impairments in memory and cognition, consistent with early AD-related pathology. Motor abilities exhibited a mild decline, potentially reflecting slower lesion progression in motor-associated brain regions. Social behavior remained largely unaffected. These distinct behavioral deficits likely reflect region-specific neuropathological progression and vulnerability during AD. Future studies incorporating multi-age tissue analysis will further delineate the stage-specific impacts of these genetic alterations on AD pathology and may facilitate identification of novel therapeutic targets.

Keywords : Alzheimer's Disease, Behavioral test, memory

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P-331

Focused ultrasound stimulation recovers abnormal ciliary defects by enhancing mitochondrial respiration

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Ventriculomegaly is a neurological condition which is caused by excessive cerebrospinal fluid (CSF) accumulation. Cilia in the subventricular zone modulate CSF circulation through ciliary beating. Mitochondria regard as providing primary energy source for ciliary beating by oxidative phosphorylation (OXPHOS). It could contribute to maintaining normal CSF outflow. Furthermore, mitochondrial dysfunction has been implicated in the progression of ventriculomegaly; however, enhancement of cilia function by upregulation of mitochondrial respiration has not been widely studied. Since focused ultrasound stimulation (FUS) has been reported to increase mitochondrial biogenesis, so we tried to apply FUS to a mouse model with mitochondrial defect in ependymal cells, which presents ventricular enlargement. First of all, we observed ventricular enlargement and shortened cilia in the subventricular zone in our mouse model. To investigate the effectiveness of FUS, we performed FUS on our mouse model and found that FUS ameliorates motor coordination and cognitive impairment. As expected, FUS administration reduced ventricular enlargement and enhanced mitochondrial respiration in the choroid plexus. Taken together, these findings suggest that FUS may serve as a promising non-invasive approach to improve cilia function through enhanced mitochondrial respiration, ultimately facilitating CSF flow.

Keywords : Focused ultrasound stimulation, Cilia, Mitochondria, Ventriculomegaly

P-332

Human-like glycosylation in mice alters neurobehavioral phenotypes

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Glycosylation is a post-translational modification in which carbohydrate chains (glycans) are enzymatically attached to proteins or lipids. This process plays a crucial role in protein folding, trafficking, stability, and cell signaling. Recently, glycosylation has been increasingly recognized as a key regulator of brain development and neurological function, with studies implicating it in synaptic plasticity, neuronal maturation, and the modulation of neural signaling pathways. Moreover, aberrant glycosylation has been reported in several neuropsychiatric and neurodegenerative disorders, including Alzheimer's disease, schizophrenia, and depression, underscoring its importance in brain physiology and pathology. Mouse models have been instrumental in elucidating these roles, as their brain N-glycan structures are broadly similar to those of humans. However, certain glycosylation-related genes—Cmah, Ggta1, and iGb3s—are either inactive or absent in humans. To better mimic the human glycosylation profile, we utilized triple knockout (TKO) mice lacking these genes and investigated whether the resulting glycan alterations affect physiological traits, particularly behavior. TKO mice exhibited increased anxiety-like behavior in the open field test and enhanced long-term recognition memory in the novel object recognition test. These findings suggest that the elimination of non-human glycan epitopes—specifically Neu5Gc, α-Gal, and iGb3—modulates anxiety and memory, indicating a phylogenetic divergence in glycosylation pathways that may underlie cognitive specialization in humans. Given that humans naturally lack these glycans, our results point to glycosylation as a possible contributing factor to species-specific neurobehavioral traits. However, direct translation of these findings to human emotional states warrants cautious interpretation and further investigation.

Keywords : Glycosylation, Human-like glycosylation, Novel object recognition, Triple knockout, Neurobehavior

P-333

Therapeutic effects of transcranial direct current stimulation in an alzheimer's disease mouse model via a glial mechanism

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Background: Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that modulates neuronal activity through low-intensity electrical currents. Alzheimer's disease (AD) is a brain disorder associated with a decline in overall cognitive functions, such as memory and attention. Sleep disturbances, commonly observed in AD, are bi-directionally associated with the disease severity. Recently, reactive astrocytosis in response to amyloidopathy in the brain has been suggested as a pathogenic mechanism for memory dysfunction and sleep disturbances. In this context, the therapeutic potential of tDCS in reducing amyloid-beta and improving cognitive functions has been

increasingly reported. However, the specific mechanisms of tDCS in AD remain unclear. Here, we hypothesized that tDCS could restore sleep disturbances by reducing reactive astrocytosis, and enhance amyloid-beta clearance via activated glymphatic system. Methods: EEG/EMG surgery, along with the installation of tDCS electrodes, was performed on all experimental mice. EEG electrodes were placed on the frontal and parietal areas, while tDCS electrodes were placed on the contralateral frontal and cerebellum areas. Twenty-minute tDCS with 200 μA was administered for two weeks. Electroencephalography was recorded to quantify sleep and 40-Hz auditory steady-state response (ASSR) before and after the tDCS treatment. Amyloid beta and astrocytic GABA were assessed by immunohistochemistry. Results: Our preliminary data showed that two-week tDCS increased NREM and REM sleep duration in 5xFAD mice. These therapeutic effects were not observed in the tDCS sham group. In addition, the count and area of amyloid plaques in both the hippocampus and cortex were reduced in the tDCS group compared to those of the sham group. Furthermore, in the tDCS stimulation group, there was an increase in 40-Hz ASSR-induced gamma power compared to the baseline. Quantification of oligodendrocytes is pending.

Keywords : transcranial direct current stimulation, Alzheimer's disease, Amyloid beta, Gamma-band oscillations, Cognition

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P-334

Sleep deprivation in adolescent mice impairs long- term memory till early adulthood via suppression of hippocampal astrocytes

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Sleep defciency is a rampant issue in modern society, serving as a pathogenic element contributing to learning and memory impair- ment, with heightened sensitivity observed in children. Clinical observations suggest that learning disabilities associated with insuffcient sleep during adolescence can persist through adulthood, but experimental evidence for this is lacking. In this study, we examined the impact of early-life sleep deprivation (SD) on both short-term and long-term memory, tracking the effects sequentially into adulthood. We employed a modifed multiple-platform method mouse model to investigate these outcomes. SD induced over a 14-day period, beginning on postnatal day 28 (PND28) in mice, led to signifcant impairment in long-term memory (while short- term memory remained unaffected) at PND42. Notably, this dysfunction persisted into adulthood at PND85. The specifc impairment observed in long-term memory was elucidated through histopathological alterations in hippocampal neurogenesis, as evidenced by bromodeoxyuridine (BrdU) signals, observed both at PND42 and PND85. Furthermore, the hippocampal region exhibited signif- cantly diminished protein expressions of astrocytes, characterized by lowered levels of aquaporin 4 (AQP4), a representative molecule involved in brain clearance processes, and reduced protein expressions of brain-derived neurotrophic factors. In conclusion, we have presented experimental evidence indicating that sleep defciency-related impairment of long-term memory in adolescence can endure into adulthood. The corresponding mechanisms may indicate that the modifcation of astrocyte-related molecules has led to changes in hippocampal neurogenesis.

Keywords : Sleep, Astrocyte, Memory, Adolescent, Adul ㅇ ㄴ

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P-335

GAT-3 inhibition restores gait and behavioral transition deficits via tonic inhibition in an ADHD mouse model

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Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by typical symptoms such as hyperactivity, impulsivity, and inattention. In addition, motor deficits are often observed in individuals with ADHD. Pharmacological treatments targeting neuromodulators are effective for cognitive symptoms of ADHD, but are less effective for behavior transition patterns and gait instability. To better understand the neurophysiological changes associated with these motor deficits, we examined tonic inhibition in several brain regions of a mouse model of ADHD, specifically the GIT1 haploinsufficient mouse. This model exhibited abnormal base of support (a measure of gait stability) and altered behavioral patterns, characterized by frequent transitions to head raising-like behavior without progression to rearing-like behavior. These abnormalities were alleviated by treatment with the tonic inhibition-modulating drug SNAP5114, a GAT-3 inhibitor. Our results suggest that tonic inhibition is involved in the pathophysiology of ADHD, and that its modulation may represent a promising therapeutic target for the treatment of motor deficits in ADHD.

Keywords : ADHD, Motor deficit, GABA, Tonic inhibition, Behavior patterns

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P-336

The astrocytic MAOB-GABA axis suppresses spinal cord regeneration by downregulating BDNF-TrkB signaling

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Neuroregeneration after spinal cord injury (SCI) is often inhibited by the glial scar, yet the molecular mechanisms underlying this inhibition remain poorly defined. Here, we identify the astrocytic monoamine oxidase B (MAOB)-GABA axis as a key molecular brake on CNS repair. In severe SCI models, excessive GABA from reactive astrocytes suppressed brain-derived neurotrophic factor (BDNF) and TrkB expression, impairing neuroregeneration. Genetic deletion of astrocytic MAOB in mice or pharmacological inhibition with KDS2010

in rats and monkeys led to functional recovery and tissue regeneration by restoring BDNF-TrkB signaling. KDS2010 further demonstrated safety and dose-proportional pharmacokinetics in a phase 1 clinical trial. These findings highlight the astrocytic MAOB-GABA axis as a therapeutic target and support KDS2010's potential for clinical translation in SCI.

Keywords : Spinal cord injury, Astrocyte, MAOB, GABA, BDNF-TrkB signaling

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P-337

Enhanced homeostatic sleep response and decreased neurodegenerative proteins in cereblon knock-out mice

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Cereblon (CRBN), a substrate receptor of the CRL4 E3 ubiquitin ligase complex, regulates energy levels by ubiquitinating AMP-activated protein kinase (AMPK). While CRBN's role in energy regulation is established, its involvement in sleep remains unclear. Thalidomide, a pharmacological modulator of CRBN, has shown to improve sleep quality, particularly by increasing slow-wave sleep (SWS) and overall sleep efficiency. This study explores the impact of CRBN deletion on sleep-wake patterns and examines parallels to thalidomide's effects. Stress-associated proteins, including phospho-Tau, phospho-α-Synuclein, DNAJA1 (DJ2), DNAJB1 (DJ1), and Heat Shock Protein 70 (HSP70), were measured via immunoblotting. Sleep deprivation reduced CRBN expression in *Crbn*$^{+/+}$ mice and elevated stress markers such as phospho-Tau, phospho-α-Synuclein, DJ2, and DJ1 in both genotypes. *Crbn*$^{-/-}$ mice showed a blunted increase in phospho-Tau and phospho-α-Synuclein but higher levels of HSP70, DJ2, and DJ1. During recovery sleep, *Crbn*$^{-/-}$ mice exhibited significantly increased slow-wave activity, suggesting heightened homeostatic sleep pressure, likely due to AMPK hyperactivation in the absence of CRBN. CRBN plays a critical role in regulating sleep homeostasis and recovery sleep, likely through its modulation of AMPK activity and stress protein responses. Interestingly, thalidomide, a CRBN modulator, has been shown to enhance slow-wave sleep and overall sleep quality in clinical studies. This improvement in slow-wave activity parallels the increased SWA observed in *Crbn*$^{-/-}$ mice during recovery sleep. This highlights a dual role for CRBN in both promoting energy balance and regulating sleep architecture. Thalidomide or related CRBN modulators could offer therapeutic benefits for improving sleep quality and mitigating neurodegeneration associated with disrupted sleep, while careful attention is needed to avoid unintended effects related to CRBN deficiency.

Keywords : Cereblon, Energy homeostasis, Sleep deprivation, Alzheimer's disease, NREM sleep

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P-338

Sleep deprivation triggers neuroinflammation and memory decline

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Sleep disorders, increasingly common in modern society, are recognized as critical risk factors for a range of health issues, including cardiovascular diseases, metabolic syndromes, cognitive impairments, and notably, memory decline. This study aims to investigate the effects of sleep deprivation on early pathological changes leading to memory decline, with a particular focus on synaptic damage and neuronal alterations in 6-month-old mice. To elucidate the mechanisms by which sleep deprivation impairs memory functions, mice were subjected to sleep deprivation (SD), while control mice maintained normal sleep. SD mice exhibited depressive-like behaviors and memory deficits. Brain tissue samples (cortex and hippocampus) from these mice were analyzed using immunostaining and Western blotting. We assessed neuronal damage, glial cell activation (as a marker of neuroinflammation), and alterations in key synaptic proteins essential for memory formation and consolidation. Our results demonstrate that sleep deprivation induces early pathological changes linked to memory decline and related diseases. Further studies will contribute to a better understanding of the mechanisms underlying sleep deprivation-induced memory impairments and may inform strategies for prevention and early intervention.

Keywords : sleep deprivation, memory, alzheimer disease

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P-339

NF-κB dysregulation impairs microglial polarization and morphology

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Alzheimer's disease (AD) involves not only amyloid and tau pathology but also chronic neuroinflammation. The NF-κB pathway plays an important role to regulate neuroinflammation, with its upstream modulators critically influencing microglial activation and cytokine production. Dysregulation of NF-κB regulatory proteins may disrupt microglial polarization, potentially exacerbating neuroinflammation and accelerating neurodegeneration. To investigate NF-κB dysregulation in microglial activity, we compared 12-month-old mice with targeted NF-κB dysregulation to age-matched wild-type (WT) controls. NF-κB dysregulated mice exhibited impaired polarization into both M1 and M2 microglial phenotypes. Morphologically, these mice showed reduced total microglial process length and increased cell body size compared to WT, despite comparable microglial numbers. Future studies will analyze inflammatory cytokines and cell death pathways (apoptosis/necroptosis) to elucidate NF-κB's role in neuroinflammation and neuronal loss.

Keywords : Alzheimer's disease (AD), Neuroinflammation, NF-κB

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P-340

Disrupted amygdala–frontal connectivity drives psychopathy-like antisocial behavior following early life stress

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Psychopathy, characterized by empathy deficits and antisocial behavior, is associated with brain abnormalities linked to early life adversity. However, whether such behavior is driven by specific neural circuits remains unclear. Here, we developed the Nosepoke-Operated Pain Assay (NOPA), a novel paradigm in which mice inflict pain on conspecifics via nosepoking, thereby modeling psychopathy-like behavior. Notably, a subset of animals exposed to chronic social stress displayed increased antisocial behavior associated with disrupted connectivity between the infralimbic medial prefrontal cortex (IL-mPFC) and the basolateral amygdala (BLA). Moreover, *ex vivo* electrophysiology revealed increased IL cortical excitability in these mice, attributed to impaired inhibitory activity. Circuit-specific optogenetic manipulations were sufficient to either induce or rescue this behavior, suggesting a causal role of IL-BLA circuitry. These findings provide a novel framework for modeling empathy-related antisocial personality disorders, and highlight potential circuit-level targets for therapeutic intervention.

Keywords : Mouse model, Early life stress, Psychopathy-like behavior

P-341

Comprehensive behavioral characterization and latent trait mapping in SHR rats: A validated model for ADHD

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The spontaneously hypertensive rat (SHR) is widely used as an animal model of attention-deficit/hyperactivity disorder (ADHD). While previous studies have reported behavioral alterations in SHR rats, few have comprehensively analyzed multidimensional behavioral traits across domains. In the present study, we first examined inter-strain behavioral differences between Sprague-Dawley (SD) and Wistar Kyoto (WKY) rats to establish a baseline. Subsequently, we conducted a comprehensive battery of behavioral tests on SHR and WKY rats and employed exploratory factor analysis to identify underlying behavioral structures. SHR rats displayed significantly altered behavior in locomotion, impulsivity, anxiety, sensorimotor gating, and compulsivity. Exploratory factor analysis extracted five interpretable behavioral domains, with SHR rats scoring significantly higher on hyperactivity and stress-related factors. These findings support the utility of SHR as a multidimensional model of ADHD and offer a data-driven framework for linking behavioral and neurobiological phenotypes.

Keywords : ADHD, SHR rat, Impulsivity, Cognitive behavior, Compulsivity

Molecular and Cellular Neuroscience P-342~P-425

P-342

N-Acetylcysteine alleviates depressive-like behaviors in adolescent EAAC1-/- mice and early life stress model rats

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Exposure to adverse experiences during early life is associated with an increased risk of psychopathology during adolescence. In a previous study, we demonstrated that neonatal maternal separation (NMS) combined with social isolation led to impulsive and depressive-like behaviors in male adolescents. Additionally, it significantly reduced the expression of excitatory amino acid carrier 1 (EAAC1) in the hippocampus. Building upon this work, we investigated the effects of N-acetylcysteine (NAC), a precursor to glutathione, in early-life stress (ELS) model rats and in EAAC1-/- mice. EAAC1 plays a dual role in transporting both glutamate and cysteine into neurons. Our findings revealed that female adolescents subjected to in the ELS model also exhibited behavioral defects similar to those of males. NAC injection rescued depressive-like behaviors in both male and female NMS models, but it improved impulsive behavior only in males. Furthermore, we observed increased reactive oxidative stress (ROS) and neuroinflammation in the ventral hippocampus (vHPC) and prefrontal cortex of NMS model rats, which were mitigated by NAC treatment. Notably, NAC reversed the reduced expression of EAAC1 in the vHPC of NMS model rats. In EAAC1-/- mice, severe impulsive and depressive-like behaviors were evident, and the NAC intervention improved only depressive-like behaviors. Collectively, our results suggest that ELS contributes to depression and impulsive behaviors during adolescence. Moreover, the cysteine uptake function of EAAC1 in neurons may be specifically related to depression rather than impulsive behavior.

Keywords : Early life stress, Neonatal maternal separation, Excitatory amino acid carrier 1 (EAAC1), N-acetylcysteine (NAC), Depressive-like behavior

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P-343

KCTD3 mutations cause neurodevelopmental disorder through DAAM1-mediated axon initial segment disruption

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Patients carrying loss-of-function variants in *KCTD3* present with neurodevelopmental disorders characterized by developmental epileptic encephalopathy (DEE), cerebellar hypoplasia, and motor dysfunction. However, the underlying mechanisms remain unclear. To investigate

the molecular function of KCTD3, we utilized a *Kctd3* knockout mouse model. Despite minimal changes in the transcriptome, proteomic analysis of embryonic brains revealed a marked reduction in DAAM1, a member of the formin family and a key regulator of actin cytoskeletal dynamics. DAAM1 is known to be a component of axon initial segment (AIS) protein complexes, regulating axonal cytoskeletal organization and outgrowth. In cultured neurons, *Kctd3* depletion reduced DAAM1 expression, leading to elongated and mislocalized ankyrin G within the AIS of hippocampal and dorsal root ganglion (DRG) neurons. The impaired AIS integrity of KCTD3-depleted neurons was rescued by DAAM1 overexpression. Functionally, neurite outgrowth and growth cone morphology were impaired, but both were restored by DAAM1 overexpression. In vivo, *Kctd3* knockdown disrupted AIS integrity and motor axon innervation at neuromuscular junctions (NMJs), potentially contributing to observed behavioral phenotypes such as limb clasping, impaired motor coordination, and respiratory defects. Together, our findings identify KCTD3 as a crucial upstream regulator of DAAM1 and AIS integrity. This study advances our understanding of AIS-related pathophysiology and highlights DAAM1 as a potential therapeutic target for *KCTD3*-associated neurological disorders.

Keywords : KCTD3, Neurodevelopmental disorder, DAAM1, Axon initial segment, Neuromuscular junction

P-344

Chronic stress-induced alterations in feeding behavior and emotional phenotypes via Glp1R and MC4R downregulation in the nucleus accumbens

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Stressful events are well-established risk factors for psychological disorders, particularly depression. Nevertheless, a substantial subset of individuals demonstrate resilience, maintaining stable psychological functioning despite repeated exposure to adversive stressors. While stress-induced symptoms such as anhedonia, dysregulated feeding behaviors, and behavioral despair are frequently observed, the precise synaptic and molecular mechanisms underlying these diverse phenotypes remain largely unknown. In this study, we examined the effects of chronic unpredictable stress (CUS) on behavior and gene expression in an inbred mouse model. Mice exposed to CUS exhibited significant behavioral alterations, including reduced sucrose preference (anhedonia), abnormal feeding patterns, and increased behavioral despair. Transcriptomic analysis using RNA sequencing revealed stress-specific gene expression changes in the nucleus accumbens (NAc), a key brain region involved in motivation and emotional regulation. Notably, we observed significant downregulation of glucagon-like peptide-1 receptor (Glp1R) and melanocortin 4 receptor (MC4R) genes in the NAc of stressed mice. Both genes play essential roles in appetite regulation, energy balance, and mood modulation. These findings suggest that stress-induced suppression of Glp1R and MC4R signaling within the NAc may contribute to disrupted feeding behavior and emotional dysregulation. Our study highlights a potential molecular pathway linking chronic stress to neurobehavioral outcomes and identifies promising targets for intervention in stress-related disorders.

Keywords : Feeding behavior, Chronic stress, Glp1R, MC4R

P-345

Autophagic regulation of myelin protein zero during myelination in Schwann cells

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The myelin sheath is essential structure for rapid impulse transmission along axons. In the peripheral nervous system, Schwann cells (SCs) are responsible for the generation of the myelin sheath. Myelin protein zero (MPZ) is the most common myelin protein in the peripheral nerves and thus quantitative control of MPZ expression is essential for normal myelination. Previous studies have found that autophagy, the lysosomal degradation of dysfunctional organelles and proteins, regulates myelin destruction during demyelination. In this study, we investigated the role of autophagy in MPZ metabolism during myelination period of SCs. To evaluate the activity of autophagy during developmental myelination and remyelination after injury, we used GFP-RFP-LC3 mice. MPZ destruction of autophagy was examined with immunofluorescent staining and western blot analysis in primary SCs culture system. Primary SCs were isolated from early postnatal rat sciatic nerve, and were treated with db-cAMP to induce differentiation. We also performed lentiviral transduction of MPZ and LC3 in SCs. We confirmed that autophagy activity was higher during postnatal myelination period than just after birth or in adulthood. After crush injury in adult mice, autophagy activity was downregulated during demyelination and reactivated during remyelination period. In differentiated SCs, we observed an increase of autophagy markers, LC3-II form and autophagosomes, and lysosomes compared to undifferentiated controls. Furthermore, MPZ was colocalized with LC3 vesicles, while E-cadherin (E-cad, mainly localized in non-compact myelin domain) was not, during SC differentiation. In addition, autolysosomal inhibition resulted in an increase in MPZ, but not E-cad levels, while forceful activation of autophagy via starvation during differentiation accelerated selective MPZ destruction. Our results suggest that autophagy plays an important role in MPZ metabolism during active myelin synthetic period in SCs.

Keywords : Schwann cells, Myelination, MPZ metabolism, Autophagy

P-346

Interleukin-2 improves insulin sensitivity through hypothalamic sympathetic activation in obese mice

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IL-2 regulates T cell differentiation: low-dose IL-2 induces immunoregulatory Treg differentiation, while high-dose IL-2 acts as a potent activator of cytotoxic T cells and NK cells. Therefore, high-dose IL-2 has been studied for use in cancer immunotherapy. We aimed to utilize low-dose IL-2 to treat inflammatory diseases such as obesity and insulin resistance, which involve low-grade chronic inflammation. Systemic administration of low-dose IL-2 increased Treg cells and decreased inflammation in gonadal white adipose tissue (gWAT), leading to improved insulin sensitivity in high-fat diet-fed obese mice.

Additionally, central administration of IL-2 significantly enhanced insulin sensitivity through the activation of the sympathetic nervous system. The sympathetic signaling induced by central IL-2 administration not only decreased interferon g (IFNγ)+ Th1 cells and the expression of pro-inflammatory cytokines, including *Il-1b, Il-6, and Il-8*, but also increased CD4+ CD25+ FoxP3+ Treg cells and *Tgfb* expression in the gWAT of obese mice. These phenomena were accompanied by hypothalamic microgliosis and activation of pro-opiomelanocortin neurons. Furthermore, sympathetic denervation in gWAT reversed the enhanced insulin sensitivity and immune cell polarization induced by central IL-2 administration. Overall, we demonstrated that IL-2 improves insulin sensitivity through two mechanisms: direct action on CD4+ T cells and via the neuro-immune axis triggered by hypothalamic microgliosis.

Keywords : Interleukin-2, Insulin resistance, Adipose tissue inflammation, sympathetic nervous system, Pro-opiomelanocortin (POMC) neurons

P-347

Neurotoxic effects of carbon black on amyloid pathology and behavior in transgenic Alzheimer's model mice

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Introduction: Alzheimer's disease (AD) is a representative neurodegenerative disorder with no fundamental cure, underscoring the need to identify modifiable risk factors for prevention and delay. Air pollution, especially particulate matter (PM), is a well-established environmental risk factor for dementia. PM has been associated with neuro-inflammation and oxidative stress. However, due to its complex composition, it is difficult to identify which specific components of PM are neurotoxic. Carbon black (CB), a component used in rubber and pigment industries, has been implicated in systemic inflammation and local oxidative stress, but its role in neurotoxicity and AD pathology remains poorly understood. Objective: This study aims to investigate whether CB exposure worsens AD pathology by promoting amyloid-beta (Aβ) accumulation and cognitive decline. Method: Carbon black (250 μg) was administered intranasally to C57BL/6J and transgenic Alzheimer's model mice once daily for 2 weeks. Neuroinflammation was assessed by immunohistochemistry (IHC) and western blot targeting GFAP and Iba-1. Aβ plaque burden was evaluated by IHC. Cognitive function was assessed in 5xFAD mice. Results: In C57BL/6J mice, CB exposure induced significant neuroinflammation, as evidenced by increased GFAP and Iba-1 immunoreactivity. However, in transgenic AD mice, CB did not further increase neuroinflammatory markers, possibly due to a ceiling effect from pre-existing pathology. Nonetheless, CB exposure led to increased Aβ accumulation and exacerbated cognitive deficits, particularly impairments in Y-maze and habituation/dishabituation tasks, suggesting its potential to aggravate AD-related pathology beyond neuroinflammation. Conclusion: This study clarifies the role of CB in AD progression and suggests that specific components of PM may contribute to neurodegeneration. The findings may support early intervention strategies for high-risk groups exposed to air pollution.

Keywords : Alzheimer's disease, Air pollution, Carbon black, Amyloid-beta, neuro-inflammation

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P-348

Could Arginine-driven polyamine synthesis explain CA2's resistance to excitotoxicity?

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Polyamines (PAs) - putrescine (Put), spermidine (Spmd) and spermine (Spm), depending on concentration, cell type, cellular localization or physiological/pathological state, support diverse neuronal processes, including both neuroprotection and excitotoxicity. Excitotoxicity, a key mechanism of neuronal death in disorders like epilepsy, stroke, or traumatic brain injury, particularly affects hippocampal CA1 neurons, while neighboring CA2 largely remains unaffected, a divergence of unidentified molecular/cellular basis. We reproduced this region-specific vulnerability in organotypic rat hippocampal slice cultures, observing substantial CA1 damage with minimal effect in CA2 following exposure to 25 μM NMDA. In our model, all three PAs, their upstream metabolite, ornithine (Orn) and its precursor, proline (Pro) were strongly depleted, while levels of alternative Orn precursor, arginine (Arg) remained unchanged. Notably, treatment with a broad range of concentrations of DFMO, an inhibitor of ornithine decarboxylase (ODC), a rate-limiting enzyme converting Orn to Put sensitized normally resistant CA2 neurons to NMDA-induced damage, despite having no toxic effect alone. In CA1, DFMO enhanced NMDA toxicity only at highest concentration. Immunohistochemical analysis of physiological distribution of PA-related enzymes revealed their significant enrichment in CA2 versus CA1, suggesting enhanced PA synthesis in this region. Strikingly, Arg2, an enzyme converting Arg to Orn, was found exclusively in CA2, suggesting that these neurons, unlike CA1, rely on Arg for their PA synthesis. Unchanged Arg levels in NMDA-exposed slices suggest that CA2 preserves its PA homeostasis in excitotoxicity via Arg-derived Orn, bypassing the impaired Pro-dependent pathway. Our findings identify PA metabolism as a key factor in region-specific hippocampal vulnerability and highlight Arg2 expression as a potential molecular basis for selective resistance of CA2 neurons to excitotoxic injury.

Keywords : Hippocampus, CA2, Polyamines, Excitotoxicity, Neuroprotection

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P-349

MICU1 perturbation impairs mitochondrial Ca^{2+} uptake and suppresses intrinsic excitability in cortical neurons

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Mitochondrial Ca^{2+} uptake is regulated by the mitochondrial Ca^{2+} uniporter (MCU) complex, with MICU1 acting as a gatekeeper that prevents Ca^{2+} overload at resting cytosolic concentrations. While the role of MICU1 in mitochondrial Ca^{2+} handling is well established, its contribution to neuronal excitability remains unclear. We used MCUi4, a specific pharmacological inhibitor of MICU1, to investigate the role of MICU1 in cultured cortical pyramidal neurons. MCUi4 treatment attenuated mitochondrial Ca^{2+} uptake and prolonged cytosolic Ca^{2+} elevations in soma following electrical stimulation, indicating impaired Ca^{2+} buffering. Whole cell recordings showed that neurons treated with MCUi4 exhibited reduced intrinsic excitability, including higher action potential thresholds and lower firing rates. These results suggest that MICU1-dependent mitochondrial Ca^{2+} uptake modulates Ca^{2+} dynamics in response to electrical activity and is required to maintain normal neuronal excitability. Our findings establish a functional link between mitochondrial Ca^{2+} buffering and neuronal excitability and identify MICU1 as a critical regulator of this process. This work sets the stage for broader investigations into the role of MICU1 in shaping neuronal function under physiological and pathological conditions.

Keywords : Mitochondria, Excitability, MICU1, Mitochondrial Ca2+, Cortical pyramidal neuron

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P-350

Trehalose-mediated neuroprotection in acute brain injury via lysosomal and zinc homeostasis

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Trehalose has been reported to mitigate neurodegenerative diseases such as Alzheimer's disease, amyotrophic lateral sclerosis (ALS), and Huntington's disease by activating transcription factor EB (TFEB), promoting lysosomal biogenesis, inducing autophagy, and reducing misfolded protein aggregation. However, the mechanisms underlying its neuroprotective effects remain incompletely understood. Recently, trehalose has shown beneficial effects in acute brain injuries such as ischemic stroke, though its mode of action in this context is unclear. Lysosomes are not only degradative organelles but also critical regulators of intracellular zinc homeostasis. In acute brain injury, zinc overload triggered by reactive oxygen species (ROS) and calcium- and zinc-mediated excitotoxicity can induce lysosomal membrane permeabilization (LMP), leading to neuronal death. In this study, we investigated lysosome- and zinc-focused mechanisms by which trehalose confers neuroprotection in ischemic stroke. In primary cortical neurons, trehalose increased lysosomal abundance, confirmed by lysosomal staining and elevated LAMP-1 expression. It also protected against zinc-induced neurotoxicity and reduced LMP, likely by enhancing lysosomal buffering capacity and maintaining zinc homeostasis. Trehalose was internalized via endocytosis and promoted lysosomal formation. Trehalose-induced TFEB activation stimulated lysosomal biogenesis. Notably, trehalose elevated cytosolic mature cathepsin B (mCTSB), indicating mild, non-lethal LMP. Zinc released into the cytosol through this process appeared to act as a signaling molecule for TFEB activation. In summary, trehalose enhances lysosomal function via endocytosis and TFEB-mediated biogenesis, and this lysosomal upregulation plays a key neuroprotective role by buffering zinc overload and reducing LMP in ischemic stroke. We further propose that mild LMP and subsequent zinc release serve as upstream signals for TFEB activation.

Keywords : Ischemic stroke, Trehalose, Lysosome, Zinc, LMP

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P-351

A novel Aβ B-Cell epitope vaccine, Aβ-10 with carrier protein OVA and KLH reduce Aβ-induced neuroinflammation in alzheimer's disease

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by amyloid-beta (Aβ) plaque deposition and neurofibrillary tangles, which collectively drive neuroinflammation, synaptic dysfunction, and cognitive decline. Here, we investigated whether a peptide epitope vaccine targeting the Aβ1–10 sequence could mitigate Aβ-induced pathology in AD mouse model. Three Aβ1–10 peptides, i.e. Aβ1–10-N, Aβ1–10-D1H, and Aβ1–10-S8R were synthesized, and Aβ1–10-S8R was further conjugated to ovalbumin (OVA) or keyhole limpet hemocyanin (KLH) to enhance immunogenicity. Among seven treatment groups, Aβ1–10-D1H and Aβ1–10-S8R, particularly when conjugated to OVA or KLH, effectively suppressed Aβ, amyloid-beta precursor protein (APP), and beta-secretase 1 (BACE-1) expression, decreased inflammatory cytokine production by astrocytes and microglia, and increased the levels of key synaptic markers (synaptophysin, synaptosomal-associated protein 23 [SNAP-23], postsynaptic density protein 95 [PSD-95]). Carrier protein conjugation also elevated immunoglobulin G (IgG) levels in the spleen, indicative of a robust humoral response. Taken together, these findings demonstrate that Aβ1–10-based immunization, especially with OVA or KLH conjugation, reduces Aβ-driven neuroinflammation, synaptic dysfunction, and memory deficits, suggesting a promising immunotherapeutic strategy for AD.

Keywords : Alzheimer's disease (AD), beta amyloid (Aβ), epitope, immunization, neuroinflammation

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P-352

Circadian clocks are modulated by compartmentalized oscillating translation

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Terrestrial organisms developed circadian rhythms for adaptation to Earth's quasi-24-h rotation. Achieving precise rhythms requires diurnal oscillation of fundamental biological processes, such as rhythmic shifts in the cellular translational landscape; however, regulatory mechanisms underlying rhythmic translation remain elusive. Here, we identified mammalian ATXN2 and ATXN2L as cooperating master regulators of rhythmic translation, through oscillating phase separation in the suprachiasmatic nucleus along circadian cycles. The spatiotemporal oscillating condensates facilitate sequential initiation of multiple cycling processes, from mRNA processing to protein translation, for selective genes including core clock genes. Depleting ATXN2 or 2L induces opposite alterations to the circadian period, whereas the absence of both disrupts translational activation cycles and weakens circadian rhythmicity in mice. Such cellular defect can be rescued by wild type, but not phase-separation-defective ATXN2. Together, we revealed that oscillating translation is regulated by spatiotemporal condensation of two master regulators to achieve precise circadian rhythm in mammals.

Keywords : Circadian rhythm, Translation, Phase separation

P-353

Dab1 expression controls Reelin-induced PI3K-Akt activation in early GABAergic neurons

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Disabled-1 (Dab1) is an adaptor protein that plays a central role in Reelin-mediated signaling, which is essential for proper brain development by regulating neuronal migration, dendritic growth, and synaptic spine formation. Upon Reelin binding to its receptors—Very Low-Density Lipoprotein Receptor (VLDLR) and Apolipoprotein E Receptor 2 (ApoER2)—Dab1 becomes phosphorylated, triggering downstream signaling cascades including Phosphoi nositide 3-kinase (PI3K)/Akt, Lis1, Crk/C3G, and Extracellular signal-regulated kinase1/2 (Erk1/2), before it is subsequently degraded via the proteasome pathway. In humans, genetic variants in *RELN* and *DAB1* have been associated with psychiatric disorders such as schizophrenia and autism spectrum disorder. While the role of Reelin in excitatory pyramidal neurons has been extensively studied, its function in inhibitory GABAergic neurons remains poorly understood. In this study, we isolated primary GABAergic neurons from the medial ganglionic eminence of mouse embryos at embryonic day 14.5, achieving a purity of over 98–99%. We quantitatively assessed Reelin signaling activity in these MGE-derived GABAergic neurons for the first time. While Reelin exposure robustly activated the PI3K-Akt pathway in excitatory neurons, the majority of GABAergic neurons showed little to no activation, except for somatostatin-positive subtypes. We found that Dab1 is transcriptionally downregulated in early GABAergic neurons, potentially restricting their capacity to engage canonical Reelin signaling during development in a cell-type-specific manner. This study provides new quantitative molecular insights into the restricted Reelin responsiveness of most GABAergic neurons during early neurodevelopment.

Keywords : Dab1, Reelin, Medial ganglionic eminence, GABAergic neurons, Phosphoinositide 3-kinase

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P-354

Molecular alterations induced by fear conditioning in the cerebellum

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While the cerebellum has traditionally been associated with motor learning, its role in non-motor functions, such as fear conditioning, is emerging. The cerebellum is highly complex and diverse in terms of molecular, physiological, and anatomical features. This heterogeneity may be associated with the cerebellum's ability to be involved in various tasks, both motor and non-motor functions. Although the cerebellar role in motor control is well established, the underlying molecular mechanisms of non-motor learning and memory are largely unknown. Here, we investigate the transcriptional changes associated with auditory fear conditioning in the cerebellum using spatial and single-nucleus sequencing. The deep cerebellar nuclei (DCN), an output region of the cerebellum, showed increased expression of immediate early genes following fear learning. In the cerebellar cortex, distinct gene expression patterns were observed in the Purkinje cell layers of vermis and hemisphere. Furthermore, specific inhibitory neurons in the DCN exhibited prominent transcriptional changes following fear conditioning, suggesting a role for this cell type in fear memory processing. Together, these findings highlight that the cerebellum, especially the DCN, is an active fear-processing region that undergoes various transcriptional changes by fear conditioning. Our findings would shed light on the molecular mechanisms underlying the cerebellum's contribution to non-motor learning.

Keywords : Cerebellum, Fear memory, Spatial transcriptomics, Single-nucleus RNA-seq

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P-355

Identification of drugs that suppress cyclin Y expression to enhance AMPA receptor trafficking during long-term potentiation

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Cyclin Y (CCNY), a cyclin family protein traditionally linked to cell cycle regulation, negatively regulates long-term potentiation (LTP), a key mechanism underlying synaptic plasticity and learning and memory. In terminally differentiated neurons, CCNY localizes predominantly to the postsynaptic compartment, where it plays a role in inhibiting the trafficking of AMPA receptors (AMPARs) during glycine-induced LTP. Our previous studies have shown that CCNY knockout mice exhibit enhanced LTP and reduced long-term depression (LTD) at hippocampal Schaffer collateral–CA1 synapses, resulting in improved spatial learning and memory flexibility, likely through altered regulation of the cofilin-actin signaling pathway. Given these findings, pharmacologically suppressing CCNY expression may represent a promising strategy for enhancing synaptic plasticity and learning and memory. To identify drugs capable of reducing CCNY expression, a fluorescence-based screening was performed using a stable HEK293T cell line expressing CCNY-WT fused to turboGFP and a publicly available drug library. After normalization and correction for intrinsic drug autofluorescence, several candidate hit compounds were identified. Subsequent validations of these candidate drugs were conducted using SEP-GluA1 (Super Ecliptic pHluorin-GluA1) in neurons to visualize LTP-induced AMPAR trafficking to synapses via time-lapse live-cell imaging. These validations confirmed that reducing CCNY levels through drug treatment enhances AMPAR trafficking and synaptic strength, reinforcing the therapeutic potential of this approach for improving synaptic plasticity and learning and memory.

Keywords : CCNY, long-term potentiation, AMPA receptors, drug screening, live-cell imaging

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P-356

Long-term suppression of glutamate decarboxylases after glutamate excitotoxicity in primary GABAergic neurons

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The excitatory/inhibitory (E/I) balance, maintained by excitatory glutamate and inhibitory gamma-aminobutyric acid (GABA), is vital for neuronal excitability, synaptic integration, and prevention of aberrant neural activity. Disruption of this balance, seen in conditions like traumatic brain injury and Alzheimer's disease, impairs neuroplasticity, elevates epilepsy risk, and contributes to cognitive deficits. Glutamate excitotoxicity and impaired GABAergic transmission are key drivers of this dysregulation, making GABA synthesis enhancement a promising therapeutic strategy. GABA is produced by glutamate decarboxylation via glutamic acid decarboxylase (GAD) isoforms: GAD67 and GAD65, which regulate GABA levels and neurotransmission. We investigated how transient glutamate excitotoxicity affects GAD expression in primary GABAergic neurons. Our results showed a sustained reduction in GAD67 and GAD65 levels for up to 5 days in vitro, due to GABAergic neuron loss and decreased GAD67 intensity per neuron. GAD mRNA levels were downregulated primarily due to reduced mRNA stability, while enhanced autophagy contributed to GAD67 protein loss. Additionally, glutamate reduced Gephyrin clustering, suggesting disrupted GABAergic postsynaptic scaffolding. These findings provide insight into mechanisms of persistent GABAergic dysfunction and E/I imbalance in excitotoxicity-related neurological disorders and highlight potential therapeutic targets to restore GABAergic function.

Keywords : Gamma-aminobutyric acid (GABA), Glutamic Acid Decarboxylases (GADs), Medial ganglionic eminence (MGE), Glutamate Excitotoxicity, Excitatory/Inhibitory (E/I) balance

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P-357

Decoding hippocampal subfield and glial responses in ischemia using single-cell transcriptomics

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Stroke affects more than 12 million individuals worldwide annually, leading to lasting physical and cognitive impairments. The peri-infarct environment in the central nervous system, comprising glial and blood vessel cells, contributes to stroke progression. The hippocampal CA1 region is particularly vulnerable to ischemia, whereas the adjacent CA3-DG region exhibits different responses. Understanding the cellular and molecular alterations in these regions before and after ischemic insult can provide insights into stroke pathology and recovery mechanisms. We conducted single-cell RNA sequencing on Sprague–Dawley rats subjected to four-vessel occlusion (4-VO) surgery, a model of transient global cerebral ischemia, and compared them with normal control rats. Cellular composition and molecular signatures of the hippocampal CA1 and CA3-DG regions were analyzed under both ischemic and sham conditions to determine differences in glial and vascular cell responses. Following stroke, there was an elevation in pro-inflammatory microglial subtypes, with distinct differences in microglial pathways depending on the hippocampal region. A unique oligodendrocyte subtype emerged in the post-ischemic hippocampus that was not present under normal conditions. Astrocytes maintained clear cluster characteristics under both normal and ischemic conditions without significant differences. Additionally, the proportion of cd74-positive pericytes increased specifically in the CA3-DG subfield after the 4-VO procedure. These findings highlight the diverse molecular signatures and functional differences of cells in specific hippocampal

regions during global cerebral ischemia. Differences in cellular functions and composition between CA1 and CA3-DG subfields suggest that glial heterogeneity may contribute to regional differences in ischemic vulnerability.

Keywords : Global cerebral ischemia, Single-cell transcriptomics, Hippocampus, Selective vulnerability, Glia

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P-358

ZCC1 attenuates ischemic stroke damage by selectively inhibiting MMP-9 and suppressing zinc toxicity

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Stroke remains a leading cause of death and long-term disability worldwide, with current therapies offering limited efficacy and considerable risk. Matrix metalloproteinase-9 (MMP-9), a zinc-dependent enzyme, is implicated in stroke pathology through its role in blood-brain barrier (BBB) disruption, edema, and neuronal injury. Thus, targeting MMP-9 represents a promising therapeutic strategy. We evaluated the therapeutic potential of ZCC1, a novel selective MMP-9 inhibitor, using both *in vivo* and *in vitro* stroke models. In a rat model of ischemic stroke induced by middle cerebral artery occlusion, ZCC1 significantly reduced infarct volume, confirmed by TTC (2,3,5-triphenyltetrazolium chloride) staining. *In situ* zymography revealed that elevated MMP-9 activity co-localized with injured regions, particularly within the parenchyma, suggesting a direct pathological role in ischemic brain damage. To investigate underlying mechanisms and direct neuroprotective effects, we performed *in vitro* cellular experiments. ZCC1 exhibited no self-toxicity and effectively suppressed zinc-induced neuronal death and reactive oxygen species (ROS) generation. However, ZCC1 did not protect against neuronal death by zinc ionophores such as zinc pyrithione or clioquinol, indicating that its effect is not due to direct zinc chelation. Notably, simultaneous blockade of NMDA, AMPA, voltage-gated calcium, and TRP channels led to only marginal reductions in zinc toxicity, whereas ZCC1 conferred significantly stronger protection. These findings suggest that MMP-9 inhibition by ZCC1 mitigates zinc toxicity by disrupting downstream intracellular processes after zinc entry. Further studies are needed to determine whether intracellular, rather than extracellular, MMP-9 activity is central to this process and to clarify its relationship with ROS. ZCC1 demonstrated robust neuroprotective efficacy without neurotoxicity, highlighting its strong potential as a therapeutic candidate for a stroke.

Keywords : Stroke, MMP-9, Zinc

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P-359

Phoenix dactylifera extract mitigates D-galactose-induced oxidative stress and neurodegeneration in the mouse hippocampus

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Aging induces oxidative stress and inflammatory responses, which impair neuronal function and are considered major contributing factors to neurodegenerative diseases such as Alzheimer's disease. In this study, we aimed to evaluate cognitive and motor deficits using a D-galactose-induced aging mouse model and to investigate the antioxidant and neuroprotective effects of *Phoenix dactylifera*(date palm) extract. Aging was induced in mice by subcutaneous (S.C.) injection of D-galactose, and *Phoenix dactylifera* extract was administered orally at various concentrations. Behavioral assessments were conducted using the Rota rod and Open field tests. Inflammatory responses and glial activation were evaluated through immunohistochemical staining (TNF-α, GFAP, Iba-1) and Western blot analysis. In the Rota rod test, the D-galactose-treated group exhibited impaired motor coordination, whereas the *Phoenix dactylifera*-treated groups showed a dose-dependent improvement in retention time. In the Open field test, the D-galactose group demonstrated reduced locomotor activity and central zone duration, both of which were gradually restored by *Phoenix dactylifera* extract treatment, indicating improved mobility and reduced anxiety-like behavior. Immunohistochemical and western blot analyses showed that the expression of inflammatory cytokines and glial markers was suppressed in a dose-dependent manner, confirming the anti-inflammatory and neuroprotective effects of the *Phoenix dactylifera* extract. *Phoenix dactylifera* extract alleviated cognitive and motor impairments in a D-galactose-induced aging model by inhibiting oxidative stress and inflammatory responses. These findings suggest that natural substances such as Phoenix dactylifera extract may serve as safe and effective therapeutic strategies to prevent age-related neuronal dysfunction. This study provides valuable foundational data for the development of neuroprotective strategies targeting aging-related brain diseases.

Keywords : Phoenix dactylifera, Aging, Behavioral analysis, D-galactose, Oxidative stress

P-360

Functional and distinct roles of Piezo2-mediated mechanotransduction in dental primary afferent neurons

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Piezo2, a mechanosensitive ion channel, serves as a crucial mechanotransducer in dental primary afferent (DPA) neurons and is potentially involved in hypersensitivity to mild mechanical irritations

observed in dental patients. Given Piezo2's widespread expression across diverse subpopulations of DPA neurons, this study aimed to characterize the mechanosensory properties of Piezo2-expressing DPA neurons with a focus on distinct features of voltage-gated sodium channels (VGSCs) and neuropeptide profiles. Using whole-cell patch-clamp recordings, we observed mechanically activated action potentials (APs) and classified AP waveforms based on the presence or absence of a hump during the repolarization phase. Single-cell reverse transcription polymerase chain reaction combined with patch-clamp recordings revealed specific associations between AP waveforms and molecular properties, including tetrodotoxin-resistant VGSCs (NaV1.8 and NaV1.9) and TRPV1 expression. Reanalysis of transcriptomic dataset of DPA neurons identified correlations between neuropeptides—including two CGRP isoforms (α-CGRP and β-CGRP), Substance P, and Galanin—and NaV1.8 and NaV1.9 expression, which were linked to defined AP subtypes. These molecular associations were further validated in Piezo2+ DPA neurons using fluorescence in situ hybridization. Together, these findings highlight the electrophysiological and neurochemical heterogeneity of Piezo2-expressing DPA neurons and their specialized roles in distinct mechanosensory signal transmission.

Keywords : Dental primary afferent neuron, Mechanoreceptor, Piezo2, Action potential, Voltage-gated sodium channels

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P-361

TARP γ-8 orchestrates AMPA receptor stability in the hippocampus

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Fast excitatory synaptic transmission and synaptic plasticity in the mammalian brain are primarily mediated by AMPA receptors (AMPARs), which are ionotropic glutamate receptors activated by the neurotransmitter glutamate. AMPARs function as tetramers assembled from combinations of four subunits: GluA1 to GluA4. AMPAR properties are tightly regulated by auxiliary subunits. Among these, transmembrane AMPAR regulatory proteins (TARPs) are critical modulators that influence receptor AMPAR trafficking, gating kinetics, and synaptic function. TARP γ-8, a subtype predominantly expressed in the hippocampus, has been identified as a key modulator of AMPAR function. In addition to modulating receptor localization and channel behavior, TARP γ-8 plays a vital role in maintaining receptor availability during synaptic activity and plasticity. This regulation is essential not only for basal synaptic transmission and long-term potentiation (LTP), thereby contributing to learning and memory. In this study, we show that TARP γ-8 not only regulates AMPAR trafficking and synaptic localization, as previously established, but also actively controls the total AMPAR protein levels. Loss of TARP γ-8 leads to a significant reduction in AMPAR protein expression, independent of transcriptional changes, indicating a post-translational mechanism of regulation. Our findings suggest that TARP γ-8 stabilizes AMPARs by protecting them from degradation, thereby ensuring adequate receptor availability for synaptic transmission and plasticity. These results reveal a previously unrecognized role for TARP γ-8 in maintaining AMPAR protein homeostasis and provide critical insight into the molecular mechanisms that govern excitatory synapse regulation.

Keywords : AMPA receptor, auxiliary subunit, TARP γ-8, Degradation, stability

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P-362

Regulation of BAT thermogenesis via TRPA1-expressing hypothalamic POMC neurons

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Pro-opiomelanocortin (POMC) neurons in the hypothalamic arcuate nucleus (ARC) play a pivotal role in regulating brown adipose tissue (BAT) thermogenesis via the sympathetic nervous system. The activation of transient receptor potential ankyrin 1 (TRPA1) has been demonstrated to enhance heat production, particularly in BAT. However, no direct evidence has been reported regarding BAT thermogenesis mediated by TRPA1-regulated ARC POMC neurons. This study investigates the role of TRPA1-expressing hypothalamic POMC neurons in BAT thermogenesis. To confirm TRPA1 expression in ARC POMC neurons, we employed single-cell RT-PCR and immunolabeling techniques. Selective TRPA1 agonists, including capsiate and ASP7663, induced depolarization of ARC POMC neurons, an effect that was inhibited by A967079, a TRPA1-selective antagonist. Furthermore, intracerebroventricular (i.c.v.) administration of ASP7663 increased BAT and core body temperature. The thermogenic effect of ASP7663 in BAT was abolished by co-administration of A967079. Among the BAT thermogenic markers, PGC-1α and PRDM16 expression was significantly upregulated following i.c.v. administration of ASP7663. However, this increase was reversed by A967079, except for PRDM16. These findings indicate that TRPA1-mediated activation of hypothalamic POMC neurons is critical in regulating BAT thermogenesis and promoting energy expenditure.

Keywords : Hypothalamus, energy balance, TRPA1, POMC, BAT thermogenesis

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P-363

Identification and characterization of intestinal cells that detect each essential amino acid

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A balanced intake of macronutrients such as proteins, carbohydrates, and fats is essential for the organism, but insufficient protein intake leads to several diseases, including kwashiorkor. Protein-deficient animals have a dietary behavior that selects food sources that contain essential amino acids (EAAs) rather than non-essential amino acids. Recently, a neuropeptide called CNMamide (CNMa) was found to be highly expressed in enterocytes of the midgut during protein depletion to modulate EAA-specific selective dietary behavior. Surprisingly, flies fed a holidic diet lacking single L-EAAs also enhanced CNMa expression, suggesting the possibility that there are cells each recognizing single L-EAAs. Moreover, it is not known whether enterocytes responding to amino acid deficiency are heterogeneous or homogeneous in response to various amino acids *in vivo* conditions. Here, we analyzed CNMa-expressing cells after amino acid deprivation using the *Drosophila* G-trace reporter to find specific cells for each amino acid and found a specific unidentified group of cells that responded only to leucine and not to other specific amino acids such as phenylalanine. Further studies have confirmed the existence of cells that respond to each amino acid in addition to leucine, and the conferment of this specificity is related to specific intracellular signaling processes such as TOR and GCN2. Taken together, our analysis suggests that specific enterocytes that recognize each amino acid deficiency are individually recognized and that these signals are relayed to the brain to modulate EAA-preference behavior.

Keywords : EAA-preference behavior, CNMa, Amino acid sensor, mTOR, GCN2

P-364

Disrupted zinc homeostasis and MMP-9 activation in L-BMAA-induced ALS models: Therapeutic potential of ZCS1

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Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by the degeneration and death of motor neurons. Among sporadic ALS cases, Guam ALS–parkinsonism-dementia complex (ALS-PDC) is a unique form presenting with overlapping symptoms of ALS, Parkinson's disease, and dementia, predominantly affecting the Chamorro population of Guam. Its incidence has been linked to dietary exposure to L-BMAA (β-N-methylamino-L-alanine), a non-proteinogenic neurotoxic amino acid produced by cyanobacteria. Elevated levels of L-BMAA have been detected in postmortem brain tissues of affected individuals, and its toxicity is believed to involve mitochondrial dysfunction and oxidative stress. In our study, treatment of primary cortical neurons with L-BMAA led to increased intracellular zinc levels, as observed by zinc-specific fluorescent staining. This suggested a role for zinc in L-BMAA-induced neurotoxicity. To further investigate the mechanism, we co-treated neurons with various agents. We found that the MMP-9 inhibitor, the zinc chelator TPEN, and the antioxidant Trolox significantly suppressed L-BMAA-induced cell death, indicating that zinc dysregulation, MMP-9 activation, and oxidative stress are key contributors to the toxic effects of L-BMAA. In an in vivo model, L-BMAA administration resulted in increased levels of neurofilament light chain (NfL) in the blood, a biomarker of neuronal damage. Notably, treatment with ZCS1, a compound that promotes lysosomal function, led to a significant reduction in NfL levels. In addition, L-BMAA-induced aggregation of 35 kDa TDP-43 was attenuated by ZCS1 treatment. These findings suggest that L-BMAA neurotoxicity involves zinc dysregulation, oxidative stress, and MMP-9 activation, and that ZCS1 may offer therapeutic potential in ALS-PDC by mitigating these pathological processes.

Keywords : ALS-PDC, L-BMAA, Zinc Homeostasis, MMP-9 Activation, ZCS1

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P-365

Astrocyte-specific regulation of clock proteins by Tmem44 in cultured mouse cortical astrocyte

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The circadian clock is an intrinsic timekeeping system that orchestrates ~24-hour rhythms in physiology and behavior by regulating rhythmic gene expression in cell type specific manner. Astrocytes, the most abundant glial cells in the central nervous system (CNS), are increasingly recognized for their essential roles in maintaining brain homeostasis and modulating neuronal function. Although circadian gene expression in astrocytes has been reported-including in our previous work-the functional significance of these rhythms remains largely unclear. In our previous study (Ryu et al., 2024), we identified 412 transcripts exhibiting circadian rhythmicity in cultured mouse cortical astrocytes. Among them, Herp was shown to regulate day–night differences in astrocytic ER calcium responsesand gap junction permeability. Building on this, we sought additional astrocyte-enriched, adult-expressed genes with high expression levels and rhythmic transcription. This approach led us to identify *Tmem44* (Transmembrane protein 44) as a strong candidate. While *Tmem44* mRNA exhibited robust circadian oscillation, the protein levels did not show this rhythmicity. Notably, knockdown of *Tmem44* resulted in a significant reduction in the protein levels of several core clock components. Ongoing studies are investigating the molecular mechanism by which Tmem44 regulates circadian clock dynamics in astrocytes.

Keywords : circadian clock, astrocyte, Tmem44, Bmal1

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P-366

Sonically enhanced adult-born neurogenesis represents a novel paradigm for improving cognitive function

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Recent advances in neuroscience have discovered possibilities for non-invasive brain stimulation techniques in enhancing cognitive functions. One such technique, focused ultrasound stimulation, has garnered attention over invasive stimulation methods and pharmacological interventions. The hippocampus is a critical brain structure for memory formation, known to undergo continuous remodeling through adult neurogenesis. Hippocampal-dependent memory is crucial for learning and spatial navigation. Emerging research suggests that non-invasive brain stimulation may positively influence the neurogenic process, thereby enhancing cognitive performance. In this context, the major objective of this study was to apply low-intensity intermittent theta-gamma coupled ultrasound to the hippocampus of WT mice and observe improvement in hippocampal memory functions. Furthermore, the involvement of adult-born neurogenesis in cognitive performance was assessed. Hippocampal-dependent memory was evaluated using the novel place recognition test and the novel object recognition test following hippocampal stimulation. Additionally, BrdU was injected intraperitoneally, and immunohistochemistry was conducted to observe changes in adult-born neurogenesis following stimulation. According to results, ultrasound paradigm applied for 14 consecutive days showed a significant increase in the discrimination index in WT mice compared to the sham group. Moreover, the application of the above ultrasound paradigm for 14 consecutive days demonstrated a significant increase in BrdU+ cell populations. In total, these findings indicate that above mentioned ultrasound paradigm might increase hippocampal-dependent memory and adult-neurogenesis, suggesting a positive correlation between these variables.

Keywords : Ultrasound neuromodulation, Hippocampal dependent memory, Adult-born neurogenesis

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P-367

Aberrant MAOB-dependent H_2O_2 cause neuropathic pain and exacerbates nocturnal pain via REVERBα-dependent MAOB disinhibi

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Neuropathic pain is a complex disorder involving spinal inhibitory dysfunction and hyperexcitability of sensory pathways, leading to chronic pain states such as allodynia. Reactive oxygen species (ROS), particularly hydrogen peroxide (H_2O_2), are major cause of this neuropathic pain, and the mechanisms by which oxidative stress drives both chronic and circadian-modulated pain remain insufficiently understood. Here, we demonstrate that H_2O_2 directly induce glial activation and neuronal sensitization in the spinal cord following peripheral nerve injury, leading to sustained pain hypersensitivity. Together with, H_2O_2 also disrupt circadian regulation by downregulating the expression of the transcriptional repressor Rev-erbα in spinal glia. This reduction in Rev-erbα leads to the disinhibition of monoamine oxidase B (MAOB), resulting in aberrant upregulation of MAOB and excessive production of H_2O_2, especially during the sleep phase. The amplified MAOB activity forms a self-reinforcing H_2O_2–REVERBα–MAOB feedback loop that accelerates ROS accumulation and exacerbates nocturnal pain. Treatment with KDS12025, a BBB-permeable ROS scavenger, restores REVERBα expression, reduces MAOB activity, and alleviates both basal and nocturnal pain hypersensitivity in a spinal nerve transection model. These findings uncover a novel oxidative–circadian mechanism of neuropathic pain and highlight the therapeutic potential of targeting the H_2O_2–REVERBα–MAOB pathway with KDS12025.

Keywords : Neuropathic pain, Circadian rhythm, Reactive oxygen species (ROS), REVERBα, Monoamine oxidase B (MAOB)

P-368

Dual CRBN-dependent and -independent neuroprotective actions of the thalidomide analog in a mild traumatic brain injury model

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Traumatic brain injury (TBI) triggers cognitive impairment and neuroinflammation, yet there are currently no FDA-approved pharmacological treatments specifically targeting the secondary inflammatory response following TBI. Thalidomide and its analogs are known for their cereblon (CRBN)-mediated immunomodulatory effects and have potential for mitigating neuroinflammation and associated diseases. We aimed to investigate the neuroprotective and anti-inflammatory effects of the thalidomide analog Compound X in a mild TBI (mTBI) mouse model and microglial cell lines. Mice were subjected to weight-drop induced mTBI and immediately treated with Compound X(1 or 10 mg/kg via IV injection). Behavioral tests (Novel Object Recognition and Y-maze) assessed cognitive recovery. Brain sections were analyzed by immunofluorescent staining for GFAP, Iba-1, and ZO-1. In vitro, BV2 and HMC3 microglial cells were stimulated with LPS ± compound X, followed by cytokine quantification and Western blot analysis. Compound X significantly reduced glial activation and improved cognitive performance in TBI mice. ZO-1 integrity was preserved, suggesting blood-brain barrier protection. In vitro, compound X suppressed the release of pro-inflammatory cytokines and modulated inflammatory signaling through both CRBN-dependent and independent mechanisms. These results suggest that Compound X functions through and independently of CRBN to inhibit neuroinflammation in a manner that can alleviate TBI-induced neurological and cognitive impairments.

Keywords : Traumatic Brain Injury (TBI), Neuroinflammation, Cereblon (CRBN), Thalidomide analog

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P-369

Regulation of cyclin Y and CYBP3 interaction with an *in silico-in vitro* integrated approach

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Cyclin Y (CCNY) is a member of the cyclin family, which is known to play crucial roles in cell cycle regulation and transcriptional processes. In the nervous system, however, CCNY inhibits long-term potentiation (LTP), the cellular basis of learning and memory, as well as spatial learning. In addition, increased interaction between CCNY and its binding protein (CCNY-binding protein 3, CYBP3) has been observed in a mouse model of dementia, leading us to hypothesize that inhibiting the CCNY-CYBP3 interaction could improve learning and memory. To test this hypothesis, we conducted *in silico* analysis to identify the CYBP3-binding region of CCNY and define its pharmacophore. We then validated this prediction using a biomolecular fluorescence complementation (BiFC) assay, in which the physical interaction of CCNY-VN173 with CYBP3-VC155 positively correlates with Venus fluorescence intensity, serving as an indicator of CCNY-CYBP3 interaction. Based on these results, we identified the CYBP3-binding region of CCNY as the pharmacophore region, which was then used to perform virtual screening and select 840 top-ranked candidates from a library of 630,000 compounds. Subsequent BiFC-based compound screening assays revealed three hit compounds capable of inhibiting the CCNY-CYBP3 interaction. These hits can be further developed into lead compounds that could improve learning and memory. The screening platform and the combined *in silico-in vitro* approach used in this study can provide an efficient strategy for identifying potential protein-protein interaction inhibitors.

Keywords : CCNY, CYBP3, BiFC, Virtual screening

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P-370

Remaining Nav1.8-positive nociceptors drive persistent tactile hypersensitivity after partial sciatic nerve crush injury in mice

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Peripheral nerve injury can lead to chronic mechanical hypersensitivity, yet the severity and persistence of pain are strongly influenced by the extent of axonal damage. Notably, partial sciatic nerve crush injury (PCI), where some nerve fibers remain intact, leads to more sustained tactile hypersensitivity than full sciatic nerve crush injury (FCI). However, the identity of these intact fibers has remained unclear. To determine the specific sensory neuron populations contributing to tactile hypersensitivity following PCI, we used fiber-specific transgenic labeling (Thy1-YFP for Aβ fibers and Nav1.8-tdTomato for nociceptors) and pharmacological silencing (QX-314 with capsaicin or flagellin) approaches to selectively manipulate fiber subtypes. Seven days after PCI, we observed a pronounced presence of Nav1.8+ nociceptive fibers in the hind paw. Moreover, selective silencing of TRPV1+ fibers with capsaicin/QX-314 produced transient analgesia, indicating direct involvement of nociceptive fibers in maintaining mechanical hypersensitivity. Whole cell recordings revealed that intact medium-sized dorsal root ganglion neurons retrogradely labeled with DiI showed decreased rheobase and increased action potential firings in response to step current injections. Besides, electrical stimulation of nociceptive fibers increased pERK expression in the spinal cord, indicating peripheral stimulation enhances nociceptive signaling in the spinal cord in the PCI. Early ablation of TRPV1+ fibers with capsaicin prevented the development of long-term tactile hypersensitivity. Collectively, our results suggest that intact nociceptors after PCI remain sensitized even during nerve repair, driving long-term tactile hypersensitivity. Targeting these intact nociceptive fibers after nerve injury may offer a potential strategy for preventing chronic pain associated with traumatic nerve injury.

Keywords : Neuropathic pain, Peripheral nerve injury, Partial crush injury, Nociceptor, Hyperexcitability

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P-371

Advancing AAV capsid engineering for targeted gene therapy using PackGene's π-Icosa platform

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We created π-Icosa, a platform merging rational design, directed evolution and AI to engineer AAV capsids that are highly specific, manufacturable and low in off-target risk. Its transformer-based targeting model, pretrained on protein language data, scored AUC 0.83 for tissue tropism. A proprietary algorithm designs diverse libraries; in vivo iterations then isolate winners. Muscle capsids PG016-18 outperformed AAV9 and MyoAAV 4A. CNS capsid PG008 plus ongoing screens delivered NHP variants with 10^3–10^6-fold higher expression. Retinal capsids PG021-22 efficiently transduced RGCs, Müller and INL cells. T-cell capsids PG009-10, PG012-13 infected primary human T cells 10× better than AAV6. A manufacturability model further yields mutants with 97 % packaging efficiency and 2–3× higher titers while expanding sequence space. π-Icosa thus unites AI, wet-lab evolution and rational design to accelerate safer, more potent gene therapies.

Keywords : AAV, CNS-targeting variant, Capsid Engineering, AI

P-372

Region-specific epigenetic regulation of cerebellar astrocytes by NFIB in motor circuits

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Astrocytes are increasingly recognized as active participants in brain function, exhibiting region-specific molecular profiles and transcriptional programs. Among these, cerebellar astrocytes remain poorly understood despite their distinct molecular features and close association with motor circuits. Here, we investigate how motor-related neuronal activity shapes astrocyte gene regulation in the cerebellum through transcriptional and epigenetic mechanisms. Using forced locomotor paradigm in mice, we observed transcriptional changes in cerebellar astrocytes accompanied by alterations in histone acetylation (H3K27ac) and methylation (H3K4me3), suggesting activity-dependent chromatin remodeling. Chemogenetic stimulation of motor cortical or cerebellar neurons revealed a long-range neuronal pathway capable of modulating cerebellar astrocyte transcription. To examine astrocyte-intrinsic regulation, we employed an adult astrocyte-specific knockout model of the transcription factor NFIB. Loss of NFIB in cerebellar astrocytes disrupted chromatin states, altered cellular morphology, reduced astrocyte density, and impaired motor performance. To understand the molecular context of NFIB function, we performed an interactome analysis, identifying multiple cerebellum-enriched NFIB-binding partners, including chromatin regulators and transcriptional modulators with known epigenetic functions. Together, these findings uncover a region-specific epigenetic program in cerebellar astrocytes that links neuronal activity to transcriptional adaptation and motor function, providing new insight into the molecular mechanisms of astrocyte contributions to cerebellar motor circuit function.

Keywords : Astrocyte, Cerebellum, Motor circuit, Transcriptional regulation, Histone modification

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P-373

Glio-vascular contributions to oxidative stress and neurodegeneration in chronic cerebral hypoperfusion mouse model

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Chronic cerebral hypoperfusion (CCH), an early feature of neuro-degenerative diseases, impairs cerebral blood supply, leading to BBB breakdown and endothelial dysfunction—events often preceding neuronal loss and cognitive decline. A key mediator in the vascular interface is the capillary endothelial glycocalyx (eGCX), whose disruption uncouples eNOS, generating excess reactive oxygen and nitrogen species (RONS). This imbalance activates astrocytes, principal regulators of vascular homeostasis. Prior work (Chun, et al., 2020) showed severe reactive astrocytes produce aberrant MAOB-dependent H_2O_2 and express iNOS, inducing oxidative stress sufficient for neurodegeneration. However, whether eGCX damage under CCH directly triggers severe reactive astrocytes and cellular ROS sources are yet to be uncovered. Using the asymmetric carotid artery stenosis (ACAS) model of CCH, 70% reduction in cerebral perfusion was observed in 35 days, accompanied by eGCX depletion, microvessel leakage, and $CD31^{+}eNOS^{+}$ endothelial activation. In the hippocampus, a 4-fold increase in GFAP intensity was observed in $iNOS^{+}MAOB^{+}$ atrophied reactive astrocytes, along with $p67^{+}Iba1^{+}$ amoeboid microglia concentrated in regions of neuronal loss, particularly within CA1, implicating the recognition memory deficits and anxiety-like behaviors observed in behavior tests. Together, these findings suggest that capillary dysfunction and eGCX depletion in CCH initiates an inflammatory state driven by eNOS uncoupling, forming a vicious cycle with astrocytes and microglia via aberrant RONS production potentially driving neurodegeneration. Notably, orally administered (ad libitum) KDS12025, a potent H_2O_2-decomposing enhancer of hemoglobin's peroxidase activity, reversed these pathological features, highlighting oxidative stress as key driver and central mechanism linking vascular injury to neurodegeneration. Targeting ROS offers a promising strategy for preventing early vascular contributions to neurodegeneration.

Keywords : Chronic cerebral hypoperfusion, Oxidative stress, Vascular dysfunction, Reactive gliosis, Neurodegeneration

P-374

Therapeutic potential of mesenchymal stem cells in cerebellar ataxia

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Defects in the ataxin-2 (ATXN-2) protein and CAG trinucleotide repeat expansion in its coding gene *Atxn-2* cause the neurodegenerative disorder spinocerebellar ataxia type 2 (SCA2). Although clinical studies have suggested that mesenchymal stem cells (MSCs) hold promise for treating different kinds of ataxia, the beneficial mechanism of MSC administration is still unclear. Herein, human bone marrow-derived MSCs (hMSCs) were injected into the cisterna magna of transgenic mice with a polyQ mutation in the *Atxn-2* gene. Our findings suggest that hMSC injection at 26 weeks can result in a significant improvement in aberrant motor performance, as well as protection of Purkinje cells in SCA2 mice up to 24 weeks after hMSC administration. In addition, the study revealed that hMSC administration upregulates the expression of follistatin-like 1 (FSTL1) protein, which in turn reduces inflammation and improves the SCA2 phenotype both behaviorally and physiologically. These findings demonstrate that hMSC-induced FSTL1 stimulates endogenous regeneration and suppresses glial-mediated inflammatory responses, pointing to a novel therapeutic strategy that could be further explored to design new clinical approaches for SCA2 patients.

Keywords : Spinocerebellar ataxia type 2, Mesenchymal stem cells, Purkinje cells, Neuroinflammation, Neurotrophic factor

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P-375

Integrative proteomic approach to reveal altered signaling modules during Alzheimer's disease progression in Tau P30

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive, functional, and behavioral impairments. Its neuropathological hallmarks include the accumulation of extracellular amyloid-β plaques and the formation of intracellular neurofibrillary tangles composed of hyperphosphorylated tau protein. In addition to these features, dysregulation of neurotransmitter systems, including dopamine, contributes to impaired synaptic transmission and neuronal communication in AD. Although the link between neurotransmitter alterations and AD pathology is recognized, comprehensive profiling of neurotransmitters and their associated proteomic changes remains limited. To address this gap, we conducted an integrated proteomic and neurotransmitter analysis across seven brain regions of PS19 (Tau P301S) transgenic mice at different stages of AD progression. Our proteomic analysis revealed distinct alterations in canonical pathways, including metabolic dysfunction, that varied across brain regions. Furthermore, profiling of neurotransmitters identified significant alterations in six neurotransmitter systems during AD progression. Through integrative analysis, we uncovered specific neurotransmitter-related signaling modules that exhibit AD progression-dependent associations with neurotransmitter alterations, particularly within the hippocampus and cerebellum. This integrated approach provides novel insights into the molecular mechanisms underlying AD progression and highlights potential signaling pathways involved in disease development.

Keywords : Integrative proteomic approach, signaling modules, Alzheimer's disease, neurotransmitters

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P-376

Molecular basis for pore blockade of Tentonin 3, a mechanosensitive channel by a conopeptide, NMB-1

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Tentonin 3 (TTN3/TMEM150C) is a mechanosensitive ion channel that responds to mechanical stimuli and exhibits distinct slow inactivation kinetics. It plays critical roles in mechanotransduction processes such as proprioception, blood pressure regulation, and insulin secretion. Structurally, TTN3 forms a tetramer with a predicted rectangular shape and a central pore. The conotoxin ρ-TIA and its synthetic analog, noxious mechanosensation blocker 1 (NMB-1), were initially developed to inhibit slowly adapting mechanically activated (MA) currents in dorsal root ganglion (DRG) neurons. Since TTN3 underlies these slowly adapting MA currents in DRG neurons, both NMB-1 and ρ-TIA were hypothesized to inhibit TTN3 activity. Indeed, NMB-1 strongly inhibited TTN3, whereas ρ-TIA had only a weak effect, and neither compound affected Piezo1. Alanine-scanning mutagenesis coupled with electrophysiological assays revealed that positively charged residues in NMB-1 are essential for its inhibitory function. Additionally, a glutamate residue (Glu126) near the TTN3 pore entrance was identified as critical for NMB-1's inhibitory action, suggesting a key electrostatic interaction between NMB-1 and TTN3. Molecular dynamics simulations further support this electrostatic interaction between the peptide ligand and the channel protein. These findings offer mechanistic insight into the selective inhibition of TTN3 by NMB-1 and provide a foundation for developing therapeutic agents targeting TTN3-related channelopathies.

Keywords : Mechanosensitive channel, Tentonin 3/TMEM150C, NMB-1, Conotoxin, Electrostatic interaction

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P-377

Downregulation of GCH1 significantly alleviates hypersensitivity in neuropathic pain models

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GTP cyclohydrolase I (GCH1), the rate-limiting enzyme for tetrahydrobiopterin (BH4) synthesis, is upregulated in the dorsal root ganglion (DRG) during neuropathic pain. Traditional analgesics often lack specificity and fail to address the root mechanisms of neuropathic pain. In this study, we developed an RNA interference (RNAi)-based adeno-associated virus (AAV) designed to selectively downregulate GCH1 mRNA across multiple species. This approach effectively reduces BH4 levels and alleviates hypersensitivity in preclinical models. We designed a series of u-siGCH1 constructs and identified the most effective multispecies-compatible candidate using RT-qPCR and western blot analysis. Adult male Sprague-Dawley rats were grouped into four groups: normal, spared nerve injury (SNI), AAV-u-shCON, and AAV-u-shGCH1. The SNI model was applied, and AAV was injected on post-operative day (POD) 16. Behavioral assessments were performed pre-surgery and on post-injection days (PID) 3, 7, 14, 21, and 28. On PID 28, rats were sacrificed, and DRG tissues and blood were collected for immunohistochemical analysis and BH4 concentration. In vitro assessments showed that the selected u-siGCH1 was remarkably effective in downregulating both GCH1 mRNA and protein levels in human, monkey, and rat cells. In neuropathic pain model, the AAV-u-shGCH1 group exhibited a progressive elevation in mechanical withdrawal threshold up to PID 28, whereas the AAV-shCON group consistently displayed persistent

hypersensitivity. Compared to SNI and AAV-shCON group, AAV-shGCH1 group immunohistochemical analysis indicated an alleviation in the expression of GCH1 in the DRG. Downregulation of BH4 using AAV-u-shGCH1 in neuropathic pain model successfully led to reduction of hypersensitive behavior in long term. It may be one of the promising gene therapy strategy to treat neuropathic pain.

Keywords : Neuropathic pain, Adeno-associated virus, Tetrahydrobiopterin, GTP cyclohydrolase I, Multispecies-compatibility

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P-378

Fine-tuning of dopaminergic synapse by microglial engulfment

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Microglia actively regulate neuronal and synaptic functions through synaptic engulfment, a process well characterized at excitatory and inhibitory synapses. However, its role at modulatory synapses, including dopaminergic synapses, remains poorly understood. Here, we demonstrate that dopaminergic presynaptic boutons in the mouse striatum are selectively engulfed by microglia under diverse physiological and pathological conditions. Notably, chemogenetic modulation of neuronal activity via DREADD GPCR activation dynamically alters microglial engulfment of dopaminergic boutons. Furthermore, we show that α-synuclein-induced mild pathology in a mouse model of Parkinson's disease enhances microglial engulfment of these boutons. These findings suggest that the activation state of dopaminergic neurons and their synaptic terminals may act as a critical cue for microglial recognition and engulfment. Our study highlights the microglial fine-tuning of dopaminergic synapses and implicates microglia in the early stage of Parkinson's disease.

Keywords : Microglia, Engulfment, Dopamine, Parkinson's disease, Dopaminergic synapse

P-379

An efficient strategy for developing a human brain cell-type-specific fluorescent probe with a molecular target

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This study proposes a streamlined approach for developing small-molecule fluorescent chemosensors (SMFCs), which target specific cell types and simultaneously identify their targeting mechanisms in the brain. It begins with the first step of screening hundreds of SMFCs to select a few promising candidates that label specific cells with high fluorescence contrast. Next, to address the bottleneck in developing brain cell-type-specific SMFCs, we applied a genome-wide activation screening platform based on CRISPR. It was used to identify the molecular target genes and elucidate the functional consequences of genetic perturbations. By repeating fluorescence-activated cell sorting (FACS), we could find F5 as a promising candidate staining a population that manifests a distinct fluorescence profile when compared to other SMFCs. Subsequently, we conducted next-generation sequencing (NGS) and identified several genes as potential regulators of F5 activity. It revealed a close association between F5-positive cells and phase II drug-metabolizing enzymes (DMEs). Simultaneously, fluorescent imaging showed the presence of F5-stained specific cell types in differentiated human neural stem and progenitor cell lines. With the identified molecular target genes and their corresponding brain cell populations, we now plan to characterize specific cell targeting through single-cell RNA sequencing after FACS enrichment. In summary, this platform can be efficiently used to validate the potential of brain cell-type-specific SMFC by identifying its molecular targets. It is also suggested that the usefulness of phase II DME substrates as potential biomarkers for defining specific brain cell types is worthy of further investigation.

Keywords : Small-molecule fluorescent chemosensors, Bioimaging, Genome-wide screening, CRISPR, Drug-metabolizing enzymes

P-380

hDPSC secretome alleviates hypoxic injury in hippocampal neurons by modulating mitochondrial function and preventing mitophagy

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Hypoxic stress, a condition of reduced oxygen availability, is a major contributor to neuronal cell death and neuroinflammation. This study explored the neuroprotective potential of the human dental pulp stem cell (hDPSC) secretome in mitigating hypoxic stress-induced damage in HT22 hippocampal neurons. Using high resolution accurate mass (HRAM) mass spectrometry for proteomics, key therapeutic proteins were identified in the hDPSC secretome. Hypoxic stress elevated mitochondrial reactive oxygen species (ROS) production, disrupted electron transport chain (ETC) activity, induced mitophagic cell death, and impaired synaptic protein expression in HT22 cells. However, treatment with the hDPSC secretome significantly reduced mitochondrial ROS levels, restored ETC complex activities (Complex I and Complex IV), inhibited mitophagic cell death, and suppressed neuroinflammatory responses by downregulating the TLR4/NF-κB signaling pathway. Moreover, the secretome enhanced anti-apoptotic protein expression and restored synaptic markers, such as synaptophysin and PSD95, thereby promoting neuronal recovery and synaptic integrity. These findings are the first to indicate that the hDPSC secretome mitigates hypoxic stress-induced neuronal damage through a multifaceted neuroprotective mechanism, including the regulation of mitochondrial function, and underscore its potential for therapeutic applications in neurodegenerative conditions.

Keywords : Secretome, Human dental pulp stem cell, Hypoxia, Mitochondrial ROS, Mass spectrometry

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P-381

Maternal transcutaneous auricular vagus nerve stimulation prevents maternal immune activation-induced behavioral deficits in offspring mice

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The fetal stage is a critical period for brain development, and excessive maternal immune activation (MIA) during pregnancy has been linked to an increased risk of neurodevelopmental disorders, such as autism spectrum disorder and schizophrenia. These effects are mediated by maternal inflammatory cytokines, including interleukin-6 (IL-6), which can disrupt key neurodevelopmental processes in the developing brain of the offspring. Cervical vagus nerve stimulation (VNS) has been reported to reduce peripheral inflammation via activation of efferent vagal pathway. Recently, transcutaneous auricular VNS (taVNS) has emerged as a non-invasive alternative that stimulates the auricular branch of the vagus nerve (ABVN) in the external ear. Similar to cervical VNS, taVNS has been shown to suppress inflammatory cytokine levels in both humans and animals. In this study, we examined whether taVNS could attenuate maternal inflammatory cytokine responses and prevent neurodevelopmental abnormalities in offspring. As a model of MIA, lipopolysaccharide (LPS) was administered to pregnant mice, and taVNS was applied to the dams at the time of LPS injection. Maternal IL-6 levels, behavioral outcomes, and microglial activation in the offspring were subsequently assessed. The taVNS significantly reduced maternal IL-6 levels two hours after LPS administration. In addition, behavioral tests conducted after the offspring reached maturity demonstrated that taVNS prevented MIA-induced behavioral impairments, including reduced social interaction, increased repetitive behavior, and elevated microglial activation in the brain. These findings suggest that applying taVNS to the mother during the acute phase of infection may reduce the risk of neurodevelopmental disorders in the offspring by suppressing maternal inflammatory cytokines such as IL-6.

Keywords : Maternal immune activation, Transcutaneous auricular vagus nerve stimulation, Neurodevelopmental disorders, Neuroinflammation, Social behavior

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P-382

Astrocytic AQP4/TRPA1/BEST1/D-serine signaling modulates brain hemodynamics and sensory perception through NMDA receptors

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Background: Neurovascular coupling matches cerebral blood flow to neuronal demand. Astrocytes are implicated, yet their direct control over cerebral blood volume (CBV) and the role of gliotransmitters remain unsettled. *Aim:* Clarify how astrocytic volume dynamics and gliotransmitter release regulate sensory-evoked and basal CBV. *Methods:* In anesthetized mice we combined whisker-evoked intrinsic optical signal imaging with local field potentials, whole-cell recordings, and arteriolar cannulation. AQP4, TRPA1, BEST1, and D-serine were manipulated pharmacologically or through conditional knock-out. *Results:* Evoked CBV rose rapidly then entered a sustained plateau that vanished after AQP4 or TRPA1 blockade. AQP4-mediated swelling triggered TRPA1 Ca^{2+} influx, which opened Ca^{2+}-dependent BEST1 channels to release D-serine. Exogenous D-serine restored the plateau in TRPA1- or BEST1-null mice; cannulation showed it did not act directly on smooth muscle but boosted neuronal NMDA currents, prolonging activity and hyperemia. At rest, tonic BEST1-dependent D-serine maintained baseline arteriolar dilation; removing it constricted vessels and narrowed the dynamic range of functional hyperemia. *Conclusion:* Astrocytes govern cerebrovascular physiology on two timescales: tonic BEST1-mediated D-serine sets basal tone, whereas activity-evoked AQP4-TRPA1-BEST1 signaling sustains prolonged functional hyperemia. Disruption of this pathway may underlie neurovascular deficits in disease.

Keywords : Neurovascular Coupling, Astrocyte, Physiology, D-serine, Hemodynamics

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P-383

Bisphenol A upregulates *CHMP2B* to promote neuron-to-glia mitochondrial transfer, accelerating neurodegeneration via exosome

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Bisphenol A (BPA), an industrial chemical prevalent in food and water containers and many consumer products, is a well-known endocrine disruptor owing to its estrogen-mimetic activity. BPA readily accumulates in the brain, where it induces mitochondrial dysfunction including elevated mitochondrial reactive oxygen species (mtROS) and dysregulated mitophagy. Here, we examined how these

perturbations reshape exosome-mediated mitochondrial transfer and promote neurodegenerative phenotypes. In human SH-SY5Y neuroblastoma cells, high-dose BPA (100 μM) markedly increased mtROS and mitophagy; both effects were mediated by reduction in membrane estrogen receptor (mER) due to internalization by BPA. BPA treatment increased exosome secretion from neuronal cells, and these vesicles were enriched with mitochondrial components, including cytochrome C protein and oxidative phosphorylation–related mitochondrial RNAs (*ND1–ND6, COX1–COX3*). Among the genes encoding components of the Endosomal Sorting Complex Required for Transport machinery (ESCRT), which regulates membrane remodeling and vesicle biogenesis, *CHMP2B* was significantly upregulated by BPA. Furthermore, overexpression of mER or knockdown of *CHMP2B* reversed the BPA-induced effects. In a hippocampal cell–astrocyte co-culture, BPA stimulated neuronal release of mitochondrial cargo into the medium, which was subsequently taken up by astrocytes. This neuron-to-glia mitochondrial transfer coincided with a significant rise in astrocytic GFAP, indicating reactive astrogliosis. Collectively, our data suggest that BPA triggers CHMP2B-driven exosomal export of neuronal mitochondria, depleting neuronal mitochondrial reserves, activating glia, and ultimately fostering neurodegenerative change.

Keywords : Bisphenol A, Exosome, Neurodegeneration, Mitochondria transfer, Gliosis

P-384

Ovariectomy alters Bone-Marrow-Associated immune and cardiovascular gene networks in the amygdala of spontaneously hypertensive rat

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[Aims] Postmenopause is linked to increased neuroinflammation and elevated blood pressure (BP) in women. Immune cell infiltration into the brain cardiovascular centers (BCCs) contributes to neuroinflammation-induced high BP in rats. We hypothesized that postmenopausal hypertension involves similar immune infiltration into BCCs. Using ovariectomized rats as a model of postmenopause, we analyzed gene expression profiles in the amygdala, a key BCC involved in menopausal symptoms and BP regulation. [Methods] Twelve female spontaneously hypertensive rats underwent sham-surgery (SHAM) or bilateral ovariectomy (OVX). One month later, amygdala brain tissues were harvested for microarray analysis. Differentially expressed genes (DEGs) were analyzed using DAVID (Database for Annotation, Visualization and Integrated Discovery) software for gene ontology (GO) and pathway enrichment analysis. Body weight and BP were measured before the surgical procedure and tissue collection. [Results] OVX rats showed significantly higher body weight and BP. A total of 1,414 DEGs were found in OVX compared to SHAM rats. Enriched GOs included cell migration (fold enrichment: 5.45 ± 0.9, $p < 0.03$) and tight junctions (4.58 ± 0.8, $p < 0.02$). Notably, *CLDN1* and *CLDN19* (Claudin-1/19) were upregulated while *CCL3* (macrophage inflammatory protein-1α), *AIF1* (allograft inflammatory factor 1), and *MMP14* (matrix metallopeptidase 14) were downregulated in OVX rats. Pathways related to T/B cell signaling, including *CCL3* and *AIF1*, were enriched, suggesting immune infiltration into the brain. Moreover, GOs related to BP regulation (fold enrichment: 4.02, $p < 0.003$) included upregulation of *C3AR1* (complement C3a receptor 1) and *COX-2* (cyclooxygenase-2), implying altered BP regulation post-ovariectomy. [Conclusion] Findings suggested a possible involvement of immune cell migration in BP regulation in OVX rats. Further functional studies are needed to clarify the function of DEGs in BCCs and BP control.

Keywords : Postmenopause, High blood pressure, Bone marrow-derived cells, Immune cells, Neuroinflammation

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P-385

Visualization of the existence of LEAP2 in the nucleus accumbens and its role in amphetamine-induced locomotor activity

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The nucleus accumbens (NAcc) is a key brain region in reward circuitry, mediating responses to psychostimulants, such as amphetamine (AMPH), including locomotor activity. This effect is known to be enhanced by the orexigenic neuropeptide ghrelin acting through growth hormone-secretagogue receptors (GHSR) expressed in the region. Recently, liver-expressed antimicrobial peptide 2 (LEAP2) was identified as another ligand for GHSR that opposes ghrelin's action. Based on its antagonism, we hypothesized that LEAP2 modulates AMPH-induced locomotor activity in the NAcc. To examine this, we first confirmed the presence of LEAP2 protein in this NAcc and observed that its fluorescent signals were predominantly localized in neurons, including medium spiny neurons (MSNs). We then investigated whether LEAP2 microinjection alters AMPH-induced locomotor activity. Our findings showed that LEAP2 inhibited acute AMPH-induced locomotor activity in a dose-dependent manner. However, its inhibitory effects were absent following chronic AMPH exposure, indicating that the effect of LEAP2 on AMPH-induced locomotor activity varies depending on drug-exposed physiological status. These results provide new insights into a state-dependent regulatory role of LEAP2 in AMPH-induced locomotor activity.

Keywords : LEAP2, Nucleus accumbens, Amphetamine, Neuropeptide, Locomotor activity

P-386

Real-time imaging and optimization of cortical neuron morphology analysis using high-content screening systems

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Live-cell imaging provides a powerful platform for real-time observation

of neuronal dynamics, thereby facilitating mechanistic studies of neurodevelopmental disorders. In the present study, we conducted a detailed characterization of morphological dynamics and optimization strategies associated with high-content screening (HCS) imaging systems. Currently, HCS imaging systems are instrumental in enabling real-time visualization of intracellular signaling pathways and dynamic molecular mechanisms in living cells. Our system is equipped with a high-speed spinning disk confocal module and a highly sensitive scientific sCMOS camera, which together offer superior temporal and spatial resolution while minimizing phototoxic effects on live specimens. The imaging system accommodates a broad range of magnifications (4× to 60×), permitting high-resolution analysis of subcellular structures and real-time monitoring of dynamic organelle behavior. Furthermore, the platform integrates specialized application modules—such as neurite outgrowth and cell cycle progression analysis—which enhance its utility in targeted neurobiological and cell-based assays. The capacity for simultaneous long-term imaging of up to 96 individual samples positions the system as a highly efficient solution for high-throughput screening of morphological and functional cellular phenotypes. Complementary software tools provide an intuitive interface that supports automated, rapid image acquisition and streamlined data processing workflows. The Brain Research Core Facilities at the Korea Brain Research Institute (KBRI) offer comprehensive support for advanced imaging modalities, including analyses of neuronal morphogenesis and ultrastructural mapping. Our overarching objective is to refine and standardize morphological imaging protocols to support the mechanistic dissection of brain function and elucidate cellular and structural correlates underlying diverse neuropathological conditions

Keywords : neuronal imaging, HCS imaging system, neuron culture, brain disorders, neuronal morphology

P-387

Identification of Aurora Kinase as a pivotal regulator of the pro-neurodegenerative phenotype in macrophages

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Macrophages play dual roles in CNS injuries such as ischemic stroke, contributing to both neuroregeneration and neurodegeneration. These effects are associated with phenotypic alterations in macrophages. We previously observed that neuron-macrophage interactions influence a pro-regenerative macrophage phenotype. However, the potential for these interactions to regulate neurodegenerative macrophage phenotype remained unexplored. To address this, we established an in vitro model of macrophage-induced neurodegeneration where conditioned medium (CM) from bone marrow-derived macrophages (BMDMs) induced substantial neurite degeneration. Notably, CM obtained from BMDMs co-cultured with neurons exhibited markedly reduced neurotoxicity. Transcriptomic analysis showed enrichment of cell cycle-related pathways in co-cultured macrophages, with Aurora kinases (AURKs) identified as key regulators. AURK inhibition increased macrophage senescence and worsened neuronal injury. Conversely, overexpression of AURKA or AURKB reduced senescence markers and alleviated neurotoxicity. The in vivo relevance of macrophage-mediated neurotoxicity was examined in a mouse photothrombotic stroke model. Splenectomy two weeks before stroke significantly reduced infarct volume, implicating infiltrating splenic macrophages in secondary neuronal injury. Transplantation of BMDMs via intravenous route into splenectomized mice resulted in an expansion of infarction volume. Conversely, infusion of AURKB, but not AURKA, overexpressing BMDMs attenuated BMDM-induced infarct aggravation, demonstrating that AURKB in macrophages can modulate the extent of post-ischemic brain damage. Taken together, our results identify Aurora kinase as a critical regulator of macrophage-mediated neurotoxicity, potentially acting through regulation of senescence-related pathways. Targeting AURK signaling may offer a novel therapeutic strategy to reprogram peripheral macrophages and limit neuronal damage following ischemic stroke.

Keywords : Macrophage, Neuron, Neurotoxicity, Aurora kinase, Stroke

P-388

Astrocytic Ankyrin2 enables memory persistence

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Ankyrin-2 (Ank2), a cytoskeletal adapter protein, is highly expressed in astrocytes, yet its role in astrocytes remains unexplored. Using mice with astrocyte-specific Ank2 deletion, we demonstrated its critical role in memory persistence, showing selective impairment of remote memory while sparing recent memory. This deficit was associated with reduced astrocytic contacts with engram neurons, as revealed by astrocyte-eGRASP, and impaired maintenance of hippocampal long-term potentiation (LTP). Mechanistically, astrocytic Ank2 deletion disrupted the TrkB.T1-IP3R2 signaling pathway, impairing BDNF-dependent astrocyte morphogenesis and preventing hippocampal BDNF infusion 12 hours post-learning from promoting memory persistence, clearly indicating that astrocytic Ank2 is essential for this process. Lastly, we developed Opto-T1, an optogenetic TrkB.T1 activation tool, to test the sufficiency of astrocytic TrkB.T1. Astrocytic Opto-T1 activation enhanced memory persistence, underscoring the importance of astrocytic TrkB.T1 signaling in this process. These findings establish Ank2 as a key regulator of astrocytic dynamics and memory persistence mechanisms.

Keywords : Astrocyte, Ankyrin2, Morphogenesis, LTP

P-389

Poster Award Candidate

Association of altered αCaMKII phosphorylation with male-specific sensorimotor gating impairments in a mouse model of Noonan syndrome

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Noonan syndrome (NS) is the most common developmental disorder among Rasopathies and exhibits a high prevalence of autism spectrum disorder (ASD). However, the neural mechanisms underlying ASD-like behavioral phenotypes in NS are not well understood. *Ptpn11*D61G/+ mice, which display NS-like symptoms such as short stature, heart deficits, and learning and memory impairments, have been used as a mouse model of NS. In this study, we report that *Ptpn11*D61G/+ mice show abnormalities in auditory sensory processing, which are one of the key features of ASD. While *Ptpn11*D61G/+ mice exhibited lowered sensitivity in auditory brainstem responses, they showed increased startle responses to acoustic stimuli, reduced habituation of startle response, and impaired sensorimotor gating in the pre-pulse inhibition (PPI) of startle response. Notably, disrupted habituation and PPI of acoustic startle response was observed in only male, not female mutant mice. As a potential mechanism underlying sex-specific impairment of auditory processing in *Ptpn11*D61G/+ mice, we found profound phospho-proteomic changes associated with synaptic organization and function in male *Ptpn11*D61G/+ mice. Specifically, phosphorylation of αCaMKII at Thr286 is significantly decreased in male *Ptpn11*D61G/+ mice compared to wild-type littermates but not in female mutants. Our results suggest that sex-specific alterations in αCaMKII Thr286 autophosphorylation may lead to sensory processing impairments in male *Ptpn11*D61G/+ mice. Our study provides new insights into the neural mechanisms underlying ASD-like behaviors in *Ptpn11*D61G/+ mice. Furthermore, these findings have implications for understanding the sex-specific phenotypes in ASD.

Keywords : Autism spectrum disorder, Sensorimotor gating, Sexual dimorphism, Prefrontal cortex, Neurodevelopmental disorders

P-390

Therapeutic potential of KBN-2202 in alzheimer's disease through modulation of microglial phagocytosis

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Alzheimer's disease (AD) is characterized by the progressive accumulation of amyloid-β (Aβ) plaques and chronic neuroinflammation. Microglia play a central role in clearing Aβ and orchestrating neuroimmune responses. In this study, we evaluated the therapeutic potential of KBN2202, a novel salicylic acid derivative, in 5xFAD transgenic mice, an established AD model. KBN2202 was administered once daily via oral gavage for 3 months, starting at 9 months of age. At the end of treatment, brain tissues were harvested following perfusion and processed for immunohistochemical analyses. Microglia were visualized using Iba1 staining, and Aβ pathology was assessed via anti-Aβ antibodies and Thioflavin-S. Lamp1 was used as a marker of lysosomal stress and neuronal injury. To assess microglial phagocytic activity, triple immunofluorescence staining for TREM2, Iba1, and ThioS was performed. Cytokine levels in brain homogenates were quantified using multiplex immunoassays. KBN2202 selectively suppressed interferon-γ (IFN-γ) without affecting other cytokines, consistent with inhibition of M1-polarized, neurotoxic microglia. Histological analysis revealed a significant reduction in Aβ plaque burden in the hippocampus, accompanied by decreased Lamp1 expression, indicating alleviation of lysosomal stress. ThioS staining confirmed a reduction in dense-core plaques, and a lower Aβ-to-ThioS ratio suggested enhanced plaque compaction and clearance of diffuse Aβ aggregates. These findings suggest that KBN2202 promotes microglial Aβ clearance, reduces neuroinflammation and lysosomal stress, and confers neuroprotection, supporting its potential as a disease-modifying therapeutic candidate for Alzheimer's disease.

Keywords : Alzheimer's disease, 5xFAD, Microglia, Phagocytosis, Amyloid beta

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P-391

Exposure to air pollutants disrupts the spontaneous activity of inner support cells in the developing cochlea

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Air pollution is the leading environmental health risk factor responsible for 6.4 million deaths/year globally. In particular, early developmental exposure appears to have greater health impact. Children and pregnant women are among the most vulnerable to air pollution-related diseases. In vitro and in vivo animal studies indicated that gestational and postnatal exposure to air pollutants impairs neurodevelopment and leads to long lasting behavioral and neurological disorders. Epidemiological studies reported that exposure to air pollutants increases the risk of hearing loss. As the cochlear synapses undergo developmental maturation similar to that of the brain, it has been postulated that early developmental exposure to air pollution exerts significant damage to cochlear synapse maturation and ultimately leads to hearing deficit. In the developing mammalian cochlea, inner support cells generate intermittent waves of spontaneous activity that are critical for the developmental maturation of auditory synaptic connections and tonotopic map. Therefore, we tested if air pollutant exposure disturbs the cochlear spontaneous activity and subsequent auditory synapse maturation. Using excised cochlear segments from postnatal rats, spontaneous activity was recorded.

Then, particulate matter (PM), a major component of air pollutants, was mixed into the extracellular solution and superfused onto the cochlear tissue. In the presence of PM, both the frequency and the average area of spontaneous activity were higher than the control values. After washing, the frequency and area of the spontaneous activity readily recovered to near-control values. These suggest that short-term PM exposure, though it may temporarily disturb the cochlear inner support cell-hair cell-afferent fiber connection, may not cause prolonged auditory damage. To reveal the critical phase and/or molecular players leading to permanent hearing deficit, repetitive or long-term PM exposure will be further examined.

Keywords : Cochlea, Air pollution, Particulate matter, Spontaneous activity

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P-392

Astrocyte-mediated synaptic trogocytosis via engineered ligand-receptor system: impact on memory in aged mice

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Cognitive decline associated with aging has emerged as a major societal concern, with hippocampal dysfunction playing a key role in memory impairments. While structural remodeling of synapses is critical for maintaining circuit flexibility, whether such remodeling can be induced in the aged brain—where synaptic plasticity is diminished—remains unclear. We investigated the functionality of the synthetic trogocytosis (SynTrogo) system, which enables astrocyte-mediated, selective elimination of excitatory presynaptic terminals, in the aged hippocampus. SynTrogo was successfully induced in astrocytes of aged mice, leading to increased astrocytic volume and targeted removal of excitatory inputs. This was accompanied by postsynaptic structural reorganization, including elevated synaptopodin expression and altered spine morphology. Notably, unlike in young mice, aged astrocytes also engulfed inhibitory pre- and postsynaptic components, resulting in widespread remodeling of astrocyte territory and CA1 synaptic composition. These structural changes contributed to improved extinction learning and enhanced remote memory retention in aged animals. Our findings demonstrate that SynTrogo remains functional in the aged brain and drives cognitive improvement via distinct astrocytic mechanisms, offering a promising therapeutic strategy for age-related memory decline.

Keywords : Aging, Astrocyte-mediated synthetic trogocytosis, Synaptic pruning, Hippocampus, Cognitve decline

P-393

Spatial alterations of N-Glycans and amino acids in photothrombosis-induced ischemic stroke models revealed by mass spectrometry imaging

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Stroke is a major neurological disorder caused by vascular damage in the central nervous system (CNS), leading to high mortality and disability rates worldwide. Ischemic stroke, the most common subtype, results from arterial occlusion that reduces or blocks blood flow to brain tissue. This condition induces the formation of fibrotic cores and glial barriers, structures regulated by extracellular matrix (ECM) glycoproteins, including collagen. Although previous studies have linked changes in glycosylation and amino acid metabolism to ischemic stroke, the spatial distribution of N-glycans and amino acids in the post-stroke brain remains poorly understood. In this study, we employed MALDI mass spectrometry imaging to visualize and quantify region-specific alterations in N-glycans and amino acids in a photothrombosis-induced ischemic stroke model. Our results showed that N-glycans with no or only one fucose residue were significantly increased in the fibrotic core, whereas N-glycans with two or more fucose residues were significantly decreased. These N-glycan changes were reversible by two different treatments that reduced both the fibrotic core and glial barrier size. Importantly, astrocyte-specific knockdown of Fut8—an enzyme critical for core fucosylation—significantly reduced fibrotic scar formation, suggesting that astrocytic N-glycosylation plays a pivotal role in post-stroke fibrotic remodeling. In a non-human primate model, we also identified significant changes in fucosylated N-glycans in the fibrotic core and glial penumbra following ischemic stroke. Additionally, we observed dynamic alterations in amino acid levels within the fibrotic core and glial barrier. Collectively, our findings underscore the importance of astrocyte-specific N-glycosylation and amino acid alterations in stroke pathology, and highlight novel molecular targets for therapeutic intervention.

Keywords : Ischemic Stroke, MALDI imaging, N-Glycan, Amino acid

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P-394

NCF1–Moesin binding controls CD8$^+$ T cell fate in neuroinflammatory conditions after ischemic stroke

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In the early phase of after ischemic stroke (IS), the cytotoxic T (Cyto T) cells infiltrating the infarct site exacerbate neuroinflammation. Previous studies have been showed that reducing Cyto T and promoting regulatory T (Treg) cells attenuated inflammatory responses. The Poly-Glu/Tyr polypeptide (Poly-YE; P-YE) has been reported as a key immune modulator that regulates T cell balance. Therefore, we focused on screening target protein that affect T cell balance by P-YE. To screen target protein, we carried out protein microarray and showed that P-YE strongly bound to neutrophil cytosolic factor (NCF1). During the inflammatory response, activated NCF1 is known to bind to moesin (MSN) and translocate to the membrane, where it contributes to the formation of the NOX complex. Among the various T cell subsets, CD8$^+$ T cells possess this NOX complex and release ROS through NOX during neuroinflammation. Also, recent study showed unbound MSN to NCF1 induces FOXP3 expression in helper T cells. Based on

these findings, we hypothesized that P-YE binding to NCF1 promotes the conversion of cytotoxic $CD8^+$ T cells into Treg-like cells under neuroinflammatory conditions. Primary $CD8^+$ T cells from 8-week-old BL/6 mouse spleens were treated with nanoparticle P-YE (3 μg/mL) and cultured in OGD-conditioned microglial medium. The results showed that NP-YE fused to the cell membrane and entered to cytosol of CD8+ T cell. In the CM group treated with P-YE, CD8+ T cells expressed FOXP3 and ROS was decreased. In Co-IP, we confirmed than binding NCF1 and P-YE liberated MSN. In addition, the proteome cytokine array showed that the P-YE group had reduced cytokine levels, and the M1 microglia was attenuated after P-YE injection in the tMCAO mouse model. Taken together, NCF1 bound to P-YE can't form NOX complex and MSN dissociated from NCF1 may lead to FOXP3 expression. Therefore, P-YE can convert CD8+ T to CD8+FOXP3+ cell through binding to NCF1 in neuroinflammatory condition.

Keywords : Ischemic stroke, Neuroinflammation, Poly-YE, CD8+FOXP3+ Treg, Moesin/NCF1

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P-395

Neurensin1 regulates social memory engram formation in the ventral hippocampus

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Social memory is a vital capability for social individuals to recognize and remember conspecific individuals, playing a crucial role in their survival and development. Studies have shown that the ventral CA1 region of the hippocampus stores social memory engram cells.However, the molecular mechanisms for their formation are remain poorly understood. Neurensin1 (NRSN1) is a synaptic vesicle membrane protein highly expressing in hippocampus which involves in neurite outgrowth via the vesicle transport system. It negatively regulates contextual fear and object location memory, but its role and mechanisms in social memory are unclear. Our results demonstrate that NRSN1 is involved in regulating the formation of social memory engram cells in the ventral hippocampus. Futher more,our studies reveals NRSN1 co-localizes with the endoplasmic reticulum (ER). APEX2 proximity labeling coupled with mass spectrometry analysis of the NRSN1 interactome reveals significant enrichment of actin cytoskeleton regulatory proteins, calcium signaling-related proteins, calmodulin-binding proteins, and et al.Preliminary findings indicate that NRSN1 potentially influences social memory engram cell functionality through its regulation of ER calcium homeostasis and synaptic protein dynamics, with detailed mechanistic pathways awaiting further investigation. These findings uncover the functional and mechanism of NRSN1 contributions to social memory formation, suggesting novel intervention strategies for disorders involving social memory deficits.

Keywords : Neurensin1, Ventral hippocampus, Social memory, memory formation, mechanism

P-396

PFOA induces cell cycle arrest mediated by ER stress in neural stem cells and impairs hippocampal neurogenesis.

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Perfluorooctanoic acid (PFOA), a synthetic perfluoroalkyl substance (PFAS), has raised significant concern due to its environmental persistence and bioaccumulative nature. PFOA is primarily absorbed into the human body through ingestion of contaminated food and water, inhalation in industrial settings, and, to a lesser extent, dermal exposure. Recently, this chemical has raised concerns due to its diverse toxic effects on the human body, including carcinogenicity, teratogenicity, reproductive toxicity, and hepatotoxicity. However, the neurotoxic effects of PFOA on neurogenesis have not yet been reported. In this study, we investigated the neurotoxic effects of PFOA on neural stem cells (NSCs) and hippocampal neurogenesis. PFOA induced cell cycle arrest via upregulation of p27 and downregulation of cyclins and cyclin-dependent kinases (CDKs), indicating suppressed NSC proliferation. PFOA also increased the expression of endoplasmic reticulum (ER) stress markers, including ATF4 and phosphorylated eIF2α. Treatment with 4-phenylbutyric acid (PBA), a known ER stress inhibitor, significantly ameliorated PFOA-mediated cell cycle arrest, indicating that the neurotoxicity of PFOA is mediated by ER stress. In an in vivo study, PFOA exerted adverse effects on hippocampal neurogenesis. PFOA reduced the proliferation of BrdU-positive cells in the hippocampus of C57BL/6 mice. Furthermore, the Morris water maze test demonstrated that PFOA administration impaired spatial learning and memory in these mice. Taken together, these results suggest that PFOA reduces NSCs proliferation through ER stress and consequently impairs hippocampal neurogenesis in C57BL/6 mice.

Keywords : Perfluorooctanoic acid, Neurotoxicity, Neural progenitor cells, ER stress, Hippocampal neurogenesis

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P-397

GPR40 activation attenuates neurodegeneration in alzheimer's disease

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Alzheimer's disease (AD) is characterized by progressive neuro-degeneration associated with mitochondrial dysfunction and chronic neuroinflammation. G-protein coupled receptor 40 (GPR40), primarily known for its role in metabolic regulation, has recently been implicated in neuronal function and inflammatory responses. In this study, we investigated the therapeutic potential of the selective GPR40 agonist TUG-469 as a candidate drug for treating AD. In the 5xFAD mouse model of AD, TUG469 administration improved cognitive performance and decreased Aβ plaque burden. Furthermore, TUG469 rescued impaired autophagy flux, as demonstrated by the regulation of LC3, p62,

and LAMP1 expression, and attenuated neuroinflammatory responses by inhibiting NLRP3 inflammasome activation and modulating microglial reactivity. These findings suggest that GPR40 activation alleviates AD pathology by restoring autophagy and attenuating inflammasome-mediated neuroinflammation. Collectively, activation of GPR40 by the selective agonist TUG469 improves cognitive function and reduces Aβ pathology in 5xFAD mice. It restores autophagic flux and suppresses neuroinflammation by inhibiting NLRP3 inflammasome activation and modulating microglial reactivity. These findings support GPR40 as a potential therapeutic target for Alzheimer's disease.

Keywords : GPR40, Alzheimer's disease, NLRP3 inflammasome, Neuro-degeneration, Neuroinflammation

P-398

Inhibition of LRRK2 kinase promotes axon regeneration after peripheral nerve injury

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Neurons in the adult mammalian central nervous system lack the regenerative capability after a traumatic injury. In contrast, neurons in the peripheral nervous system can regenerate axons after injury through robust activation of a pro-regenerative transcriptional program. Leveraging a previously published large-scale transcriptomic dataset, we identified that the level of *Lrrk2*, a gene that encodes leucine-rich repeat kinase 2, is significantly downregulated following nerve injury. LRRK2, a kinase implicated in both familial and sporadic Parkinson's disease, has been the target of extensive small-molecule inhibitor development, including compounds currently in clinical trials. However, the physiological role of non-pathogenic LRRK2 in axon regeneration remains largely unknown. Consistent with the transcriptomic data, we observed a reduction in both mRNA and protein levels of LRRK2 in sciatic dorsal root ganglion (DRG) neurons after sciatic nerve crush (SNC) injury. Genetic and pharmacological inhibition of LRRK2 promoted regenerative axon growth of primary DRG neuron in culture. Phosphoproteomic profiling further identified molecular pathways associated with LRRK2 inhibition that may underlie this regenerative response. Finally, oral administration of LRRK2 kinase inhibitors significantly promoted axon regeneration *in vivo* after SNC injury. These findings suggest a role for non-pathogenic, endogenous LRRK2 in axon regeneration and highlight the potential for repurposing small-molecule LRRK2 inhibitors on therapeutic approaches to promote axon regeneration.

Keywords : Axon regeneration, Peripheral nerve injury, Dorsal root ganglion, LRRK2

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P-399

Piezo1 activation promotes glial anti-inflammation and tau dephosphorylation in human Alzheimer's disease model

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Piezo1 is a mechanosensitive ion channel that has recently been recognized to mitigate Alzheimer's Diseases (AD) pathological signatures such as Aβ clearance and microglial neuroinflammation. However, the impact of Piezo1 channel in tauopathy remains unclear, partly due to the complex neuroglia interactions involved in tau pathogenesis. This study aims to investigate how Piezo1 modulates glial neuroinflammation in tau phosphorylation and identify key factors mediate tauopathy. We utilized a 3D human AD minibrain model that recapitulates key pathological features of AD, including Aβ accumulation, glial neuroinflammation, tau hyperphosphorylation, and neuronal loss to investigate the effects of Piezo1 channel activation on tauopathy through neuron-glia interactions. We found that Piezo1 activation rescued neurodegeneration of Aβ accumulation, tau hyperphosphorylation, synapse and neuronal loss in our AD model (Fig. a-e). We observed that Piezo1 activation suppressed microglial nuclear factor-kB (NFκB) (Fig. f,g), while promoting Aβ clearance, reducing oxidative stress and C-X-C Motif Chemokine Ligand 1 (CXCL1) production. Piezo1 also mitigated tau phosphorylation by inhibiting STAT3-mediated A1 astrocytic neuroinflammation (Fig. h), reducing the production of Interleukin-8 (IL-8) and C-C Motif Chemokine Ligand 2 (CCL2). Notably, we found that Piezo1 facilitated tau dephosphorylation and reduced tau hyperphosphorylation by independently enhancing protein phosphatase 2A (PP2A) activity and inhibiting cyclin-dependent kinase 5 (CDK5) in neurons (Fig. i-k). In conclusion, we elucidated the roles of mechanosensitive ion channel Piezo1 activation in alleviating tauopathy. We observed the rescue of neurodegenerative brains with decreased glial neuroinflammation, Aβ accumulation, tauopathy, and neuronal loss. Our findings highlight Piezo1 as a promising multitarget therapeutic strategy for tauopathy-mediated neurodegeneration.

Keywords : Piezo1, tau dephosphorylation, neuroinflammation, amyloid beta clearance, Alzheimer's disease

P-400

Immune-neural crosstalk and divergent cell-specific immune programs are modulated by diet in *Drosophila Melanogaster* ischemic stroke

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Ischemic stroke, driven by restricted oxygen and glucose availability, disrupts immune–neural balance and metabolic function. To model this condition, we exposed adult male Drosophila melanogaster to 2.5 hours of hypoxia (0.4% O_2 at 25°C). This treatment induced acute suppression of feeding behavior, which gradually recovered over two days. Bulk RNA sequencing of brains one day after hypoxia revealed

significant upregulation of immune-related genes. Flies eclosed from a sucrose-supplemented diet had lower survival rates and diminished feeding recovery compared to those eclosed from a nutritious-food. Furthermore, the hypoxia-induced immune response was suppressed in sucrose-fed flies. Through comparative transcriptomic analysis, we identified three diet-sensitive immune genes: *Listericin, CG4847*, and *Drosomycin*. Analysis of single-nucleus RNA sequencing data revealed their distinct cellular expression patterns for these genes. Two genes were predominantly expressed in glial clusters, while one was enriched in hemocyte-like clusters. This suggests that immune activation may have diverse cellular sources. These findings demonstrate how diet modulates immune–neural interactions and cell-type-specific immune responses under ischemic stress. This model provides a foundation for investigating diet-related effects on ischemic stroke outcomes.

Keywords : Ischemic stroke, Innate Immune, Hypoxia, Transcriptomic analysis, Drosophila

P-401

Identification of a neuroprotective compound for the treatment of ischemic stroke through drug repurposing

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Ischemic stroke is the second leading cause of death and disability globally. It is mainly due to blockage or disruption of blood flow to the brain. Narrow treatment window and complexity of the brain tissue limits the development of drugs for ischemic stroke. Here we utilized drug repurposing strategies to identify neuroprotective agents that could enhance recovery after the treatment. We screened 54 biologically active compounds related to neurological process under in vitro ischemic stroke models: Oxygen-glucose deprivation/Reoxygenation (OGD/R) and glutamate toxicity. We identified a phosphodiesterase inhibitor, X, treatment rescues cell viability and decreases Reactive oxygen species (ROS) level under the OGD/R condition in neuroblastoma cells. We also tested the effect of compound X in the novel in vivo stroke model (L-NAME-UCAO). X treatment significantly increases survival rate and slightly lowers infarct volume in the new model. We will further examine the mechanism underlying X's neuroprotective effect in ischemic stroke

Keywords : Ischemic stroke, Drug repurposing, Neuroprotection

P-402

Down-regulation of glucocorticid receptor modulates glial cell inflammatory response and neural stem cell proliferation

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Major depressive disorder (MDD) is characterized by dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and heightened neuroinflammation, with the glucocorticoid receptor (GR) serving as a critical mediatorin both processes. Although GR typically functions to suppress inflammation through negative feedback regulation of the HPA axis, its role in MDD remains complex and not fully understood. In this study, we investigated the impact of GR signaling on neuroinflammatory responses by treating BV-2 microglial cells and primary astrocytes with dexamethasone (DEX), a synthetic GR agonist. Unexpectedly, DEX induced a pro-inflammatory response rather than the anticipated anti-inflammatory effect in primary astrocytes. Furthermore, DEX treatment led to reduced GR expression and decreased cell proliferation in neural progenitor cells (C17.2) and neural stem cells (NSCs). Astrocytes pretreated with DEX showed increased glial fibrillary acidic protein (GFAP) expression when exposed to the neurotoxin MPP^+, indicating enhanced astrocyte activation. In vivo experiments further demonstrated that corticosterone administration impaired neurogenesis in the hippocampus of young male C57BL/6 mice, providing additional support for the involvement of GR in neuroinflammation. These findings suggest that altered GR signaling in glial and neural stem cells contributes to the neuroinflammatory environment observed in MDD. Targeting GR pathways may thus represent a promising therapeutic approach for alleviating depressive symptoms and restoring neural function in affected individuals.

Keywords : Major depressive disorder, Neuroinflammation, Glucocorticoid receptor, Hypothalamus – pituitary – adrenal axis, Hippocampal neurogenesis

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P-403

The role of dopamine receptors on microglial functions and motor-related behaviors

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Microglia, the resident immune cells of the brain, play a key role in maintaining central nervous system homeostasis and are implicated in various neurodegenerative and psychiatric disorders. To fulfill these roles, microglia must detect and respond to environmental changes, including neuronal activity. While recent studies have shown microglial responses to classical neurotransmitters like glutamate, GABA, and norepinephrine, their role in dopaminergic signaling remains unclear. Here, we demonstrate that microglia are closely associated with dopamine boutons and express dopamine D1 and D2 receptors, enabling them to respond to dopamine signals. Additionally, microglia-specific deletion of the D2 receptor reduced microglial numbers, altered morphology, and changed cytokine expression. These microglial alterations weakened the extracellular matrix and reduced the excitability of parvalbumin (PV) interneurons in the striatum. Furthermore, changes in PV interneuron-derived inhibitory synapses led to deficits in motor-related behaviors. Our findings highlight the significance of dopamine receptor-mediated signaling in microglia for striatal synaptic functions and motor-related behaviors.

Keywords : Microglia, Dopamine receptor, Striatum, PV interneuron, Extracellular matrix

P-404

Pulsatile GnRH signaling in the hippocampus promotes neurotrophic effects

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Gonadotropin-releasing hormone (GnRH), a master regulator of reproduction in the hypothalamus, has recently been linked to cognitive function and aging. Although pulsatile restoration of GnRH appears to support brain function in the hypothalamus, it remains unclear whether these effects originate from GnRH directly or are mediated by downstream hormones due to feedback mechanisms. To address this, we aimed to investigate the neuroprotective effects of GnRH signaling in the hippocampus, which is free from hormonal feedback and strongly associated with cognition. We selectively expressed a chimeric optogenetic receptor composed of an optoXR extracellular domain and a GnRHR intracellular domain in the hippocampus and applied pulsatile optogenetic stimulation to the dentate gyrus of the male mice to mimic physiological GnRH rhythms. The opto-GnRHR stimulation significantly increased BDNF expression, indicating that pulsatile GnRH signaling in the hippocampus can exert neurotrophic effects. The presence of both GnRH and its receptor in the extrahypothalamic regions further supports its emerging role beyond reproduction. Our study suggests that the previously observed neurogenic and anti-Alzheimer's disease effects of systemic GnRH may originate from this hippocampal action even under pathological conditions. This study highlights the potential of GnRH as a therapeutic target for promoting neuroprotective effects.

Keywords : GnRH, optogenetic, BDNF, anti-AD

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P-405

TWIK-1 regulates mitochondrial homeostasis and protects against acoustic stress

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Two-pore domain potassium (K2P) channels are pivotal in maintaining cellular excitability and homeostasis across diverse physiological contexts. Among these, TWIK-1 (K2P1.1), a member of this family, is broadly expressed in excitable and non-excitable cells, including those in the central nervous system and the cochlea. To investigate its physiological function in the inner ear, we used cochlear-derived UB-OC1 cells and found that TWIK-1 is expressed not only at the plasma membrane but also robustly localized within mitochondria. TWIK-1 knockdown markedly increased mitochondrial ROS, impaired mitochondrial membrane potential (ΔΨm), and disrupted Ca^{2+} homeostasis, indicating compromised mitochondrial function. In vivo, BAC transgenic mice revealed TWIK-1 expression in cochlear hair cells. Immunohistochemistry in wild-type mice further demonstrated co-localization of TWIK-1 with mitochondrial markers, supporting its mitochondrial localization. Functionally, TWIK-1 KO mice exhibited significantly greater auditory threshold shifts following acoustic overstimulation, accompanied by increased hair cell loss and exacerbated mitochondrial impairment relative to WT controls. Mitochondrial dysfunction in TWIK-1 KO cochleae was marked by reduced OCR and increased OXPHOS and UPRmt protein levels. Notably, AAV-mediated restoration of TWIK-1 expression in KO mice significantly reduced noise-induced hair cell loss, highlighting its protective role under stress. Furthermore, age-related decline in cochlear TWIK-1 expression was observed, which correlated with progressive hearing loss, and TWIK-1 KO mice showed an even more severe auditory deficit with aging. Collectively, our findings identify TWIK-1 as a key mitochondrial regulator that preserves mitochondrial function and cochlear integrity under both acoustic and age-related stress, supporting its potential as a therapeutic target for sensorineural hearing loss.

Keywords : Twik-1, Mitochondria, Oxidative stress, Noise-induced hearing loss, Cochlear hair cells

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P-406

Optimal low-dose pregabalin enhances functional recovery after spinal cord injury

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Spinal cord injury (SCI) induces profound and often irreversible impairments in motor, sensory, and autonomic function due to a combination of initial mechanical trauma and secondary injury mechanisms. These include excitotoxicity, calcium overload, oxidative stress, mitochondrial dysfunction, blood–spinal cord barrier disruption, chronic neuroinflammation, and glial scar formation, all contributing to a regeneration-inhibitory environment. Pregabalin (PGB), a gabapentinoid that binds to the α2δ subunit of voltage-gated calcium channels, is widely prescribed for neuropathic pain. Recent studies suggest that early post-injury administration may support motor recovery via modulation of neuroinflammation and synaptic plasticity. However, systematic evaluation of its dose-response efficacy and histological outcomes remains limited. This study investigated PGB's neuroprotective effects using in vitro and in vivo preclinical models. Primary cortical neurons were exposed to hydrogen peroxide to simulate oxidative injury and then treated with PGB (5, 50, and 500 μM). PGB significantly improved cell viability and neurite outgrowth, with the strongest effects at 5 μM. In vivo, rats underwent moderate thoracic contusion SCI and received daily intraperitoneal PGB (5, 15,

30, 60, and 120 mg/kg). Motor function was assessed using the Basso, Beattie, and Bresnahan (BBB) scale and the horizontal ladder test over 8 weeks. Low concentrations (5 and 15 mg/kg) demonstrated the most consistent and significant improvements in locomotor function and coordination. Histological analysis at 8 weeks post-injury revealed that PGB-treated spinal cords exhibited reduced lesion volume, improved myelin preservation, and decreased microglial and macrophage activation. These findings suggest that early, low-dose PGB not only improves motor recovery but also preserves spinal tissue and reduces inflammation. This supports its potential as a clinically relevant neuroprotective intervention for SCI.

Keywords : Spinal cord injury, Pregabalin, Neuroprotection, Synaptic plasticity, Inflammation

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P-407

Gap junction-mediated modulation of neural circuit function in the thalamus

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Astrocytes contribute to the maintenance of microenvironmental homeostasis by forming interconnected networks through gap junctions. Multiple connexin subtypes—including Cx30, Cx32, Cx43, and Cx47—are expressed across different brain regions. While both the hippocampus and thalamus express Cx30 and Cx43, Cx43 predominates in the hippocampus, whereas Cx30 is more abundantly expressed in the thalamus. Despite this regional enrichment, the functional role of Cx30 in the thalamus remains poorly understood. In this study, we investigated how astrocyte-specific deletion of *Gjb6* (encoding Cx30) influences thalamocortical activity. Using *ex vivo* electrophysiological recordings from the ventrobasal (VB) nucleus of the somatosensory thalamus in adult mice, we found that astrocytes lacking Cx30 exhibit reduced gap junctional coupling. This disruption of astrocytic network communication was associated with altered neuronal activity in the VB, suggesting that Cx30-mediated astrocytic connectivity plays a critical role in modulating thalamocortical circuit function. These findings highlight the thalamus-specific contribution of astrocytic Cx30 to synaptic activity and circuit integration.

Keywords : Astrocyte, Oligodendrocyte, gap junction, Connexin, Thalamus

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P-408

Microplastics promote extracellular vesicle-mediated Amyloid-beta release

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The production and consumption of plastic have increased rapidly over the past few decades, posing a serious threat to both the environment and human health. Among plastic pollutants, microplastics (MPs) are of particular concern, as they can cross the blood–brain barrier and infiltrate the central nervous system, where they may exert neurotoxic effects and contribute to amyloid-beta (Aβ) accumulation. However, the mechanisms by which MPs impact amyloid pathology have yet to be fully elucidated. Therefore, this study investigated the mechanism of extracellular Aβ accumulation induced by microplastics using SH-SY5Y cells. Screening results revealed that only 5 μm and 10 μm diameter MPs contributed to the increased accumulation of Aβ42. This elevation was not caused by a conventional amyloidogenic pathway, as neither BACE1 expression nor γ-secretase inhibition by DAPT altered Aβ42 levels. Conversely, treatment with N-Smase inhibitor GW4869 reduced Aβ42 levels, implying that its release is mediated by extracellular vesicles (EVs). Supporting this observation, targeted screening of ESCRT complex components involved in EVs formation revealed that *CHMP2B* and *RAB11FIP2* were significantly upregulated. Silencing these genes via siRNA significantly decreased EVs, verifying their functional role in MP-induced vesicle formation. These results indicate that the increase in Aβ following MP exposure is not due to enhanced amyloidogenic processing, but rather to EVs-mediated secretion. In conclusion, *CHMP2B* and *RAB11FIP2* mediate microplastic-induced Aβ release via EVs, highlighting their potential as therapeutic targets for Alzheimer's disease.

Keywords : Microplastics, Extracellular vesicle, Amyloid pathology, Alzheimer's disease

P-409

GenX exposure alters cortical organization and synaptic function in cerebral organoids.

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GenX is a next-generation chemical in the PFAS group and was made to replace PFOA in various industrial processes, most notably in the manufacturing and production of fluoropolymers. Despite being considered less harmful than PFOA, GenX has been increasingly detected in water sources and biological systems, raising concerns about its potential neurotoxicity. To clarify the neurotoxic effects of GenX, we evaluated its impact on human cerebral organoids as a model for brain development. GenX exposure induced significant developmental alterations in cerebral organoids, including reduced organoid size, indicating impaired growth and maturation. Analysis of cortical organization revealed decreased rosette diameter and ventricular zone (VZ) area, demonstrating disrupted neural differentiation and altered cortical architecture. Functionally,

neurons from GenX-exposed organoids exhibited abnormal synapse formation and compromised synaptic activity. Transcriptomic analysis identified downregulation of critical pathways governing neuropeptide signaling, synapse assembly, postsynaptic organization, and calcium ion homeostasis, providing molecular insight into the observed functional deficits. These findings demonstrate that GenX exposure disrupts both cortical organization and synaptic function in developing brain tissue, suggesting significant risks to human neurological health during critical developmental periods. Also given the widespread detection of GenX in environmental and biological samples, this study emphasizes the need for further research into its neurodevelopmental toxicity.

Keywords : GenX, PFAS, Neurodevelopmental toxicity, Cerebral organoids, Neurotoxicity

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P-410

VPS26B enhances motor learning ability via glutamate receptor recycling in the primary motor cortex in a parkinsonian mouse model

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Parkinson's disease (PD) patients have motor learning impairment associated with disrupted synaptic plasticity in the primary motor cortex (M1). Cortical synaptic plasticity depends on glutamate receptor recycling via molecular transporters or glutamate receptor phosphorylation regulated by dopamine receptors. However, in the PD context, dopaminergic degeneration from the ventral tegmental area (VTA) projecting to M1 leads to insufficient dopamine receptor activation. Here, in the strategy of increasing motor learning ability for the MPTP-induced PD mouse model, we focus on supporting glutamate receptor recycling via overexpression of VPS26B, a component of retromer, which is a molecular trafficking machine. We found in the MPTP-induced PD mouse model that pretreatment with VPS26B into M1 increases surface and overall glutamate receptor in M1. This result may explain why level of proteins related to synaptic plasticity were protected in VPS26B overexpressing mice groups even under MPTP condition. Moreover, VPS26B knockout mice had the shortest running time in the rotarod test, indicating that reducing VPS26B contributes to the motor learning impairment in PD. Noteworthy, VPS26B showed interactions with D1 and D2 dopamine receptors. We anticipate our research to be a starting point for using retromer components as a valuable treatment for neurodegenerative diseases.

Keywords : VPS26B, Parkinson's disease, Glutamate receptor trafficking, Synaptic plasticity, Motor learning

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P-411

Acetate-induced Cathepsin B expression in reactive astrocytes of GBM patients

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Reactive astrogliosis is a hallmark of glioblastoma (GBM), yet its metabolic regulation remains unclear. Using PET imaging with ^{11}C-acetate and ^{18}F-FDG, we visualized reactive astrocytes in GBM patient brains. We observed that Cathepsin B (CTSB) expression is significantly elevated in IDH1-wildtype GBM compared to IDH1-mutant astrocytoma, particularly in tumor-associated astrocyte regions. Single-cell RNA sequencing further revealed CTSB as a top upregulated gene in acetate-stimulated astrocytes. These findings suggest that acetate acts as a metabolic cue activating lysosomal pathways, leading to CTSB upregulation. This acetate-induced CTSB may contribute to extracellular matrix degradation, potentially promoting GBM invasiveness.

Keywords : Glioblastoma, astrogliosis, Cathepsin B, PET, Acetate

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P-412

Griseofulvin attenuates rotenone-induced dopaminergic cell toxicity by modulating microtubule dynamics and Autophagy

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Pesticides are a significant environmental risk factor implicated in the development of neurodegenerative disorders. Griseofulvin, a pesticide, induces apoptosis and mitotic arrest by disrupting microtubule function in various cancer cell lines. In this study, we investigated the effect of griseofulvin using a dopaminergic cell line, MN9D. Griseofulvin showed minimum cytotoxicity in low-dose treatment, as assessed by WST assay and PI-staining. Notably, a non-toxic concentration of griseofulvin attenuated rotenone-induced cell death including necrotic cell death. Mechanistic studies revealed that rotenone treatment led to microtubule depolymerization which was effectively attenuated by griseofulvin co-treatment. Concurrently, griseofulvin reduced rotenone-induced microtubule hyperacetylation in MN9D cells, suggesting its dual role on polymerization and acetylation of microtubule. Furthermore, griseofulvin suppressed the rotenone-induced accumulation of autophagosomes and autolysosomes. These results suggest that griseofulvin exerts neuroprotection by stabilizing microtubules through promoting polymerization and facilitating deacetylation, while normalizing autophagic pathways. These findings highlight its potential as a new therapeutic strategy for neurodegenerative disorders associated with microtubule dysfunction, such as Parkinson's disease.

Keywords : Pesticide, Microtubule, Ttubulin, Neurodegeneration, Autophagy

Acknowledgements : This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center (KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (Grant number: HU23C0199).

P-413

PAD4-mediated NEMO (IKKγ) citrullination in microglia promotes neuroinflammation in the post-ischemic brain

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Peptidylarginine deiminase 4 (PAD4) catalyzes the post-translational conversion of positively charged arginine residues to neutral citrulline residues. This modification, known as citrullination, are implicated in various pathological conditions, including those affecting the central nervous system. This study investigated the pro-inflammatory role of PAD4 in microglia in an MCAO (middle cerebral artery occlusion) animal model of ischemic stroke. While PAD4 was detectable in most brain cell types of sham controls, we observed a significant increase in PAD4 expression and subsequent accumulation of citrullinated proteins in activated microglia following ischemia. This PAD4 induction and protein citrullination in microglia persisted for up to 4 days in both the ischemic penumbra and core regions. Notably, we demonstrate that PAD4 induces citrullination of NEMO (IKKγ), a key regulator that activates the NF-kB signaling pathway by promoting the formation of NEMO-IKKa/IKKb triple complex, thereby driving a pro-inflammatory cascade in the post-ischemic brain. Treatment with BBCA (a PAD4 inhibitor) and specific knockdown of PAD4 blocked this pro-inflammatory function mediated by PAD4-induced NEMO citrullination in both activated microglia and in the post-ischemic brain. Furthermore, inhibition of NEMO citrullination by a NEMO-binding domain peptide (NBDp) or co-treatment of NBDp and BBCA, further supports a crucial role for PAD4-mediated NEMO citrullination in post-ischemic neuroinflammation. Importantly, intranasal administration of BBCA provided robust neuroprotection in the post-ischemic brain in a broad therapeutic window. Collectively, these results suggest that PAD4 plays a critical role in pro-inflammatory processes following cerebral ischemia by upregulating NEMO citrullination and subsequent NEMO-IKKa/IKKb complex formation.

Keywords : PAD4, NEMO, Stroke, citrullination, neuroinflammation

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P-414

Mass screening of FDA-approved compounds identifies neuroprotective and neuroregenerative agents for treatment of spinal cord injury

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Spinal cord injury (SCI) remains a serious clinical condition for which no approved pharmacological treatments currently exist to restore neurological function, highlighting the urgent need for therapeutic strategies that can be rapidly translated into clinical application. Drug repositioning, which leverages compounds with established safety and pharmacokinetic profiles, offers a practical and time-efficient approach to addressing this unmet need. In this study, we conducted high-throughput screening of 3,120 FDA-approved small molecules to identify agents capable of enhancing neuronal viability and promoting neurite outgrowth under oxidative stress conditions relevant to the pathophysiology of SCI. Primary cortical neurons were isolated from fetal Sprague-Dawley rats and cultured for 10 days. Oxidative injury was induced by treatment with 150 μM hydrogen peroxide for 30 minutes. Each compound was applied at concentrations of 5 μM and 25 μM for 16 hours. Neuronal viability and morphological changes were evaluated by quantitative image analysis following immunocytochemical staining with βIII-tubulin. From this screening, 56 out of 1,920 compounds significantly improved neuronal survival compared to negative controls, and among these, 15 compounds also demonstrated statistically significant neurite elongation. These active compounds were classified according to previously known pharmacological mechanisms, including anti-inflammatory action, modulation of neuromodulatory receptors, and attenuation of oxidative stress—all of which are associated with neuronal regeneration pathways. Pathway analysis of these compound classes suggests that complementary mechanisms of neuroprotection and structural recovery may be involved. This study proposes a set of promising drug candidates with strong preclinical potential to address the unmet therapeutic need in SCI treatment and provides a pharmacological rationale for future *in vivo* validation.

Keywords : Drug repositioning, Spinal cord injury, Neuroregeneration, Compounds screening, Oxidative stress

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P-415

ATP acts as a neurotransmitter for Type III cells in the fungiform papillae taste buds

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Although ATP was considered a candidate neurotransmitter for Type III taste bud cells because blocking ATP signaling through pharmacological or transgenic approaches reduces sour taste responses, ATP release has not been observed either in vitro or in vivo. To better understand real mechanism for sour transduction in vivo, we performed in vivo functional screening on taste bud of transgenic mouse model which expressed ATP or 5-HT GRAB sensor at the taste bud. By this method, we found that ATP is repeatedly released in response to sour stimulation contrast to 5-HT, and its release pattern is closely associated with the activity of Type III cells and afferent nerves. This trend persisted across different types, concentrations, and durations of sour stimulation, showing strong similarity, and was also closely associated with the responses of Type III cells and afferent nerves. Also, spatial domain of ATP release by sour taste was totally separated from sweet/umami or bitter taste, which is only mediated by type II cell. Furthermore, RNA FISH and immunohistochemistry analyses of the regions where ATP was released in response to sour stimulation revealed that the cells

in these areas expressed Car4 mRNA and protein, a marker for Type III cells, and that P2X3-positive nerves were closely apposed to these regions. Injection of BoNT/A between the epithelial sheet and tongue muscle selectively reduced ATP release in response to sour stimuli, but not to sweet stimuli, indicating that ATP release from Type III cells is mediated by a synaptic vesicle-dependent pathway. Finally, blocking purinergic receptors with AF-353 reduced afferent responses and impaired sour taste discrimination, whereas Htr3a knockout had no significant effect on either neural or behavioral responses compared to wild-type mice. These findings allow us to conclude that ATP functions as a neurotransmitter released from Type III cells via a synaptic vesicle-dependent pathway.

Keywords : Taste bud, Type III cell, ATP, 5-HT

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P-416

Agbl4 knockout mice display autistic-like behaviors and prefrontal dysfunction

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social interaction and communication, along with restricted and repetitive patterns of behavior. ASD arises from diverse neurobiological factors that disrupt brain development, leading to broad impairments in social functioning, language, cognition, emotional regulation, and sensory processing. Recent genetic studies have implicated *Agbl4*, which encodes cytosolic carboxypeptidase 6 (CCP6), as a potential ASD-associated gene due to its role in tubulin deglutamylation and microtubule regulation. However, the functional significance of *Agbl4* in the brain, particularly in regions involved in social behavior such as the medial prefrontal cortex (mPFC), remains largely unknown. In this study, we investigated the behavioral and neurophysiological consequences of *Agbl4* deficiency using *Agbl4* knockout (KO) mice. Through a multi-modal approach combining behavioral assays, immunohistochemistry, electrophysiological recordings, and transcriptomic analyses, we demonstrate that loss of *Agbl4* leads to synaptic and circuit-level disruptions in the mPFC, accompanied by impairments in social behavior. Furthermore, we identify potential therapeutic strategies targeting the observed pathophysiological changes. These findings confirms that *Agbl4* as a key molecular factor in the regulation of mPFC-dependent social behavior and suggest that its dysfunction may contribute to the pathophysiology of ASD. While ASD is widely recognized as a polygenic disorder, our results underscore the importance of *Agbl4* in shaping core behavioral domains relevant to the disorder, offering a potential target for therapeutic intervention.

Keywords : Autism spectrum disorder, Agbl4 deficiency, Medial prefrontal cortex, Social behavior

P-417

Two distinct RhoGTPase pathways regulating post-tetanic potentiation

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Functional synaptic plasticity is driven by the dynamic remodeling of presynaptic actin. However, the mechanism by which actin is regulated in the context of plasticity remains largely unknown. In Drosophila, previous reports have identified the small Rho GTPase Rac1 as an actin regulator that controls post-tetanic potentiation (PTP), a form of activity-dependent short-term plasticity. However, whether other Rho family GTPases are involved in PTP remains untested. Here, I show that Cdc42, another Rho GTPase, also regulates PTP induction via a different cellular process than Rac1. I also report that RhoGEF3 functions downstream of the cAMP-Epac-Rap1 signaling pathway to activate Cdc42 during PTP induction. Moreover, I find that Rac1 and Cdc42 induce PTP by facilitating an increase in RRP size and vesicular release probability, respectively, indicating that the two pathways are molecularly distinct. Finally, I show that the increase in vesicular release probability is accompanied by enhanced calcium channel clustering. Based on these results, I propose that cAMP-mediated post-tetanic potentiation depends on changes in both RRP size and vesicular release probability, each governed by two distinct molecular pathways. These pathways bifurcate from Rap1 signaling to activate Rac1 and Cdc42, which are responsible for regulating changes in RRP size and vesicular release probability, respectively.

Keywords : Synapse, Drosophila, Synaptic plasticity

P-418

Therapeutic effects of ifenprodil on pain and neuroinflammation in a rat model of chronic polyarthritis

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Chronic arthritic pain remains a debilitating condition that is often insufficiently managed by existing therapies. Ifenprodil, a selective N-methyl-D-aspartate receptor-2B (NMDAR-2B) antagonist, has demonstrated efficacy in neuropathic pain models; however, its effects in arthritis-related pain have yet to be fully explored. This study aimed to evaluate the therapeutic potential of ifenprodil in modulating pain and inflammation in a rat model of chronic polyarthritis induced by complete Freund's adjuvant (CFA). CFA-induced arthritic rats received intrathecal ifenprodil (0.5 or 1.0 μg/μL) or sodium diclofenac (6 μg/μL, positive control) for 7 consecutive days. Pain behaviours were evaluated using von Frey and hot-plate tests on day 0 (baseline), day 15 (pre-treatment), and day 23 (post-treatment). ELISA assays were performed on L4–L5 spinal cord segments, and histopathological evaluations were conducted on ipsilateral hind paws and ankle joints. Statistical analyses involved one-way ANOVA and repeated measures ANOVA with post-hoc tests ($p<0.05$). Ifenprodil at 0.5 μg/μL significantly reduced

thermal hyperalgesia and tactile allodynia, showing strong pain relief. It also reduced ankle joint oedema, indicating anti-inflammatory effects. At a molecular level, 0.5 μg/μL ifenprodil significantly downregulated NR2B, TNF-α, BDNF, and Substance P in the spinal cord, suggesting it suppresses central sensitisation. Histopathological analysis showed reduced inflammatory cells and improved joint structure. In conclusion, intrathecal ifenprodil, especially at 0.5 μg/μL, exhibited significant anti-nociceptive and anti-inflammatory effects comparable to sodium diclofenac. These findings underscore the therapeutic potential of targeting NMDAR-2B to modulate both central and peripheral mechanisms involved in chronic arthritic pain.

Keywords : Complete Freund's adjuvant, Tactile allodynia, Thermal hyperalgesia, Paw oedema, Polyarthritis

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P-419

The role of LRRK2 in stress granules formation

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Stress granules (SGs) are membraneless ribonucleoprotein structures that assemble in response to cellular stress and serve to regulate mRNA triage and translation. Their formation is primarily initiated by the phosphorylation of eIF2α, which suppresses translation initiation and promotes the condensation of RNA-binding proteins such as G3BP1. Emerging evidence has linked SG dysregulation to the pathogenesis of various neurodegenerative diseases, including Parkinson's disease (PD). Leucine-rich repeat kinase 2 (LRRK2), a multidomain serine/threonine kinase, is the most frequently mutated gene in familial PD and also contributes to some sporadic cases. LRRK2 is known to regulate intracellular processes such as vesicle trafficking, cytoskeletal dynamics, and autophagy, mainly through phosphorylation of Rab GTPase substrates. However, its potential involvement in SG regulation remains poorly understood. This study aims to explore the possible connection between LRRK2 and SG biology, with a particular focus on how LRRK2 activity and its interaction with members of the Rab GTPase family might influence translation control under stress conditions. A better understanding of this relationship may provide new insight into the molecular mechanisms underlying neuronal stress responses and PD.

Keywords : LRRK2, Stress granules, Rab, Parkinson's disease, eIF2α

P-420

Synaptoporin is essential for the structural integrity and functional plasticity of hippocampal mossy fiber synapses

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Synaptoporin (Synpr), a synaptic vesicle protein belonging to the synaptophysin (Syp) family, is highly enriched in mossy fiber (MF) terminals of dentate gyrus (DG) granule cells. Despite its distinct localization, the functional role of Synpr in regulating MF synaptic architecture and plasticity remains poorly understood. To address this, we generated Rbp4-Cre;Synpr$^{fl/fl}$ mice, allowing for DG-specific Synpr deletion via Cre-dependent recombination. Confocal imaging of GFP-labeled MF boutons showed no significant difference in bouton volume between control and Synpr-deficient mice. However, correlative light and electron microscopy (CLEM) revealed striking ultrastructural alterations in Synpr-deficient MF boutons, including disrupted synaptic vesicle organization, fragmented lamellate structures, and reduced incorporation of postsynaptic thorny excrescences (TEs) into the bouton core—indicating compromised presynaptic integrity. To assess functional consequences, we performed field excitatory postsynaptic potential (fEPSP) recordings in the CA3 region following high-frequency stimulation of the MF pathway. Synpr-deficient mice exhibited significantly attenuated long-term potentiation (LTP) compared to controls, suggesting impaired synaptic plasticity. Although behavioral phenotypes in Synpr-deficient mice are yet to be explored, these findings establish Synpr as a key regulator of both the structural complexity and functional plasticity of hippocampal MF-CA3 synapses. Our study provides novel insights into the molecular mechanisms underlying MF synapse organization, highlighting Synpr's essential role in maintaining the integrity of the DG-CA3 circuit.

Keywords : Synaptoporin, Vesicle protein, Hippocampus, Mossy fiber terminal, CLEM

P-421

Minimally invasive chemogenetic modulation of the Dorsal Motor Nucleus of the Vagus

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This study presents a novel and minimally invasive approach to brain function regulation through chemogenetic modulation of the dorsal motor nucleus of the vagus (DMV) using vagus nerve stimulation without direct brain viral injection. The researchers utilized adeno-associated viral (AAV) vectors to achieve activation and modulation of physiological behaviors such as feeding, water intake, and metabolic activity. Vagus nerve injections were validated by GFP expression localized within the DMV, and following clozapine administration, electrophysiological recordings demonstrated altered firing rates in GFP-positive neurons, confirming functional control over these cells. Immunohistochemical staining verified that DMV neurons expressing the hM3Dq-eYFP receptor were selectively activated, while behavioral analysis revealed a notable decrease in food intake alongside increased energy expenditure trends. Additional locomotor assessments indicated that clozapine administration at a specific dose did not affect overall movement, as measured by total distance traveled and mobility parameters. These findings suggest that vagus nerve-mediated chemogenetic stimulation could serve as a viable therapeutic strategy for central nervous system disorders, offering a less invasive alternative to traditional brain-

targeted approaches, particularly for conditions affecting autonomic and metabolic regulation.

Keywords : Vagus nerve, chemogenetic, hM3Dq, clozapine, Dorsal motor nucleus of vagus

P-422

Age-dependent alterations of SELENBP1 in microglia of 5XFAD mice

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SELENBP1, a selenium-binding protein implicated in various diseases such as cancer and schizophrenia, has also been found to be upregulated in several brain areas of individuals with Alzheimer's disease (AD). However, its role in AD development remains unclear. The present study investigated changes in Selenbp1 in the hippocampus and prefrontal cortex of wild-type and 5XFAD transgenic mice, a widely used animal AD model, across different ages (1.5, 3, and 6 months). Using Western blot analysis and immunofluorescence staining, we measured age-dependent alterations in Selenbp1 levels and examined cellular locations of Selenbp1. The hippocampus, a region critically involved in memory and one of the first affected by AD, was examined for Selenbp1 levels and cellular location in microglias, astrocytes, and neurons using markers Iba-1, GFAP, and NeuN. Results showed that Selenbp1 levels increased with age in both brain regions, regardless of genotype. Although 5XFAD mice displayed a tendency toward higher hippocampal Selenbp1 levels at 1.5 and 3 months compared to wild-type mice, the differences were not statistically significant. No genotype-dependent differences were observed in the prefrontal cortex. Importantly, immunofluorescence staining revealed increased Selenbp1-positive signals in the hippocampus of 5XFAD mice, primarily localized in microglia, with minimal expression in astrocytes and neurons. These results suggest that SELENBP1 may play a regulatory role in modulating microglial activation, a key feature of AD-related neuroinflammation.

Keywords : Alizheimer's disease, SELENBP1, Microglia

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P-423

TMEM43 tunes hippocampal networks *via* an astrocytic gap junction

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The *TMEM43* gene has been reported to play supportive but critical roles in many human diseases, such as cancer, arrhythmogenic right ventricular cardiomyopathy (ARVC), and auditory neuropathy spectrum disorder (ANSD). However, direct characterization of the TMEM43 protein is missing, and its role in the brain remains unexplored. Here, we demonstrated that TMEM43 confers ion channel activities via the lipid bilayer reconstitution of purified TMEM43 protein. We further characterized TMEM43 as a pH-sensing cation channel in the heterologous expression system. In the hippocampus of TMEM43 knockout (KO) mice, we observed impaired dye diffusion and electrical coupling among astrocytes, increased neuronal excitability, and alteration in AMPA/NMDA ratio. Additionally, TMEM43 KO mice exhibited impaired long-term potentiation (LTP). Finally, we found that the electrophysiological changes in the hippocampus of the KO mice lead to a disturbance in memory recall, which was rescued by astrocyte-specific TMEM43 overexpression. These results indicate that astrocytic TMEM43 actively participates in the gap junction networks in the hippocampus, preventing neurons from hyperexcitability, which is critical for memory retrieval. Together, our study elucidates the molecular and functional identities of TMEM43 and underscores its role in the brain.

Keywords : TMEM43, Gap junction, Hippocampus, Dye diffusion, Electrical coupling

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P-424

c-Kit signaling confers damage-resistance to sweet taste cells upon nerve injury

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Taste buds relay taste sensory information to the primary taste neurons but depend on those same neurons for essential components to maintain function. While denervation-induced taste bud degeneration and subsequent regeneration were discovered decades ago, the mechanisms underlying these phenomena (e.g., heterogenous cellular responses to nerve injury and the signaling pathways involved) remain poorly understood. Here, using mouse genetics, nerve injury models, pharmacologic manipulation, and taste bud organoid models, we identify a specific subpopulation of taste cells, predominantly c-Kit-expressing sweet cells, that exhibit superior resistance to nerve injury. We found the c-Kit inhibitor imatinib selectively reduced the number of residual c-Kit-expressing sweet cells at post-operation week 2, subsequently attenuating the re-emergence of other type II cells by post-operation week 4. In taste bud organoids, c-Kit-expressing cells were resistant to R-spondin withdrawal but susceptible to imatinib, while other taste cell types showed the opposite behavior. We also observed a distinct population of residual taste cells that acquired stem-like properties, generating clonal descendent cells among suprabasal keratinocytes independent of c-Kit signaling. Together, our findings reveal that c-Kit signaling confers resilience on c-Kit-expressing sweet cells and supports the broader reconstruction of taste buds during the later regenerative stage following nerve injury.

Keywords : taste, taste buds, denervation, nerve injury, c-Kit

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P-425

Investigating cortical adenosine dynamics during the sleep-wake cycle of the mouse

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Adenosine is known as the neuromodulator which is crucial for sleep regulation. Neurons expressing either A1 or A2A adenosine receptors are widely distributed over the central nervous system. It has been suggested that brain activity during wakefulness accumulates extracellular adenosine in various brain regions such as basal forebrain and cerebral cortex, resulting in induction of sleep. Slow-wave activity (SWA), a brain wave within the frequency of 0.5-4 Hz, is usually observed in the non-rapid eye movement (NREM) sleep and considered as a marker for sleep depth. Researchers had discovered that prolonged wakefulness increases the power of SWA during the following NREM sleep. Although the role of adenosine in sleep homeostasis had been studied mainly in the basal forebrain, the SWA is known to be generated in cerebral cortex, while the propagation and modulation would be mediated by the cortico-thalamo-cortical circuit. The mechanism of the generation of SWA is still not understood well. To study the relationship between sleep states and cortical extracellular adenosine, we investigated dynamics of extracellular adenosine in the cerebral cortex of the freely moving mouse using GRAB Ado 1.0 sensor while simultaneously monitoring its brain states by EEG and EMG recording. Result shows that the adenosine concentration fluctuated across the wakefulness and sleep states. The adenosine was mostly abundant during the wakefulness compared to NREM sleep. The rapid increase of extracellular adenosine was observed at the onset of wakefulness and REM sleep episodes, while it slowly decayed during NREM sleep. Our study shows that dynamics of cortical adenosine fluctuate brain-state dependently.

Keywords : Adenosine, Slow-wave activity, Cerebral cortex, Sleep

Neuroengineering P-426~P-443

P-426

Locomotor kinematics shapes spatial patterns of cortical activity and connectivity

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Locomotion in a given environment requires integrating sensory inputs with feedforward and feedback signals while coordinating motor commands. The neural mechanisms underlying locomotion have been extensively studied, with evidence indicating that the projection of signals from the cerebral cortex to subcortical and spinal regions plays a crucial role in regulating movement, however, intercortical sensory-motor integration is unclear. In this study, we monitored widefield calcium signals in head-fixed Thy1-GCaMP6f mice during locomotion on a treadmill, wheel, or disk. We computed cortical activity and inter-regional connectivity to understand how locomotor kinematics shape spatial patterns of cortex wide. The activity and connectivity in the cortex calculated by removing the influence of motion captured behavior variables for locomotion different in types of tracks. The treadmill, a linear and stable track, exhibited robust connectivity across widespread cortical regions despite reduced activity. Notably, the medial region of secondary motor cortex (M2) showed reduced connectivity during treadmill walking. These findings suggest that cortical dynamics depend on the locomotor environment, with reduced sensory-driven connectivity in medial M2 potentially supporting stable sensory-motor integration. Taken together, we suggest that the choice of behavioral models needs to take into account the kinematics of the body and the corresponding cortical responses.

Keywords : Widefield imaging, Cortical activity, Cortical connectivitiy, Locomotion, Sensory-motor

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P-427

A wireless autonomous soft optogenetic stimulator with neural signal monitoring for freely behaving animals under indoor ambient light

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Optogenetics has made significant contributions to the advancement of neuroscience by enabling the control of cellular activities in living tissues using light. To achieve effective optogenetics in real-time for freely moving animals, many optical stimulation and monitoring systems utilizing wireless technology have been developed. However, existing systems have limitations such as the need for periodic battery replacement, constraints of coil-based power systems that allow charging only within specific cages, and the restricted applicability of conventional solar cells, which function only outdoors under sunlight. Perovskite solar cells offer a unique advantage in that they support energy harvesting not only under outdoor sunlight but also under indoor ambient lighting conditions, making them suitable for optogenetics stimulation using LEDs in freely moving animals. In this research, we present a wireless stimulation and monitoring device integrated with compact perovskite solar cells that can harvest energy from indoor light. The device is equipped with a low-power Bluetooth system that enables wireless control of brain stimulation over extended periods. In addition, the device supports real-time measurement of neural activity by recording local field potentials, allowing simultaneous monitoring of neural responses during stimulation. This wireless, self-powered dual-functionality supports long-term behavioral experiments. Furthermore, these capabilities provide a base for future closed-loop systems, in which stimulation parameters can be dynamically adjusted in response to neural activity. The ability to operate and charge indoors is critical for enabling long-duration experiments in standard lab settings. By increasing autonomous function and enabling wireless interaction through a Bluetooth user interface, this platform can be applied to a

range of neuroscience research and further extended to preclinical neuromodulation research.

Keywords : Optogenetics, Wireless interface, Perovskite solar cell, Local field potential monitoring, Indoor energy harvesting

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P-428

Flexible high-definition active neural interface for single spike neural recording

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Over the last decade, neuroscience has been a central focus of scientific inquiry, driving the exponential development of neural interfaces as critical tools for interpreting neural signals. Extensive research has aimed to enhance these interfaces, specifically in terms of biocompatibility and resolution. A main approach for achieving high biocompatibility involves deploying flexible substrates. Unlike conventional rigid electrodes, which cause tissue damage and trigger adverse immune responses when implanted in the brain, flexible substrates overcome these issues by closely matching the mechanical properties of brain tissue. High-resolution neural interfaces are essential due to the inherent complexity of neural circuits. To effectively decipher these signals and read individual spike signals from single neurons, a large number of sufficiently small electrode channels are crucial. While the number of electrode channels in neural interfaces has improved significantly through active arrays using multiplexing, the size of individual electrodes remains large due to current manufacturing limitations, hindering single-spike signal acquisition. Herein, we propose an active neural interface designed to achieve single-spike resolution through significantly reduced electrode size. The miniaturization was achieved by a modification of the on-electrode transistor circuit architecture. Specifically, we reconfigured the conventional active array design by relocating the multiplexer transistors from within each electrode to the back-end circuitry. This approach allowed us to shrink the size of individual electrodes to 400μm^2. The transistors demonstrated excellent performance even when fabricated on a flexible polyimide (PI) substrate. We observed a gate threshold voltage of 1.2V and an on-off ratio of 8.73×10^5, while the uniformity across the entire array of electrodes was successfully maintained, ensuring reliable and consistent neural signal acquisition.

Keywords : Single spike recording, Neural interface, Actively-multiplexed array

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P-429

Miniaturized implantable stimulator using liquid crystal polymer for deep brain stimulation targeting the ventral posterolateral nucleus (VPL)

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Introduction: Deep brain stimulation (DBS) delivers electrical pulses to modulate brain regions associated with neurological disorders. It is a promising therapy for intractable pain, especially in patients unresponsive to drugs or surgery. This study presents a miniaturized, head-mounted DBS device using liquid crystal polymer (LCP), featuring an ultra-thin electrode approximately one-tenth the thickness of conventional ones. The fully implantable system allows wireless stimulation in freely moving rodents, offering new opportunities for preclinical neuromodulation research. Methods: To assess the efficacy of the proposed DBS system, we used an in vivo behavioral test on a rat model of neuropathic pain model called spared nerve injury (SNI) method which is reliable and highly responsive rodent model. For pain relief, we inserted electrode at ventral posterolateral nucleus (VPL). Electrical stimulation was delivered at a fixed frequency of 130Hz and pulse width of 60μs, while the stimulation amplitude was varied to evaluate changes in pain threshold at different levels. Results: Mechanical threshold was 1.297 ± 0.2546 g before DBS application. However, when a current stimulation of 100μA, the threshold increased up to 5.996 ± 1.413 g (* $p < 0.05$). At 500μA was applied, the threshold rose to 10.27 ± 1.236 g (*** $p < 0.001$). When 1mA amplitude was applied, the threshold was similar to that on stimulation with a current of 500μA (10.24 ± 1.236 g; *** $p < 0.001$). Conclusion: A fully implantable, miniaturized DBS device utilizing biocompatible LCP was developed for rodent models, offering lightweight form factor and compatibility with scalable fabrication. For future clinical translation, critical challenges include wafer size expansion for human-scale production and integration of real-time neural recording to ensure precise electrode targeting. The proposed platform demonstrates strong potential for advancing preclinical neuromodulation research.

Keywords : Deep brain stimulation, Neuropathic pain, Rodent model, Liquid crystal polymer, Miniaturized device

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P-430

An AAV toolset for microglia-specific transgene targeting across species

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Microglia, the resident immune cells of the central nervous system, are critical to brain health and disease. Despite advances in AAV capsid

and promoter engineering, achieving precise and efficient viral targeting of microglia across brain regions and species remains challenging. Here, we introduce an AAV toolset that enables stable, specific, and robust transgene expression in microglia across diverse brain areas and species. Using single-cell chromatin accessibility sequencing, we identified a 446-bp microglia-specific regulatory element (MSRE). We also developed the AAV variant 2/9.m, which provides higher production yields and improved transduction efficiency. To address suboptimal expression of certain genes, we devised a microglia-specific codon optimization strategy. Therefore, this system enables sensor expression, DREADD-based chemogenetics and gene knockout in microglia. This will provide a powerful tool for further manipulation of microglia and functional study. The AAV2/9.m-MSRE system supports robust microglia-specific transgene expression in healthy and diseased mice, rats, non-human primates, and human ex vivo brain slices. This versatile platform advances microglial gene delivery for basic research and enhances the therapeutic potential of AAVs for neurological disorders.

Keywords : microglia, AAV vector, Cis-regulatory elements, codon optimization, gene editing

P-431

Disentangling attention dynamics through EEG-based relative phase analysis

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In the study, we employed a novel analytical approach termed Relative Phase Analysis(RPA), which leverages phase lead/lag relationships between neural signals, to detect rapid neuro-dynamics during shifts in attentional state. Additionally, we aimed to characterize the stable neural activity patterns and information processing mechanisms underlying sustained attentional engagement. The study involved 20 participants (ages 29.5±6.5 years) to examine attention fluctuations and sustained performance using the gradual CPT(Esterman et al., 2013). Based on participants' reaction time variability, their attentional states were classified into 'zone-in' (smaller variability: more focused to the task) and 'zone-out' (longer variability: less focused to the task) periods based on reaction time variability. EEG-based RPA was applied to both transitional periods between attentional states and periods of stable attention to identify frequency-specific differences in neural oscillatory activity. The results of the RPA revealed a significant phase pattern differences between the zone-in and zone-out states in the alpha and low-beta frequency band during the −300 ms to 0 ms interval preceding stimulus image appearance ($p<0.05$). The zone-in state was characterized by a higher order cognitive frontal area phase-leading pattern, suggesting top-down information flow being more dominant, whereas the zone-out state exhibited a frontal-lagging configuration, suggestive of bottom-up flow dominance. These results may suggest elevated activation of higher-order dorsal prefrontal cortex which plays significant role of attention modulation during zone-in period. Our findings support an integrative interpretation of attentional dynamics within the zone-in/zone-out framework and the hierarchical processing model. Moreover, the observed phase patterns provide a potential basis for the development of neural markers capable of detecting attention-related brain states in real time.

Keywords : EEG, Top-down/Bottom-up, Attention, Relative Phase Analysis, Phase dynamics

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P-432

Electrochemical impedance sensing of dopamine for real-time neurochemical monitoring in neuroengineering

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Dopamine (DA) is a key neurotransmitter involved in regulating mood, cognition, and motor control. Abnormal dopaminergic signaling is closely linked to neurological disorders such as Parkinson's disease, schizophrenia, and addiction. Therefore, real-time and reliable dopamine monitoring technologies are essential for both neuroscience research and clinical diagnostics. Conventional dopamine detection methods—such as fluorescence imaging and fast-scan cyclic voltammetry (FSCV)—have contributed significantly to understanding dopamine dynamics, but they often suffer from limitations like poor temporal resolution, background interference, and the need for electrical stimulation, which may disrupt the physiological environment. To address these challenges, we present an impedance-based sensing platform using a flexible neural probe functionalized with dopamine-specific antibodies. This design allows for selective, real-time, label-free dopamine detection without enzymatic conversion or voltage cycling. The flexible architecture ensures mechanical stability and biocompatibility for in vivo applications, while minimizing tissue damage. The impedance changes correlate linearly with dopamine concentration and maintain high specificity even in the presence of common interfering molecules such as ascorbic acid and uric acid. Unlike FSCV, our system does not require high-voltage biasing, which helps preserve the native neural environment. This method enables high-resolution, real-time monitoring of dopamine in physiological and pathological conditions, and offers a promising foundation for future development of closed-loop neuromodulation systems and dopamine-responsive brain–machine interfaces.

Keywords : Dopmaine, Impedance-based, Flexible neural probe, Real-time monitoring

P-433

Development of TMP-tag based chemigenetic neuromodulator sensors for multiplex imaging

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The brain consists of tens of billions of neurons that communicate primarily via neurochemicals (neurotransmitters and neuromodulators),

the fine-tuning of which is essential for proper function under varying conditions. Understanding the dynamics and functions of these neurochemicals will help elucidate brain working mechanisms and potential therapeutic strategies for neurological diseases. Given the diversity and complexity of neurochemical signaling, there is an urgent need for tools that enable simultaneous monitoring of multiple neurochemicals. Using the GRAB (GPCR Activation-Based) strategy, our lab has developed a series of green and red fluorescent neuromodulator sensors with high spatial and temporal resolution. Building on this work, we combined the GRAB strategy with a chemigenetic approach to extend the imaging spectrum (≥ 650 nm) for multiplex detection of three or more neuromodulators. Briefly, we utilized the TMP-tag, an engineered self-labeling tag that covalently binds its ligand without additional reagents, along with bioavailable chemical dyes, to develop far-red and near-infrared (NIR) chemigenetic sensors. To date, we have developed cpTMP-tag based chemigenetic sensors for dopamine (DA), norepinephrine (NE), serotonin (5-HT), melatonin (MT), corticotropin-releasing factor (CRF), and oxytocin (OT). For example, the TMP-DA sensor shows a comparable response to DA both*in vitro* and *in vivo*. These sensors can be labeled with far-red and NIR rhodamine dyes, enabling multiplex imaging alongside existing green and red fluorescent sensors. Notably, beyond intensity changes, these cpTMP-tag based chemigenetic sensors also exhibit significant lifetime shifts upon ligand binding, suggesting their potential for real-time quantitative imaging *in vivo*.

Keywords : Neuromodulator, TMP-tag, Chemigenetic sensor, Multiplex imaging, Fluorescent lifetime

P-434

Proprioception can be recalibrated by sensory deception in arm matching task

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Proprioception is the capacity to sense the body movement, posture, and interaction force. The loss or impairment of proprioception may affect the control of muscle tone, and result in significant deficits in the spatiotemporal movement capability. Therefore, the restoration of proprioception has been regarded as a primary consideration in motor rehabilitation and learning. To this end, a number of studies have investigated proprioceptive recalibration. Previous studies have demonstrated that, after moving the body with visuo-proprioceptive mismatch, proprioception is partially recalibrated to be matched with the vision. However, the change of proprioceptive recalibration has been reported to vary widely across studies, ranging from 10% to 80%. In this study, we suggest two hypotheses regarding the conditions that effectively induce proprioceptive recalibration. The first hypothesis is that participants' awareness of error influences the effect of misaligned visual feedback on proprioceptive recalibration. The second hypothesis is that electro-tactile feedback promotes proprioceptive recalibration. During the experiment, participants were asked to adjust their right elbow joint to the left elbow joint, which was fixed at a specific angle using an angle block (30° or 40°). During the training session, visual or electro-tactile feedback was provided as being misaligned to proprioception. After the training, participants again attempted to match their right elbow joint angle to their left elbow joint angle, and the extent of proprioceptive recalibration was assessed based on the error between the left and right elbow joint angles. On average, we observed shifts in perceived elbow joint angle of approximately 67% following training with misaligned visual or electro-tactile feedback. Furthermore, these shifts were maintained at around 59% even 72 hours after the training.

Keywords : Proprioception, Proprioceptive recalibration, Sensory deception, Arm matching

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P-435

Microcoil-based magnetic stimulation in a Parkinson's disease mouse model

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Deep brain stimulation (DBS) has long used electrical currents to treat drug-resistant neurodegenerative diseases. However, conventional electrical stimulation often leads to broad current spread and reduced long-term efficacy due to encapsulation layers. As an alternative, magnetic stimulation using microcoils is gaining attention for its potential to achieve more precise and durable effects. However, the efficacy of microcoil-based stimulation has so far been validated only in brain slice experiments and limited in vivo studies at the cortical level. Therefore, in vivo validation at the deep brain level is essential to assess its therapeutic potential, and this study aims to address that need. We investigated the feasibility of using microcoils to stimulate the subthalamic nucleus (STN), a key deep brain target in Parkinson's disease. Electric field simulations in Maxwell 3D guided the design of rectangular microcoils, fabricated without semiconductor processes. The in vivo experiment targeted the right STN of a Parkinson's disease mouse model induced by 6-hydroxydopamine (6-OHDA). As a result, the PD mouse exhibited a marked reduction in its clockwise rotational bias following magnetic stimulation, and additional c-Fos imaging confirmed accurate placement of the microcoil in the STN with approximately a 30% decrease in neural activity. These results demonstrate that magnetic stimulation using microcoils is effective not only at a theoretical level but also in deep brain regions, highlighting its potential as a therapeutic approach for neurodegenerative diseases.

Keywords : Microcoil stimulation, Magnetic stimulation, Deep brain stimulation, Parkinson's disease, Subthalamic nucleus

P-436

Theoretical approach to high-frequency magnetothermal dissipation in ferrofluids for wireless deep brain stimulation

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Thermal dissipation in magnetic nanoparticles (MNPs) arises predominantly from two relaxation mechanisms: Brownian and Néel relaxation. While both pathways contribute to energy loss, Brownian rotation generally results in greater heat generation than Néel relaxation. However, because it relies on the physical motion of particles, Brownian rotation not only raises concerns about inducing cellular damage through mechanical agitation, but is also limited in biological environments where nanoparticles are often immobilized or entraped to cellular structures, making it unsuitable for deep brain stimulation (DBS) applications. In this study, we experimentally and theoretically investigate Néel relaxation-driven heating under high-frequency alternating magnetic fields toward enabling a scalable wireless neuromodulation. We synthesized 13 nm Fe_3O_4 MNPs and injected only 200 nL of ferrofluid into the hippocampal region of the mouse brain. Applying an external magnetic field, we confirmed localized temperature elevation, verifying heat dissipation via unrotative Néel relaxation in contrained environment. To complement the experiments, we utilized analytical expressions based on the Debye model of complex susceptibility to evaluate frequency-dependent power loss, accounting for both Brownian and Néel relaxation mechanisms. The resulting theoretical predictions showed excellent agreement with experimental measurements, validating the underlying mechanism. These findings establish a robust framework for magnetothermal neuromodulation that circumvents mechanical particle rotation, enabling low-invasive platform for chronic, wireless DBS. They provide quantitative design guidance for ferrofluid-based high-frequency applications—from magnetic hyperthermia to wireless thermal actuators—while deepening the fundamental understanding of dual relaxation phenomena in ferrofluids.

Keywords : Magnetic nanoparticles, Néel relaxation, Debye model, High frequency, Deep brain stimulation

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P-437

Correlation between number of stimulation channel and therapeutic effects of transcutaneous nerve stimula

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Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that commonly occurs in childhood and can persist into adulthood, characterized by core symptoms such as inattention, hyperactivity, and impulsivity. These core symptoms cause significant functional impairment in various areas of an individual's life, including academic, occupational, and social functioning, and are considered a major public health issue worldwide (1,2). Previous studies have reported the possibility of a correlation between stimulation and response in neural modulation therapy using microcurrents. Reports indicate that higher frequency and intensity of microcurrent stimulation promote neural plasticity and improve motor function (5). Additionally, precise measurement of evoked compound action potentials (ECAP) using spinal cord stimulation (SCS) and real-time adjustment of stimulation intensity have shown that higher doses and stimulation intensities exceeding the ECAP threshold are associated with better pain relief (6). Object of this study is 1) to confirmation of the inhibitory or reductive effects on inattention and hyperactivity indicators through neurostimulation and 2) clarification of the stimulus-therapeutic response correlation according to the increase in the number of stimulation channels. We used SHR rat model to represent ADHD, total 100 rats(control included) were examed. During the intervention, MBT, Y-mase, open field trial(OFT), cliff avoid test(CAT) were performed by timeline. After the 10 days of intervention(neurostimulation), subject were sacrificed immediately and prep to ELISA test. We administrated neurostimulation once a day for 10 minutes over a 10-day period. The stimulation is a biphasic waveform with a current of 0.5 mA, a frequency of 60 Hz, and a pulse width of 500 μs. We showed that neurostimulation, especially dual channel neurostimulation reduced hyperactive behavior at SHR rat, using MBT, NOR and CAT behavior test.

Keywords : Neuroengineering, Neurostimulation, ADHD, Dose-effect correlation

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P-438

Modeling motor learning as hysteresis: a quantitative approach to assess aftereffects of sensory modulation

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Human motor learning is a process where sensory input shapes an internal sensory reference adjusting motor output. To develop rehabilitation therapies and neuromorphic systems, a quantitative model of human motor learning is necessary. However, the quantitative relationship between sensory input and motor learning remains poorly understood. Motor aftereffects following sensory modulation is a well-known phenomenon, observed in paradigms such as split-belt treadmill training. In these cases, a modified motor pattern persists after the external sensory stimulus is removed, demonstrating that altered sensory input leaves a lasting influence on motor output. Previous research has been limited to confirming the existence of these aftereffects. Quantitative analysis between sensory input and corresponding motor aftereffect has been lacking. Prevailing concepts, like the internal model, miss the temporal dynamics of how the sensory reference and motor output evolve. This absence of a dynamic model has hindered a full understanding of motor learning and aftereffects. In this work, we propose a hysteresis model of motor learning. This is because the sensory reference adapts to changes in sensory input

with a time lag. By conceptualizing sensory input as the external field and the sensory reference as the internal state, this model may explain the temporal dynamics of motor learning, i.e., motor aftereffect. To validate the efficacy of the hysteresis model, we selected mastication as our experimental model. Based on its feedforward-dominant nature, motor output directly reflects sensory reference. Our results show that sensory augmentation during mastication strengthened the masticatory force, while sensory augmentation during rest weakened it. These force modulations persisted as an aftereffect after stimulation was stopped. These results suggest that the hysteresis model well explains the dynamic relationship between sensory input and motor output.

Keywords : Motor learning, Sensory modulation, Hysteresis, Aftereffect, Mastication

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P-439

Enhanced tool end-effector control accuracy and retention through multi-modal augmented feedback in virtual reality environments

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Precise tool manipulation is crucial ability to maximize productivity in medical and sports fields, as suggested by the rapid growth of surgical and golf simulator markets. However, traditional approaches such as verbal and visual feedback have not been effective, mainly because of their real-time processing challenges and variability in interpretation. Moreover, visual augmentation feedback can easily cause cognitive overload because of the intrinsic engagement of vision for daily tasks. To address these, novel approaches of somatosensory augmentation feedback, such as E-tactile feedback, offer low processing need and intuitive information mapping (i.e., low variability). Further, E-tactile feedback provides low mechanical instability and high spatiotemporal resolution, which is advantageous to enhance control accuracy. This study investigates multi-modal augmented feedback, combining visual and E-tactile feedback, on enhancing tool's end-effector control accuracy in VR Golf simulations and XR Fitts's law tasks. We hypothesized that the combined augmented feedback would yield superior accuracy and stronger after-effects compared to the visual augmentation feedback alone. Our results from two distinct tasks consistently showed that the group receiving both visual and E-tactile augmented feedback achieved significantly higher accuracy improvement and better retention than the group receiving only visual augmented feedback, supporting our hypothesis. The results also indicate that augmented feedback did not enhance precision, which suggests that distinct underlying mechanisms may apply to accuracy and prevision, respectively. The increase in accuracy with E-tactile augmented feedback was retained for 24 hours post-training, which needs further investigation.

Keywords : Augmented feedback, Multi-modal feedback, E-tactile feedback, Motor learning, XR

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P-440

Microchannel-structured nerve conduits enhance functional recovery following peripheral nerve injury in rats

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Peripheral nerve injuries (PNIs) remain a significant clinical challenge, as current treatments such as autologous nerve grafts (ANGs) are limited by donor site morbidity and tissue availability. To overcome these limitations, we developed a novel polymer-based nerve conduit incorporating phosphate glass fibers within a polycaprolactone (PCL) matrix. This design forms aligned microchannels and nanopores to enhance directional axonal guidance, facilitate nutrient diffusion, and support metabolic waste removal. In vitro, nerve conduit prototypes were fabricated to evaluate the optimal microchannel configuration for neurite outgrowth, using models with varied fiber alignment speeds. The 400 RPM group showed the greatest mean neurite extension (173.84 ± 6.22 μm), outperforming the non-aligned control (120.41 ± 0.50 μm) and comparable to 200 RPM (166.10 ± 13.88 μm) and 800 RPM (163.64 ± 4.91 μm) groups. In vivo, a 10-mm sciatic nerve transection model was established in 16-week-old male Sprague–Dawley rats. At 2 weeks post-implantation, axonal outgrowth from the proximal stump averaged 4,450.65 ± 172.29 μm in the conduit group, significantly exceeding the hollow tube control (1,877.58 ± 54.33 μm) and similar to the ANG group (3,273.72 ± 585.28 μm). At 16 weeks, histomorphometric analysis revealed axon densities of 3,623.66 ± 792.24 axons/mm² in the conduit group, closely approximating the ANG group (3,933 ± 397) and significantly higher than the hollow tube group (1,186.66 ± 318.43). Behavioral assessments confirmed improved sensory and motor recovery in the conduit group compared to controls. These results show that our microchannel-structured nerve conduit supports guided axonal regeneration and promotes functional recovery similar to autologous grafts. Its reproducible regenerative performance, biocompatibility, and precisely defined architecture underscore its potential clinical applicability as a synthetic alternative in future peripheral nerve repair strategies.

Keywords : Peripheral nerve injury, Nerve conduit, Microchannel, Axonal regeneration, Funtional recovery

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P-441

Poster Award Candidate

Multi-BRET biosensors for resolving biased Gα coupling dynamics in GPCRs

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G protein-coupled receptors (GPCRs) regulate various physiological responses via coupling to G proteins. GPCRs were traditionally believed to couple with a single Gα subtype, but growing evidence suggests they can interact with multiple Gα proteins, leading to diverse downstream signaling pathways. For example, 5-HT7R, generally known to associate with Gαs, can also interact with Gα12, playing a crucial role in early neuronal development. Thus it is important to develop a system to accurately distinguish Gα subtype coupling preference for the effective drug discovery targeting GPCRs. Here we developed a multicolor BRET-based assay, which can directly compare Gα preference to target GPCRs. First, we modified the TRUPATH assay to create R-TRUPATH, by reversely inserting fluorescent protein (FP) into Gα and luciferase into Gβγ. Based on these advances, we designed a multi-BRET system utilizing a single luciferase and two FPs including large stokes shift FP. We optimized the multi-BRET R-TRUPATH system by minimizing spectral interference and improving the signal-to-noise ratios. The multi-BRET biosensors allowed simultaneous monitoring and direct comparison of two Gα coupling events to target GPCRs, such as DRD2 and 5-HT7R. Therefore, the multi-BRET R-TRUPATH system provides a novel platform for competitive evaluation of GPCR-Gα binding preferences, offering a valuable screening tool for biased ligand discovery and advancing GPCR signaling research.

Keywords : GPCR, Gα coupling, BRET, Large stokes shift

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P-442

Poster Award Candidate

Reliable cortical mapping using randomized I/O curve in transcranial magnetic stimulation

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Transcranial magnetic stimulation (TMS) is a neurostimulation technique used to localize cortical functional areas and has clinical significance in preoperative motor and language function mapping. To identify cortical functional areas, a recent approach leverages input-output (I/O) curves, where the input is the computed TMS-induced electric field in the brain and the output is the corresponding measured TMS-generated motor evoked potentials (MEPs). The cortical site showing the highest coefficient of determination (R2) between input and output is identified as the stimulation target. However, generating reliable I/O curves typically requires a large number of stimuli. To reduce acquisition time, downsampling strategies using random coil position and orientation have been proposed, though their effect on mapping stability remains unclear. This study systematically investigated how randomization of coil position and orientation affects stability in the I/O curve-based cortical mapping. Specifically, mappings were performed under controlled random variations in coil orientation (±10° to ±60°, in 10° steps) and position (radii of 5, 10, 20, and 30 mm). Cortical position stability was quantified by calculating the mean distance differences between cortical mapping results across all condition pairs. The results showed that for orientation variation, cortical positions differed significantly under ±10°to ±30°conditions, while ±40° to ±60° yielded consistent cortical mappings. For positional variations, mapping stability improved significantly over 10 mm. These findings demonstrate that robust cortical mapping can be maintained even under randomized coil conditions, provided the range is sufficiently broad. This supports the feasibility of protocol standardization and optimization for clinical TMS.

Keywords : Transcranial magnetic stimulation (TMS), Brain mapping, Motor Evoked Potentials (MEPs), Input-Output Curve (I/O Curve), Random Sampling

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P-443

Poster Award Candidate

Therapeutic effects of low-intensity focused ultrasound neuromodulation in a mouse model of tic-like behavior using clinically relevant parameters

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Tourette syndrome (TS) is commonly managed with pharmacological treatments, which often exhibit limited efficacy and lead to tolerance over time. As alternatives, neuromodulatory approaches such as deep brain stimulation (DBS) and transcranial magnetic stimulation (TMS) have gained attention for treating tic disorders. Despite their potential, these techniques are constrained by invasiveness and lack of spatial precision. To overcome these challenges, we employed low-intensity focused ultrasound (LIFU), a promising noninvasive modality previously applied in various neurological conditions. We established a bicuculline-induced mouse model of tic disorder and validated the presence of tic-like features through behavioral analysis and recordings of neural and electrophysiological activity. LIFU stimulation was delivered using a 250-kHz ultrasound transducer with parameters relevant to clinical use. We identified effective stimulation protocols, and targeted stimulation of the secondary motor cortex (M2) resulted in significant reductions in tic-like behaviors and pathological EEG spikes by 38% and 61%, respectively, relative to sham controls. These findings indicate that LIFU can effectively suppress tic-related symptoms in a preclinical TS model. Given the clinical compatibility of the stimulation parameters, this work provides a strong foundation for translational research toward human applications in tic disorder treatment.

Keywords : Low-intensity focused ultrasound, Tic disorder, Tourette syndrome, Electrophysiology, Therapeutic effect

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Others P-444~P-471

P-444

Poster Award Candidate

Visual reconstruction based on temporal encoding information of visual cortex neurons

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Visual neural decoding is critical for understanding how the brain processes visual information and is a prerequisite for developing cortical prosthetics for precise visual restoration. Our research aims to develop better strategies for visual neural decoding. Methods: Electrophysiological recordings were performed using Neuropixels2.0 electrodes in the primary visual cortex (V1) of anesthetized C57 mice. Responses of nearly 5000 neurons to natural scenes, grayscale videos, and color videos were recorded. We propose an end-to-end visual neural decoding approach consisting of three modules: 1) a pulse sequence enhancement module based on learnable wavelets, which enhances the representation of neuronal temporal pulse signals; 2) a neuron-to-visual scene mapping module, which identifies the mapping relationships between neurons and the pixels of the stimulus scene; 3) a visual scene reconstruction enhancement module, which decodes the pixel-level visual scenes based on an autoencoder.

Keywords : Visual neural decoding, Electrophysiological recordings

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P-445

Poster Award Candidate

Discovery and optimization of a series of vinyl sulfoximine-based analogues as potent Nrf2 activators for the treatment of multiple sclerosis

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Multiple sclerosis (MS) is an immune-mediated neurodegenerative disease of the central nervous system (CNS), which leads to demyelination, axonal loss, and neurodegeneration. Increased oxidative stress and neurodegeneration have been implicated in all stages of MS, making neuroprotective therapeutics a promising strategy for its treatment. We previously have reported vinyl sulfones with antioxidative and anti-inflammatory properties that activate nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that induces the expression of cytoprotective genes against oxidative stress. In this study, we synthesized vinyl sulfoximine derivatives by modifying the core structure and determined therapeutic potential as Nrf2 activators. Among them, 10v effectively activated Nrf2 (EC50 = 83.5 nM) and exhibited favorable drug-like properties. 10v successfully induced expression of Nrf2-dependent antioxidant enzymes and suppressed lipopolysaccharide (LPS)-induced inflammatory responses in BV-2 microglial cells. We also confirmed that 10v effectively reversed disease progression and attenuated demyelination in an experimental autoimmune encephalitis (EAE) mouse model of MS.

Keywords : Multiple Sclerosis, Nrf2 Activator, Vinyl Sulfoximine, Experimental Autoimmune Encephalomyelitis

P-446

Poster Award Candidate

Serotonin 2C Receptors Expressed by CRH and TRH Neurons Regulate Metabolism

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The central nervous system contains several important endocrine structures, including the hypothalamic-pituitary-adrenal (HPA) axis, which controls homeostasis. The corticotropin-releasing hormone (CRH) and thyrotropin-releasing hormone (TRH) neurons are neurohormone-expressing neurons involved in HPA axis and regulate metabolism. Since it has been previously shown that CRH and TRH neurons express serotonin 2C receptor (Htr2c) that controls many aspects of metabolism, we aimed to identify the metabolic role of Htr2c expressed by CRH and TRH neurons. We conducted experiments with Crh-ires-cre::Htr2cflox/Y and Htr2cflox/Y mice and Trh-ires-cre::Htr2cflox/Y and Htr2cflox/Y mice. We measured body weight, food intake, energy expenditure and performed GTT, ITT, and PTT. We also conducted a fasting-refeeding experiment with an Htr2c agonist, WAY161503, and GR antagonist, RU486. In addition, we measured corticosterone (CORT) levels using ELISA. We recorded the electrical activity of neurons using patch-clamp technique with Crh-ires-cre::tdTomato and Trh-ires-cre::tdTomato reporter mice. We observed that anorexia induced by WAY160503 was attenuated in the Crh-ires-cre::Htr2cflox/Y mice, without affecting other metabolic phenotypes. Among the CRH neurons expressed in various brain region, those in the paraventricular nucleus of the hypothalamus (PVH) were inhibited by WAY161503. This attenuated anorexia was reproduced in when *Htr2c* was knocked-down only in PVH CRH neurons. Decreases of CORT level by Htr2c agonist was also blunted in the knock-down model. Htr2c agonist induced anorexia was restored by GR antagonist. In the Trh-ires-cre::Htr2cflox/Y mice, we did not observe any differences in body weight, food intake, energy expenditure, GTT, ITT and PTT. However, we found that WAY161503 inhibits TRH neurons within both the PVH and the DMH. Our findings provide new insights into how Htr2c expressed by CRH and TRH neurons differentially regulate metabolism.

Keywords : Hypothalamus, serotonin 2c receptor, CRH neuron, TRH neuron, metabolism

P-447

Drawn to delight: A vicarious reward paradigm unveils neural circuits of positive empathy

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Empathy fosters social bonding by enabling individuals to share affective states. However, the neural basis of positive empathy, particularly the transmission of rewarding emotions, remains elusive, partly due to the lack of robust animal models. In this study, we developed a novel rodent behavioral assay in which observer mice were exposed to conspecific demonstrators undergoing wireless medial forebrain bundle (MFB) stimulation (WBS), serving as an incentive reward. Observer mice exhibited real-time social preferences toward demonstrators receiving WBS, indicating vicarious reward perception. This behavioral phenotype was dependent on auditory sensation. Furthermore, observer mice formed a lasting rewarding memory, as evidenced by social conditioned place preference (sCPP) tested 24 hours post-conditioning, suggesting that the conditioning experience served as a strong social reward. Using whole-brain Fos-TRAP mapping and chemogenetic interventions, we identified the paraventricular nucleus of the thalamus (PVT) as a key node mediating these behaviors. Further optogenetic analyses revealed a critical projection from the PVT to the zona incerta (ZI), whose selective modulation was both necessary and sufficient for expressing vicarious reward. Notably, inhibition of the PVT-to-ZI pathway during a sucrose preference test did not alter direct reward-seeking behavior, suggesting that this circuit is specifically tuned to socially derived, rather than primary, reward processing. Collectively, our findings establish a robust animal model for investigating the neural substrates of positive empathy and highlight the specialized role of the PVT-to-ZI pathway in mediating socially transmitted rewarding experiences.

Keywords : Vicarious reward, Positive empathy, Paraventricular thalamus

P-448

Postprandial sodium sensing by enteric neurons in *Drosophila*

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Sodium is essential for all living organisms. Animals including insects and mammals detect sodium primarily through peripheral taste cells. It is not known, however, whether animals can detect this essential micronutrient independently of the taste system. Here, we report that *Drosophila Ir76b* mutants that were unable to detect sodium became capable of responding to sodium following a period of salt deprivation. From a screen for cells required for the deprivation-induced sodium preference, we identified a population of anterior enteric neurons, which we named internal sodium-sensing (INSO) neurons, that are essential for directing a behavioural preference for sodium. Enteric INSO neurons innervate the gut epithelia mainly through their dendritic processes and send their axonal projections along the oesophagus to the brain and to the crop duct. Through calcium imaging and CaLexA experiments, we found that INSO neurons respond immediately and specifically to sodium ions. Notably, the sodium-evoked responses were observed only after a period of sodium deprivation. Taken together, we have identified a taste-independent sodium sensor that is essential for the maintenance of sodium homeostasis.

Keywords : post-ingestive sensor, sodium, salt appetite, drosophila, enteric neurons

P-449

Organoid modeling of functional neuromuscular junctions and therapeutic screening of natural extracts for sarcopenia

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Human induced pluripotent stem cell (iPSC)-derived organoids offer a powerful platform to model human diseases in genetically diverse backgrounds. Neuromuscular organoids (NMOs), which recapitulate functional neuromuscular junctions (NMJs), have emerged as valuable tools for investigating muscle innervation, atrophy, and regeneration *in vitro*. Sarcopenia, defined by the age-related decline in skeletal muscle mass and function, remains a critical unmet clinical need due to a lack of effective therapies. Previously, through high-throughput screening using a split GFP-based C2C12 myoblast system integrated with the CellCyte platform, we identified Extracts A, B, and C as promising candidates that enhance myocyte differentiation and reverse dexamethasone-induced muscle atrophy. In this study, we established a functional NMO model that mimics NMJ formation and muscle innervation and evaluated the therapeutic potential of the selected natural extracts. By day 50 of NMO maturation, skeletal muscle fibers expressing Fast MyHC localized distinctly from TUJ1-positive neuronal clusters. Moreover, α-bungarotoxin (α-BTX) staining revealed acetylcholine receptor (AChR) clusters near TUJ1-positive neurites adjacent to muscle fibers, indicating successful NMJ formation. The selected extracts significantly increased muscle fiber development, as evidenced by upregulated myosin heavy chain expression and increased the number of α-BTX-positive puncta in the organoids. Notably, Extracts B and C exhibited strong protective effects against dexamethasone-induced atrophy in the NMO model. In conclusion, we present a physiologically relevant NMO model that recapitulates key features of NMJ development and sarcopenia pathology. The observed protective effects of natural extracts, particularly B and C, support their potential as therapeutic candidates. This organoid system also offers a scalable platform for high-throughput drug screening in neuromuscular disorders.

Keywords : Sarcopenia, Neuromuscular organoid, Neuromuscular junction, Natural extracts

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P-450

Network meta-analysis identifies epigenetic mechanisms supporting functional recovery after spinal cord injury

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Spinal cord injury (SCI) remains a major clinical challenge, with limited treatment options and highly variable outcomes. Numerous in vivo studies have reported functional improvements using pharmacological or genetic interventions; however, the underlying mechanisms vary widely across studies, limiting translational insight. In particular, while epigenetic mechanisms such as histone acetylation and RNA modifications have recently gained attention, their relative contribution alongside classical biological processes remains unclear. To address this, we performed a comprehensive systematic review and network meta-analysis (NMA) of 29 preclinical rodent studies, covering 252 experimental comparisons involving drug- or gene-based treatments aimed at functional recovery. Each intervention was classified into one of three mechanistic categories: epigenetic regulation (six types), classical recovery mechanisms (five types), and intracellular signaling pathways (nine types). Functional outcomes were extracted across motor, histological, and electrophysiological domains. NMA was conducted using standardized mean differences and surface under the cumulative ranking curve (SUCRA) to evaluate both individual treatments and mechanism groupings. The results showed that certain epigenetic mechanisms—particularly histone acetylation and RNA methylation—were consistently associated with improved functional outcomes, often comparable to classical mechanisms such as neuroregeneration and inflammation control. Several intracellular pathways, including JAK/STAT and apoptosis signaling, also demonstrated positive but heterogeneous effects. Overall, the findings suggest that functional recovery after SCI is not driven by a single mechanism but arises from an interplay of epigenetic, classical, and signaling processes. This study provides a comparative mechanistic framework to guide future therapeutic strategies and promote more targeted clinical translation.

Keywords : Spinal cord injury, Epigenetic mechanisms, Network meta analysis, Functional recovery, Preclinical rodent studies

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P-451

Dual delivery of light/prodrug nanoparticles using tumor-implantable micro light-emitting diode on a optofluidic system for combinational glioma tr

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Introduction: Glioma is one of the most lethal types of tumors with a bad prognosis, however, the existence of the blood-brain barrier (BBB) and skull significantly limits the therapeutic approaches. Herein, an implantable microLED device with a micro-syringe chip (LED-SC) is newly proposed for the dual delivery of light/prodrug nanoparticles (PNPs) to glioma tumors in the brain. Materials: The LED-SC combines microLED and SC to enable intratumoral administration of light and PNPs for chemophotodynamic therapy. PNPs, self-assembled nanoparticles of verteporfin (VPF)-doxorubicin (DOX) prodrug, are cleaved by the enzyme cathepsin B, releasing active drugs specifically within tumor cells. Results:In vitro studies show that PNPs are taken up by glioma cells and exhibit enhanced cytotoxicity under light irradiation. The PNPs-loaded LED-SC can be implanted into glioma, wherein PNPs are slowly diffused through the tumor, bypassing the BBB, and it also ensures effective light delivery in glioma beneath the skull, boosting chemo-photodynamic therapy. In glioma mouse models, PNP-loaded LED-SC implantation showed a 3.9-fold improvement in PNP delivery efficiency over intravenous administration, leading to better drug distribution and therapeutic results. Conclusions: LED-SC-mediated intratumoral administration of PNPs and light is fully demonstrated as a promising method, successfully overcoming the major obstacles in glioma therapy.

Keywords : Glioblastoma, Tumor specific-delivery, Light/drug administration, Chemo-photodynamic therapy, Implantable device

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P-452

Enhanced optical clearing for efficient imaging of genetically encoded fluorescence and multicolor staining in mouse brain tissue&

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Optical tissue clearing is essential for high-resolution imaging of thick biological samples; however, many existing aqueous clearing methods suffer from high viscosity, inadequate refractive index (RI) matching, and significant fluorescence signal loss. We introduce AICI (Aqueous high refractive Index matching and tissue Clearing solution for Imaging), a novel iodixanol-based clearing agent designed to overcome these limitations. AICI exhibits low viscosity and a high RI of 1.466, enabling efficient RI matching and rapid optical clearing in a single step. It renders 1-mm-thick mouse brain slices fully transparent within 90 minutes while preserving tissue morphology with minimal shrinkage (<2.2% after 24 hours). AICI also maintains fluorescence signal stability over time (GFP retains >50% intensity after 10 days) and remains chemically stable in liquid form for more than 30 days under ambient conditions, allowing for consistent and flexible experimental workflows. Compared to iohexol-based RI matching solutions commonly used in other protocols, AICI demonstrates superior optical transparency and tissue penetration, likely due to the optimized physicochemical properties of iodixanol. When used with fluorescent protein-expressing mice, AICI enables

direct imaging without the need for additional labeling, streamlining the workflow and facilitating efficient visualization of target structures. At imaging depths of several tens to hundreds of micrometers, it also supports multiple rounds of immunostaining, enabling high-resolution multicolor imaging in cleared tissues.

Keywords : Tissue clearing, Refractive index matching, Iodixanol-based clearing agent, Multicolor 3D imaging

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P-453

The role of the prefrontal cortex in the emotional evaluation of ambivalent stimuli

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Emotional evaluation, the ability to assess the affective value of environments or stimuli, is critical for adaptive behavior, yet it often varies substantially across individuals. To investigate the neural basis of such variability, we developed a mouse model to examine the medial prefrontal cortex (mPFC) contributes to individual differences in emotional valuation. Mice were placed in a two-chamber apparatus where one chamber was paired with a specific type of stimulation: either a positive stimulus (chocolate), a negative stimulus (foot shocks), or an ambivalent combination of both. The other chamber remained neutral. Contextual preference tests revealed significant individual variability in chamber preference across all stimulation types. To better understand behavioral heterogeneity, we applied DeepLabCut for pose estimation and used t-distributed stochastic neighbor embedding (t-SNE) to uncover microstructure patterns in behaviors. Unsupervised clustering identified three distinct behavioral patterns associated with the different affective context. We then recorded mPFC neural activity using fiber photometry with the calcium indicator, GCaMP8f. Strikingly, mPFC activity was selectively elevated during behaviors associated with ambivalent (conflicting) affective contexts. These findings suggest that the mPFC is specifically engaged in processing emotionally ambiguous or conflicting information and may underlie individual variability in emotional evaluation.

Keywords : Emotional valence, Individual difference, The mPFC, Behavioral clustering

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P-454

Area postrema detects circulating tumor-derived soluble factors at the earliest stage of cancer associated cachexia

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Cancer cachexia is a systemic wasting syndrome associated with advanced malignancies, involving both peripheral and central mechanisms. However, the brain regions that detect early tumor-derived signals remain poorly characterized. To identify neural correlates of early cachexia, we used a syngeneic colon cancer mouse model and stratified animals into control, pre-cachexia, and cachexia stages. Whole-brain c-Fos mapping revealed seven regions with cachexia-associated neuronal activation: PVH, Arc, SFO, ME, PBN, AP, and NTS. Among them, only four regions—PVH, PBN, AP, and NTS—were activated in the pre-cachexia stage. Notably, the area postrema (AP) was the only region that showed consistent activation in both pre-cachexia and cachexia. The AP is a sensory circumventricular organ that lacks a blood-brain barrier (BBB), allowing direct exposure to circulating soluble factors. This anatomical feature suggests that the AP may serve as a primary neural sensor of peripheral tumor-derived signals. To further examine its functional engagement, we performed Stereo-seq-based spatial transcriptomics in the cachexia stage. Transcriptomic alterations in the AP were evident, supporting its sustained activation and potential role in mediating brain responses to systemic tumor burden. These findings suggest that the AP functions as an early and persistent brain sensor in cancer cachexia, linking peripheral signals to central regulatory pathways.

Keywords : Cancer associated cachexia, Area postrema, Colon cancer

P-455

Frequency-based imitation as an independent learning heuristic

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Learning is widely believed to require outcome-based feedback. However, in real-world environments, such feedback is often ambiguous or uncertain. What strategies, then, support learning under such conditions? We propose that humans guide learning by imitating others, driven by their social inclination to cooperate—even in the absence of clear feedback. Specifically, we suggest that humans rely on frequency-based imitation—the tendency to adopt behaviors simply because they are more frequently observed in others, regardless of actual outcomes. While previous studies have reported frequency-based imitation in outcome-neutral settings, we demonstrate that it persists even when some outcomes are more rewarding than others. We conducted a behavioral experiment in which participants selected among visual stimuli associated with varying reward probabilities, aiming to learn which were more rewarding and to maximize earnings. Before each choice, participants observed selections made by artificial agents, with some stimuli chosen more frequently than others. Crucially, the agents' choice frequencies were uncorrelated with reward. Results showed that participants preferred stimuli more frequently chosen by agents, even when they offered no reward advantage. Notably, participants exhibited the strongest preferences for stimuli that were both frequently chosen and highly rewarding, indicating that frequency- and reward-based learning can operate concurrently. Furthermore, while reward bias increased over time as participants learned to identify high-reward stimuli, frequency bias remained stable. These findings demonstrate that frequency bias persists independently

of the presence or strength of reward bias, suggesting it is not merely a fallback strategy under uncertainty but a robust and persistent feature of human learning. We propose that frequency-based imitation functions as a core heuristic supporting learning in outcome-ambiguous real-world environments.

Keywords : Learning, Fequency-based Imitation, Social behavior, Human behavior, Reward Learning

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P-456

Unfairness affects the perception of pain and altruistic behavior

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A sense of fairness can trigger emotional and motivational changes that influence individuals' perceptions and behaviors. In healthcare settings, perceived unfairness has been linked to increased pain sensitivity and poorer health outcomes. Unfair allocation of resources can also reduce altruistic motivation, such as providing medical care. Despite its clinical relevance, few studies have examined how unfairness affects pain perception and altruistic behavior. This study comprises two experiments. In the first experiment, participants received painful stimuli under fair or unfair conditions based on task performance. They rated the perceived unfairness, intensity, and unpleasantness of the stimuli. Results showed that pain was perceived as more intense and unpleasant under unfair conditions, with a positive correlation between unfairness ratings and pain ratings. In the second experiment, a subset of participants from the prior study received fair or unfair monetary allocations in a dictator game. They then decided how much to donate to a pain-related charity while viewing empathy-inducing painful or neutral faces. During the donation decision-making, the hemodynamic responses were measured using a functional near-infrared spectroscopy system. Donations decreased after unfair allocations, even with empathy cues and this reduction was linked to decreased activity in orbitofrontal cortex. Notably, those who perceived greater pain in the first experiment showed greater reductions in donation in response to unfairness. Together, our findings show that perceived unfairness amplifies pain and reduces altruistic behavior, highlighting how social context can influence perceptual and behavioral responses. These findings suggest that unfair experience can worsen personal suffering and weaken social connectedness. Understanding these effects may offer valuable insights for improving patient care and promoting more equitable healthcare environments.

Keywords : Altruistic behavior, Charitable donation, Inequity, Pain, Unfairness

P-457

Fluorinated THK-5320 derivatives for in vivo PET imaging of ApoE-binding amyloid plaques

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Apolipoprotein E (APOE) is the most significant genetic risk factor for Alzheimer's disease (AD). ApoE is known to colocalize with amyloid plaques. Postmortem studies have suggested that ApoE-binding plaques may elicit a stronger glial response than other plaque types. The recent identification of several rare protective ApoE variants further suggests that ApoE plays a crucial role in modifying AD progression. Interestingly, these cases exhibited a distinct regional ApoE-immunoreactive pattern that correlated with activated microglia. In vivo imaging of ApoE-binding plaques would offer a valuable window into the dynamic processes of senile plaque development and heterogeneity, potentially revealing important distinctions between benign and neuroinflammatory pathogenic amyloid deposition. Positron Emission Tomography (PET) is a practical tool for the in vivo visualization of amyloid-β (Aβ) and tau in the human brain. While many fluorescent probes targeting Aβ plaques and tau tangles have been developed as research tools, we identified a unique fluorescence probe, THK-5320, which differentially stained amyloid plaques in two colors (red and blue). Detailed characterization revealed a correlation between the red plaques and ApoE-binding plaques. The discovery of THK-5320 may pave the way for the development of novel PET tracers that specifically target ApoE-binding plaques. In this study, we synthesized and evaluated fluorinated THK-5320 derivatives for the in vivo imaging of ApoE-binding plaques. Biodistribution studies in mice have demonstrated good brain uptake and rapid washout from the normal brain tissue. In vitro autoradiography further showed that several ^{18}F-labeled THK-5320 derivatives highly accumulated in the CA1 region of the hippocampus, which contains ApoE-binding plaques. Further characterization is required to validate the selective detection of ApoE-binding plaques in vivo.

Keywords : Alzheimer's disease, Apolipoprotein E, Amyloid plaques, Positron Emission Tomography

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P-458

The neural signature of music preference: Musical complexity, ratings, and relative phase

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People have a wide range of musical preferences, but is there a way to quantify them? Prior research indicates that music appreciation is influenced by complexity, which can be computed using Information Content (IC) and entropy via the Information Dynamics of Music (IDyOM)

algorithm. General listeners displayed an inverted U-shaped relationship between the IC and liking ratings, with musical stimuli of intermediate IC exhibiting the highest likability. Our study explores how experts and non-experts differ in their music preference profiles and whether this distinction is reflected in neural responses. To investigate this, we conducted simultaneous EEG-fMRI recordings as participants listened to classical music excerpts and gave ratings. Specifically, we measured the relative phase of the EEG response for each musical stimulus and examined its relationship with the IC for both expert and non-expert groups. The relative phase was calculated by subtracting the global mean phase from each electrode's phase, revealing lead-lag patterns in EEG signals that reflect temporal brain dynamics. We also analyzed the correlation between the IC and participants' ratings. Interestingly, only non-experts demonstrated an inverted U-shaped curve in their ratings of likability, attention, and emotional valence. Experts showed increased transitions between different phase-lead-lag patterns in EEG as the IC increased, suggesting more dynamic brain activity as the song became more complex. Through these analyses, we identified the differences in responses between experts and non-experts, as well as differences in the EEG phase dynamics changes as the musical complexity increases. These findings demonstrate that musical preferences can be quantitatively characterized, offering novel insights into the neural and cognitive mechanisms underlying aesthetic appreciation. Future research will explore the relationship between aesthetic factors and differences in brain activity.

Keywords : Human brain, Music cognition, State transition, Phase dynamics, EEG

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P-459

Neurobehavioral and histopathological assessment of 3-Fluorophenmetrazine neurotoxicity in mice

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3-Fluorophenmetrazine (3-FPM), a synthetic stimulant structurally related to phenmetrazine, has emerged as a novel psychoactive substance (NPS) with significant abuse potential. This study evaluated the neurotoxic effects of 3-FPM in male C57BL/6 mice through cognitive, neurobehavioral, and histopathological analyses. Mice received intraperitoneal injections of 3-FPM (10 or 30 mg/kg), either as a single dose or once daily for 14 days. Motor coordination was significantly impaired following acute 30 mg/kg administration, as evidenced by decreased latency in the rota-rod test ($p < 0.001$). Spatial working memory deficits were observed in the Y-maze test at both 10 and 30 mg/kg under acute and repeated exposure conditions ($p < 0.01$). The Irwin test revealed transient neurobehavioral abnormalities, including hyperlocomotion, increased touch sensitivity, and heightened nociceptive responses, particularly after acute high-dose administration. Immunohistochemical analyses showed dose-dependent reductions in tyrosine hydroxylase (TH)-positive neurons in the substantia nigra pars compacta and decreased TH-positive fiber density in the striatum following repeated 3-FPM exposure. These findings demonstrate that 3-FPM induces dose-dependent dopaminergic neurotoxicity accompanied by measurable cognitive and neurobehavioral impairments.

Keywords : Neurotoxicity, Rota-rod, Y-maze, Irwin test, Dopaminergic neurons

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P-460

Suppression of BDNF-CREB signaling by prenatal RF exposure in wild-type mice: Insights into developmental sensitivity versus AD pathology

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Brain-derived neurotrophic factor (BDNF) and its downstream signaling via TrkB and CREB play critical roles in neuronal development and memory-related synaptic plasticity. Dysregulation of this pathway is commonly observed in Alzheimer's disease (AD), including decreased expression of BDNF and reduced phosphorylation of CREB. However, the effects of prenatal exposure to radiofrequency electromagnetic fields (RF-EMF) on this neurotrophic pathway, particularly in the context of AD pathology, remain unclear. In this study, we examined the impact of prenatal RF-EMF exposure on postnatal brain development in both wild-type (WT) and 5xFAD transgenic mice, a familial AD model. Pregnant mice were exposed to 1,950 MHz WCDMA RF-EMF at 4 W/kg for 2 hours daily from gestational days 1 to 17. At 3 weeks of age, hippocampal mRNA and protein levels of BDNF and TrkB were found to be reduced in RF-exposed WT offspring, along with decreased phosphorylation of CaMKII, ERK, and CREB. Notably, p-CaMKII and p-CREB levels were also diminished, indicating suppression of the BDNF-TrkB-CREB signaling axis. Despite these molecular changes, no alterations in hippocampus-related behaviors were observed in WT mice at 6 months of age. In contrast, AD transgenic mice showed baseline reductions in BDNF-TrkB-CREB signaling compared to WT, but prenatal RF exposure did not further affect molecular or behavioral outcomes at either time point. These findings suggest that prenatal RF-EMF exposure may transiently suppress neurotrophic signaling in healthy juvenile brains, while having limited impact on brains already undergoing AD-related pathology.

Keywords : Prenatal exposure, RF-EMF, BDNF-TrkB-CREB signaling

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P-461

Effects of RF-EMF exposure on impulsive behavior and immediate-early gene expression in the striatum

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The developing brain is highly susceptible to environmental stressors, including radiofrequency electromagnetic fields (RF-EMFs). Epidemiological evidence has linked early-life mobile phone use to increased risk of attention-related disorders such as ADHD, but the underlying neural mechanisms remain unclear. To investigate the biological impact of RF-EMF exposure during early development, we conducted behavioral assessments—open field (OF) and cliff avoidance reaction (CAR) tests—and transcriptomic analysis via RNA-sequencing (RNA-seq) on striatal tissue from 4-week-old C57BL/6 mice exposed to 1950 MHz LTE signals for 4 weeks (specific absorption rate [SAR]: 4 or 6 W/kg; 6 h/day, 7 days/week). Mice exposed to 6 W/kg RF-EMF exhibited significantly reduced center time in the OF test and increased risk-taking in the CAR, indicating elevated anxiety-like and impulsive behavior. RNA-seq analysis revealed significant upregulation of immediate-early genes (IEGs), including Arc, Fos, and Egr1, in response to RF-EMF exposure. These transcriptomic changes were confirmed by qPCR analysis, which validated the increased expression of Arc and other IEGs in the striatum. Furthermore, immunohistochemistry showed that Arc expression was selectively elevated in the dorsomedial striatum (DMS). Together, the upregulation of Arc in the striatum region, coupled with impulsive behavioral phenotypes, suggests that RF-EMF exposure might affect fronto-striatal circuits involved in impulse control. These findings provide mechanistic insight into how high-SAR RF-EMF exposure during development may increase vulnerability to behavioral dysregulation.

Keywords : RF-EMF, Impulsive behavior, Immediate-early genes, RNA-sequencing

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P-462

Liquid metal based flexible electrodes for neural stimulation and recording

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Objectives: Conventional DBS for neuropathic pain typically uses rigid metal electrodes, which can damage adjacent brain tissue, cause inflammation, and reduce stimulation accuracy. These issues limit long-term stability of neural recording and stimulation. This study evaluates the efficacy of soft neural electrodes made from EGaIn liquid metal for stimulation and recording in a rat model of neuropathic pain. Methods: Flexible electrodes were fabricated by filling polyimide tubing with EGaIn and coating the tips with platinum black to enhance biocompatibility and electrochemical properties. Their functionality was first validated in vivo by recording neural signals from the nucleus accumbens (NAc) after medial forebrain bundle (MFB) stimulation. The stimulation capability was also tested via von Frey test with continuous ventral posterolateral nucleus (VPL) stimulation using implanted electrodes (130 Hz at 100 μA and 50 Hz at 80 μA). Additionally, chronic implantation studies showed VPL stimulation with the same electrodes reliably induced turning behavior in freely moving rats, confirming long-term stability. Results: In vivo recordings showed that neuronal firing rate in the NAc increased significantly after MFB stimulation (pre: 21.8 ± 3.6 Hz, post: 36.45 ± 4.4 Hz, *p<0.05). Biphasic current (50 Hz, 80 μA) effectively modulated pain sensitivity, indicated by increased withdrawal threshold (10.51 g). During chronic tests, turning behavior and rotation angle increased with higher VPL stimulation currents. Conclusion: EGaIn-based soft electrodes demonstrated effective stimulation and recording while minimizing tissue damage. These results suggest they are promising alternatives to rigid electrodes for long-term neuromodulation in neuropathic pain. However, implantation methods require further refinement to suit liquid metal properties.

Keywords : DBS, Neuropathic pain, Liquid metal

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P-463

Reward-related functional connectivity: comparing self-rewards and filial motivation in adolescents

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Understanding the neural basis of reward processing is key to explaining motivation, decision-making, and social behaviour. While general reward responses are well studied, less is known about how the reward recipient—self vs. others—modulates functional connectivity (FC) in the brain's reward network. This study compared FC patterns between individuals motivated by self-reward (cash) and filial (parental) reward during anticipation and task execution. Twenty-eight healthy Malaysian participants (mean age 22.71 ± 1.08 years) underwent fMRI while performing the N-back tasks (2-back) under four reward conditions: self-reward (cash), filial reward, certificate reward, and a neutral condition. Each condition included an anticipation (reward cue) and task execution (2-back) phase. Based on 2-back scores, participants were grouped into "cash" (n=14) and "filial" (n=14). Seed-to-voxel FC analyses were conducted using the ventral striatum (VS) as the seed via Conn Toolbox. The FC was compared between the two groups. During the anticipation phase, there are functional connectivity differences for three cues. Under the cash cue, increased FC was found between the left VS and right supramarginal gyrus and also the right precentral gyrus. The filial cue showed increased FC between the right VS and bilateral lingual gyrus, as well as the right superior parietal lobule. Also, the left VS and the right postcentral gyrus. Certificate cues also revealed group differences. During task execution, the filial group showed stronger FC for the filial n-back between the left VS and precuneus. These regions are associated with empathy and self-referential processing. Findings suggest self-rewards engage sensorimotor networks, while filial rewards activate socio-emotional areas, offering insights into adolescent motivation and implications for promoting prosocial behaviour in education and therapy.

Keywords : reward, prosocial decision-making, functional connectivity, filial, adolescent

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P-464

Theory of mind mediates adolescents' age-related increase in interest-based gossip sharing

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Gossip—the transmission of social information about absent third parties—is a central yet often overlooked feature of human conversation. Although developmental studies have suggested that gossip behavior changes during adolescence, few have examined how these changes unfold or what mechanisms drive them. To address this, we collected behavioral data from 98 adolescents (52 female, mean age 13.8, range = 10–18) using a structured gossip-sharing task. Participants evaluated various scenarios on multiple dimensions, including how interesting or useful they found the information, and then chose whether to share it. Using hierarchical Bayesian modeling, we found that adolescents became increasingly likely to share gossip they perceived as interesting or useful, with both effects strengthening with age. Notably, interest-based sharing was positively associated with Theory of Mind (ToM), as measured by the Korean RMET. Structural equation modeling further revealed that ToM mediated the relationship between age and interest-based sharing. A separate sample of adults (N = 102; 59 female, mean age 23.8, range = 20–32) exhibited higher overall interest-based sharing than adolescents, and although a subtle age-related decrease was observed, this pattern contrasts with the age-related increase seen in adolescents—suggesting that ToM may support interest-based sharing in a developmentally specific manner. Finally, resting-state fMRI from a subsample of adolescents (N = 38; 25 female, mean age 14.5, range = 10–18) revealed that interest-based sharing was associated with intrinsic functional connectivity in a seed-to-voxel analysis using the right posterior superior temporal sulcus (pSTS)—a region implicated in both social perception and ToM. This effect was specific to the pSTS, suggesting that intrinsic functional organization supporting mentalizing processes may contribute to adolescents' motivation to share interesting social information.

Keywords : Gossip, Theory of Mind, Adolescence

P-465

Sex differences in modifiable risk factors influencing cognitive decline

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Backgrounds: Men and women exhibit different patterns of brain aging; the specific neuroanatomical mechanisms underlying these differences are poorly defined. The impact of health risk factors on brain structure and cognitive function is also unclear. Therefore, we investigated the relationships between modifiable health risks, brain volume, and cognition in middle-to-old-aged men and women. Methods: A total of 3,003 adults between the ages of 49 and 80 from the Korean Genome and Epidemiology Study (KoGES) with complete T1-weighted MRI, cognitive testing, lifestyle, and psychological data were included in this cross-sectional study. Two-way analysis of covariance tested age and sex interactions on various memory and executive tests. Mediation analyses first tested whether health risk factors mediated the relationship between age and cognition, followed by a separate model with brain volume as the mediator. Results: Both sexes showed executive decline, with greater decline in women during later life. In women, age-related impairments in Stroop and trail-making function were mediated by elevated depression scores and longer sleep latency, respectively. Smoking deteriorated age-related Stroop performance in men. Age-related cognitive decline was then mediated by cortical atrophy in different brain regions across sexes. Discussion and conclusion: This study suggests that health risk factors contribute to the rapid progression of cognitive aging, with different neural mechanisms in women and men. Sex-based modifiable interventions, including enhancing sleep, alleviating depression, and smoking control, may help delay cognitive aging.

Keywords : Health risk factors, Sex, MRI, Brain aging, Cognition

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P-466

Inactivation of Protein X by HDAC8 represses myogenic differentiation via miR-18b/CTGF/TrkA/Erk1,2 signaling pathway in Duchenne muscular dystrophy

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Duchenne muscular dystrophy (DMD) is a degenerative disorder caused by the lack of dystrophin. Dystrophin is connected to the transmembrane complex called a dystroglycan complex, which maintains the myotube structure and its integrity. The absence of dystrophin leads to muscle degeneration without regeneration due to repeated sheer force of skeletal muscle. HDAC8 is a histone deacetylase enzyme that is significantly increased in DMD. Studies have found that HDAC8 inhibits myogenic differentiation of skeletal muscle. Here, we studied how

HDAC8 changes the molecular mechanism of myogenesis. Protein X mediates the formation of myotube. Connective tissue growth factor (CTGF/CCN-2) is involved in the induction of fibrosis in muscle degenerative diseases. In *mdx* mouse, a DMD mouse model, CTGF is significantly increased whereas the dystrophin is decreased. Through epigenetic modification, the activation of Protein X is regulated by a histone deasctetylase, HDAC8. miR-18b is modulated by Protein X in that Protein X motifs bind to the promoter region of miR-18b controlling its transcription. miR-18b post-transcriptionally regulates CTGF in a myoblast. Dysregulated miR-18b induces CTGF overexpression, inhibiting myogenic differentiation via CTGF/TrkA/Erk1,2 signaling pathway. Taken all together, our data indicate that myogenesis is affected by epigenetic modification changing the intracellular signaling pathway. Overexpressed HDAC8 in differentiated myoblast represses Protein X. miR-18b is involved in the regulation of CTGF and mediated by Protein X. miR-18b modulated by Protein X at its promoter region plays a significant role in the regulation of CTGF expression, which would not only promote the development of fibrosis but also inhibit the myogenesis. Our study suggests a novel mechanism to understand the pathophysiology of DMD.

Keywords : duchenne muscular dystrophy, dystrophin, myogenesis, fibrosis, histone modification

P-467

A Naturalistic decision-making task revealing differences in explore–exploit trade-offs in addiction

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Traditional laboratory tasks have long been invaluable for probing cognitive mechanisms under controlled designs. The multi-armed bandit (MAB) paradigm, widely used to study the explore–exploit trade-off, offers clear insights but gathers limited behavior and omits spatial or temporal costs. Understanding how people handle such costs is vital, especially in clinical populations where decision bias contributes to maladaptive behaviors like addiction. Although addiction studies report an exploitation preference, how this bias emerges in spatially grounded settings is unclear. We therefore developed a 3D reinforcement-learning task in Minecraft, extending the restless MAB with distance-based costs and 10 Hz recordings of locomotion and gaze. The task captures movement entropy, path length, visual entropy, and pitch/yaw variance. We compared non-smokers (N = 25), abstinent smokers (N = 22), and satiated smokers (N = 20), controlling abstinence duration. A hierarchical Bayesian Kalman-softmax model estimated inverse temperature (β) and decay parameter (λ), where β reflects reliance on option values and λ controls the decay of past rewards over time. We also tested linear, hyperbolic, and exponential cost functions with parameter γ, which reflects spatial cost sensitivity. We hypothesized stronger group differences in 3D than 2D, predicting that abstinent smokers would show higher β, lower λ, and reduced cost sensitivity (lower γ). We also predicted the decision type (explore vs. exploit) would interact with locomotion and gaze. The results supported our predictions: 2D showed no group differences, whereas in 3D abstinent smokers exhibited the expected parameter profile. Locomotion and gaze metrics likewise showed the largest explore–exploit contrasts in this group. The results suggest that a naturalistic 3D task thus captures individual differences better than conventional designs and provides an ecologically valid tool for studying decision-making in addiction.

Keywords : Naturalistic decision making, Addiction, Smoking, Exploration-Exploitation

P-468

Astrocytic calcium mirrors neuromodulator release in the hippocampus during anxiogenic contexts

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Astrocytes act as major receivers of neuromodulators. Astrocytes, activated by neuromodulators, influence synapses, local circuits, and ultimately behavior. Neuromodulators are involved in regulating mood and mood-related behaviors. In particular, norepinephrine and serotonin released in the hippocampus regulate mood such as anxiety. Moreover, hippocampal astrocytic activity has been shown to modulate anxiety-like behavior. However, it remains unclear whether hippocampal astrocytes can regulate mood-related behaviors through neuromodulator dynamics. Here, we recorded astrocytic activity with fiber photometry by expressing calcium (GCaMP) and neuromodulator(norepinephrine, dopamine, serotonin) indicators (GRAB) in hippocampal astrocytes while mice were exposed to various risky stimuli: elevated plus maze (EPM), tail suspension test (TST), and electrical shock chamber. We found that when mice confronted an anxiogenic context, such as entering the open area of the EPM, astrocytic calcium increased and simultaneously only norepinephrine among neuromodulators released to hippocampal astrocytes. Furthermore, we showed that dampening astrocytic calcium (hPMCA2w/b) in the hippocampus did not alter anxiety-like behavior in mice, suggesting that astrocytic intracellular signaling triggered by neuromodulator-mediated GPCR activation may be involved. Taken together, we propose that norepinephrine dynamics in hippocampal astrocytes are associated with the astrocytic calcium level in accordance with anxiety-like behaviors.

Keywords : Astrocyte, Neuromodulator, Norepinephrine, Hippocampus, Anxiety

P-469

Deterioration and compensation of episodic memory in aging

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Episodic memory is defined as the binding of an object (*what*) and a place (*where*) with temporal order (*when*). While the hippocampus integrates these components into a coherent memory, distinct cortical regions contribute differently across memory components. Although past studies have shown that the temporal organization of episodic memory

is particularly impaired in aging, it is not clear whether this is due to its heightened vulnerability to age-related decline in hippocampal function or the involvement of distinct compensatory cortical mechanisms across what, where, and when memory. In this study, we aimed to understand the neural correlates of component-specific decline and compensation in aging, particularly in the middle age range, when hippocampal function begins to decline. We conducted an event-related fMRI experiment in 113 participants (42 young (19-33), 71 middle-aged (49-63)). Participants were instructed to memorize visual scene stimuli and then were asked to retrieve the objects from the scenes, their spatial locations, and the temporal order in which the scenes were presented. Behavioral accuracy for all three episodic memory components decreased with aging, and temporal memory accuracy was significantly lower than that of other episodic memory components. A reduced activation in the medial temporal lobe, including the hippocampus, was found in older adults and correlated with age-related decline in the temporal component of episodic memory. Interestingly, older participants showed higher activation in various cortical regions as well. Those with better episodic memory overall showed greater activation in the middle frontal, but additional component-specific effects were found in the left inferior parietal region for 'what' memory, and the right inferior parietal region for '*where*' and '*when*' memory suggesting evidence of domain-specific compensatory mechanisms.

Keywords : Episodic Memory, Aging, fMRI, Compensation

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P-470

Glial scar formation in the peritumoral reactive astrocytes via the TGF-β2 signaling pathway regulates glioblastoma progression

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Glioblastoma (GBM) is the most common and aggressive primary brain tumor. One of its pathological features is the formation of a glial scar in the peritumoral region, which acts as a dense physical barrier primarily composed of reactive astrocytes and extracellular matrix (ECM) components. Astrocytes are not merely peritumoral cells but serve as regulators that respond to the tumor microenvironment and influence its structural and functional properties. Transforming growth factor beta (TGF-β) signaling has been widely implicated in tumor progression by promoting reactive astrogliosis and enhancing the expression of ECM molecules such as chondroitin sulfate proteoglycans (CSPGs), thereby contributing to robust glial scar formation. However, the extent to which TGF-β-mediated regulation of astrocyte reactivity contributes to glial scar formation – and how this, in turn, influences GBM progression – remains unclear. The underlying cellular and molecular mechanisms also have yet to be fully elucidated. In this study, using both *in vitro* and *in vivo* GBM models, we demonstrate that TGF-β2 drives reactive astrogliosis and increases CSPG deposition. Gene silencing of TGF-β2 led to reduced levels of GFAP and CSPGs, accelerated tumor growth, and shortened survival in GBM-bearing mice. Conversely, astrocyte-specific overexpression of TGF-β2 promoted glial scar formation and significantly prolonged survival of GBM model mice. These findings indicate that through TGF-β2 signaling, reactive astrocytes contribute to tumor containment by forming glial scars that function as physical barriers to tumor spread. Taken together, our results demonstrate that astrocyte-derived TGF-β2 promotes glial scar formation that restricts GBM progression and highlight TGF-β2 as a potential therapeutic target in GBM.

Keywords : Glioblastoma, Glial scar, Reactive astrocyte, Transforming Growth Factor-β

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P-471

Fixative-eXchange (FX)-seq: a platform for transcriptomics analysis of PFA-Fixed and FFPE Samples

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Single-cell transcriptomic profiling of fixed tissues holds immense potential to bridge molecular biology with structural and clinical insights. Paraformaldehyde (PFA)-fixed samples provide essential spatial context in neuroscience, while clinical formalin-fixed paraffin-embedded (FFPE) archives offer access to annotated pathological specimens and patient outcomes. Yet, this promise has remained largely unrealized due to fixation-induced damage that severely compromises reverse transcription (RT) efficiency, limiting current protocols to fresh or frozen tissues. Here, we introduce Fixative-eXchange sequencing (FX-seq), a robust and scalable method for single-nucleus RNA sequencing from PFA-fixed and FFPE-treated specimens. FX-seq integrates two key innovations: (1) an organo-catalyst that removes PFA crosslinks under mild conditions to improve *in situ* RT yield, and (2) a regiospecific platinum-based crosslinker that prevents RNA leakage without inhibiting RT. Using FX-seq, we obtained high-quality transcriptomic data from PFA-fixed mouse brain and FFPE-preserved human cancer tissues, demonstrating its broad utility. By leveraging the intrinsic stability of fixed samples, FX-seq enables efficient multiplexed profiling across multiple timepoints and subjects. This flexibility supports diverse applications, including single-nucleus spatial transcriptomics, multiplexed tissue analysis, and high-resolution snRNA-seq from small anatomical subregions. FX-seq thus establishes a powerful framework for unlocking transcriptomic information from archival and structurally preserved specimens across both basic and clinical research domains.

Keywords : Single nucleus RNA sequencing, Single cell genomics, Spatial transcriptomics, Methods Development

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Synapses and Circuits P-472~P-495

P-472

Investigation of synaptic connectivity between CA1 and ACC during systems consolidation

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For remote memory formation, the hippocampus interacts with cortical regions and transfers the memory trace, a process known as systems consolidation. Previous studies have focused on individual properties of the hippocampus and anterior cingulate cortex (ACC) in remote memory formation. In a recent study, the CA1-ACC circuit is directly involved in systems consolidation through increasing axonal projection. In this study, we investigate the synaptic dynamics during systems consolidation in the CA1-ACC circuit. We tested engram reactivation in CA1 and ACC using Arc-CreERT2 systems. CA1 neurons are reactivated during recent retrieval, while ACC neurons are reactivated during both recent and remote retrieval. Also, inhibition of ACC projecting CA1 neurons impaired remote memory partially. Through these results, we hypothesized that synapse change between CA1 and ACC occurs during the recent period, and this synapse might be an enlarged structure or recruit new engram synapse formation. By using dual-eGRASP and in vivo two-photon imaging, we will visualize synaptic dynamics at multiple time points and reveal the synaptic mechanism for systems consolidation.

Keywords : Dual-eGRASP, Synapse, Systems consolidation, Memory, Two-photon imaging

P-473

Astrocytic Slitrk2 competitively constrains neuronal Slitrk2-mediated excitatory synaptic functions

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Slitrk2 (SLIT and NTRK-like protein 2) is a postsynaptic cell-adhesion molecule (CAM) that binds to LAR-RPTPs, TrkB and PDZ domain-containing proteins to regulate excitatory synaptic properties in the hippocampal neural circuits. Although Slitrk2 is expressed in both neurons and astrocytes, it remains unclear whether astrocytic Slitrk2 functions at tripartite synapses. Here we find that conditional knockout (cKO) of astrocytic Slitrk2 causes an increase in excitatory, but not inhibitory, synaptic transmission in co-cultured hippocampal cultured neurons. Moreover, the cKO of astrocytic Slitrk2 induced an enhancement in α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid receptor (AMPAR)-mediated, but not N-methyl-D-asparate receptor (NMDAR)-mediated, postsynaptic responses. Consistent with the *in vitro* results, acute deletion of astrocytic Slitrk2 increased the basal excitatory synaptic transmission in the hippocampal CA1 of adult mice. Molecular replacement experiments further showed that astrocytic Slitrk2 requires the binding activities toward both LAR-RPTPs and PDZ domain-containing proteins for negatively regulating excitatory synaptic transmission. Ongoing experiments include the identification of Slitrk2-interacting PDZ proteins expressed in astrocytes and elucidation of astrocytic Slitrk2-mediated astrocytic functions and related mechanisms *in vivo*.

Keywords : Tripartite synapses, Astrocytic adhesion molecules, Slitrk2, Excitatory synaptic properties

P-474

Anatomical and functional evidence for vestibular-auditory integration via the LVN-IC pathway

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The vestibular system plays a critical role in maintaining balance and spatial orientation. It functions independently, but it works more effectively when it cooperates with other sensory systems. While sensory integration is important, relatively few studies have specifically addressed the interaction between the vestibular system and auditory processing. Evidence suggests a connection via the lateral vestibular nucleus (LVN); a study found LVN projections to the dorsal cochlear nucleus co-labeled with VGLUT2, implying a potential anatomical link. However, the precise neural pathways in vestibular auditory interaction are still not well understood. This study investigated the interaction between the inferior colliculus (IC), a hub that integrates auditory inputs, and the LVN, and evaluated whether the LVN plays a key role in integration of auditory-vestibular system. Retrograde virus injection into the IC resulted in labeled neurons in the LVN, and anterograde virus injection into the LVN revealed labeled fibers in the ventromedial region of the IC. In addition, retrograde virus injection into the LVN led to labeling in uvula, suggesting that the LVN receives afferent input from uvula. Virus tracing revealed double-labeled neurons in the LVN following retrograde injection into the IC and anterograde injection into the uvula. Optogenetic stimulation of the LVN, electrophysiological recordings from the IC revealed a strong modulation in the firing rate of IC neurons with short latency. To investigate whether IC- projecting LVN neurons response not only to vestibular system but also to auditory stimuli, we conducted a sound exposure experiment. After sound exposure, c-fos expression in the LVN was observed in response to 8, and 32 kHz sound. This result indicates that IC-projecting LVN neurons are also activated by auditory stimulation. Taking together, these findings suggest that the LVN and IC may be functionally connected as part of a sensory-motor system.

Keywords : vestibular system, auditory, lateral vestibular nucleus, inferior colliculus

P-475

Parafascicular thalamic glutamatergic activity encodes the transition from alcohol consumption to motivational engagement

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The parafascicular nucleus (Pf) of the thalamus provides dense glutamatergic input to the dorsal striatum, which regulates reward seeking and habituation, and further drives transitions across the behavioral phases. However, the contributions of Pf glutamatergic neurons to these shifts from voluntary taking to motivated seeking, remains unclear. We investigate how Pf glutamatergic neurons dynamically involved in emerging alcohol addiction phases. We conceptualized the alcohol addiction framework into two phases: (1) an alcohol-taking phase, modeled by the Drinking-in-the-Dark (DID) paradigm combined with a two-bottle choice test in a three-chamber apparatus to assess voluntary intake and preference; and (2) a motivated alcohol-seeking phase, assessed using an operant conditioning task in which lever presses resulted in ethanol delivery, capturing instrumental reward-seeking behavior. In vivo calcium imaging identified phase-specific dynamics of Pf glutamatergic neurons across all phases. During three chamber two bottle choice task after alcohol taking period(DID), Pf activity displayed precisely aligned calcium transients with alcohol drinking events. In contrast, during the operant phase, Pf glutamatergic activity dissociated from direct consumption event and showed anticipatory peaks preceding instrumental actions, indicating a transition toward encoding reward expectation and action planning. Although Pf astrocyte activity was also monitored, it remained lacked phase-specific modulation, suggesting a limited contribution to these motivated transitions. These results identify Pf glutamatergic neurons as dynamic encoders of behavioral state, selectively responsive to shifts from reflexive intake to motivated action. This functional reorganization of Pf activity may constitute an early neural marker of maladaptive motivational drive and represents a potential node for targeted circuit modulation in alcohol use disorders.

Keywords : Alcohol addiction, Parafascicular nucleus, Glutamatergic neuron, Thalamostriatal circuit, Habitual behaviors

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P-476

Activation of pallidal prototypic neurons regulates behavioral flexibility

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Behavioral flexibility allows animals to adjust actions to changing environments. While the basal ganglia are critical for adaptation, the specific role of the external globus pallidus (GPe) is unclear. This study examined the contributions of two major GPe cell types—prototypic neurons projecting to the subthalamic nucleus (ProtoGPe→STN neurons) and astrocytes—to behavioral flexibility. Using longitudinal operant conditioning with context reversals, we found that ProtoGPe→STN neurons dynamically represent contextual information correlating with behavioral optimality. In contrast, GPe astrocytes exhibited gradual contextual encoding independent of performance. Deleting ProtoGPe→STN neurons impaired adaptive responses to changing action-outcome contingencies without altering initial reward-seeking acquisition, highlighting their specific role in enabling behavioral flexibility. Furthermore, we discovered that ProtoGPe→STN neurons integrate inhibitory striatal and excitatory subthalamic inputs, modulating downstream basal ganglia circuits to support flexible behavior. This research elucidates the complementary roles of ProtoGPe→STN neurons and astrocytes in cellular mechanisms of flexible reward-seeking behavior.

Keywords : Pallidal Prototypic Neurons, Behavioral Flexibility

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P-477

In vitro electrophysiological analysis of taurine function and receptor expression in rat primary cultured neurons and astrocytes

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Taurine has been proposed as a neurotransmitter in the brain, particularly due to its ability to activate chloride channels, thereby inducing hyperpolarization of neuronal membranes and exerting inhibitory effects. Recent magnetic resonance spectroscopy (MRS) analyses have revealed that the concentration of taurine in the medial prefrontal cortex (mPFC) of women suffered from depression decreases from 1.13 mM to 0.91 mM, suggesting a potential mechanism of taurine on depression. However, the precise mechanisms by which reduced taurine levels contribute to the pathophysiology of depression remain unknown. To first address whether taurine exhibits cytotoxicity toward neurons and astrocytes, we evaluated cell viability using the Cell Counting Kit-8 (CCK-8) assay. Across a broad range of taurine concentrations 0.5, 1, 3, 5, 10 mM, no cytotoxic effects were observed in both neurons and astrocytes, indicating that taurine is a highly biocompatible bioactive molecule. Subsequently, we investigated whether taurine induces receptor-mediated Ca2+ transients in astrocytes; however, no evidence of Ca2+ transients was detected. To further examine the function of taurine as an inhibitory neurotransmitter, we measured chloride currents with the Nernst equation set to 0mV. Under these conditions, substantial inward chloride currents were observed at taurine concentrations of 0.1, 1, 10 mM, indicating that taurine modulate neuronal membrane potential. Moreover, we observed a tendency for increased frequency of inhibitory postsynaptic currents (IPSCs) following taurine application, suggesting

the presence of taurine-responsive receptors on neuronal membranes. Based on these findings, we plan to investigate taurine activity as well as the expression and function of taurine receptors in ovariectomized female rodents. We provide the molecular mechanism how reduced taurine affects depressive disorder.

Keywords : Taurine, electrophysiology, depression, neurotransmitter, inhibitory current

P-478

Lateral hypothalamus directs stress-induced modulation of acute and psoriatic itch

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Stress and anxiety are well-known modulators of both physiological and pathological itch. Acute stress suppresses itch, while chronic stress exacerbates it. These effects are mediated by neural circuits within the brain, though the precise mechanisms remain poorly understood. In this study, we investigate the role of neurons in the stress-sensitive lateral hypothalamic area (LHA) in modulating itch. Using neural activity-dependent genetic labeling and chemogenetic tools, we selectively engaged a population of LHA neurons (LHAstress-TRAP neurons) responsive to stress. Transient stimulation of these neurons induced anxiety-like behaviors, conditioned place aversion, and suppressed acute (chloroquine-induced) and chronic (psoriatic) itch. Conversely, the inhibition of the LHAstress-TRAP neurons enhanced acute and chronic itch. Interestingly, LHAstress-TRAP neurons did not respond to acute itch stimuli, but their activity was temporally correlated with scratching episodes in mice with psoriasis. Ex vivo whole-cell patch-clamp recordings revealed that these neurons exhibit heightened excitability in psoriatic animals. Anterograde viral tracing demonstrated that LHAstress-TRAP neurons project to brainstem regions implicated in itch modulation, including the periaqueductal gray (PAG), rostral ventromedial medulla (RVM), and lateral parabrachial nucleus (LPBN). Furthermore, chemogenetic activation and optogenetic silencing of LHAstress-TRAP axon terminals revealed that bidirectional modulation of itch is primarily mediated through projections to the PAG. Together, these findings identify a previously unrecognized central mechanism by which stress modulates itch, centered on a specific population of LHA neurons and their downstream brainstem targets.

Keywords : Itch, Optogenetics, Psoriasis, Hypothalamus, Chemogenetics

P-479

Analgesic effects of 10 kHz low-intensity DBS in agranular insular cortex for neuropathic pain rat model

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Introduction: Deep brain stimulation (DBS) is a promising technique for the control of intractable pain. Recent studies have confirmed that ultra-high-frequency stimulation of acute 10 kHz is not only effective in improving motor symptoms in DBS patients with movement disorder but also tends to reduce side effects. In this study, we investigated the effects of 10 kHz low-intensity DBS applied to the rostral agranular insular cortex (RAIC) involved in maintaining persistent pain conditions to modulate neuropathic pain. Methods: Male Sprague-Dawley rats (200 - 220g) were used in this study. Using spared nerve injury (SNI) model for neuropathic pain. The rats were divided into the following experimental groups: the NM (normal) group, the SNI group, the 50 Hz STIM (SNI + 50Hz 120 μA stimulation) group and the 10 kHz STIM (SNI + 10 kHz 30 μA stimulation) group. 2 weeks after SNI surgery, microelectrodes were implanted in the contralateral to the injury site RAIC for DBS. The Von Frey tests were performed to assess the analgesic effects and brain tissue underwent immunohistochemistry to assess microenvironmental changes under DBS parameters. Results: Repeated 10 kHz low-intensity stimulation significantly reduced mechanical allodynia, with its effects progressively increasing over time (mechanical threshold at 1 hr on Day 1: 3.088 ± 0.3623 vs. Day 5: 8.599 ± 0.8682, $p < 0.05$). Additionally, the stimulation promoted an astrocyte-mediated anti-inflammatory response, suggesting that ultra-high-frequency DBS effectively modulates neuroinflammation in neuropathic pain. Conclusion: This study shows that 10 kHz low-intensity DBS of the RAIC safely reduces pain without inducing nerve damage, highlighting its potential as an effective neuromodulation approach for chronic neuropathic pain. Suggests it may serve as a viable and effective strategy for pain relief.

Keywords : Neuropathic pain, Deep brain stimulation, Ultra high frequency, Insular cortex, Anti-inflammation effect

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P-480

Behavioral benefits of prolonged exercise rely on plasticity in cerebellar granule cell networks

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Regular exercise offers benefits from enhanced motor learning to anxiolysis or antidepressant effects, but it remains unclear which changes in specific brain regions underlie these wide-ranging outcomes. Recent findings suggest that the cerebellum—traditionally recognized for its role in motor control—also contributes to cognitive and emotional functions, raising the possibility that prolonged exercise-induced changes in the cerebellum play a role in its diverse effects. Although cerebellar granule cells (GCs) in specific lobules are known to be active during exercise, how the GC network across the entire cerebellum adapts to prolonged exercise remains unknown. To investigate this, we employed the voluntary wheel-running paradigm in mice and examined the spatial distribution of activated GCs throughout the cerebellar cortex using immunohistochemistry of c-Fos, a widely used marker of neuronal activity. Our analysis revealed a distinct macroscopic pattern of GC activation across several cerebellar lobules, including the paramedian

lobule. Interestingly, prolonged exercise resulted in a reduction in the number of activated GCs compared to short-term exercise, without altering the overall spatial pattern of activation. Furthermore, prolonged exercise decreased GC network activity, as indicated by reduced synaptic transmission from exercise-associated GCs to Purkinje cells. These findings suggest that prolonged exercise induces neuroplasticity in GCs, potentially enhancing sparse coding. To assess the functional relevance of this enhanced sparse coding, we developed a method to selectively disrupt exercise-induced neuroplasticity by knocking down $GABA_A$ receptor subunits specifically in active GCs during exercise. Our current data indicate that this manipulation impairs the enhancement of motor learning typically observed following prolonged exercise. Together, the results support that GC neuroplasticity contributes to behavioral modulation induced by prolonged exercise.

Keywords : Cerebellum, Neuroplasticity, Cerebellar granule cell, Long-term exercise, Network

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P-481

Hindbrain cold-sensitive neurons orchestrate integrated homeostatic responses

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Thermoregulation is a fundamental physiological process critical for survival, yet how the brain represents peripheral cold sensory information and coordinates the diverse responses remains incompletely understood. Here, using activity-dependent genetic labeling (Targeted Recombination in Active Populations, TRAP) in mice, we characterize cold-activated neurons in the external lateral parabrachial nucleus (abbreviated as PB^{Cold} neurons) as primary recipients of cold sensory input in the brain. PB^{Cold} neurons exhibit rapid and sustained activation to various cold stimuli, with response amplitude increasing progressively as temperature deviates from thermoneutrality. Functional inhibition of these neurons impairs essential cold-induced responses across multiple domains, including autonomic (brown adipose tissue thermogenesis and tail vasoconstriction), behavioral (cold avoidance), metabolic (cold-induced hyperphagia), and affective (dopamine release to rewarding cool stimuli) adaptations, and compromises survival under severe thermal stress. Conversely, targeted activation of PB^{Cold} neurons promotes warmth-seeking behavior and enhances food intake without causing weight gain, suggesting an elevation in energy expenditure that offsets increased caloric intake. Molecular profiling reveals highly specific markers for subsets of PB^{Cold} neurons, whereas activity-dependent TRAP-labeling provides both high specificity and broader coverage for comprehensive targeting. Collectively, our findings establish PB^{Cold} neurons as a critical integrative center coordinating cold-responsive adaptations, providing insights into central mechanisms of thermal homeostasis.

Keywords : TRAP, Thermoregulation, Parabrachial nucleus, Cold sensation, Homestasis

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P-482

Sexual dimorphism in social recognition following resocialization after social isolation in mice

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Social recognition is a fundamental aspect of social behavior that enables individuals to distinguish and remember conspecifics. Previous studies have shown that male and female mice exhibit distinct behavioral and neural responses to chronic social stress, yet the long-term effects of social isolation followed by regrouping remain poorly understood. In this study, we investigated how prolonged social isolation and subsequent regrouping influence social recognition in juvenile male and female mice. Animals were single-housed for 8 weeks and then returned to group housing for an additional 4 weeks. Consistent with our earlier findings, male mice exhibited persistent deficits in social recognition even after regrouping. In contrast, while female mice showed impaired social recognition immediately after isolation, their performance recovered following the regrouping period, as assessed using the three-chamber social interaction test. To identify neural correlates of these behavioral differences, we performed whole-cell patch-clamp recordings from infralimbic (IL) prefrontal cortex neurons projecting to the nucleus accumbens shell (NAcSh), a circuit implicated in social recognition. Immediately after isolation, both sexes showed reduced excitability in IL–NAcSh neurons compared to group-housed controls. However, after regrouping, excitability was restored only in females, while males continued to show reduced excitability. Moreover, chemogenetic inhibition of IL–NAcSh neurons impaired social recognition in both sexes, underscoring the critical role of this pathway. These results suggest that while the IL–NAcSh circuit is essential for social recognition in both male and female mice, females exhibit greater neural resilience or plasticity in response to social stress, enabling behavioral recovery following regrouping.

Keywords : social recognition, social isolation, resocialization, infralimbic cortex, nucleus accumbens

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P-483

The role of Myosin V in synaptic plasticity

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Myosin V plays a crucial role in neuronal vesicle transport, axonal growth

and neural connectivity. As a key actin-based motor, Myosin V mutations are associated with neurological disorders, highlighting its importance in maintaining neural function. While previous studies have mentioned that Myosin V facilitates Hebbian plasticity by transporting NMDA receptors and enhancing synaptic strength during long-term potentiation (LTP), the role of Myosin V in miniature neurotransmission remains poorly understood. In this study, we demonstrate that Myosin V deficiency in cortical neurons enhances synaptic transmission, as evidenced by increased miniature excitatory postsynaptic current (mEPSC) frequency and amplitude. Using in vitro live imaging, we further reveal synaptic vesicles (SVs) accumulate in presynaptic boutons, and exhibit reduced trafficking between boutons. Notably, we identify that a reduction of Myosin V expression in activity deprived neurons. Our findings suggest that Myosin V is essential for maintaining neuronal stability and synaptic plasticity.

Keywords : Myosin V, Vesicle transport, Synaptic transmission, Synaptic plasticity

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P-484

Role of hypothalamic circuitry for social interaction under threatening conditions

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Appropriate responses to the social environment are vital for survival and support the cohesion of social communities. Under threatening conditions, individuals often engage in adaptive social interactions to maintain physiological safety. However, the neural mechanisms driving such selective social behaviors in response to external threats remain poorly understood. In this study, we developed a novel behavioral paradigm using both visual and auditory looming stimuli to investigate changes in social approach behavior following threat exposure. Repeated looming sessions led to significant alterations in social interaction patterns. Using fiber photometry and chemogenetic manipulation, we identified a hypothalamic circuit activity as a key mediator of social adaptation, causally regulating social behaviors. Given the distinct activity patterns and the predominance of inhibitory neurons within this circuit, we aim to examine how neurotransmitter release to downstream targets modulates neural activity in threat-conditioned social contexts. Collectively, this study introduces a new behavioral paradigm that links threat-driven social adaptation to hypothalamic circuit mechanisms, offering insights into how specific neurotransmitter systems contribute to flexible social behaviors under threatening conditions. These findings may have implications for understanding disorders such as social anxiety and stress-related dysfunction.

Keywords : social interaction, Looming stimulus, Hypothalamic circuit

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P-485

Recalled NR2D- NMDARs in the hippocampal GABAergic interneurons regulate E/I balance during epileptogenesis

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NR2D subunit-containing N-methyl-D-aspartate receptors (NMDARs) gradually disappear during brain maturation but can be recalled by pathophysiological stimuli in the adult brain. Here, we report that NR2D-NMDARs recall generated an Mg^{2+}-resistant tonic NMDA current (I_{NMDA}) in the hippocampal GABAergic interneurons of pilocarpine-injected mature male mice. The tonic activation of NR2D NMDARs upregulated the ongoing firing in GABAergic interneurons and facilitated the presynaptic GABA release in CA1 pyramidal neurons in pilocarpine-injected wild-type mice. Genetic NR2D intervention abolished the generation of Mg^{2+}-resistant tonic I_{NMDA} in the GABAergic interneurons, and prevented the facilitation of presynaptic GABA release shown by decreased sIPSC frequency in the pilocarpine-injected NR2D KO mice, causing aberrant excitation of the CA1 neurons. The excitatory shift of E/I balance increased the seizure susceptibility with CA1 neuronal death, which resulted in recurrent spontaneous seizures in NR2D KO mice. NR2D rescue in GABAergic interneurons efficiently blocked the pilocarpine-induced CA1 neuronal death and recurrent spontaneous seizure activity in NR2D KO mice. These results show that NR2D recall in GABAergic interneurons upregulates GABAergic tone in postsynaptic CA1 pyramidal neurons to restrain the excitatory shift of E/I balance in the pilocarpine-injected hippocampus, preventing recurrent seizures. The state-dependent NR2D recruitment could be a novel therapeutic target for mitigating cell-type-specific neuronal death and chemical-induced epileptogenesis.

Keywords : NMDARs, NR2D, E/I balance, GABAergic Interneurons, Status Epilepticus

P-486

Bergmann glia activation induces Purkinje cell suppression via interneurons

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Bergmann glia (BG) are radial glial cells in the cerebellar cortex that have multiple functions. They interact with Purkinje cells (PCs) by modulating synaptic inputs, regulating excitability via potassium concentration, and affecting PCs through neurotransmitter release. We revealed that BG activation decreases PC activity in painful situations, specifically during acute tonic pain induced by capsaicin injection, which modulates PC firing through α1-adrenergic receptors in BG. However, the mechanism of neuron-glia interactions in the cerebellum remained unclear. In this study, we genetically expressed hM3Dq in BG through GFAP-promoter-contained AAV virus. We showed that this BG-PC regulation is mediated by the NMDA receptor and GABAA receptor.

Furthermore, using calcium imaging, we confirmed that BG activation induces MLI activation. Taken together, we concluded that glutamate released from BG induces GABA release from MLI, which in turn inhibits PC activity. Our findings provide a cellular mechanism for understanding the role of BG in the modulation of neuronal activity in the cerebellum.

Keywords : Bergmann glia, Purkinje cell, Interneuron, Cerebellum

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P-487

Neuromodulator effects on ARC neurons: Unraveling mechanisms of feeding regulation in the CNS

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The regulation of appetite and feeding behavior is governed by a complex neural circuit within the central nervous system (CNS), with the arcuate nucleus (ARC) playing a central role in integrating peripheral signals to modulate feeding. However, the precise neurophysiological functions of neuromodulators within the ARC remain poorly understood. In this study, we explored the effects of various neuromodulators on the activity of ARC neurons. We found that leptin and Vaspin both reduced food intake 24 hours post-ICV injection. Leptin decreased spontaneous firing, neuronal excitability, AMPAR amplitude, and modestly reduced NMDAR amplitude in NPY-positive ARC neurons. Vaspin also reduced spontaneous firing, decreased AMPAR amplitude, but increased sEPSC frequency in these neurons. These findings provide valuable insights into how neuromodulators regulate ARC neuronal activity and synaptic plasticity, thereby influencing feeding behavior.

Keywords : appetite, feeding, hypothalamus, arcuate nucleus, neuromodulator

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P-488

Pathway-specific chemogenetic modulation of BLA projections to PrL and NAc subregions controls amphetamine-induced conditioned place preference

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Individuals with substance use disorders develop maladaptive associative memories, linking environmental contexts with drug experiences. The basolateral amygdala (BLA), prelimbic cortex (PrL), and nucleus accumbens (NAc) are central components of the neural circuitry underlying these associations. However, it remains unclear how specific BLA outputs differentially regulate the expression of contextual drug memories. Using designer receptors exclusively activated by designer drugs, we selectively modulated neuronal activity with deschloroclozapine as the activating agent during the expression of amphetamine-induced conditioned place preference (CPP) in the BLA pathways to the PrL, NAc core, and NAc shell. Our findings revealed a dissociation between these pathways: the BLA-to-PrL circuit exerted bidirectional control over CPP expression, with inhibition significantly enhancing and activation attenuating drug-context associations. In contrast, BLA-to-NAc core manipulations selectively modulated locomotor aspects of conditioned responses without affecting place preference, while BLA-to-NAc shell manipulations produced no significant effects on CPP expression. These results demonstrate that the BLA has a distinctive pathway-specific roles in the expression of contextual drug memory.

Keywords : Amphetamine Conditioned place preference, DREADD, Basolateral amygdala, Prelimbic cortex, Nucleus accumbens

P-489

The influence of internal state changes on social behavior

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Internal states play a critical role in generating adaptive behaviors by integrating external environmental stimuli. Although such internal state changes profoundly influence social behavior, the underlying neural mechanisms remain largely unclear. In this study, we investigated how different types of internal state changes affect social interaction patterns and associated neural activity in mice. We utilized local field potential (LFP) recordings to compare the effects of social stimuli, involving exposure to either female or male intruders, and physiological stimuli, including water deprivation and water re-access, on social behavior and neural dynamics. Both forms of social stimuli led to reductions in social interaction, with male intruders inducing a stronger and more sustained decrease. In the physiological stimulus group, social interaction tended to increase. C-fos expression analysis revealed distinct activation patterns in the anterior insular cortex (AI), anterior cingulate cortex (ACC), and lateral hypothalamus (LH) depending on the type of internal state. LFP analysis further demonstrated that social stimuli primarily modulated ACC-centered networks, whereas physiological stimuli affected LH-centered networks. These findings suggest that social and physiological challenges regulate social behavior through distinct neural mechanisms. This study provides new insights into the neural pathways underlying internal state-dependent modulation of social behavior and advances our understanding of the neurobiological basis of social interaction.

Keywords : Internal state, Social interaction, Local field potential, Neural network

P-490

The vDB-vHPC cholinergic projection mediates long-term social memory deficits

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Numerous neurological disorders are associated with impairments in

social memory, including Alzheimer's disease and autism spectrum disorders. Social memory plays a crucial role in the survival and reproduction of mammals. While the ventral hippocampus (vHPC) is well-established as a key brain region for storing social memories, the upstream neural circuits providing social information to the hippocampus remain poorly understood. In this study, we have identified a cholinergic projection from the ventral diagonal band of Broca (vDB) to vHPC that specifically regulates long-term social memory in mice. Approximately 54.2% of vHPC neurons receive cholinergic input from vDB. Inhibition of cholinergic neuronal activity in vDB during social memory encoding prevents normal acetylcholine release in vHPC, leading to aberrant activation of parvalbumin (PV)-expressing interneurons in vHPC. This results in abnormal expansion of social memory engram cells in vHPC and subsequent failure to retrieve correct social memory information during recall, ultimately causing social memory impairment. The relationship between excessive PV neuron activity and excitatory neuron dysfunction in vHPC is currently under investigation.

Keywords : vDB, vHPC, long-term social memory, choline, PV interneuron

P-491

Brainstem enkephalinergic neural circuit underlying cold-induced pain relief in mice

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The application of cold or cold-mimicking compounds, such as agonist of transient receptor potential melastatin 8 (TRPM8), to the skin has long been recognized as an effective means of alleviating pain. However, the underlying neural mechanisms have remained elusive. In this study, we identified a specific neuronal subset within the lateral parabrachial nucleus (lPBN)—a thermosensory relay center in the hindbrain—as a critical mediator of cold-induced analgesia, through enkephalinergic signaling and descending pain modulation pathways. We demonstrated that activation of cold-responsive lPBN neurons and their projection to ventrolateral periaqueductal gray (vlPAG) significantly increased hot and mechanical pain threshold. Conversely, ablation of these neurons attenuated the analgesic effect of cold-mimicking chemical. Neural population sorting and subsequent RNA sequencing analysis revealed that cold-responsive neurons in lPBN express Penk, a precursor gene for enkephalin. Furthermore, activation of these neurons or peripheral exposure to cold stimuli increased enkephalin levels within the vlPAG. Supporting these results, local administration of enkephalin-neutralizing antibody or opioid receptor antagonist naloxone to vlPAG bolished cold-mimicking chemical-induced analgesia, highlighting the involvement of endogenous opioid system in cold-induced pain relief. Analgesic cold stimuli activated vlPAG and rostral ventrolateral medulla (RVM), suggesting the engagement of descending pain modulation pathway. In accordance with this, activation of cold-responsive neurons in the lPBN or RVM suppressed noxious mechanical stimuli-induced Fos expression in the lumbar spinal cord. Collectively, these findings provide novel insights into the neural circuitry underlying cold-induced analgesia and highlight a pivotal role of the lPBN-to-vlPAG pathway in cold induced analgesia, which could be a novel target for pain treatment.

Keywords : TRPM8, parabrachial nucleus, periaqueductal gray, enkephalin, Pain

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P-492

Mapping of the gut-brain axis induced by PINK1 deficiency using viral tracing

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Parkinson's disease (PD) is a neurodegenerative disorder primarily characterized by motor symptoms resulting from the selective loss of dopaminergic neurons in the substantia nigra, often accompanied by pathological aggregation of alpha-synuclein.. Recent evidence suggests that pathological alpha-synuclein aggregation may originate in the gut and subsequently propagate to the brain via the vagus nerve, supporting the gut-brain axis hypothesis in PD pathogenesis. Mutations in PTEN-induced kinase 1 (PINK1) commonly observed in early-onset PD patients. Although PINK1 knockout (KO) mice typically do not exhibit overt phenotypes, they develop PD-like symptoms following gut infection; however, the impact of PINK1 deficiency on gut-brain connectivity and disease progression remains unclear. In this study, we investigated the consequences of altered gut-brain connectivity by PINK1 deficiency. We employed pseudorabies virus (PRV) as a retrograde trans-synaptic neuronal tracer, specifically using PRVB152—a PRV Bartha variant (an attenuated strain widely used for neuronal circuit mapping) expressing EGFP. PINK1 KO mice exhibited significantly increased viral labeling in most hindbrain regions, particularly the nucleus of the solitary tract (NTS) and the dorsal motor nucleus of the vagus (DMV), compared to WT controls. Conversely, the parasubthalamic nucleus(PSTh) showed reduced signal in PINK1 KO mice. These findings indicate that PINK1 deficiency enhances neural connectivity between the gut and lower brainstem regions, while potentially weakening upstream connections to the hypothalamus. Such alterations may influence the propagation of alpha-synuclein pathology from the gut to the brain in PD. Future studies will assess alpha-synuclein transport following gut administration to further elucidate the role of PINK1 in modulating gut-brain axis dynamics and PD pathogenesis.

Keywords : Parkinson's disease, Gut-Brain Axis, PTEN-induced kinase 1, Pseudorabies virus

P-493

The role of SST interneuron in early life adversity-induced deficits in empathic freezing

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Early life adversity (ELA) refers to adverse experiences during childhood, including emotional or physical abuse and neglect. Depending on the period of brain development, ELA can alter neural plasticity in the PFC, hippocampus, and amygdala, resulting in social and emotional impairments. While the effects of ELA on aggression, anxiety, depression, and sociability have been revealed, how adverse childhood experiences influence empathic-like behaviors remains poorly understood. To investigate the underlying neurobiological mechanisms, we focused on somatostatin (SST) interneurons in the anterior cingulate cortex (ACC). Our previous work demonstrated that ACC SST neurons bidirectionally regulate observational fear, a form of emotional contagion in mice. Here, we found that observational fear is significantly impaired in two distinct mouse models of ELA: repeated maternal separation and post-weaning social isolation, but not peripubertal stress. We investigated the functional impact of ELA on ACC SST neurons by examining in vivo Ca2+ activity. Our study reveals how early life adverse experience disrupts the SST-mediated ACC microcircuit, providing insights into the neural basis of ELA-related social and emotional dysfunction.

Keywords : Early life adversity, SST interneuron, Empathy

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P-494

Poster Award Candidate

A GFRAL–spinal circuit links mitochondrial stress to sympathetic thermogenesis and adipose remodeling

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Growth differentiation factor 15 (GDF15) is a mitochondrial stress–induced cytokine that suppresses appetite via GFRAL-expressing neurons in the hindbrain. Beyond its anorexigenic role, its ability to engage central autonomic circuits and drive peripheral energy expenditure remains unclear. Here, we examined whether GDF15 activates a hindbrain–spinal circuit that modulates sympathetic outflow and thermogenesis. Sympathetic preganglionic neurons (SPNs) activity was assessed by c-Fos immunostaining and electrophysiological study. Retrograde tracing with pseudorabies virus (PRV-CAG-EGFP) was used to visualize hindbrain neurons that innervating interscapular brown (iBAT) and inguinal white adipose tissue (iWAT). As a model of mitochondrial stress–induced GDF15 elevation, we generated *Ucp1*-Cre::*Crif1flox/flox* (Crif1BKO) mice. *Gfral*-targeting antisense oligonucleotide (ASO) was administered via ICV injection. GDF15 ICV injection acutely increased c-Fos expression in SPNs in spinal cord and elevated their firing frequency, despite the absence of *Gfral* expression in these neurons. Retrograde neuronal tracing using PRV injected into iBAT and iWAT labeled neurons that co-localized with APGFRAL neurons, confirming their synaptic connection to iWAT and iBAT. In Crif1BKO mice, we observed a marked increase in circulating and cerebrospinal GDF15 levels, reduced food intake, increased energy expenditure, and browning of inguinal WAT. These metabolic alterations were accompanied by elevated c-Fos expression in both APGFRAL neurons and SPNs. *Gfral* knockdown abolished the increased energy expenditure and restored food intake observed in Crif1BKO mice, and significantly reduced UCP1 expression in iWAT. Our results reveal a GFRAL-mediated neural circuit linking mitochondrial stress to central sympathetic outflow and thermogenesis, highlighting a brainstem-driven mechanism by which the CNS integrates peripheral mitochondrial stress to regulate whole-body energy balance.

Keywords : GDF15–GFRAL signaling, Sympathetic nervous system, Hindbrain–spinal circuit, Thermogenesis, Adipose tissue browning

P-495

Infantile silent engram cells modulate memory formation during adulthood

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Infantile amnesia refers to the inability to consciously recall early-life experiences, despite their lasting influence on adult behavior. Recent evidence suggests that memory traces formed during infancy may persist in a silent engram state. However, whether and how these silent engram cells contribute to memory formation during adulthood remains unclear. To address these questions, we first examined whether experiences during the infant period affect later memory formation during adulthood using the retraining paradigm of contextual fear conditioning in mice. Consistent with previous studies, we observed a strong infantile amnesia phenomenon as indicated by almost complete forgetting 30 days later. Interestingly, despite amnesia, these mice exhibited memory enhancement when retrained during adulthood, suggesting an effect of silent infantile engram on adult memory formation. Notably, this effect on memory was context-specific, thus excluding the possibility of a nonspecific stress effect. Using an activity-dependent tagging system (TRAP2 x Ai14 mice), we tracked infant engram cells activated during contextual fear conditioning in infancy. We found that retraining recruited infantile silent engram cells into the adult engram in the cortex. These findings provide direct evidence that infantile engrams in the cortex can be reactivated by adult learning in a context-specific manner and contribute to memory enhancement. This suggests a developmentally persistent mechanism through which early experiences are selectively integrated into adult memory systems under matching contextual conditions.

Keywords : Infantile amnesia, Dormant state, Retraining, Infantile memory, Silent engram

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Systems and Computational Neuroscience P-496~P-545

P-496

Phase preservation of EEG reflects distraction control of visual working memory

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Distractor resistance is a hallmark of working memory. However, how working memory can tolerate distraction remains as an area to be explored. To examine the processes involved in distractor control, we designed two blocks of delayed color estimation task. In the first block and one-third trials of the second block, participants remembered the colors of two or four targets and reported one of them after a short period of retention interval. In the other two-third trials of the second block, distractors that have high- or low-impact were presented in the middle of retention interval. To manipulate their distraction magnitude, we assigned task-relevant features to high-impact distractors (colored digits), but not to low-impact distractors (black digits). Participants showed a better performance when two targets were present than four targets were present. Even though high-impact distractors damaged the performance under both set sizes, low-impact distractors disturbed performance only when set size was four. To examine cognitive processes of distractor control, we obtained phase coherence in theta-band oscillation; EEG phase preservation across trials. Distractors as well as targets evoked theta-band phase coherence at frontal and parietal electrodes which remained elevated after withdrawing distractors. Specifically, low-impact distractors elicited higher coherence than high-impact distractors when participants maintained two targets but comparable coherence when four targets were maintained. Additionally, phase coherence at the parietal electrode after distractor withdrawal was positively correlated with individual visual working memory capacity, measured independently; participants with higher capacity showed greater coherence after distractors were withdrawn. Taken together, phase coherence at the parietal electrode indicates distractor control process in visual working memory.

Keywords : Working memory, Distractor control, Electroencephalogram (EEG)

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P-497

Comparative analysis of spike-timing correlation in wild-type and optogenetically-treated degenerate retinas

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The visual system processes continuous streams of sensory input while maintaining consistent representation of external scenes. However, in retinal degenerative diseases such as retinitis pigmentosa and age-related macular degeneration, progressive loss of retinal neurons gradually disrupts this process, resulting in impaired visual recognition. To restore visual function, photosensitive opsins such as channelrhodopsins (ChR2) have been introduced into retinal cells via optogenetic approaches, enabling degenerate retinas to respond to light. However, it remains unclear whether their expression can restore the temporal heterogeneity of spike patterns among retinal ganglion cells (RGCs) observed in healthy retinas. To investigate this, we used a 256-channel multielectrode array (MEA) system to record population-level retinal activity and examined whether light stimulation induces comparable spike-time correlations in wild-type (*wt*) retinas (C57BL/6J) and ChR2-expressing retinal degeneration 10 (*rd10*) retinas (B6.CXB1-*Pde6b*rd10/J) via AAV2-CAG-ChR2(H134R)-EGFP transduction. To quantify these correlations, we employed the spike time tiling coefficient (STTC), which measures the temporal correlation between RGC spike trains. In conclusion, *wt* retinas exhibited significantly higher spike-time correlations than ChR2 retinas under both white and blue full-field stimulation. STTCs in *wt* were 0.570±0.237 (white) and 0.716±0.203 (blue), while ChR2 retinas showed 0.371±0.159 and 0.378±0.141, respectively. The differences were statistically significant (white and blue: $p<0.001$). These findings suggest that, although light responsiveness was restored via optogenetic treatment, the temporal coordination among RGCs was not fully recovered. These results highlight the limitations of current optogenetic strategies. Future research should focus on improving optogenetic approaches to restore not only light responsiveness but also the temporal precision of retinal circuits and function.

Keywords : Retina, Optogenetics, Correlations, Multielectrode array (MEA)

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P-498

A neural circuit integrating sensory and memory signals underlying social novelty preference

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Social novelty preference (SNP)—the inclination to preferentially interact with novel over familiar conspecifics—is vital for adaptive social behaviors and impaired in multiple neuropsychiatric disorders. Despite its significance, the precise sensory origins and neural mechanisms integrating incoming sensory cues with social memory remain unresolved. Here, we show in mice that SNP critically depends on olfactory signals detected by the main olfactory epithelium (MOE), rather than the traditionally emphasized vomeronasal organ. MOE-driven olfactory information is relayed via the main olfactory bulb to the anterior medial amygdala (MeAa), where it converges with top-down social memory signals originating specifically from ventral CA1 (vCA1) hippocampal neurons. Two-photon calcium imaging revealed that MeAa neurons robustly discriminate novel from familiar conspecifics

during social encounters. This novelty-selective encoding arises via a feed-forward inhibitory mechanism: vCA1-derived social memory inputs recruit a subset of calbindin+ local interneurons in the MeAa that suppress MeAa responses to familiar individuals. MeAa excitatory neurons, in turn, transmit this integrated novelty signal downstream to a genetically distinct population of *Tac2*+ neurons in the posterolateral bed nucleus of the stria terminalis (plBNST). Selective inhibition of these plBNST*Tac2* neurons abolishes SNP without impairing general sociability. Together, our results uncover a previously unidentified main olfactory-to-limbic circuit that dynamically integrates bottom-up sensory and top-down memory information to drive adaptive social behavior, providing mechanistic insights into the neural basis of social cognition and its dysregulation in related neuropsychiatric disorders.

Keywords : Social Novelty Preference, Social Behavior, Olfaction, Medial Amygdala, BNST

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P-499

Spatial context and past experiences build spatial memory

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Successful navigation relies on concrete spatial memory, which may be built upon either an egocentric reference frame or an allocentric reference frame. Egocentric reference frame encodes information relative to the navigator, whereas allocentric reference frame encodes static positions in a global reference frame. Although prior studies suggest that these two systems work in parallel, how they interact is yet difficult to discern from behavior. Here, we set out to find their respective navigational advantages. Participants were asked to collect diamonds in a 5×5 maze either from a first-person (egocentric) or third-person (allocentric) perspective. During the training phase, walls were visible and physically present. In the test phase, however, the walls remained present but were rendered transparent, requiring participants to rely on their memory to avoid collisions. Participants completed the task more quickly and with fewer collisions when the spatial context remained consistent across phases (e.g. egocentric training phase is followed by an egocentric test phase). This suggests that participants learn and retrieve the spatial layout more efficiently in the congruent spatial contexts than incongruent ones (e.g., an egocentric training phase is followed by an allocentric test phase). We then investigated which memory component contributes to accurate retrieval by identifying an individual behavioral pattern called “Motif” for both training and test phases. This pattern enables us to trace back the most representative trajectory for each location based on past experiences. Motifs were also similar when participants were both trained and tested in the same spatial contexts. Our findings echo the notion that spatial memory is more easily retrieved in the same spatial context, and we suggest that frequent visits to a certain location increase the likelihood of revisiting that location in the future, anchored to concrete spatial memory across both reference frames.

Keywords : Navigation, Spatial Memory, Virtual Reality

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P-500

Systematic proteogenomic analysis identifies causal plasma proteins and subtype-specific biomarkers for Alzheimer’s disease

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Alzheimer’s disease (AD) is a multifactorial neurodegenerative disorder with high heritability and growing public health impact. Although recent studies have identified numerous blood-based biomarkers for early AD detection, the lack of causal evidence has limited their translational utility. We aimed to identify blood proteins with a potential causal role in AD using large-scale proteomic and genetic datasets. We conducted Mendelian randomization (MR) analyses using plasma pQTL summary statistics from 54,219 individuals and AD-related GWAS datasets, collectively covering over 1.1 million individuals. These GWAS covered diverse AD phenotypes, including clinically diagnosed AD, late-onset AD, tau levels, hippocampal volume, and cardiovascular comorbidities. To evaluate causality and directionality, we employed genetic epidemiology approaches and assessed genetic colocalization to identify shared causal signals. Among approximately 25,000 protein–trait pairs, 71 candidates showed consistent evidence of a directional relationship with AD-related phenotypes. Of these, 15 proteins were further supported by shared genetic architecture, highlighting their potential causal relevance. This study demonstrates a comprehensive proteogenomic approach to nominate and prioritize plasma proteins as putative biomarkers or therapeutic targets for AD.

Keywords : Alzheimer’s disease, Mendelian randomization, Plasma proteomics, Biomarker discovery, AD subtypes

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P-501

A noradrenergic brainstem-to-hypothalamus circuit for sustained appetite suppression following stress

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Stress triggers adaptive behavioral shifts that override homeostatic drives such as appetite, yet the underlying neural mechanisms remain poorly understood. Here, we identify a noradrenergic brainstem-to-hypothalamus circuit that mediates stress-induced appetite suppression in mice. Using in vivo fiber photometry, we found that noradrenergic locus coeruleus (LC^{NA}) neurons exhibit persistent activity extending beyond acute restraint stress, temporally aligned with feeding suppression. Inhibition of LC^{NA} neurons or their projections

to the paraventricular hypothalamus (PVH) prevents stress-induced appetite suppression, whereas optogenetic activation of LC^{NA} neurons mimics stress effects that suppress feeding. Real-time norepinephrine recordings in the PVH show sustained elevation after restraint stress, correlating with the duration of feeding suppression. Pharmacological blockade of α1-adrenergic receptors abolishes stress-induced appetite suppression. Notably, this circuit is also required for feeding suppression after chronic stress. Our findings pinpoint the LC^{NA}-$PVH^{\alpha 1}$ noradrenergic circuit as a key driver of sustained appetite suppression following stress, uncovering a direct link between brainstem arousal center and hypothalamic feeding circuits.

Keywords : Stress, Appetite suppression, Norepinephrine, Locus coeruleus, Paraventricular hypothalamus

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P-502

EEG Analysis of hierarchical processing in deviant auditory stimuli: Oddball paradigm

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Previous studies show that prediction errors deviating from a global standard evoke distinct EEG responses: early mismatch negativity (MMN) and later P3b (a late positive deflection linked to conscious deviance detection and cognitive updating). These components emphasize top-down predictive processing over passive adaptation and may serve as clinical markers of conscious perception. This study explores the directionality of information flow using a novel relative phase method applied to EEG data from an auditory oddball paradigm. We analyzed 64-channel EEG recordings from 28 participants. Each trial included 125–130 sequences of five brief tones—either identical in pitch (standard sequence) or ending with a deviant final tone (local deviant sequence). In each trial, one sequence type (either standard or local deviant) occurred infrequently (20%), while the other predominated (80%). The rare sequence type was labeled a “global deviant,” introducing implicit global irregularity. Each participant completed eight trials. Preprocessing included down-sampling, filtering, and bad channel removal. Using the Hilbert transform, we extracted each signal’s phase and computed relative phase to infer information flow (Park et al., 2025, BioRxiv, DOI:10.1101/2025.03.12.642768). A positive relative phase indicates phase-leading (source of information); a negative value, phase-lagging (sink). MMN appeared ~150 ms after local deviants in frontal areas. P3b followed ~300 ms after global deviants in central-parietal regions. Critically, relative phase analysis showed a shift from central to frontal phase-leading during global deviants—suggesting a transition from bottom-up (sensory) to top-down (cognitive) processing, absent in local deviants. These results support MMN and P3b as sequential neural markers. The frontal-leading pattern during global deviants reflects prediction error signaling, consistent with hierarchical predictive coding models (Wacogne et al., 2011; Chao et al., 2018).

Keywords : Mismatch negativity (MMN), P3b, Relative phase analysis, EEG, information flow

P-503

Human analogical reasoning violates geometric assumptions of vector-based model

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Analogical reasoning is identifying a relationship between two things and mapping the relationship onto novel pairs. It is often modeled using vector-based word embeddings, where relational similarity is represented geometrically. A key example is the parallelogram model, which assumes that relationships between pairs can be captured as vector differences. These models assume that relational similarity follows geometric constraints such as the triangle inequality, which in mathematics means that the sum of any two sides of a triangle is greater than or equal to the third side. In analogy, if A is similar to B and B to C, then A should be similar to C. However, such models assume a pair's similarity is stable and context-independent. We hypothesized that when there are two types of relationships for one pair, it would lead to context-dependent violations and challenge the assumptions of vector-based models. We developed an analogy task where participants revealed four masked images through fixation and rated the similarity between pairs. We created 18 questions, each of four pairs of related items labeled A, B, C, and D. Pairs AB, AC, and BC share the same relation; pair AD has a different relation, while pairs BD and CD have no meaningful relation. This formed two comparison triangles: one with AB, AC, and BC, and another with AB, AD, and BD. This enabled us to test if relational similarity judgments followed the triangle inequality within a consistent relation, and if that pattern was violated when a different relation was introduced. We found that the inequality was often violated in the mixed-relation triangle, but preserved in the consistent-relation one. This suggests that human relational similarity judgments are context-sensitive. To determine if this was unique to human reasoning, we tested the same questions on LLMs. The results showed fewer violations and more geometry-consistent patterns, reflecting the assumptions of vector-based representations.

Keywords : Analogical Reasoning, Vector-based Models, Relational Similarity, Triangle Inequality

P-504

Metabolically-informed dynamic causal modeling of ketogenic therapy in childhood epilepsy

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Drug-resistant childhood epilepsy—particularly Lennox-Gastaut syndrome, infantile spasms, Dravet syndrome, myoclonic-astatic epilepsy, and metabolic epilepsies such as GLUT-1 or PDH deficiency—often responds better to ketogenic diet (KD) than to further medications. KD

modifies brain energy metabolism by enhancing mitochondrial function, activating neuronal KATP channels, and reducing oxidative stress, thus lowering network excitability and seizure risk. Functional neuroimaging also implicates altered default mode network (DMN) connectivity in various pediatric epilepsies, observed both interictally and peri-ictally. To investigate whether KD-induced metabolic changes improve network stability, we integrated bioenergetic parameters into a Dynamic Causal Modeling (DCM) framework. Based on a multiscale thalamocortical model [1–2], we added parameters for ATP consumption and KATP channel gating [3–4], and applied the model to resting-state EEG from children before and after KD therapy. The DMN was selected as the key circuit of interest, guided by EEG-fMRI studies linking it to seizure propagation. For each subject, we compared DMN dynamics pre- and post-treatment. Simulated perturbations (brief excitatory pulses and synaptic noise) were used to assess network resilience, evaluated using Lyapunov- and variance-based metrics. The model reproduced cross-spectral EEG features and showed greater stability under KD-like metabolic conditions, suggesting reduced susceptibility to perturbation. These findings support the idea that KD improves energy-dependent stability in brain networks. Metabolically-informed DCM offers a mechanistic bridge between cellular bioenergetics and large-scale dynamics, supporting personalized modeling of metabolic therapies in drug-resistant childhood epilepsy.

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Keywords : EEG, Seizure, Epilepsy, Dynamic Causal Modeling, Metabolism

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P-505

Insights in rats: Behavioral investigation in Tolman's Maze

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When faced with complex problems, both humans and animals may exhibit sudden, unexpected shifts in behavior—commonly interpreted as evidence of "insight." Although this phenomenon was first described nearly a century ago in Tolman and Honzik's three-way maze study, its underlying mechanisms remain poorly understood, partly due to limitations in behavioral quantification. In this study, we present a novel approach that combines a recreated classic maze and AI-based video analysis to systematically detect and characterize insight-like behavioral transitions in rats. By integrating historical paradigms with modern computational tools, our framework enables a unique dissection for the behavioral dynamics of problem-solving insight. We hypothesize that insight-driven behavior is not random, but emerges from a structured sequence of exploratory behaviors that precede sudden task success. These behavioral transitions, although abrupt in outcome, may be anticipated by identifiable behavioral motifs—such as vicarious trial-and-error (VTE), a pause at decision points during which the animal's head sweeps back and forth between alternatives—as well as hesitation or prolonged decision latency. To test this, we replicated the three-way maze environment and utilized AI-based video analysis for automated behavioral tracking and quantification. Our approach offers a new avenue for probing cognitive flexibility in animals, and lays the groundwork for future integration with large-scale neural recordings. Ultimately, this study advances our understanding of high-level cognition such as creativity and insight by grounding it in observable, quantifiable behavior.

Keywords : Insight, Problem-solving, AI-based behavior analysis, Cognitive flexibility, Tolman's maze

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P-506

Effect of motion speed expectation on visually guided oculomotor behavior

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The Bayesian inference hypothesis combines prior expectations with current sensory evidence to generate adaptive motor behaviors, suggesting that motor programming relies on prediction-modulated sensory information. Our behavioral experiments demonstrate that prior expectations about the speed of moving stimuli influence the speed of smooth pursuit eye movements. Participants had to perform a smooth pursuit eye movement task with the target blanking paradigm. In which the visual motion target moved diagonally, momentarily disappearing in the middle and reappearing at the center with 3 different speed conditions, fast, same and slow. Despite the actual pursuit target moving at the same speed, the speed of participants' smooth pursuit eye movements was biased toward the speed of the target presented before the blanking. This provides behavioral evidence that participants formed prior expectations about motion speed based on the speed of preceding stimuli. This suggests that visually-guided oculomotor tracking behavior regarding the speed of moving objects can be explained by the Bayesian inference hypothesis. To further identify the neural signature of motion speed prediction, we recorded electroencephalography (EEG) activity during same session and applied the inverted encoding model (IEM) to decode the predicted motion speed. Since changes in stimulus speed also alter the time it takes for the stimulus to traverse the screen, we performed decoding along the position axis rather than the time axis. By using IEM, we extracted the predicted speed of the moving stimulus by investigating the speed representation while the motion stimulus was turned off. In contrast to the behavioral results, the neural representation of speed was biased toward the speed of the pursuit target rather than the speed of the preceding stimulus. This finding suggests that an interaction occurs between speed prediction and the actual pursuit target speed during sensorimotor processing.

Keywords : Bayesian inference, Speed decoding, Inverted encoding model, EEG, Represenstation of speed

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P-507

Movement shapes decisions via multiplexing neurons in the mesencephalic locomotor region

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Animals continuously integrate dynamic movement states and external sensory signals to make adaptive decisions. Yet, the neural mechanisms underlying such state-dependent decision-making remain unclear. To address this, we developed a novel go/no-go perceptual decision-making task on a treadmill, allowing mice to perform under varying self-paced walking speeds. We focused on the mesencephalic locomotor region (MLR) as a candidate region for integrating internal movement states with external task-relevant cues. Using a general linear model (GLM), we found that individual MLR neurons multiplex both kinematic (e.g., walking, licking) and external task-relevant (e.g., sensory cues, rewards) information. MLR neurons exhibited distinct encoding patterns depending on task events and movement dynamics. Clustering based on task-aligned activity revealed subpopulations selectively responsive to external cues, and modulated by movement states. To link neural activity with decision behavior, we applied a drift-diffusion model (DDM) and found that walking speed predominantly altered the drift rate, indicating movement state-dependent modulation of evidence accumulation. Importantly, firing rates of specific multiplexing neuron clusters correlated with this drift rate, suggesting they contribute directly to adaptive decision formation. These findings demonstrate that MLR neurons integrate movement states and external cues to modulate decision-making dynamics. These results establish the MLR as a subcortical hub for integrating cognitive- motor integration in context-dependent adaptive decision control.

Keywords : Perceptual decision-making, Multiplexing, Mesencephalic locomotor region, Drift-diffusion model, Cognitive-motor integration

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P-508

Psychobehavioral analysis and neural decoding of food addiction in non-human primates: From model development to pharmacological intervention

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Food addiction is increasingly recognized as a neurobehavioral disorder involving disrupted reward regulation rather than mere excessive intake. Unlike drug addiction, food is biologically necessary, creating ambiguity at the computational level—what goal is the brain pursuing? This complicates mechanistic interpretation across the algorithmic and implementation levels. Grounded in Marr's framework, we aim to dissect the neural basis of food addiction in non-human primates by integrating behavior, neuroimaging (fMRI, PET), and circuit-targeted intervention. We established a primate model of binge eating using fixed intermittent access to palatable food. A second paradigm employing unpredictable intermittent access is underway. Behavioral phases—motivational drive, compulsivity, and relapse—are quantified via high-resolution SLEAP-based pose tracking, detecting microbehaviors (e.g., cue-triggered approach, anhedonia-like signs). Planned resting-state fMRI will assess connectivity among the nucleus accumbens (NAcc), orbitofrontal cortex (OFC), and ventromedial prefrontal cortex (vmPFC). PET will quantify striatal dopaminergic signaling using [18F]-fallypride to map D2 receptor binding potential. Binge-eating monkeys exhibited escalated intake (90 kcal/min, 5.6× baseline), withdrawal-induced rebound, and approach behavior peaking at month 4. Preliminary evidence suggests chronic intermittent feeding may alter mesocorticolimbic function—inducing NAcc hyperactivity and D2R downregulation, potentially reflecting a shift to compulsive seeking. We expect future neuroimaging to confirm weakened prefrontal regulatory control. Anti-obesity treatments were tested in the fixed-intermittent group; GLP1R-targeted interventions are planned for the unpredictable-access group. This study offers a systems-level view of food addiction, advancing primate-based models for understanding motivational disorders and informing circuit-specific obesity interventions.

Keywords : Food addiction, Non-human primate model, Dopaminergic signaling, Binge eating and relapse behavior, SLEAP-based behavior tracking

P-509

Forelimb trajectory stability in reach-to-grasp task reflects long-term motor learning progression

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The reach-to-grasp task is a widely used behavioral paradigm for probing skilled forelimb motor control in rodents. It requires the animal to reach through an aperture, grasp a food pellet, and retrieve it, engaging precise coordination of the wrist and digit. This task is especially valuable for studying natural motor learning, as performance typically improves progressively over 2-3 weeks of training, reaching expert-level execution within approximately two weeks. In this study, we examined how forelimb kinematic trajectories evolve over the course of 13 days of reach-to-grasp training in rats. Using DeepLabCut, a deep learning-based markerless motion tracking tool, we analyzed the 2D spatial trajectories of the wrist and digit during each reach attempt. Here, we present representative trajectory data from Days 1-3 (early learning phase) and Days 11-13 (expert performance). Early trajectories exhibited broad spatial dispersion, irregularity, and inconsistency in endpoint locations. By contrast, late-stage trajectories on Days 11-13 demonstrated spatial refinement, tighter clustering, and higher stereotypy, indicative of consolidated motor patterns. Furthermore, we investigated the correlation between daily success rate—defined as the percentage of successful retrievals—and trajectory stability. Preliminary analyses suggest that higher task success is associated with more constrained and goal-directed movement patterns, particularly in distal effectors (wrist and digit), highlighting the utility of trajectory features as potential markers of learning state. These findings support the use of

the reach-to-grasp task as a powerful model for assessing experience-dependent motor plasticity and provide insights into how skilled limb use emerges and stabilizes through practice.

Keywords : Motor learning, Reach to grasp, DeepLabCut

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P-510

Neural basis of approximate object counting in human single-neuron activity

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The ability to estimate quantities and process numerical information is a core cognitive function that emerges early in development and is conserved across species 1. A prevailing theory posits that distinct neural systems support different number ranges: small quantities (typically 1-4) are processed rapidly and precisely, whereas larger quantities are estimated more slowly and with greater, number-dependent variability 2,3. Additionally, symbolic counting in humans likely relies on a separate system based on exact, sequential processing. However, how these systems interact to enable flexible numerical cognition remains unclear. To tackle this question, we designed a number-estimation task in which participants freely viewed visual stimuli containing 1–16 objects for two seconds and reported the estimated number. During task performance, we recorded single-neuron activity from multiple cortical areas—including the hippocampus, entorhinal cortex, anterior cingulate cortex, and orbitofrontal cortex—in neurosurgical patients (N=6). Participants exhibited significantly greater response errors when estimating large numbers of dots (12–16) than when estimating small numbers (1–4) ($t(458) = 9.9007$, $p < 0.001$). We found that approximately 20% of neurons exhibited number-selective tuning, with a notable bias: about 40% of these were tuned to small numbers (1-4). Preliminary analysis of population dynamics revealed that neural trajectories in state space diverged according to numerical magnitude, with greater separation for smaller numbers. This pattern may underlie the enhanced precision for small-number estimation and reflect the number-dependent scalar variability. Together, these findings shed light on how distinct representations may contribute to different numerical ranges.

Keywords : Electrophysiology, Human, Number

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P-511

Explainable machine learning EEG data analysis framework for predicting vagus nerve stimulation effects in epilepsy patients

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1. Research Background: Vagus nerve stimulation (VNS) has emerged as an effective adjunctive therapy for drug-resistant epilepsy. However, predicting individual patient response to VNS remains a significant clinical challenge. Accurate prognosis prior to VNS implantation would greatly aid in selecting suitable candidates and optimizing treatment strategies. This study aims to address this gap by developing a machine learning-based predictive framework that not only achieves high accuracy but also ensures neuroscientific interpretability. 2. Method: The proposed pipeline comprises four key stages: (1) preprocessing; (2) seizure-state classification; (3) VNS outcome prediction; and (4) post-hoc neuroscientific interpretation. For preprocessing, EEG signals undergo feature extraction using TQWT(tunable Q-factor wavelet transform) into five frequency bands. Subsequently, DMD(dynamic mode decomposition) is applied to extract dynamic patterns(eigenmodes) within each band, capturing transient and nonlinear dynamics. A Random Forest classifier is trained on the TUH EEG dataset and applied to EEG sessions of VNS-treated patients from Yonsei Severance Hospital(hereinafter VNS-EEG) labeled by neurologists into three prognosis categories to distinguish ictal and interictal intervals. The VNS outcome predictor, based on GNNs and attention mechanisms, handles inputs derived from the frequency-eigenmode domain of the VNS-EEG dataset. 3. Result: The proposed preprocessing pipeline, seizure-state classifier, and GNN-based VNS outcome predictor modeling have been successfully implemented. Application of the full pipeline to the VNS-EEG dataset is currently underway, with hyperparameter tuning and evaluation in progress. Concurrently, development of a visualization GUI is in progress for high-level analysis, not only enhancing the interpretability and clinical utility of the model but avoiding unnecessary invasive therapy procedures and serious side effects in clinical domain.

Keywords : Neuroscience, Electroencephalography, Epilepsy, Deep learning, Vagus nerve stimulation

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P-512

Latent Attractor Dynamics in OFC and RSC During Naturalistic Foraging

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The brain is well-equipped to learn information across multiple timescales. While prior studies have illuminated how neural populations support

short-timescale learning driven by immediate rewards, the mechanisms underlying long-timescale learning with sparse, delayed rewards remain unclear. Here, we investigated how neuronal populations in the orbitofrontal cortex (OFC) and retrosplenial cortex (RSC) support learning under such conditions. Two nonhuman primates were trained on a first-person 3D virtual navigation task in which the spatial layout remained fixed across days, but the goal location varied daily and the starting position changed on each trial. Because each trial began from a random location, subjects sampled different trajectories and had to integrate information across trials to infer the goal location, thereby promoting learning over extended timescales. To uncover the underlying population dynamics, we applied a recurrent switching linear dynamical system (rSLDS) model to multi-neuron recordings from OFC and RSC. As behavioral performance improved with increases in choice optimality, line attractor dynamics emerged in both regions, with neural trajectories progressing along the axes of line attractors in a manner predictive of choice optimality. Additionally, we observed that the amount of line integrals akin to perturbations and relaxations around the line attractors showed correlations with choice optimality. These findings highlight the utility of dynamical systems approaches for revealing how distributed neural populations support long-term learning in naturalistic settings.

Keywords : Long-term learning, Virtual navigation, Orbitofrontal cortex, Retrosplenial cortex, Attractor dynamics

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P-513

Comprehensive analysis of naturalistic behaviors enables tailored diagnosis of depressive disorder in mice

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Major depressive disorder (MDD) is an etiologically diverse psychiatric disease with heterogeneous manifestations, making it difficult to diagnose with conventional assessment standards. In addition, the obvious incompatibility of the standard survey-based tests for human MDD and the behavioral assays for depressive-like phenotypes in mice makes clear the requirement for a non-invasive method for quantifying the onset of depression in naturalistic contexts. Here, we introduce a self-supervised machine learning platform, CLOSER (Contrastive Learning-based Observer-free analysis of Spontaneous behavior for Ethogram Representation), to monitor the spontaneous behavior in a depressive disease model with enhanced precision, reliability, and efficiency. This framework incorporates 3D pose skeleton data and kinematic features in a unique data augmentation strategy to characterize semantic behavioral syllables with a high-quality feature space. Using CLOSER, we uncovered distinct motion profiles in chronically stressed mice across both sexes and different disease stages. Furthermore, we quantified the drug-specific recovery of psychomotor symptoms, highlighting CLOSER's discriminative power for identifying drug efficacy. In offering a comprehensive analysis of exploratory behaviors, CLOSER proposes the standardization of depressive disorder diagnosis in mice, thereby unifying preclinical and clinical assays for psychiatric drug discovery.

Keywords : psychomotor, depressive disorder, naturalistic behavior, antidepressant, machine learning

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P-514

Frequency-Selective Sound Localization Mechanism in Drosophila Mediated by WV-WV Interneurons

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Sound localization is one of the most important abilities for survival and communication across wide range of animals. While humans localize sound using interaural time and level differences, *Drosophila melanogaster* relies on a unique mechanism. Here, I explore how *Drosophila* localizes sound using antennae and central brain circuitry, focusing on the role of the WV (Wedge-VLP) interneurons. I hypothesized that WV neurons in the central brain integrate input from both sides of the antennal mechanosensory and motor center B (AMMC-B) and project to descending neurons. Using whole-brain connectome data (FAFB), I designed a numerical model simulating this network. The model reveals that WV neurons act as subtractive calculators, enabling frequency-specific sound localization and behavior modulation, consistent with a Braitenberg vehicle type 2a structure. Behavioral experiments confirmed these predictions. Silencing WV neurons via Kir expression abolished frequency-specific preferences, supporting its role in sound-localization. Furthermore, I observed unpredicted behavioral responses at some frequencies suggesting additional mechanisms, possible involving the other parts of AMMC or structural factors like mounting compliance. Together, these findings reveal a novel neural computation for sound localization in *Drosophila*, driven by frequency tuning and mechanical resonance, and highlight WV interneurons as key components in directional auditory processing.

Keywords : Sound-localization, Frequency selectivity, Drosophila, Braitenberg vehicle, Auditory

P-515

Dopamine neurons flexibly compute reward proximity during foraging competition

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Living with multiple potential goals, we take into account our current status and reward statistics when making decisions. We developed a novel task to model this more realistic reward environment using mice.

In a square chamber, an LED cue is positioned at the center of each side, with a water port installed beneath each cue. When one of the four visual cues is randomly activated for a second, a drop of water is dispensed from the port below the activated cue. As mice learned the association between LED cue and reward delivery, they gradually approached reward with shorter latency. As expected, we observed that the latency increased with the mouse's distance to the reward and visual angle of the cue (< 120 deg from the midline). We questioned whether these geometric parameters (distance, angle) are embedded in the dopaminergic activity. To monitor dopamine (DA) activity, we injected a dopamine sensor (DA2m, DA3m) into the ventral striatum and dorsomedial striatum . DA responses to cues decreased with distance and angle, suggesting that mice internally estimate time-to-reward ('predicted latency') based on spatial parameters and this process is reflected in dopaminergic responses. Next, we examined how the competitive context influences DA responses by adding another animal. To estimate which animal may win the competition, we computed the predicted latency for each mouse based on both its own geometric parameters and those of the competitor. This predicted latency reflects each animal's estimated time to reward. Interestingly, when the mouse is closer than the competitor, the DA activity reliably decreases as the predicted latency increases. However, when the competitor is closer, this relationship is weaker. Across sessions, the effect of the predicted latency on DA responses became stronger. These results suggest that mice flexibly incorporate both their own and others' physical parameters to compute reward proximity, reflected in adaptive dopaminergic activity.

Keywords : foraging, competition, reward, dopamine signaling

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P-516

Acetylcholine enhances deviance detection in Hodgkin-Huxley neuronal networks

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The brain continuously generates predictions about the environment, with unexpected events eliciting a deviance detection (DD), a neural manifestation of prediction error. While acetylcholine (ACh) is known to be essential for attention, its potential computational mechanisms for DD remain unresolved. In this study, we used the Hodgkin-Huxley (HH) model to investigate the effects of cholinergic modulation on DD. We constructed a network of 160 excitatory and 40 inhibitory neurons with a 5% connection probability. ACh levels were modulated by the slow K^+ current conductance, gks, where a range of 0 to 1.5 corresponded to a decrease in ACh from maximum to zero. To investigate DD, we designed three sequences: a standard sequence (80% stimulus A, 20% stimulus B); a deviant sequence (20% A, 80% B); and a multi-standard control sequence (20% each of stimuli A, B, C, D, E). Simulation results showed that the model exhibited DD in the absence of ACh, responding more strongly to the same stimulus A when it appeared in a deviant sequence compared to a control sequence, despite both having an equal probability of 20%. However, when a small amount of ACh was added (by reducing gks from 1.5), DD was enhanced, reaching a maximum at gks value of 1.3. Further increases in ACh levels led to a decline in DD, eventually reducing it to zero. Furthermore, we demonstrated that ACh enhances DD through spike frequency adaptation (SFA), an intrinsic neural property in which a neuron's firing rate decreases in response to a repeated stimulus. SFA is modulated by both gks and synaptic currents. Our simulations showed that SFA was maximized with a moderate level of ACh given the synaptic current amplitudes in our networks. This induced local suppression in response to the frequent stimulus, effectively freeing up larger portions of the network to remain responsive to rare, deviant stimuli. Our study offers a mechanistic account of how ACh facilitates DD without long-term plasticity.

Keywords : Neuromodulator, Deviance detection, Perception, Predictive coding

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P-517

Neural geometry of relational representation in the monkey posterior parietal cortex

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Abstract relational reasoning is crucial for flexible cognition. A leading theory has proposed that such reasoning requires 1) explicit representations of abstract relations, and 2) appropriate binding of these relations to the sensory attributes (Doumas et al. 2008). We take this problem to the brain, asking how the neural population represents relational information and integrates it with sensory information. Specifically, we focused on 7a of the posterior parietal cortex (PPC), which has been implicated in encoding spatial relations between object parts (Chafee et al., 2007). To address our question, we trained monkeys on a relational memory task in which they remember the spatial relation between a cue and a target, and later apply the relation to a new cue location to make a saccade to the final target location. Animals learned the task successfully and were able to rapidly generalize to new relations and cue locations. We first tested whether spatial relations are encoded independently of absolute spatial locations by analyzing Neuropixels recordings from 7a while monkeys were performing the task. We found that cue-target relations and cue locations were represented in independent low-dimensional subspaces of the neural population. These subspaces preserved the two-dimensional spatial layout of both cue positions and cue-target relations, and the spatial layout of the relational memory was reorganized in incorrect trials. Next, we asked how these separate representations are integrated to compute a saccade vector. Population geometry analysis on the delay period data suggests that the 7a dominantly encodes the remembered spatial relations, while the integrated saccade target signal was present but weaker. Overall, we show that 7a supports relational reasoning by encoding relations and locations in separable low-dimensional subspaces, and robustly maintaining the relation representations during the memory period to enable flexible, goal-directed actions.

Keywords : Relational reasoning, Posterior parietal cortex, Electrophysiology, Non-human primate

P-518

Inferring Temporally Resolved Directionality Transition Dynamics in fMRI via Phase Analysis

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We introduce a novel approach to estimate directionality transitions in fMRI signals using Relative Phase Analysis (RPA), originally developed for EEG (Park et al., 2025, bioRxiv: https://doi.org/10.1101/2025.03.12.642768). RPA computes the instantaneous phase of each BOLD time series using the Hilbert transform and defines relative phase as the difference between each vertex's phase and the global mean phase. This enables a temporally resolved view of signal flow across the brain, where positive values indicate leading and negative values lagging activity. To validate this method, we compared the principal components derived from RPA-applied BOLD signals with those from PCA and CPCA (complex PCA; Bolt et al., 2022), which captures global spatiotemporal patterns by applying PCA to complex-valued BOLD signals derived via Hilbert transform. The first principal component (PC1) from RPA showed a strong spatial correlation with the PC1 phase map from CPCA (r = 0.64), indicating shared sensitivity to large-scale propagation patterns. In contrast, higher-order components (PC2, PC3) exhibited minimal correspondence, suggesting that RPA captures distinct temporal features. Notably, the first component (PC1) revealed a global anterior-to-posterior propagation pattern, while PC2 reflected transitions between attention-related and sensorimotor regions. PC3 showed more localized dynamics, potentially capturing internal transitions within the default mode network. Unlike CPCA, which extracts global temporal modes through complex decomposition, RPA preserves native temporal resolution and allows each time point to be projected into the principal component space, enabling real-time tracking of dominant directionality states. This real-time compatibility makes RPA well-suited for studying dynamic brain processes in naturalistic settings. Its simplicity and sensitivity support future applications such as neurofeedback and adaptive cognitive paradigms.

Keywords : Relative phase analysis, fMRI directionality, Complex principal component analysis, Brain dynamics, Principal component analysis

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P-519

Establishing Awake Monkey fMRI Platform for Whole-Brain Imaging and Perturbation

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Functional magnetic resonance imaging (fMRI) is a powerful tool for investigating whole-brain function, albeit being mainly used in humans. Expanding fMRI to non-human primates allows direct cross-species comparisons, bridging the gap between human and animal research. Additionally, when combined with direct stimulation and inactivation of a brain region, monkey fMRI allows for causal inference of the targeted region's functional role, enabling us to go beyond correlational analyses. Many monkey fMRI studies still rely on anesthetized monkeys or passive viewing paradigms due to the technical challenges. However, fMRI in awake task-performing monkeys is essential to study the link between brain activity and behavior. Here, we establish awake behaving monkey fMRI using two well-known paradigms for the non-human primates. First, we trained a monkey to fixate the eye at the center of the screen and presented face stimuli while scanning the whole brain. Consistent with previous findings that identified face-selective patches, we observed localized activations in the superior temporal sulcus, validating our fMRI set up and imaging protocols. Second, we trained the animal for the memory-guided saccade task, a widely used paradigm for studying working memory and oculomotor planning in monkeys. In this task, animals are required to make a saccade to the remembered location of the briefly presented target after a delay. Based on previous experiments, we predicted task-related activation in the posterior parietal cortex and frontal cortex. We monitored the animal's eye movement in the MRI scanner environment and the animal was able to perform the task reliably inside the scanner. Furthermore, consistent with previous findings, we found activations in the frontoparietal cortices. These preliminary results demonstrate our setup's potential for integrative whole-brain imaging and causal perturbation.

Keywords : Awake monkey fMRI, Non-human primate, Neuroimaging , Cognitive Neuroscience, Casual perturbation

P-520

Connectome-based Cognitive Prediction Models: Integrating Functional and Structural Brain Networks

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[Introduction] Advances in neuroimaging techniques have enabled more precise characterization of the human connectome and its relationship to cognition[1]. Yet, how functional and structural brain networks jointly inform cognitive prediction across the adult lifespan remains underexplored. This study introduces a multimodal connectome-based framework that integrates functional and structural connectivity and morphological features to predict individual cognitive abilities in healthy adults across age groups and sexes. [Methods]We developed a hybrid prediction model that combines a Graph Attention Network (GAT)[2] with a deep multilayer perceptron (MLP) to incorporate both graph-based connectivity information and morphological features (e.g., cortical thickness, volume). Using lifespan neuroimaging data from the Human Connectome Project, we trained separate models to predict multiple domains of cognitive function. The interpretability of the model was assessed through analysis of attention weights at both the node and edge levels and extraction of SHAP-based feature importance. [Results] Analysis of node-level attention revealed distinct patterns of regional importance across age groups and sexes. At the edge level, high-attention connections were identified within known cognitive networks, highlighting the model's sensitivity to functional integration between regions. These patterns varied systematically with age, reflecting known developmental and

compensatory mechanisms in cognitive aging. [Conclusion] Our findings demonstrate that connectome-based GAT+MLP fusion models can uncover biologically meaningful and interpretable patterns of brain connectivity relevant to cognitive function. This data-driven approach offers a scalable and explainable framework for cognitive prediction and provides new opportunities to study how brain network organizations support cognitive variability across age groups and sexes.

Keywords : Connectome, Cognition, Functional Connectivity, Structural Connectivity, GAT Fusion model

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P-521

Context-dependent reward processing reflected in central positivity

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Reward processing enables flexible behavioral adjustments in response to dynamic environments. Previous research has identified frontal negativity and parietal positivity as neural markers of reward-related signals, typically using probabilistic choice tasks that induce prediction errors. However, such tasks often lack structured models that reflect real-world decision-making, where individuals rely on internal representations and adjust behavior based on contextual cues. To bridge this gap, the current study explores how reward processing operates when a stable task structure is preserved but the rewarding context changes. Participants first completed a Basic Association Task (association task), acquiring baseline stimulus-action-outcome associations through binary choices. This was followed by the Adaptive Contextual Choice Task (choice task), which introduced two distinct color-coded contexts (green and blue) with varying reward contingencies of associations. Each context was presented in two consecutive runs. Although accuracy of choice task initially declined sharply after context transitions, it quickly recovered, indicating efficient adaptation in associative learning. By the end of the first context, performance had plateaued, suggesting that associative learning was fully established. While the amplitude of central positivity following reward was greater in the first context and reduced in the second context, the reduction in its amplitude from the first to the second run within context was greater at the vertex electrode, which is more closely associated with error-related processing, than at the parietal electrode. These findings suggest that central positivity is associated with contextual reward processing.

Keywords : Associative learning, Reward processing, EEG

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P-522

Rhythmic but fading: damped oscillation reveals the temporal dynamics of retroperception

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Although perception and cognition are often described as continuous, emerging evidence suggests they operate rhythmically, reflecting neural oscillations. Several studies have shown that such rhythms exist in perception and attention by presenting a cue before a target stimulus with varying interval between pre-cue and target stimulus. However, it remains unknown if this rhythmic sampling occurs in retro-cue conditions where a cue follows a target. Previous retro-cue studies have employed retro-cues at only a limited number of timepoints and thus have failed to characterize the temporal dynamics of perception and attention and dynamic relationship between the two. Current study investigated whether the relation between visual awareness and attention exhibit intrinsic rhythmicity in retro-cue conditions. With an established retro-cue paradigm and dense sampling of behavioral reports, participants performed target orientation discrimination and visibility rating tasks. Irregular Resampling Auto-Spectral Analysis (IRASA) revealed that both discrimination accuracy and subjective visibility rhythmically fluctuated at individual peak frequencies in the theta band. To characterize the temporal structure of retroperception, we compared three models: monotonically decaying, monotonically decaying rhythmic oscillation, and monotonically decaying damped oscillation. Model fitting using Takeuchi's Information Criterion (TIC) revealed that the monotonically decaying damped oscillation model best captured the temporal dynamics of both behavioral accuracy and subjective visibility. Furthermore, we demonstrated the phase coherence between perceptual and attentional oscillations at theta frequency, advocating a functional interplay between perception and attention. Collectively, our finding of monotonically decaying damped oscillatory dynamics of retro-cued perception reveals the temporally flexible yet bounded nature of our conscious experience.

Keywords : Attention, Perception, Retroperception, Conscious access, Rhythmic sampling

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P-523

Comparison of BGRU, EEGNet, and EEG Conformer from the Perspectives of Performance and Design Principles in EEG-Based Emotion Recognition

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EEG-based emotion recognition is a core technology for decoding human emotional states by capturing real-time electrical activity in brain regions such as the cerebral cortex and limbic system, which are responsible for emotional processing. This technology holds great significance in both neuroscience and neuroengineering, as it enables understanding of emotional mechanisms and supports applications such

as real-time emotion feedback, early prediction of mental disorders, and the development of personalized brain-computer interfaces. However, extracting and modeling emotional patterns from high spatiotemporal EEG data is challenging due to complex nonlinear relationships. In this study, we conducted a comparative analysis of three representative artificial intelligence-based models: BGRU(Bidirectional Gated Recurrent Unit), EEGNet, and EEG Conformer. BGRU effectively captures continuous emotional changes through bidirectional sequential learning but has limitations in efficiently processing spatial information in high-density EEG data. EEGNet, with its lightweight convolutional neural network structure, efficiently learns from high-density channel data and can extract key features across temporal and spatial patterns, though it may be somewhat constrained in capturing complex nonlinear temporal contextual relationships. EEG Conformer, a state-of-the-art model combining convolution and self-attention mechanisms, is designed to learn not only temporal sequences but also nonlinear and complex inter-channel relationships. This design makes it highly effective at extracting multidimensional contextual and semantic emotional patterns from high spatiotemporal density EEG data. Experiments using the DEAP and SEED datasets showed that EEG Conformer achieved the highest performance. This study analyzes the design principles, strengths, and limitations of each model and demonstrates their practical applicability in EEG-based emotion recognition.

Keywords : EEG, Emotion Recognition, Artificial Intelligence, EEG Conformer, Neuroscience

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P-524

Dynamic Control of Neural Activity via Real-Time Brain-Machine Interface Across Brain Regions

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Thorndike's law of effect posits that behaviors followed by reinforcement are more likely to be repeated. In neural terms, activity patterns followed by reinforcement may occur more frequently. To test this, we developed a closed-loop brain-machine interface (BMI) that reinforces spontaneous spike patterns. Using DAT-Cre C57BL/6 × CD1 F1 hybrid mice, we recorded single-unit activity from multiple brain regions, including the prelimbic cortex, and delivered phasic optogenetic stimulation to dopaminergic neurons in the ventral tegmental area (VTA) in real time. Our adaptive decoder gradually adjusted the spike count threshold during the session to regulate the frequency of dopamine stimulation. Starting with a low threshold, the system progressively increased selectivity, allowing reinforcement to become more contingent on specific neural patterns. Our dynamic decoder successfully tracked ongoing neural activity and delivered dopamine stimulation in real time. As the session progressed, stimulation became increasingly aligned with structured spike patterns, even in the absence of external cues or behavioral tasks. Across brain regions, we observed region-dependent changes in firing rates, suggesting that dopaminergic reinforcement interacts distinctively with neural representations. These findings indicate that real-time feedback can shape spontaneous neural activity while the decoder continues to adapt, providing a foundation for stabilizing control signals and improving the robustness of closed-loop BMI systems. Thus, dopaminergic reinforcement does not exert uniform effects across the brain but rather engages region-specific plasticity. This heterogeneity highlights differences in how neural circuits integrate value signals and adapt their dynamics. Our approach provides a novel framework for dissecting the organizational principles of reinforcement pathways and developing BMI systems tailored to the intrinsic learning capacities of distinct brain regions.

Keywords : BMI, multi-region, real-time, dynamic control, closed-loop

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P-525

Neural Circuit Dynamics During the Acute Phase of Stroke Recovery

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Stroke is one of the leading causes of death worldwide, and it is a severe condition that causes permanent loss of function in the damaged area, leaving people with disabilities. Although rapid neurological recovery is commonly observed within the first month after stroke, the underlying mechanisms at the microcircuit level remain poorly understood. Moreover, most studies have focused on the chronic phase of recovery, with relatively few addressing the neural dynamics during the acute phase. In this study, we aim to observe neuronal activity changes during the acute and chronic phase of stroke recovery using Neuropixels probes. Spike data were obtained during a virtual reality (VR) task from the ipsilateral striatum and motor cortex adjacent to the right primary motor cortex (M1), as well as from the contralateral M1. Behavioral observations show that mice develop a bias, preferentially turning toward the ipsilateral side after stroke induction. We analyze how neuronal activity in the acute phase changes by comparing pre-stroke and post-stroke states. In particular, we investigate alterations such as firing rates in the penumbral region and possible compensatory changes in the contralateral M1. Single-unit analyses are conducted to characterize potential shifts in cue-evoked selectivity. We will present to conduct chronic longitudinal recordings during the acute recovery phase to track the progression of neural circuit reorganization and neuroplasticity over time. The significance of this research lies in its potential to elucidate the mechanisms underlying stroke recovery at the neural circuit level. By understanding these processes, we may identify novel therapeutic targets for neural repair, and the insights gained could also be applied to the development of artificial neural networks inspired by biological recovery mechanisms.

Keywords : Stroke, Recovery, Acute, Neural plasticity, Circuit

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P-526

Weighted Maximum Likelihood Estimation: Explanation of biased visual-proprioceptive integration

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Current motor rehabilitation therapy or learning mainly relies on the repetition of a target movement with additional sensory information. However, this therapeutic approach is inefficient and time-consuming. To enhance current practice, understanding the interaction between proprioception and other sensory modalities is crucial, as proprioception is the key modality for motor control and learning. Its integration with other sensory modalities, especially with vision, provides more optimal motor outcomes. Therefore, full comprehension of visual-proprioceptive integration is necessary to prescribe optimum therapy for motor rehabilitation. Integration between different sensory modalities has been explained by the maximum likelihood estimation (MLE) framework based on the Bayesian theorem. However, this framework is limited in explaining biased situations, especially in the presence of proprioceptive feedback from the motor output that is intrinsically engaged with proprioception. To fully understand how proprioceptive information is integrated with other sensory modalities, we've conducted a finger aperture matching task. Our results suggest that visual-proprioceptive integration does not follow the traditional MLE framework; instead, proprioceptive modality should have additional sensory weight over the visual modality. Based on this result, we propose that the brain puts more weight on proprioceptive modality during the multisensory integration between vision and proprioception, when the expression contains proprioceptive information as feedback. This emphasizes the critical role of proprioception in motor rehabilitation or learning. Moreover, this result highlights the significance of proprioceptive information in enhancing motor rehabilitation or learning efficiency.

Keywords : Multisensory integration, Proprioception, Maximum likelihood estimation

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P-527

Emergence of aesthetic preference from hierarchical neural circuits

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Aesthetic sensitivity to specific spatial proportions has long been observed across human cultures, with the golden ratio (GR, $\phi \approx 1.618$) frequently cited as a preferred visual configuration. Although widely documented in visual composition and biological structures, the origins of this preference remain poorly understood. Previous research has reported neural and behavioral sensitivity to GR in adults (Bartolo, 2021; Rizzolatti, 2007), and even early ratio discrimination in infants and non-human animals (McComb, 1994; Pallet, 2010). These findings suggest that GR sensitivity may not depend entirely on experience. However, the mechanisms by which such selectivity could emerge within the visual system are still unknown. To examine this question, we first conducted a behavioral experiment in which participants compared face images with and without GR-based modifications. Participants more frequently selected GR-structured faces as more visually appealing, consistent with a long-proposed perceptual bias favoring this proportion. In a follow-up eye tracking experiment, we compared gaze responses to GR and non-GR face stimuli. Participants showed different gaze dynamics across conditions, supporting the notion that GR structure influences perceptual processing. To explore whether such sensitivity could emerge from neural architecture, we developed a two-dimensional hierarchical model with sparse connectivity, mimicking early visual processing. Receptive fields were recursively constructed across layers, and aspect ratios were extracted from the resulting spatial integration patterns. We found that the aspect ratio distributions in deeper layers exhibited increased density near the golden ratio. This pattern was absent in fully connected control models. These findings suggest that golden ratio selectivity may arise from structural wiring constraints alone, offering a mechanistic explanation for the emergence of aesthetic preferences without the need for training.

Keywords : Golden ratio, Hierarchical neural network, Neuroaesthetics, Perception

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P-528

Real-Time Individual Sleep Prediction Enabled by Probabilistic Modeling of Wearable Data and Functional Brain Activity Analysis

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Insomnia is a major health concern in modern society. However, sleep drive, which plays a significant role in sleep regulation, is not directly observable, making it hard to intervene effectively. We propose a probabilistic model that estimates individual sleep drive and its uncertainty in real time. The model infers sleep drive using only heart rate, sleep onset time, and wake time, and demonstrates a significant improvement over an existing model that does not consider uncertainty. Using wearable data from both the healthy group and the insomnia group (N = 32), cross-validation showed that the model significantly predicted wake time, total sleep time, and wake duration on days not used for training. In addition, we examined the relationship between the model's key parameters and prefrontal brain activity measured during Stroop and N-back tasks using functional near-infrared spectroscopy (fNIRS). The sleep model parameters were significantly correlated with task difficulty-related changes in brain activation, particularly in the orbitofrontal cortex (OFC) and dorsolateral prefrontal cortex (DLPFC). These findings indicate that our model can reveal individual differences in sleep regulation and their neurobiological mechanisms using digital phenotype data collected from wearable devices. Our model may be useful for clinical subtyping of insomnia based on digital phenotypes and personalized sleep interventions.

Keywords : Sleep, Insomnia, Functional imaging, Drift-diffusion model, Digital Phenotype

P-529

Spontaneous social change driven by Stochastic Individual Behavior

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Imitation can drive large-scale shifts in collective social behavior, yet the mechanisms behind such transitions remain largely unknown. Prior studies suggest that the emergence of new social conventions requires a minority of individuals reaching a critical mass (Centola, 2018), grounded in two key assumptions: (1) the presence of a committed minority that persistently exhibits new behaviors, and (2) the remainder of the population engages in conformist imitation — copying the most frequently observed behavior while ignoring fewer common alternatives. Here, we present a fundamentally different framework in which social tipping could emerge spontaneously, without the need for any critical mass of committed individuals. This can be driven by random imitation, where individuals probabilistically copy others in proportion to the frequency of observed behaviors, rather than conforming strictly to the majority. In addition, instead of relying on a committed minority as a persistent source of novelty, we introduce a randomly exploring minority who stochastically adopts new behaviors without consistency. Using a multi-agent simulation and a Markov chain-based model, our results reveal that social tipping can arise even in the absence of any individual persistently performing a new behavior to initiate the transition. Notably, the model shows that the entire population can shift to a new behavioral state even when no individual initially adopts the new behavior. Unlike previous models, our framework captures a novel dynamic in which the system exhibits spontaneous trend cycles, wherein dominant behaviors are periodically replaced by new ones over time without any deliberate intent or external intervention. Taken together, our findings suggest how individual-level randomness in both imitation and innovation drives tipping and cyclical changes in social conventions without requiring committed minorities, offering new insights into the collective dynamics.

Keywords : Social dynamics, Collective behavior, Imitation, Multi-agent system, Markov chain

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P-530

Population-level encoding of mixed tones from the auditory neural assemblies

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Understanding how the auditory cortex encodes complex sounds is essential for decoding neural representations of acoustic information. We conducted in vivo calcium imaging in the primary auditory cortex (A1) of C57BL/6 mice using AAV-CaMKII-GCaMP8f and a Prism lens based Miniscope system. Mice were passively presented with pure tones (4–32 kHz, 0.5-octave steps) and two-tone combinations (mixed tones). Population activity was analyzed by calculating average firing rate vectors for each sound, followed by agglomerative hierarchical clustering. Clustering revealed distinct subpopulations of neurons that responded either positively or negatively to specific pure tones. Notably, in response to mixed tones, these neurons preserved their polarity with respect to the component pure tones. This suggests that the encoding of mixed stimuli may be largely explained by linear or nonlinear summation of responses to individual tones. To examine whether such selectivity requires recurrent dynamics, we implemented a recurrent neural network (RNN) model with 64 hidden units and no within-layer connections. Despite the absence of recurrence, the model reproduced the polarity-preserving responses observed in biological data. These findings suggest that input-driven properties, rather than recurrent computations, may predominantly shape population-level auditory encoding in passive listening states, at least for simple tone combinations.

Keywords : Auditory cortex, In vivo calcium imaging, Neural population dynamics, Mixed tone encoding, Recurrent neural network model

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P-531

One-Shot Preconditioning for Robust and Efficient Neural Learning

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Learning, in both biological and artificial systems, depends on synaptic modification driven by feedback signals that correct errors. Early-stage feedback, particularly its directional precision, critically influences learning accuracy and efficiency. Backpropagation, the foundation of modern machine learning algorithms, updates synaptic weights using precisely computed gradients. Yet this method enforces strict symmetry between forward and backward connections throughout training, incurring high memory demands, synchronization overhead, and vulnerability to noise and adversarial perturbations. Feedback alignment (FA) offers an alternative by replacing exact weight transport with random fixed feedback connections, enabling approximate error correction at significantly lower computational cost (Lillicrap, 2016). However, this simplification sacrifices early guidance, leading to slower, less stable convergence and reduced accuracy. To bridge the above crucial gap, we propose Initial Feedback Alignment (IFA)—a one-time soft alignment between forward and backward weights at initialization. This single preconditioning step establishes a reliable initial teaching signal that corrects the noisy, misdirected gradients of random feedback and drives rapid, stable error minimization across the loss landscape. Subsequent spectral analyses reveal that such pre-alignment smooths error flow and promotes convergence toward flatter minima, thereby enhancing both trainability and generalization. Furthermore, as training progresses, IFA permits gradual relaxation from its initial alignment, enabling adaptive learning dynamics that improve robustness to input corruption and resistance to adversarial attacks. These findings demonstrate that a single soft alignment at the outset leverages early guidance to efficiently shape the entire learning

trajectory and achieves stable, resilient performance in a biologically plausible manner.

Keywords : Feedback alignment, Error propagation, Synaptic preconditioning, Adversarial robustness, Biologically plausible learning

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P-532

Oxytocin dynamically gate prefrontal-amygdala-auditory networks to enable selective processing of socially salient cues in awake mice

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Neuromodulators must flexibly reshape large-scale brain dynamics to allow selective access to behaviorally relevant information. Here, we show that oxytocin acts as a dynamic gating agent, transiently reconfiguring mesoscopic brain network dynamics to enhance processing of socially salient auditory cues in awake mice. We employed CBRAIN–a wireless neural recording system for social animal developed in our lab (Kim et al., 2020)–to record local field potentials (LFPs) from the medial prefrontal cortex (mPFC), basolateral amygdala (BLA), and auditory cortex (A1). Using these recordings, we characterized resting-state network states following intraperitoneal oxytocin injection and compared them to those observed in saline-treated controls. Oxytocin induced broadband hypoactivity–significant suppression of spectral powers across θ_{high}, β, and γ bands–accompanied by reduced inter-regional coherence and Granger causality among mPFC, BLA, and A1. Specifically, oxytocin enhanced bottom-up influence from A1 to mPFC (θ_{high}) while suppressing top-down mPFC→A1 and bidirectional BLA mPFC coupling, indicating selective attenuation of internal predictive and affective signals. In parallel, oxytocin increased the spectral slope, consistent with reduced cortical excitability and enhanced inhibitory tone, consistent with known synaptic and circuit effects of oxytocin in the cortex (Froemke and Young Annu Rev Neurosci 2021). All effects were transient and reversible, delineating a temporally bound “gating window” during which internal dynamics are suppressed and sensory pathways reorganized. Taken together, these results support a model in which oxytocin does not globally amplify neural activity but instead establishes a state-dependent, directionally asymmetric network mode aligned with selective social signal processing. This oxytocin-driven dynamic gating mechanism enables the brain to flexibly balance internal and external information flow in a behaviorally adaptive manner.

Keywords : oxytocin, dynamic gating, resting state, oscillations, network connectivity

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P-533

Reconstructing latent neural attractors during motor learning with false-nearest-neighbor-regularized autoencoders

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Withdrawn

Recent advances in the study of neural population activity emphasize analyzing neural ensemble activity—also referred to as the neural manifold—rather than single-neuron tuning. However, limited simultaneous access to the full neural population and multiple brain regions with conventional techniques restricts the application of dynamical systems analysis. To overcome this partial observability, we applied a novel autoencoder framework regularized by a false-nearest-neighbor (FNN) loss function to reconstruct latent full attractors from population activity in the primary motor cortex (M1) of rats performing a 13-day motor learning task. This method yielded parsimonious yet faithful representations of neural dynamics, capturing the full attractor dimension without redundant dimensions. Our results show that the variance of the attractor decreases during the middle stage of learning. This attractor convergence then diminishes again as learning proceeds to the later stage, suggesting an involvement of motor cortex dynamics in the transition from manifold exploration to manifold consolidation. Moreover, inputs from other brain regions are implied through decreased effective dimensions, which is supported by infered input from sequential auto-encoders. Overall, our framework demonstrates robust nonlinear analysis of neural state trajectories, even under sparse experimental observations.

Keywords : Neural manifold, Autoencoder, Attractor reconstruction, Motor learning, False-nearest-neighbor

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P-534

Neural correlates of interleaved practice explaining superior motor learning

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The choice of motor practice structure significantly affects motor learning. The contextual interference (CI) phenomenon highlights the motor learning advantage afforded by using interleaved practice (IP) compared to repetitive practice (RP) when acquiring multiple motor skills concurrently. Despite robust behavioral advantages of IP, limited studies has explored the neural mechanisms underlying IP’s advantage. To address this gap, we conducted a systematic review on neural correlates of the CI effect in motor learning. Included studies directly compared IP and RP and reported both behavioral and neuroimaging outcomes. Ten studies met our inclusion criteria, spanning 1979–2025: eight used functional magnetic resonance imaging (fMRI), one diffusion-weighted imaging (DWI), and one magnetic resonance spectroscopy

(MRS). fMRI studies showed that IP enhanced inter-regional connectivity, especially between the contralateral dorsolateral prefrontal cortex (DLPFC) and premotor cortex (PMC). During retention, IP elicited reduced BOLD signals in the DLPFC, PMC, and posterior parietal cortex, suggesting more efficient neural processing. With extended IP, connectivity expanded to the supplementary motor area, caudate nucleus, cerebellum, and parietal regions, reflecting practice-dependent neural networks. DWI findings linked IP-related retention performance correlated with fractional anisotropy (FA) in the corticostriatal tract from the left sensorimotor cortex to the posterior putamen. RP was associated with FA in the right forceps minor and lateral prefrontal pathways. MRS showed decreased GABA+ in the occipital cortex after IP, but increased after RP, indicating distinct neurochemical plasticity. Behavioral outcomes consistently showed better learning with IP than RP, aligning with neuroimaging results. Final analysis will use activation likelihood estimation meta-analysis to identify converging activation patterns.

Keywords : Contextual interference, Interleaved practice , Practice structure, Motor learning, fMRI

P-535

A hypothalamus-to-dorsal pons circuit for palatability-guided consummatory behaviors

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Animals engage in diverse consummatory behaviors like feeding and drinking in response to homeostatic deficits. *Vgat*-expressing GABAergic neurons in the lateral hypothalamus (LH^{Vgat}) are critical for food and water consumption. However, how these neurons are modulated by internal state or palatability and guide diverse consummatory behaviors remains elusive. Using two-photon calcium imaging, we identified a subpopulation of LH^{Vgat} neurons that encode consumption regardless of the type of ingesta. These neurons are scaled based on food palatability and homeostatic need. Notably, the palatability encoding is attenuated by GLP1R agonism. Consumption-encoding LH^{Vgat} neurons preferentially encode food-reward delivery and lick response, rather than food cues. Furthermore, we demonstrated that LH^{Vgat} projections to the peri-locus coeruleus (periLC) in the dorsal pons are activated during liquid food and water consumption, not by the olfactory food cue. Closed-loop optogenetic stimulation of LH^{Vgat}-periLC projections elicited voracious feeding and drinking. Together, these findings reveal how hypothalamic circuits integrate distinct physiological states and orchestrate diverse ingestive behaviors through hindbrain targets.

Keywords : Consummatory behavior, Palatability, Hypothalamus, Dorsal pons, Two-photon calcium imaging

P-536

Brain's dynamic functional connectivity predicts general attention

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Attention is a fundamental cognitive ability that allows the brain to prioritize meaningful stimuli over distractions. Despite its dynamic nature, most fMRI studies have focused on static functional connectivity (sFC). i While sFC has been shown to predict general attention, the contribution of temporal variability remains unexplored. ii This study investigates whether temporal variability can predict general attention and generalize across tasks. We analyzed 89 participants' task fMRI data while they performed three attention tasks. Dynamic functional connectivity (dFC) was generated by computing sliding-window Pearson's correlations between all pairs of nodes. General attention was defined as the mean of z-scored performance across three tasks. Connectome-based predictive modeling (CPM) was used to predict general attention from dFC, with cross-task prediction assessing model generalizability. Models were trained and evaluated using 10-fold cross-validation. We also explored a combined sFC+dFC approach to test whether it could improve prediction. The dFC-based models successfully predicted general attention within and across different tasks. Within-task predictions were significant for gradCPT($r = 0.35$, $p<0.001$) and VSTM ($r = 0.28$, $p <0.01$). In cross-task predictions, models better predicted general attention when tested on gradCPT-FC, regardless of the training task (all r's >.35, all p's <.001). While the models based on combined sFC and dFC did not substantially improve predictive power compared to using sFC alone, they resulted in enhanced statistical power. All nine models with sFC and dFC yielded highly significant results (all p's < .001). Our results suggest that moment-to-moment fluctuations in brain connectivity may provide complementary and generalizable neural markers of attention, beyond those identified through static connectivity analyses alone.

Keywords : Dynamic functional connectivity, Task-fMRI, General attention, Connectome-based predictive Modeling(CPM), Sliding-window

P-537

Selective attention in spiking neural network

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Introduction Selective attention is considered a key cognitive process that enables organisms to prioritize goal-relevant inputs. In this study, we implemented an attention mechanism in a spiking neural network composed of two-compartment neurons, where the excitability of each neuron was modulated based on task-related cue signals. We trained and tested the model using an ambiguous input dataset designed to assess the model's ability to selectively attend to task-

relevant input features and correctly identify the target. Methods Our network model is composed of an input layer, three hidden layers, an output layer, and a small group of attention signal neurons. We trained the model using an overlapped MNIST dataset, where each image contains two semi-transparent, superimposed digits. The model learned to allocate attention to the target digit based on the cue provided by the attention signal neurons. As hidden-layer neurons receive the attention signal, their baseline membrane potentials are adjusted, modulating their excitability to enhance or suppress neuronal responses. Results The model achieved 79% accuracy with the overlapped MNIST dataset, showing a significant improvement in resolving reversed predictions (selecting the incorrect digit from the overlapping pair) compared to a model without an attention mechanism. Also, the model could generate a representation of the target digit when the attention signal was applied. Moreover, layer 3, the deepest layer, emerged as the most effective target of attention, with the most distinct divergence pattern in the attention weight matrix. Discussion Our results show that the attention mechanism helped the model selectively focus on target digit. Also, the attention altered cell firing patterns, working with feedback input. Layer-wise analysis revealed that attention exerted the strongest influence in the deepest hidden layer which resonates with biological evidence that higher cortical areas play a central role in attention.

Keywords : Selective attention, Top-down attention, Spiking neural network, Neuromodulation, Canonical microcircuit

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P-538

Long-Tail Structure Enables Functional Flexibility in Brain Networks

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Neuronal connectivity in the brain is structurally asymmetric, with diverse features such as connection degree, inter-neuronal distance, and synaptic strength following long-tail distributions. These patterns reflect the presence of hub neurons and rare but strong or long-range connections, indicating that such heterogeneity may play a crucial role in shaping brain function. However, the influence of these asymmetric structures on temporal neural dynamics at the cellular level remains insufficiently understood. In this study, we conducted a high-resolution connectivity evaluation in the zebrafish brain by integrating calcium imaging (Ca^{2+} imaging) data with synapse-level structural information. This enabled the construction of both structural connectivity (SC) and functional connectivity (FC) networks at single-cell resolution. Statistical analysis revealed that SC exhibits heavy-tailed distributions, and that inter-regional connectivity includes both high–high and high–low degree connections, underscoring the network's structural diversity. To investigate how this architecture influences time-varying neural interactions, we tracked functional gradients—low-dimensional representations of FC—over time. We found marked spatial heterogeneity in gradient dynamics, with frontal regions showing greater temporal variability than occipital areas. To assess causality, we developed a large-scale spiking neural network model (~30,000 neurons) in which we systematically flattened long-tail features in SC while preserving its topology. Only networks retaining moderate asymmetry reproduced realistic transitions between functional segregation and integration. These results demonstrate that structural asymmetry, revealed through fine-scale connectivity evaluation, is essential for regulating dynamic functional gradients in the brain.

Keywords : long-tail structure, large-scale simulation, zebrafish

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P-539

Differential Value Coding in CA1 and Medial Entorhinal Cortex

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Although the hippocampal formation is known to process value-related information, how different subregions work together to represent value remains unclear. In this study, we compared value-related activity in the medial entorhinal cortex (MEC) and CA1. We trained Wfs1-Cre mice in a classical conditioning task using odor cues associated with three levels of reward probability (0%, 25%, and 75%). During this task, we measured the activity of CA1 pyramidal neurons and MEC layer 2 pyramidal (L2P) neurons using in vivo calcium imaging. Both regions exhibited significant value signals, but three differences emerged. First, population activity in CA1 increased monotonically as a function of value, whereas MEC L2P neurons exhibited decreasing activity. Second, although both regions preserved similar value-dependent activity across the two cue sets at the population level, only individual MEC L2P neurons maintained consistent value-related responses, unlike CA1 neurons. Third, specific odor cue-selective responses were stronger in CA1 than the MEC L2P neurons. These differential activity patterns suggest that the two regions may employ distinct neural coding strategies to represent value. Future investigations into the functional interactions between these regions may reveal how value signals are organized and integrated within the MEC-CA1 circuit.

Keywords : Entorhinal cortex, Hippocampus, Reward, Value, Classical conditioning

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P-540

Encoding of vocal communicative contexts by marmoset prefrontal neurons

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Human speech is characterized by our ability to flexibly adapt its structure and acoustics across varying contexts, including conversational

history, interpersonal proximity between speakers and listeners, and ambient noise levels. This flexibility requires the integration of communicative contexts with vocal motor commands. Although the frontal cortex has been demonstrated as a key neural substrate for vocal planning, initiation, and articulation, it remains unknown how this region incorporates vocal motor commands with communicative contexts. To uncover the neural computations underlying this process—particularly at the single neuron level—we recorded local field potentials (LFPs) and single-unit spiking activity from the prefrontal cortex of marmosets, a primate species exhibiting context-dependent vocal flexibility, while they produced vocalizations under experimentally controlled contexts. We specifically manipulated two behavioral contextual dimensions: social distance from a partner monkey and environmental noise. Consistent with humans, marmosets demonstrated context-dependent vocal behavior, modifying call type usage and acoustic properties. Prefrontal activity increased immediately before vocalization (pre-vocal activity), with theta and high-gamma band power in LFPs encoding call type information. At the single-neuron level, spiking activity was found to encode both call types and experimental contexts. Population dynamics analysis revealed distinct neural trajectories across contexts during the pre-vocal period. Notably, classification based on decoding these trajectories showed that social distance contexts are more distinct than environmental noise contexts, suggesting a greater prefrontal contribution to social contextual integration. Altogether, these findings suggest that the prefrontal cortex integrates vocal motor commands with communicative contexts, with a preferential role in processing social contexts over environmental ones.

Keywords : Non-human primate, Vocal motor control, Vocal flexibility, Prefrontal cortex, Social communication

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P-541

Neuromodulation supports projection-specific roles of the anterior cingulate cortex in visuomotor transformation

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The anterior cingulate cortex (ACC) projects to both the visual cortex (VC) and the dorsomedial striatum (DMS), regions involved in perceptual behavior. However, how distinct ACC projections contribute in parallel to visual decision-making remains unclear. To investigate this, we identified anatomically segregated ACC populations projecting either to the VC (ACC→VC) or the DMS (ACC→DMS) using dual retrograde tracing. We then performed in vivo Ca^{2+} imaging of these populations while mice engaged in a visual detection task. Notably, ACC→DMS neurons responded to visual stimuli only when the mice made a correct behavioral response, whereas ACC→VC neurons responded consistently, regardless of behavioral outcome. These findings suggest that ACC→DMS neurons facilitate visuomotor transformation, while ACC→VC neurons primarily contribute to sensory processing, rather than to the transformation itself. To explore the neuromodulatory mechanisms underlying the behavioral output-dependent visual activity of ACC→DMS neurons, we recorded photometry signals of acetylcholine (ACh) and dopamine (DA), two neuromodulators known to influence frontal cortical dynamics. ACh and DA levels in the ACC were higher when mice correctly responded to visual stimuli compared to when they missed, suggesting that these neuromodulators enhance ACC→DMS activity supporting visuomotor transformation. Systemic infusion of ACh or DA receptor antagonists further revealed that both muscarinic (mAChR) and nicotinic ACh receptors (nAChR) are required for perceptual behavioral responses, whereas D1-like DA receptors are essential for spontaneous responses. Additionally, single-cell RNA sequencing of ACC→DMS neurons showed high expression of the M1 muscarinic ACh receptor (M1 mAChR), suggesting direct cholinergic modulation of this projection via M1 mAChRs. Together, our results indicate that ACC→DMS neurons mediate visuomotor transformation through distinct cholinergic and dopaminergic modulation.

Keywords : Anterior cingulate cortex, Visuomotor transformation, Acetylcholine, Dopamine, Mouse

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P-542

Who do you want to team up with? How reward probability and partner support guide decision-making

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Withdrawn

Traditional behavioral economics and neuroeconomics frame decision-making as evaluating the expected value of each option, typically calculated as the reward magnitude multiplied by the probability of obtaining that reward. However, this conventional framework overlooks the decision-making process that a reward often depends on an individual's capability to pursue and secure it effectively, referred to as an affordance. Since the affordance depends on both one's own competence and external collaborative support. Thus, a comprehensive model must integrate not only individual competencies but also collaborative affordances into the evaluation of expected outcomes. Here, we investigate whether individuals weigh both collaborative support and reward probability when making decisions in a collective hunting task. Participants (n = 12) selected between two partners who provided varying levels of assistance by reducing the speed of moving targets during pursuit. Each partner differed systematically in how effectively they facilitated target capture (competency-based affordance) and the likelihood of successfully obtaining the reward (reward probability). The task employed a block design wherein partner characteristics changed implicitly without explicit notification, prompting participants to continuously update their expectations and decisions based on observed partner performance and historical reward outcomes. Participants were sensitive to both the history of reward probability and variations in partner-specific facilitation that affected their success during the hunt. To understand how these factors jointly influenced decision-making, we examined whether their effects combined additively or multiplicatively. The results indicated a multiplicative interaction: reward probability scaled the influence of perceived partner competency, shaping how individuals translated their assessment of partner effectiveness into behavioral commitment under uncertainty.

Keywords : Decision-Making, Pursuit Task, Competency, Partner Selection Task, Neuroeconomics

P-543

Number concepts and Bayesian inference in Large Language Models and Humans

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Recent Large Language Models (LLMs) have shown impressive performance across a wide range of reasoning tasks. One of the domains at which LLMs particularly excel is mathematical and numerical reasoning. Yet it is unclear how LLMs achieve this reasoning capacity and how they are different from humans. To address this, we compare LLM and human in a structured inference task for number concept. In the task ('number game'), subjects infer a numerical concept behind a set of example numbers (e.g., {2, 4, 6}) and predict whether a new target number (e.g., 8) belongs to the same concept. In prior work (Bigelow & Piantadosi, 2016), human responses reflected both rule-based generalization, with sparse responses at specific target numbers (e.g., multiples of 5 for {15, 70}), and interval-based generalization, with responses concentrated near the example numbers (e.g., {15, 11}). Similarly, GPT exhibited both rule- and interval-based generalizations. But its behaviors were distinct from humans in three aspects: first, GPT relied more on the rules than humans do. Second, GPT did not generalize from one example number as humans do in one-shot fashion. Third, GPT showed evidence for use of more compositional numerical concepts. We next used a Bayesian model to better understand how GPT is different from humans. In the model (Tenenbaum, 1999), each number concept is assigned a prior probability, which is then combined with its likelihood for example numbers to compute the posterior probability. The model captured key features of human behavior including flexible generalization based on numerical rules or intervals. Consistent with this, human behaviors aligned better with the model than GPT's. Model fits to GPT responses also confirmed a stronger reliance on rule-based reasoning compared to humans. These findings suggest that LLMs developed rich and complex number concepts and used them in a Bayesian manner for numerical reasoning, despite their quantitative difference from humans.

Keywords : Bayesian inference , Number concepts, Numerical reasoning, Large Language Models (LLMs), Human-AI comparison

P-544

Disrupted Synchrony of Egocentric Spatial Cells in 5XFAD Mouse Model of Alzheimer's disease

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Neurons that represent egocentric space have been found in the retrosplenial cortex (RSC), which are important in constructing an egocentric cognitive map. Interestingly, the RSC has also been reported to be one of the earliest brain regions affected by amyloid beta accumulation in Alzheimer's disease (AD), characterized by deficits in episodic memory and spatial navigation. However, it is yet unknown how amyloidosis in AD affects egocentric neural representation. To address this question, we performed *in vivo* Ca^{2+} imaging of GCaMP-expressing excitatory neurons in the RSC while the control mice and 5XFAD mice freely explored a square open chamber. Our results reveal that there is a significant disruption in neuronal synchrony among egocentric spatial cells in 5XFAD mice. In addition, functional clustering of neurons became more dispersed and fragmented in the AD model, and cluster identity was unstable upon re-exposure to the same environmental context. These findings suggest that amyloid pathology disrupts the temporal coordination and contextual stability of egocentric spatial representations in the RSC.

Keywords : Synchrony, Alzheimer's disease, Egocentric spatial representation, Retrosplenial cortex, Calcium imaging

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P-545

Neural and behavioral correlation of mating decision-making in female mice

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Female mice face critical trade-offs during mating, balancing reproductive benefits with potential social and physiological costs. To make informed decisions, they engage in social behaviors such as facial touches and sniffing, to gather information about potential mates before behavioral acceptance or rejection. However, the circuit-level neural dynamics underlying this decision-making process remain poorly understood. To investigate this, we employed CBRAIN device – a wireless neural recording system for freely moving social animals - to record local field potentials (LFPs) from the medial prefrontal cortex (mPFC), basolateral amygdala (BLA), and nucleus accumbens (NAc). Male-female mouse pairs were tested in a structured interaction paradigm comprising three phases: habituation (5 min), restricted interaction through acrylic barriers (10 min), and free interaction (5 min). During the restricted phase, mice could engage social information gathering behaviors through the barriers. In the free interaction phase, females could either accept or avoid male advances. Behavioral data were collected using overhead and under-floor cameras, a depth sensor, and ultrasonic vocalization (USV) microphone. Additionally, we developed a custom GUI-based tagging interface for manual micro-behavior annotation. During the restricted phase, both sexes actively investigated each other. In the free interaction phase, while most males initiated courtship, not all exhibited active approaches. Female responses varied: many initially avoided the male, with some later transitioning to approach behaviors, while others maintaining avoidance. Our ongoing analysis focuses on linking neural activity during the restricted phase to subsequent female behavioral outcomes (avoidance vs. acceptance). Specifically, we aim to quantify the changes of theta (4-7 Hz), beta (13-30 Hz), and gamma (40-120 Hz) band activity using burst detection and cross-frequency coupling analyses.

Keywords : Male-female interaction, Avoidance, Acceptance, Socio-sexual decision making, Local field potential (LFP)

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Translational and Clinical Neuroscience P-546~P-564

P-546

Grabody B, an IGF1R-Targeting Molecular Shuttle, Enhances Brain Penetration via Multiple Novel Transcytosis Pathways

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Efficient delivery of therapeutic antibodies across the blood-brain barrier (BBB) is a critical challenge in neurotherapeutics. Insulin-like growth factor 1 receptor (IGF1R) is a receptor tyrosine kinase highly expressed in brain microvessels and neurons in both rodents and humans. Grabody B, an IGF1R-targeting molecular shuttle, enhances the BBB penetration by distinct transcytosis mechanisms. Unlike conventional monoclonal antibodies (mAbs) that are largely confined to brain surfaces, ventricles, and perivascular regions, Grabody B-fused bispecific antibodies (GB BsAbs) penetrate deep into the brain parenchyma, achieving more effective target engagement. Imaging mAb and GB BsAb signals after brain clearing demonstrates that GB BsAbs distribute extensively throughout the brain, including deeper cortical layers. GB BsAbs rapidly internalize into human brain microvascular endothelial cells (HBMECs) within 30 seconds, closely associating with filamentous actin (F-actin). This rapid uptake is distinct from transferrin receptor (TfR)-based shuttles, which internalize more slowly through Clathrin-dependent pathways and predominantly colocalize with the early endosomal marker Rab5, resulting in degradation in late endosomes. In contrast, Grabody B utilizes multiple internalization routes, including Clathrin, caveolin, and fast endophilin-mediated endocytosis (FEME), as evidenced by strong colocalization with endophilin A2, and minimal overlap with Rab5, potentially avoiding rapid lysosomal degradation. This unique mechanism may explain the deep parenchymal distribution and sustained brain penetration observed in animal models. These findings establish Grabody B as a versatile and efficient platform for delivering therapeutic antibodies to the brain, offering new opportunities for treating neurological diseases through improved target engagement and enhanced tissue penetration.

Keywords : BBB, BBB shuttle, Antibody therapeutics, Transcytosis, Grabody B

P-547

The development of new dopamine with less toxicity and less autoxidation

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Levodopa (L-DOPA), the gold standard drug for Parkinson's disease, supplements dopamine but induces side effect called L-DOPA-induced dyskinesia (LID) because of its toxicity. In our recent study, we proposed dopamine-modified hyaluronic acid (DA-HA) as a dopamine mimetic with less autoxidation and preserved dopamine functionality-two essential criteria for developing safer dopamine replacements. However, DA-HA's high molecular weight limits its permeability to cross the blood-brain barrier (BBB). To resolve these problems, we selected five materials with a similar structure to dopamine. Here, we report a series of evidence that 2-PTA and DA-HA, which are new dopamine candidates, show similar functionality as dopamine and low neurotoxicity with no autoxidation. Using a genetically encoded GPCR-activation-based DA ($GRAB_{DA2m}$) sensor, we evaluate functionality as dopamine. 1 mM 2-PTA as well as 1 μM DA-HA showed identical peak amplitude of GFP transients as 20% GFP transients induced by 1 μM dopamine. However, tyrosine, paracetamol, N-methyltyramine and phenylalanine showed no responsiveness on GFP transients of $GRAB_{DA2m}$. After 72 h incubation, 100 μM DA-HA showed low autoxidation level and 100 μM 2-PTA showed no autoxidation compared to that dopamine did show autoxidation. Moreover, both 100 μM 2-PTA and DA-HA exhibited low neurotoxicity. Our study suggests that 2-PTA and DA-HA, with their dopamine-like functionality and low neurotoxicity, represent promising tools for treating Parkinson's disease.

Keywords : Dopamine , L-DOPA, BBB, autoxidation, function

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P-548

Regional transcriptomic differences of cortical dysplasia in human focal cortical dysplasia

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Focal cortical dysplasia (FCD) is a structural and cellular abnormality of the cortex that is a common pathology for drug-resistant epilepsy. However, the transcriptomic characteristics in cortical dyslamination and their role in hyperexcitability are poorly understood. In this study, brain tissues with cortical dyslamination were selected from fresh surgical specimens of epilepsy patients through anti-NeuN staining to assess neuronal arrangement. We performed spatial transcriptomics analysis using the Nanostring CosMx spatial molecular imager with a 6000 plex RNA panel, and analyzed the differences between regions

with and without cortical dyslamination using the AtoMx platform. Cell segmentation was performed using an in-house AtoMx pipeline optimized for brain tissue, and cell typing was conducted with the InSituType supervised method, referencing the CosMx brain cell atlas. Regions of interest, including cortical dyslamination and adjacent normal cortex, were manually selected based on IHC images. Gene ontology(GO) analysis of differentially expressed genes(DEGs) revealed that genes associated with glutamatergic synapses in the cellular component were upregulated in the FCD region. This may reveal specific genes that play critical roles in the dysregulation of structural development and suggest a target for new treatment options for patients with refractory epilepsy.

Keywords : Focal cortical dysplasia, Spatial transcriptomics, Epilepsy

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P-549

Manipulating autophagy pathways strengthens the tumor-killing capabilities of photodynamic therapy for glioblastoma

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Glioblastoma (GBM) is an aggressive brain tumor with high recurrence rates. Photodynamic therapy (PDT) is a promising treatment, but its efficacy is often limited by protective mechanisms like autophagy, which promotes cancer cell survival. This study investigated if modulating autophagy could enhance PDT's anti-tumor effects in GBM. Using C6 glioma cells for *in vitro* and *in vivo* rat models, we evaluated PDT efficacy when combined with an autophagy inducer (Rapamycin) or an inhibitor (Bafilomycin A1). *In vivo*, the combination of Bafilomycin A1 and PDT showed markedly superior tumoricidal activity and prevented tumor regeneration, consistently outperforming PDT alone or with Rapamycin. The Rapamycin combination, in contrast, was ineffective at inhibiting regrowth. This discrepancy may be due to poor drug delivery; our results suggested Rapamycin has limited brain penetration, unlike the photosensitizer (Ce6) which crossed the compromised blood-tumor barrier (BTB). *In vitro*, the drugs alone were not significantly cytotoxic. Our findings confirm that autophagy is a critical pro-survival mechanism for GBM cells under PDT stress. Therefore, inhibiting autophagy with Bafilomycin A1 is a powerful synergistic strategy to potentiate PDT for GBM. This work highlights that both the biological target and drug delivery are crucial for developing effective therapies and demonstrates the Bafilomycin A1-PDT combination's strong potential for clinical translation.

Keywords : Glioblastoma (GBM), Photodynamic therapy (PDT), Autophagy, Cobination therapy, Blood-Brain Barrier (BBB)

P-550

Standardization of brain lesioning in real time thermal monitoring radiofrequency ablation by sEEG electrodes

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Background: Epilepsy surgery is the most effective treatment for drug-resistant epilepsy patients although various antiepileptic drugs have been developed. Radiofrequency (RF) ablation is widely used for epilepsy surgery, and its safety and efficacy have been demonstrated. However, most existing RF ablation devices lack the capability for real-time thermal monitoring via sEEG electrodes. Standardizing lesion volume by thermal dose could further enhance the safety and efficiency of this therapy. In this study, we aim to develop a new RF thermal ablation device with real-time thermal monitoring through sEEG electrodes. Method: Thermal ablation was performed using a radiofrequency device developed by Starmed. Ablations were conducted at temperatures of 60°C, 70°C, and 80°C for durations of 10 and 30 seconds. A PMT sEEG electrode was modified for use in a monopolar setup, and ablation was performed using a two channel. The safety and lesion sizes were evaluated using Magnetic Resonance Imaging (MRI), and H&E staining was performed to assess the lesion variations between lesions formed under the same parameter. Result: MRI confirmed well-formed, safe lesions in all experimental conditions. Lesion size increased with higher temperatures and longer ablation durations. The experimental animals remained alive throughout the procedures. H&E staining revealed clear border lines between the lesion and surrounding tissue, and the variation between lesions formed under the same parameter was minimal. Conclusion: Although RF ablation is widely used, there is limited information on the lesion size formed at specific temperatures. This device enables real-time temperature monitoring, allowing for safer ablation procedures and quantification of temperature-dependent lesion changes. This technology holds promise for safer surgeries and more precise lesion formation in future clinical applications. Furthermore, it holds potential for effective treatment in patients with epilepsy.

Keywords : Epilepsy, Radiofrequency ablation, sEEG

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P-551

AI-powered 3D pathology provides novel visualizations and quantifications with clinical diagnostic value

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Background and Aim: Accurate diagnosis and understanding of gastrointestinal (GI) diseases such as ulcerative colitis (UC) and Hirschsprung's disease (HSCR) remain limited by traditional two-dimensional (2D) histopathology, which cannot fully capture the complex three-dimensional (3D) architecture and dynamic microenvironment of GI tissues, especially the enteric nervous system (ENS). Methods: We developed an integrated platform combining tissue-clearing 3D imaging with artificial intelligence (AI)-based analysis. Colon biopsy samples from UC patients and full-thickness surgical specimens from HSCR patients were imaged volumetrically. AI algorithms were trained to detect and quantify ENS components, epithelial crypts, and other structures. The performance was compared to conventional 2D histology. Results: The AI-powered 3D imaging revealed detailed ENS networks from mucosa to serosa, often missed in 2D. In UC biopsies, crypt distortion and ENS changes were quantitatively assessed. In HSCR tissues, full-thickness ENS architecture and aganglionic zones were visualized. This approach significantly improved diagnostic accuracy, allowed earlier detection of pathological changes, and uncovered spatial relations critical for understanding disease mechanisms. Conclusions: Integrating 3D imaging with AI overcomes limitations of 2D histology, providing scalable and objective GI tissue analysis. This method bridges clinical diagnostics and basic research, offering potential to revolutionize GI disease diagnosis, improve patient care, and advance translational neurogastroenterology research.

Keywords : Enteric nervous system, Tissue clearing, Artificial intelligence, Ulcerative colitis, Hirschsprung disease

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P-552

Suppression of Astrogliosis and Significant Functional Recovery in Traumatic Spinal Cord Injury via Combined Pharmacotherapy and Rehabilitation

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Traumatic spinal cord injury (SCI) results in neuronal death, glial scar formation, and impairment of motor and sensory functions. In the United States, approximately 79,000 spinal fractures occur annually, with nearly half leading to complete paralysis. Despite extensive efforts to promote spinal cord regeneration, current treatment strategies remain limited to pain management and rehabilitation, with no available therapies that induce actual functional recovery. To address these limitations, this study proposes an integrated therapeutic approach. Pathologically, SCI progresses through three phases: acute, subacute, and chronic. In the acute phase, astrocytes become reactivated in response to stimuli such as H_2O_2 and ATP. During the subacute and chronic stages, reactive astrocytes form a glial barrier and release cytokines and chemokines that trigger immune responses. H_2O_2 and GABA produced in this environment contribute to further neuronal damage and inhibit neural regeneration (Lee, Jang et al. 2025). In this study, we used the newly developed H_2O_2-decomposing peroxidase enhancer KDS12025 (Won, Lee et al. 2024) and the MAO-B inhibitor KDS2010 to suppress reactive astrogliosis, thereby reducing the release of H_2O_2 and GABA that contribute to neuronal toxicity and hinder regeneration. To promote functional recovery, these pharmacological treatments were combined with a structured rehabilitation protocol. Mice underwent treadmill training at a speed of 3 m/min for 20 minutes, five times per week, for 6 weeks. As a result, animals receiving the combined treatment (KDS12025 + KDS2010 + Rehab) showed a significant improvement in locomotor performance, achieving a Basso Mouse Scale (BMS) score of 3.5, compared to 1.1 in the vehicle-treated rehabilitation group. These findings suggest that a multimodal therapeutic strategy targeting both molecular and functional pathways may offer a promising avenue for future regenerative treatments for SCI.

Keywords : Spinal cord injury, Glial scar formation, Neuroinflammation, astrogliosis, Combined therapy

P-553

Functional network alterations among tau-based alzheimer's subtypes and their association with cognitive decline

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Alzheimer's disease (AD) is a heterogeneous neurodegenerative disorder, with variable cognitive trajectories shaped by the regional distribution of tau pathology. However, the functional brain network mechanisms underlying this heterogeneity remain unclear. In this study, we applied the Subtype and Stage Inference (SuStaIn) model to tau PET imaging data to identify four tau-based subtypes. Resting-state functional MRI (rs-fMRI) was used to assess subtype-specific alterations in functional brain architecture through gradient mapping and graph-theoretic analysis. Compared to tau-negative individuals, tau-positive participants exhibited a global reduction in functional hierarchy, as indicated by lower gradient dispersion and decreased network segregation. Subtype-level analyses revealed distinct patterns of early-stage network reorganization. The limbic-predominant subtype showed increased within- and between-network dispersion in the limbic system, which was positively associated with preserved global cognition, suggesting a compensatory response. The lateral temporal subtype demonstrated reduced local efficiency across the cortex and worse language performance, reflecting impaired regional information transfer. The posterior subtype showed disrupted hierarchical organization in the dorsal attention network, coupled with accelerated visuospatial decline. These findings indicate that the initial site of tau spread differentially shapes functional reorganization pathways across subtypes, contributing to heterogeneous cognitive trajectories. Our results highlight the importance of considering early-stage functional dynamics in AD subtyping and suggest that functional gradient and graph-based metrics may serve as candidate biomarkers for network-level vulnerability and subtype-specific intervention.

Keywords : Alzheimer's disease (AD), Tau-based subtype, Subtype and Stage Inference (SuStaIn) model, Functional gradient, Graph-theoretic analysis

P-554

GLP-1 modulates cognitive satiation via dopaminergic and hypothalamic pathways in mice and humans

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Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have emerged as highly effective treatments for obesity, influencing food-related cognition and pre-ingestive satiation. However, the precise neural mechanisms underlying their effects remain unclear. Here, we identify two distinct pathways through which GLP-1 signaling modulates feeding behavior in mice and humans: a hypothalamic circuit encoding pre-ingestive satiation and a striatal mechanism altering dopamine pathways triggered by food anticipation. We administered GLP-1RAs to obese patients and observed a heightened sense of cognitive satiation even before swallowing food. Analysis of human and mouse brain samples pinpointed GLP-1R neurons in the dorsomedial hypothalamus (DMH) as candidates for encoding cognitive satiation. Optogenetic inhibition of these neurons prolonged bout duration, whereas activation immediately terminated ingestion, confirming their sufficiency in satiation control. Using fiber photometry and micro-endoscopy, we demonstrate that GLP-1R-expressing neurons in the dorsomedial hypothalamus play a central role in pre-ingestive satiation. In addition, GLP-1RA administration increased the activity of DMH GLP-1R neurons during the pre-ingestive phase compared to saline administration, which was sustained throughout the ingestive phase. This effect was attenuated by optogenetic inhibition, confirming the necessity of these neurons in GLP-1RA-induced pre-ingestive satiation. In parallel, real-time dopamine activity in wild-type mice revealed that GLP-1RA administration suppressed dopamine levels in the nucleus accumbens at food anticipation. In vivo recording of lateral septum (LS) GLP-1R neurons revealed potentiation of calcium signal activity at the anticipatory stage. Neuroactivation of LS GLP-1R neurons suppressed phasic dopamine levels without altering tonic dopamine levels before ingestion, suggesting that GLP-1 signaling also modulates pre-ingestive food reward perception.

Keywords : GLP-1, GLP-1R agonist, Obesity, Cognition

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P-555

Potential effects of ambroxol-modified new drug in α-synuclein(A53T)-upregulated animal model of Parkinson's disease

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Parkinson's disease (PD) is characterized by dopaminergic neurodegeneration and pathological α-synuclein (α-syn) accumulation. In an adeno-associated virus-mediated [AAV-α-syn(A53T)] model of PD, we investigated the therapeutic potential of a novel small molecule, AST-X, structurally derived from ambroxol. Daily administration of AST-X via drinking water for 24 weeks markedly improved motor deficits and preserved dopaminergic markers in the substantia nigra and striatum. Notably, AST-X maintained striatal dopamine levels, indicating functional preservation of the nigrostriatal pathway. It also restored lysosomal integral membrane protein 2 expression, a lysosomal trafficking receptor for glucocerebrosidase (GCase, a key lysosomal enzyme involved in α-syn clearance), without altering its total levels. Our results demonstrate that AST-X confers neuroprotection by modulating lysosomal GCase trafficking, preserving mitochondrial function, and suppressing neuroinflammation, and may represent a novel disease-modifying strategy for PD.

Keywords : Parkinson's disease, AST-X, Neuroprotection, Lysosomal function, Neuroinflammation

P-556

Optimized imaging protocols for visualization of human dura mater

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The dura mater is the outer most meningeal layer that envelops the brain and spinal cord. It consists chiefly of densely packed collagen bundles interwoven with fenestrated blood and lymphatic vessels, fibroblasts, immune cells, and nerves. Once viewed merely as a robust mechanical shield, it is now recognized as a critical interface for neuro-immune communication, suggesting its potential vital role in neurological diseases. However, despite this growing attention, the human dura remains poorly characterized due to a research landscape dominated by rodent models. Additionally, the dura's densely collagenous composition poses technical challenges for immunohistochemical analysis. In this study, we investigated postmortem human dura using a series of optimized immunohistochemistry (IHC)-based imaging protocols. We examined the effects of different paraformaldehyde (PFA) fixation concentrations on vascular endothelial immunolabeling and tested various fluorescence quenching strategies to reduce collagen-associated autofluorescence using confocal microscopy. These methodological advances allowed high-resolution visualization of key cellular components, including vascular and immune cells. To employ lightsheet fluorescence microscopy for volume imaging and three-dimensional reconstruction of the cellular composition of the dura mater, we compared two different tissue clearing methodologies and established an optimized protocol using a modified iDISCO method. Our findings establish a robust imaging framework for the human dura. This work offers foundational tools and perspectives for advancing research in neuroimmunology, CNS inflammation, and human meningeal biology.

Keywords : Human Dura, immunohistochemistry, Confocal microscopy, Lightsheet fluorescence microscopy, Tissue clearing

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P-557

Effects of the use of mindfulness-based mobile application on sleep in nocturnal phone users

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Mindfulness Meditation (MM) is an effective non-intervention measure for improving the wellbeing of people. Previous studies indicated its effects on reducing stress, anxiety, and depression and improving sleeping. MM practice is commonly conducted in-person under the instructors' guidance. However, mobile application training programme has become a popular alternative in users with its features of less expensive and more accessible. The main goal of the study was to explore whether MM mobile application could help reduce stress and improve both subjective and objective sleep quality in extensive nocturnal smartphone users. Young adults aged 18 to 30 in Hong Kong were recruited to perform a four-week MM training by using the mobile app "Peace and Awareness". The objective and subjective outcomes of sleep were collected pre-MM and post-MM training, by using the wearable device and the self-reported questionnaire respectively. Stress condition of subjects was assessed by the Depression, Anxiety and Stress Scale 21 (DASS 21) and salivary cortisol concentration. The t-test was used to compare the pre-MM and post-MM differences of objective sleep and the cortisol level. And the Mann-Whitney U test was used to compare the self-reported sleep quality and stress level. Results showed a significant increase of light sleep percentage, the decrease of salivary cortisol level, and the improvement of self-reported sleep quality after mobile MM training. This study suggested that the use of MM mobile app could improve sleep quality in nocturnal phone user by decreasing the stress level.

Keywords : Mobile app, Mindfulness app, wearable device, sleep quality, cortisol

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P-558

Slice Based High Density Micro Electrode Array Assay for Circuit Level Evaluation in Painful Diabetic Neuropathy

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We established a high-density micro-electrode array (HD-MEA) platform to characterize electrophysiological signatures of cortical and spinal circuits in a painful diabetic neuropathy (DN) model. Male C57BL/6 J mice received five consecutive intraperitoneal injections of streptozotocin (50 mg/kg), inducing hyperglycemia and mechanical allodynia by day 28. Behavioral changes were assessed with von Frey testing and Motion Sequencing (MoSeq). Acute 300 µm slices from motor cortex and lumbar (L4/L5) spinal cord were recorded using a CMOS MEA (64×64 electrodes, 17.5 µm pitch, 10 kHz, 3dBrain, Inc). The recording protocol included a 2 min baseline, 2 min 8 mM K^+ challenge, 5 min wash, and 2 min washout recordings. Data were processed to extract spikes, LFPs, and current-source-density (CSD) maps. Extracted features included active electrode count, mean spike rate, LFP variance, 1/f slope, peak CSD sink amplitude, sink–source depth, and K^+-evoked wind-up (spinal cord slices only). DN spinal slices showed a 2.1-fold higher CSD sink amplitude and 1.8-fold greater wind-up ($p<0.01$), while motor cortex slices exhibited a 35% increase in LFP variance and a 0.18 steeper 1/f slope ($p<0.05$). CSD maps revealed superficial dorsal horn hyper-excitability without ventral involvement. This platform offers a robust, multi-parametric assay for DN-associated circuit dysfunction and provides a quantitative baseline for future dose–response and machine-learning-driven analgesic screening.

Keywords : High-density microelectrode array (HD-MEA), Spinal cord electrophysiology, Current source density (CSD), electrophysiology, machine-learning

Acknowledgements : The research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (RS-2023-00264409, RS-2023-00302281, RS-2025-00522868, RS-2025-00573499) and the Brain Pool program funded by the Ministry of Science and ICT through the NRF of Korea (RS-2023-00304323) and GIST AI Grant 2025.

P-559

Repurposing procaine and valproic acid to enhance motor recovery after spinal cord injury in rats

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Spinal cord injury (SCI) causes profound and often permanent motor deficits, and no pharmacological interventions have yet demonstrated meaningful functional recovery in the clinical setting. Drug repositioning offers a clinically pragmatic approach by utilizing compounds with established human safety profiles. In this study, we investigated the therapeutic potential of procaine and valproic acid—both clinically. In vitro experiments using primary cortical neurons subjected to hydrogen peroxide-induced injury revealed that treatment with 10µM procaine and 100µM valproic acid promoted neuronal survival and neurite outgrowth. In vivo, adult Sprague-Dawley rats underwent a moderate contusion injury at the T10 level, followed by daily intraperitoneal administration of procaine (5, 25, 100 mg/kg), valproic acid (50, 200, 400 mg/kg), or saline vehicle for two weeks. Functional outcomes were assessed using the Basso, Beattie, and Bresnahan (BBB) locomotor scale and the horizontal ladder test. Histological analyses evaluated lesion morphology and neuroinflammatory responses. Procaine-treated animals exhibited significantly improved locomotor recovery on the BBB scale compared to both valproic acid and control groups ($p < 0.01$), with earlier onset and sustained improvements over eight weeks. Histological findings included reduced lesion cavity volume and diminished ED1-positive microglial/macrophage infiltration at one week post-injury, as well as enhanced axonal preservation at eight weeks. While valproic acid showed modest neuroprotective effects, its functional benefits were less prominent. In conclusion, procaine demonstrated a superior capacity to enhance motor recovery and mitigate histopathological damage following SCI compared to valproic acid. Given its clinical availability and favorable safety profile, procaine warrants further investigation as a candidate for spinal cord repair strategies.

Keywords : Spinal cord injury, Procaine, Valproic acid, Neuroprotection, Motor recovery

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P-560

Optimized Fixation and Autofluorescence Reduction Methods for Correlative Light and Electron Microscopy in Postmortem Human Brain Tissue

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Correlative light and electron microscopy (CLEM) enables the spatial integration of molecular and ultrastructural information in biological specimens, but its application to postmortem human brain tissue is challenged by the need to preserve ultrastructure, retain antigenicity, and minimize background autofluorescence. Here, we present an optimized CLEM workflow for postmortem human medial prefrontal cortex using a modified Tokuyasu cryopreservation technique. We systematically compared three fixation regimens—(1) 4% paraformaldehyde (PFA), (2) 4% PFA with 0.2% glutaraldehyde (GLA), and (3) 2.5% GLA—and evaluated their effects on immunolabeling quality, ultrastructural preservation, and autofluorescence. Autofluorescence quenchers, sodium borohydride and Sudan Black B, effectively reduced background signals and autofluorescence within cells without compromising the fluorescence intensity of major neuronal and glial markers, although they introduced minor ultrastructural artifacts. Among the fixatives tested, 4% PFA + 0.2% GLA provided superior ultrastructural preservation compared to 4% PFA alone. This fixation also enabled high-quality CLEM imaging, yielding well-preserved neuronal ultrastructure with corresponding specific immunolabeling. Notably, the protocol allows for delayed antibody selection, enabling flexible postmortem tissue banking and retrospective molecular analysis. Together, our findings establish a robust and adaptable workflow for CLEM applications in archived human brain tissue.

Keywords : Electron microscopy, CLEM, postmortem human brain, autofluorescence, fixation

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P-561

Injection of an engineered hydrogel promotes structural tissue repair in a rat model of intracerebral hemorrhage

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Intracerebral hemorrhage (ICH) leads to irreversible tissue damage and chronic cavity formation due to hematoma formation and related secondary tissue degeneration. Long-term cystic spaces may hinder repair by inhibiting axonal growth and cell integration. In this study we aimed to apply an engineered imidazole-conjugated polymer hydrogel to ICH model to prevent chronic cavity formation and facilitate tissue repair. We first investigated the temporal evolution of lesion morphology to define an optimal window for the hydrogel intervention in collagenase-induced rat ICH model. Serial histological and MRI assessments revealed that at 7 days post-injury (dpi), lesion volume peaked with prominent edema. From 14 to 30 dpi, the lesion progressively transformed into a fluid-filled cavity accompanied by ventricular expansion, suggestive of atrophic changes due to secondary degeneration. immunohistochemical analysis demonstrated that at 7 dpi, fibronectin and GFAP signals were highly intermingled, reflecting active ECM and astrocyte interaction. This overlap declined by 14 dpi. Similarly, IBA-1$^+$ microglial/macrophage activity was highest at 7 dpi and declined, confirming the subacute inflammatory phase. According to these findings, hydrogel was injected into the lesion cavity at 7 dpi. MRI and histology in hydrogel group showed successful cavity filling, fibronectin-rich matrix formation, and astrocyte integration. Microglial presence within hydrogel-treated lesions was minimal, suggesting a localized immunomodulatory effect. However, behavioral tests (ladder rung walking, cylinder test, single-pellet reaching) revealed no significant motor recovery compared to controls. These findings identify 7 dpi as a critical time point for structural intervention and show that hydrogel enables tissue reconstruction. Nevertheless, structural repair alone was insufficient to promote functional recovery, highlighting the need for combinatorial approaches to enhance neuroregeneration.

Keywords : Intracerebral hemorrhage, Hydrogel, Regeneration, Extracellular matrix, Functional recovery

P-562

Personalized SEEG Stimulation Framework for Epileptogenic Zone Targeting Using FEM and Reciprocity Principle

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Introduction Stereoelectroencephalography (SEEG) has been widely used to identify the epileptogenic zone (EZ) in drug-resistant epilepsy. However, conventional methods often lack precision in targeting deep brain regions for each patient. This study proposes a simulation pipeline combining individual anatomical modeling and computational optimization to address this limitation. By generating patient-

specific 3D brain models and simulating SEEG stimulation, we aim to improve accuracy in identifying epileptogenic regions and inform seizure-inducing protocols to support surgical planning. Methods The pipeline starts with creating a finite element method (FEM) brain mesh from each patient's T1-weighted MRI. SEEG electrode positions are extracted from a post-implantation CT co-registered to the MRI and mapped onto the mesh. A leadfield matrix is computed assuming sources at brain nodes, representing how neural activity appears at the electrodes. For stimulation modeling, where electrodes act as current sources, the reciprocity principle is applied to derive a stimulation-specific leadfield. Least-squares optimization calculates electrode currents that focus stimulation on a region of interest (ROI) while minimizing spread. Additionally, we simulate temporal interference (TI) stimulation using two high-frequency currents with a slight frequency offset to generate a low-frequency envelope reaching deeper targets. Results Applying the pipeline to predefined ROIs, we demonstrate that precise, patient-specific SEEG stimulation is feasible. This approach enables tailored targeting aligned with individual anatomy and electrode placement. The strategy offers a foundation for more effective neuromodulation in epilepsy. As a next step, we plan to build a brain network–based seizure model to simulate stimulation patterns that induce seizures. Integrating this model with the current framework aims to improve EZ identification and support personalized surgical planning.

Keywords : Epilepsy, SEEG stimulation, Reciprocity principle, ROI targeting, FEM

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P-563

Increased Sensitivity to Loss during Reversal Learning in Individuals with Food addiction and Bulimia nervosa

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Objectives : Food addiction and eating disorders are forms of problematic eating behavior that are associated with cognitive characteristics such as impulsivity, craving, and loss of control. The present study aimed to examine whether adults exhibiting problematic eating behaviors (i.e., food addiction and eating disorders) differ from healthy individuals in terms of response inhibition, attentional bias, and cognitive flexibility. Methods : A total of 72 Korean adults (aged 19–39 years) completed self-report psychological questionnaires, including the Yale Food Addiction Scale (YFAS) and the Eating Disorder Diagnostic Scale (EDDS). Based on these assessments, participants were categorized into two groups: those with food addiction and/or bulimia nervosa (FA+BN) and healthy controls (HC). Three cognitive tasks were administered: the stop-signal task, the flanker task, and the reversal learning task. The stop-signal and flanker tasks employed food-related stimuli contrasting high-calorie and low-calorie items. Results : No significant group differences were found in either the stop-signal task or the flanker task. However, in the reversal learning task, significant group differences were observed in lose-switch behavior: the FA+BN group showed a greater tendency to switch following loss outcomes. Conclusions : These results suggest that eating disorders and food addiction may be associated with heightened punishment sensitivity, indicating that individuals with problematic eating behaviors may respond more sensitively to negative outcomes.

Keywords : bulimia nervosa, food addiction, stop signal task, flanker task, reversal learning task

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P-564

Therapeutic index of acupoints based on effective and hazardous depth measurement

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Acupuncture needle can be used to treat a variety of diseases conditions, but also might produce serious adverse events. Therapeutic index, originally developed in pharmacology to quantify the safety margin between effective and toxic doses, offers a valuable framework for evaluating anatomical safety in acupuncture. In this study, we applied the therapeutic index concept to two commonly used acupoints—GB21 and ST36—by quantifying the ratio between effective needling depth (eliciting *de-qi*) and hazardous depth (approaching vital anatomical structures). Using ultrasound-guided measurements in 39 participants, we calculated the therapeutic index for each point and constructed cumulative distribution functions to visualize the therapeutic window and calculate the therapeutic index. GB21 had a therapeutic index of 1.54, suggesting a relatively broad safety margin, while ST36 had a therapeutic index of 1.09, indicating a narrow and potentially risk-prone margin. These findings highlight the importance of anatomical variability and underscore the need for personalized depth control in acupuncture practice. Our study provides preliminary evidence supporting the integration of therapeutic index into acupuncture safety assessment, paving the way for more individualized, data-driven needling strategies.

Keywords : acupuncture, anatomy, depth, safety, therapeutic index

KSBNS 2025

The 28th Annual Meeting of The Korean Society for Brain and Neural Sciences: K-Brain 2025 & The 3rd CJK Neuroscience Meeting

Poster Session 3

P565-P844

Day 3(Aug 26, 2025)	13:30-18:00	[Exhibition/Poster Hall]
Day 4(Aug 27, 2025)	9:00-12:30	[Exhibition/Poster Hall]

Mechanisms of Brain Disorders	P-565 ~ P-621
Molecular and Cellular Neuroscience	P-622 ~ P-706
Neuroengineering	P-707 ~ P-723
Others	P-724 ~ P-751
Synapses and Circuits	P-752 ~ P-776
Systems and Computational Neuroscience	P-777 ~ P-825
Translational and Clinical Neuroscience	P-826 ~ P-844

Mechanisms of Brain Disorders P-565~P-621

P-565

Poster Award Candidate

Top-down modulation of acupuncture in Parkinson's disease: Enhancing gut function via MCH neurons

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Recent clinical and experimental evidence in Parkinson's disease (PD) has highlighted the concept of the brain-gut axis, which explains the interactions between the central nervous system and the gut microbiota. Despite recent increases in reports of the anti-parkinsonian effects of acupuncture, it remains unclear how the gut and brain communicate to maintain intestinal inflammation homeostasis and improve symptoms. Here, we show that acupuncture-induced activation of melanin-concentrating hormone (MCH) neurons in the lateral hypothalamus is an upstream regulator that can improve the intestinal environment by changing the peripheral nervous system, thereby improving symptoms and restoring microbiota balance. We used a chemogenetic approach with Gq- and Gi-DREADD (hM3Dq and hM4Di) in the MPTP mouse model of PD to investigate the mechanism for the anti-parkinsonian effects of acupuncture via MCH neurons. We demonstrate that cell-type-specific chemogenetic activation or inhibition of MCH neurons recapitulates or blocks the effects of acupuncture on intestinal function recovery and gut microbiota remodeling, respectively. Notably, these changes were reversed by performing a subdiaphragmatic vagotomy. These results elucidate a top-down pathway in which MCH neuron activation due to acupuncture stimulation regulates the intestinal environment through the vagus nerve. These findings are meaningful in that they provide the first experimental evidence that acupuncture-induced MCH neuron activation can attenuate PD by regulating the brain-gut axis.

Keywords : Parkinson's disease, Acupuncture, Brain-Gut axis, Melanin-concentrating hormone

Acknowledgements : This research was supported by NRF-2021R1A2C2006818, RS-2024-00409969, RS-2024-NR121316, and RS-2022-NR071818.

P-566

Poster Award Candidate

Abnormal N-Glycosylation in the mPFC Contributes to Cognitive Impairment in Schizophrenia

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Schizophrenia is a complex and debilitating disorder characterized by positive, negative, and cognitive symptoms. However, current antipsychotics fail to effectively address cognitive deficits, including working memory impairments. In this study, we uncovered a novel molecular mechanism linking abnormal N-glycosylation to schizophrenia-related cognitive dysfunction. Using Plcβ1 knockout (KO) mice, a well-established schizophrenia model, we performed glycomics analysis and identified a significant reduction in high-mannose-type N-glycans within the prefrontal cortex (PFC), a key region for cognition, of KO mice compared to wild-type (WT) controls. Consistently, RNA sequencing revealed Man1a2, an enzyme involved in high-mannose-type N-glycan biosynthesis, was markedly downregulated. ATP1B2 was identified as a major glycoprotein target affected by N-glycosylation changes in Plcβ1 KO mice. In our glycoproteomics analysis among which the high-mannose-type glycopeptides at the N238 site exhibited a marked reduction in Plcβ1 KO mice, indicating a site-specific glycosylation deficit linked to disease pathology. Knocking down Man1a2 or Atp1b2 in the medial PFC (mPFC) induced severe spatial working memory deficits, resembling those in Plcβ1 KO mice. Notably, overexpressing Man1a2 in the mPFC not only restored cognitive function but also rescued neuronal excitability in Plcβ1 knockdown mice. Furthermore, combining Man1a2 and Atp1b2 overexpression with the antipsychotic haloperidol in Plcβ1 KO mice alleviated both positive symptoms and cognitive deficits. By establishing a direct link between disrupted N-glycosylation and cognitive impairments, our findings not only open new avenues for targeted therapeutic strategies but also suggest combinational therapies alongside current antipsychotics to mitigate schizophrenia-related cognitive symptoms.

Keywords : Schizophrenia, Atp1b2, Glycosylation, Plcβ1, Cognition

Acknowledgements : This work was supported IBS-R001-D2 from the Institute for Basic Science.

P-567

Poster Award Candidate

Microglial HIF-1α–CCL2 axis mediates radiation-induced cognitive impairment: evidence from single-cell transcriptomics

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Cranial radiotherapy is a standard treatment for brain tumors, while it frequently leads to long-term side effects such as cognitive decline, significantly impairing patients' quality of life. Nevertheless, the cellular and molecular mechanisms underlying radiation-induced brain injury (RIBI) remain poorly understood. Here, we employed a mouse model of RIBI to elucidate the cellular basis of injury and identify potential therapeutic targets. Mice received a single cranial dose of 10 Gy, and brain tissues including hippocampus and cortex were analyzed using single-cell RNA-sequencing (scRNA-seq). Our analysis revealed a robust reduction in microglial abundance and associated intercellular signaling, validated by additional molecular analyses, including immunostaining, quantitative PCR, and immunoblotting, leading to further investigation focused on microglial functional changes. Microglial transcriptional states significantly shifted from homeostatic-like to an activated-like state. We also observed microglia-specific upregulation of hypoxia-inducible factor-1 alpha (HIF-1α) signaling, which was not

apparent in bulk-tissue analyses. Pharmacological inhibition of HIF-1α ameliorated radiation-induced cognitive deficits and suppressed neuroinflammatory responses, particularly through downregulation of *Ccl2*. This microglia-specific HIF-1α-CCL2 axis not only uncovers a novel mechanistic link between radiation exposure and neurocognitive effects, but also offers a novel therapeutic potential for interventions aimed at preserving cognitive function in patients undergoing radiotherapy for brain tumors. These findings position microglial HIF-1α signaling as a viable therapeutic target for mitigating radiation-induced cognitive impairment.

Keywords : Cranial irradiation, Microglia, Single-cell RNA sequencing

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P-568

Activation of perineural microglial cells supports functional axon regeneration following Facial Nerve Injury

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The peripheral nervous system (PNS) neurons exhibit robust axonal regeneration after injury, unlike central nervous system (CNS) neurons. Recent studies showed that interactions between neurons and on-neuronal cells contribute to enhanced axon regeneration in PNS injuries. We previously demonstrated that neuron-macrophage interaction promotes axonal regeneration of dorsal root ganglia neurons following sciatic nerve injury. However, applying this model to CNS neurons has been challenging, as their cell bodies reside in the CNS. Previous studies reported that microglia depletion worsens spinal cord injury outcomes, and additionally, neonatal microglia transplantation supports axonal regeneration in adult spinal cord, suggesting that microglia may support regeneration after CNS injury. To test if neuron-microglia interaction is involved in axon regeneration, we examined microglial activation in the facial motor nucleus (FMN) following facial nerve crush injury. The number of microglial cells markedly increased being positioned very closed to facial motor neurons. We depleted microglia using PLX5622, CSF1R inhibitor. PLX5622 effectively reduced FMN microglia after injury. In PLX5622 treated mice, recovery of facial function (eye closure and vibrissa movement) was significantly delayed compared to the control (AIN-76A chow). Axonal regeneration of facial motor neurons was reduced by nearly 50% assessed by FluoroGold retrograde tracing. These results suggest that FMN microglia are play a key role in spontaneous facial nerve regeneration. To explore the molecular profile of pro-regenerative microglia, we will perform bulk RNA-seq on microglia isolated from the FMN using FACS from CX3CR1-GFP mice. We propose that targeting pro-regenerative microglia may offer therapeutic strategies for CNS injuries like stroke and spinal cord injury.

Keywords : Microglia, Facial motor nucleus, PLX5622, Neuron-microglia interaction, PNS injury

P-569

Astrocytic putrescine degradation by polyamine acetyltransferase mediates astrocytic GABA synthesis and memory impairment in Alzheimer's disease.

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Astrocytic synthesis of γ-aminobutyric acid (GABA) plays a pivotal role in regulating brain function and pathophysiology, particularly in neurodegenerative disorders such as Alzheimer's disease (AD). In astrocytes, GABA synthesis is coupled to the degradation of putrescine. While most enzymes in the putrescine-to-GABA pathway have been identified, the enzyme initiating the metabolic cascade has remained elusive. Here, we identify polyamine acetyltransferase (PAT), also known as spermidine/spermine *N1*-acetyltransferase 1, as the key enzyme catalyzing the conversion of putrescine to *N1*-acetylputrescine, the substrate for monoamine oxidase B (MAO-B). Knockdown of PAT in astrocytes markedly reduced GABA synthesis and release *in vitro* and suppressed tonic GABA currents induced by putrescine incubation in *ex vivo* mouse hippocampal slices. To further dissect the underlying mechanism, we used whole-cell patch-clamp recordings combined with direct infusion of metabolites and inhibitors. Through this approach, we demonstrated that both pharmacological and genetic inhibition of PAT reduced tonic GABA currents induced by putrescine infusion, and that co-application *N1*-acetylputrescine reversed the effect of PAT. We further demonstrate that overexpression of ornithine decarboxylase 1 (ODC1) in hippocampal dentate gyrus astrocytes elevated putrescine levels, enhanced GABA synthesis, and impaired cognitive performance, and that these effects were reversed by PAT inhibition. Finally, PAT inhibition ameliorated cognitive deficits and reduced tonic GABA inhibition in a mouse model of AD (APP/PS1). These findings identify PAT as a critical regulator of astrocytic GABA synthesis and highlight its potential as a therapeutic target in Alzheimer's disease.

Keywords : Polyamine degradation, Astrocytes, Alzheimer's disease, GABA synthesis

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P-570

Functional and Regional Validation of an AAV-delivered Human DRD1 Promoter for Targeted Genetic Manipulation in the Mouse Brain

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Dopamine D1 receptor (DRD1)–expressing neurons underlie critical brain functions such as learning, memory, reward processing and motor control, yet tools for their selective manipulation typically rely on transgenic models. Here, we report the development and validation

of a human DRD1 promoter (hDRD1) optimized for adeno-associated virus (AAV) packaging that enables efficient, cell-type-specific transgene expression in mice. Following stereotaxic delivery of AAV-hDRD1 constructs into the medial prefrontal cortex, dorsal striatum and nucleus accumbens, immunohistochemical analyses revealed that 83.4 %, 91.9 % and 86.1 % of transduced neurons, respectively, co-expressed endogenous D1 markers. Furthermore, we compared the electrophysiological characteristics of native mouse DRD1 neurons and hDRD1+ neurons, and expected that their electrophysiological properties would be highly similar (experiment in progress). Chemogenetic activation of hDRD1-positive cells elicited robust contralateral rotation behavior, confirming functional engagement of the targeted population. These results establish hDRD1 as a versatile, transgenic-free tool for precise genetic targeting of DRD1 neurons in vivo, opening new avenues for dissecting basal ganglia circuit dynamics in motor control and Parkinson's disease, dopamine-mediated mechanisms of reward and addiction, and D1-dependent cognitive processes in neuropsychiatric disorders.

Keywords : DRD1, AAV, viral promoter

P-571

Hippocampal SARS-CoV-2 Spike Protein accumulation Induces Cognitive Decline via Pyroptosis and Neuroinflammation with Glial Reactivation

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The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to numerous reported cases globally, with patients experiencing a range of symptoms including respiratory issues, fever, and neurological complications such as cognitive impairment and brain fog. Despite the prevalence of these neurological manifestations among COVID-19 survivors, the underlying mechanisms remain largely unexplored, and reproducible models for post-COVID syndrome (long COVID) are still being developed. This study investigates cognitive deficits associated with the persistent intracellular accumulation of SARS-CoV-2 spike protein in the hippocampus and elucidates the underlying mechanisms. We generated a lentivirus expressing SARS-CoV-2 spike protein and confirmed its expression and intracellular accumulation in vitro. Following administration into the mouse hippocampus, specifically the CA1 region, behavioral assessments revealed cognitive impairments without anxiety-like behavior three weeks post-infection. Notably, cognitive dysfunction was accompanied by a significant reduction in neuronal density in the CA1 pyramidal layer, alongside the presence of reactive astrocytes and microglia. Furthermore, bulk RNA sequencing and protein-protein interaction analysis indicated a marked progression of pyroptosis and intensified neuroinflammation, contributing to neuronal destruction. Collectively, our findings suggest that pyroptosis and severe neuroinflammation, driven by the accumulation of intracellular SARS-CoV-2 spike protein in the hippocampus, may represent critical mechanisms underlying long COVID.

Keywords : COVID-19, Cognitive impairment, Pyroptosis, Neuroinflammation, Glial reactivation

P-572

Hippocampal Progranulin Alleviates Mood Disorders via Autophagy in Estrogen Withdrawal Mice

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Background: Mood disturbances are common among perimenopausal women due to estrogen withdrawal, yet current alternatives to hormone replacement therapy (HRT) are limited in efficacy and safety. Progranulin (PGRN), an estrogen-responsive neuroprotective glycoprotein, has recently been linked to emotional regulation, though its role in stress resilience during menopause remains unclear. Methods and Results: We demonstrate that neuronal PGRN in the hippocampus is critical for maintaining stress resilience in female mice. Estrogen deprivation via ovariectomy (OVX) resulted in a marked reduction of Grn expression in the hippocampus, which was reversed by estrogen supplementation. Overexpressing Grn in hippocampal neurons alleviated OVX-induced anxiety- and depression-like behaviors, while knockdown of neuronal—but not microglial—Grn increased susceptibility to stress. Mechanistically, PGRN maintained autophagic flux by preserving lysosomal function, as evidenced by enhanced LC3-II turnover and the restoration of cathepsin D activity. The therapeutic benefits of PGRN were further validated by both intracerebral administration and targeted hippocampal overexpression in mice models of 4-vinylcyclohexene diepoxide (4-VCD)-induced premature ovarian insufficiency, as well as naturally aging female mice. In addition, the PGRN-derived peptide fragment GRN-E has the ability to cross the blood-brain barrier and holds potential for anxiolytic and antidepressant effects. Conclusion: Our findings establish PGRN as a key estrogen-dependent regulator of stress resilience via autophagy in neurons. This highlights PGRN and related GRN fragments as a promising therapeutic target for mood disorders associated with menopausal transition, offering a novel alternative to conventional HRT.

Keywords : Progranulin, Menopause, Estrogen, Anxiety, Depression

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P-573

Reactive astrogliosis drives neuronal hypometabolism and tau hyperphosphorylation via acetate-induced, MAOB-dependent oxidative stress in GBM

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Reactive astrogliosis and neuronal tau hyperphosphorylation are

common pathological features of neurodegenerative diseases and glioblastoma multiforme (GBM). While previous positron emission tomography (PET) studies demonstrated elevated 11C-acetate uptake in reactive astrocytes accompanied by neuronal glucose hypometabolism (18F-FDG PET) in Alzheimer's disease, whether reactive specifically drives neuronal tau pathology within the unique metabolic context of GBM remains unclear. We combined 11C-acetate and 18F-FDG PET imaging to identify metabolic alterations in GBM patient biopsies and patient-derived xenograft (PDX) models. Tau phosphorylation and GLUT3 expression were assessed in targeted biopsies and validated in PDX and astrocyte-neuron co-culture models. Pharmacological (MAO-B inhibition) and genetic (MCT1 knockdown) approaches were used to examine mechanistic pathways. Biopsies from GBM regions with high acetate and reduced glucose uptake showed increased tau phosphorylation and decreased neuronal GLUT3 expression, findings replicated in GBM PDX models. Blocking reactive astrogliosis pharmacologically or genetically restored GLUT3 expression and reduced tau pathology. Mechanistically, acetate-induced reactive astrogliosis increased astrocytic release of hydrogen peroxide (H_2O_2) and gamma-aminobutyric acid (GABA), leading to neuronal oxidative stress. This oxidative stress activated glycogen synthase kinase-3β (GSK3β), subsequently promoting tau hyperphosphorylation and neuronal glucose hypometabolism. Reactive astrogliosis induces neuronal hypometabolism and tau pathology in GBM through acetate-driven, MAO-B-dependent oxidative stress. This astrocyte–neuron metabolic interaction provides novel PET imaging biomarkers and therapeutic targets to improve neuronal integrity in GBM.

Keywords : Reactive astrogliosis, PET imaging, Tau hyperphosphorylation, Oxidative stress, Glioblastoma

P-574

Sleep Loss Impairs Neuropathic Pain Modulation through Homer1a-Dependent Synaptic Remodelling

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Introduction: Neuropathic pain (NP) frequently coexists with sleep disturbances, but the underlying mechanisms remain poorly defined. The immediate early gene Homer1a, a key regulator of synaptic scaling and plasticity, is upregulated in both NP and sleep deprivation. We hypothesize that disrupted sleep contributes to NP maintenance by driving Homer1a-dependent dendritic spine remodeling, thereby impairing endogenous pain modulatory circuits. Methods: Mice underwent 6-hour, 12-hour, or 5-day total sleep deprivation. Mechanical and thermal sensitivity were assessed using von Frey and Hargreaves tests. Homer1a mRNA expression in the ventrolateral periaqueductal gray (vlPAG) was quantified by RT-qPCR. To examine dendritic spine dynamics in vlPAG-to-RVM projection neurons, AAV1-DIO-ChR2-EGFP was injected into the vlPAG, and AAVrg-hSyn-Cre into the RVM. Confocal imaging and Imaris software were used to analyze spine morphology three months post-injection. Results: Sleep deprivation increased mechanical and thermal hypersensitivity and elevated Homer1a expression in the vlPAG. Spine analysis showed that 24-hour sleep loss reduced spine density and shifted morphology toward immature forms, indicating impaired synaptic maturation. Similar changes were observed after sciatic nerve injury, suggesting both sleep loss and nerve injury induce maladaptive plasticity in the descending pain pathway. Conclusion: These findings highlight Homer1a-mediated dendritic spine remodeling as a shared mechanism linking sleep disruption to impaired descending pain inhibition, offering new insight into how sleep loss contributes to NP development.

Keywords : Sleep deprivation, Neuropathic pain, Dendritic spine remodelling, Homer1a

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P-575

Hypothalamic circuit plasticity drives pain sensitization and anxiety in neuropathic pain

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Objective Neuropathic pain is a chronic condition often accompanied by affective disturbances such as anxiety. While brain circuits integrating these sensory and emotional components remain poorly defined. The hypothalamus (HY) is recognized for its role in stress responses and homeostasis. However, whether it drives the chronicity of neuropathic pain remains unknown. In this study, we aimed to identify central circuits engaged by abnormal peripheral inputs and to define their structural and functional plasticity under neuropathic conditions. Methods Herpes simplex virus-based whole-brain trans-synaptic tracing was performed in spared nerve injury (SNI) mice to map somatosensory network reorganization. Viral tracing and circuit-specific labeling were integrated to systematically map the connectivity changes of the sensory neural network under neuropathic pain conditions. Long-term inhibition and optogenetic manipulations were used to probe the functional role of altered pathways in pain and anxiety-like behaviors. Results (1) SNI mice exhibited enhanced hypothalamic connectivity within the somatosensory network, particularly with enhanced connectivity to dorsomedial hypothalamic nucleus (DMH) and paraventricular hypothalamic nucleus (PVH). (2) Neuropathic pain induced increased morphological complexity of contralateral lateral parabrachial nucleus (LPB) neurons. (3) PVH mainly receives injury information directly from the spinal cord, while DMH mainly receives injury information relayed by LPB. (4) Enhanced SC-PVH and LPB-DMH connectivity regulate the comorbid anxiety associated with neuropathic pain. Conclusion The hypothalamus is a previously unrecognized hub integrating nociceptive and affective dysfunction. The LPB-DMH and SC-PVH circuit drives neuropathic pain by integrating sensory and affective pathology, providing a theoretical foundation for treating neuropathic pain and its emotional comorbidities.

Keywords : Neuropathic pain, DMH, PVH, Neural circuit, Anxiety

P-576

Neuroprotective Effect and Mechanism of Transcutaneous Auricular Vagus Nerve Stimulation in a Parkinson's disease model

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Parkinson's disease (PD) is a representative neurodegenerative disorder characterized by the loss of dopaminergic neurons, leading to impaired motor function. Current clinical treatments primarily focus on symptom management, while there is an urgent need for therapies that can slow or halt disease progression. Recent studies suggest that transcutaneous auricular vagus nerve stimulation (taVNS) may inhibit neuroinflammation and contribute to neuroprotection in PD models, although its mechanisms of action remain insufficiently understood. Therefore, the objective of this study is to specifically evaluate the effects of taVNS on neuroinflammatory responses and neuroprotection. Parkinson's disease was induced in mice by intraperitoneal injection of MPTP for 5 consecutive days. Following this, taVNS was applied once daily for 15 minutes over a period of 12 days. After the experimental period, immunostaining for c-Fos, GFAP, and Iba1 was performed to assess neuronal activation and inflammatory responses. Additionally, tyrosine hydroxylase (TH) staining was conducted to quantitatively evaluate dopaminergic neuronal damage. c-Fos screening was performed across various brain regions, with a significant increase in expression observed in the LC, indicating a neural activation effect of taVNS. Additionally, GFAP and Iba1 staining in the LC revealed a reduction in neuroinflammatory responses, suggesting that taVNS effectively suppresses inflammation. In the striatum and substantia nigra, TH staining showed preservation of dopaminergic neurons, supporting the potential neuroprotective effects of taVNS. These findings suggest that taVNS may inhibit neuroinflammation and contribute to the protection of dopaminergic neurons in a Parkinson's disease mice model. Further studies are expected to validate its clinical applicability, potentially offering a novel approach for Parkinson's disease treatment.

Keywords : Parkinson's disease, Vagus nerve, Transcutaneous auricular vagus nerve stimulation, Neuroinflammation, Neuroprotection

P-577

Microstate-specific functional connectivity in Alcohol Use Disorder using resting-state EEG

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Alcohol Use Disorder (AUD) is often described as a “disconnection syndrome,” reflecting the neural dysfunction typically associated with chronic and heavy alcohol use. However, previous studies on functional connectivity (FC) of resting-state EEG (rsEEG) in AUD have reported inconsistent findings—some showing hyperconnectivity, others hypoconnectivity or no significant differences—possibly due to overlooking the brain’s dynamic resting-state nature. Here, we applied microstate (MS) analysis to assess FC of rsEEG in AUD by capturing transient brain states. Specifically, we hypothesized that applying this method would reveal subtle FC differences between young adults with AUD and healthy controls (HC). We analyzed rsEEG data from 26 individuals with AUD (m/f = 19/7, age = 27.62 ± 5.39) and 35 HC (m/f = 25/10, age = 24.94 ± 2.90), recorded for 5 minutes with eyes closed. Four MSs (A–D) were identified for each group using a modified k-means algorithm and were back-fitted to individual rsEEG data. FC was calculated using EEG coherence within 230 ms non-overlapping windows where a given MS persisted for at least 210 ms. FC matrices were averaged per MS, and graph-theoretical measures (e.g., clustering coefficient, betweenness) were used to identify hub nodes. Network efficiency was assessed using small-worldness. MSs C and D occurred more frequently in AUD, whereas HC showed a more balanced MS distribution. Each MS exhibited distinct FC patterns. Although the overall FC structure was comparable between groups, no hub nodes were identified in AUD, suggesting overly localized connectivity and weakened global communication. In addition, network efficiency in MS C—associated with the default mode network—was significantly lower in AUD compared to HC (p_{FDR} = 0.001). Our findings show FC characteristics uniquely observable within transient microstates in rsEEG, offering a more detailed account of how alcohol use affects the brain’s FC in young adults.

Keywords : Alcohol Use Disorder, Resting-state EEG, Functional connectivity, Microstates, Network neuroscience

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P-578

Stress responsiveness shapes neuronal dynamics in the lateral habenula

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Exposure to acute stress leads to abnormal activation of the lateral habenula (LHb), a brain region involved in stress responses and depression. We hypothesized that within the heterogeneous LHb population, a distinct subset of stress-activated neurons undergoes persistent physiological changes that contribute to depressive-like behavior. We labeled stress-responsive neurons (SRs) using two independent activity-dependent tagging methods, including a viral vector approach and a transgenic mouse line based on c-fos expression. To induce neuronal activation, we used the acute learned helplessness (aLH) paradigm, which involves one hour of inescapable and unpredictable foot shocks. Both tagging methods enabled us to identify neurons activated by aLH. Compared to non-responsive neurons (NRs), which exhibited tonic or silent activity, SRs predominantly showed burst firing and enhanced excitatory synaptic transmission, which was likely mediated by an increased presynaptic vesicle release probability. To examine how stress intensity affects these responses, we labeled neurons activated by mild stress. These neurons did not initially exhibit SR-like properties. However, after aLH exposure, they showed burst firing and enhanced presynaptic release, suggesting that excessive stress induces lasting physiological changes in stress-responsive neurons. We confirmed these changes in vivo using fiber photometry, which revealed dynamic LHb activity patterns consistent with ex vivo findings. These findings offer mechanistic insights into how excessive

stress reshapes specific LHb circuits, potentially driving the emergence of depressive-like behavior.

Keywords : stress, depression, lateral habenula

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P-579

Linking VWA7-Associated ECM Dysregulation to Cerebellar Dysfunction in Schizophrenia

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Schizophrenia (SZ) is a complex psychiatric disorder affecting about 1% of the global population. While research has traditionally focused on cortical and dopaminergic dysfunction, recent studies highlight the cerebellum as a key region involved in cognitive and emotional regulation via the cerebello-thalamo-cortical (CTC) circuit. However, the molecular mechanisms underlying cerebellar dysfunction in SZ remain poorly understood. One emerging factor is the extracellular matrix (ECM), which shapes synaptic plasticity, glial-neuronal signaling, and ion homeostasis. Postmortem studies suggest ECM disruption in SZ, but region-specific effects and functional outcomes are unclear. Among SZ-associated genes, VWA7—identified through genome-wide association studies—shows altered expression in patient brains, yet its biological function remains unknown. In this study, we investigate how cerebellar ECM remodeling contributes to SZ pathology by focusing on VWA7. Using a VWA7 knockout mouse model, we observed reduced prepulse inhibition (PPI), indicating deficits in sensorimotor gating, a behavioral hallmark of SZ. We also employed AVATAR (AI Vision Analysis for Three-dimensional Action in Real-time) combined with unsupervised clustering using the SUBTLE (Spectrogram-UMAP-based Temporal Link Embedding) algorithm to analyze mouse behavioral patterns in a high-dimensional space. To probe the underlying mechanisms, we plan electrophysiological recordings to evaluate excitatory and inhibitory synaptic transmission in granule and Purkinje cells. Concurrently, we are analyzing ECM components and glial markers using immunohistochemistry and western blotting. Our findings aim to clarify how VWA7 deletion alters cerebellar function through ECM dysregulation. This study offers new insights into non-cortical contributions to SZ and proposes VWA7 and cerebellar ECM as novel targets for therapeutic development.

Keywords : Schizophrenia, ECM, Cerebellum

P-580

Histological and Behavioral Characterization of TDP-43^{A315T} Mice

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Objectives: Dysfunction of TAR DNA-binding protein 43 (TDP-43) is a principal hallmark of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), but its pathological mechanisms related to oligodendrocyte and myelin which might contribute to FTD remain unclear. This study investigated TDP-43A315T pathology associated with myelin and cognitive impairment by analyzing histology, behavior, and gene expression. Moreover, we treated the mice with blebbistatin, an inhibitor of nonmuscle myosin IIb, to investigate rescue effects of gene expression related to myelin and cognitive dysfunction. Methods: TDP-43A315T transgenic mice were used at ages of 8 and 16 weeks old. Open field test (OFT), Y-maze test, and novel object recognition (NOR) test were conducted to assess cognitive impairment at 16 weeks old mice. Histological analysis and mRNA sequencing were performed to examine myelin deficits. Results: 16 weeks old mice showed significant impairment in discriminating novel object in NOR test, while there was no significant difference in exploration or working memory performance in OFT and Y-maze test. Furthermore, mRNA sequencing revealed alteration of gene expression following blebbistatin treatment, especially reduction of *Bcas1*, a gene associated with oligodendrocyte maturation and myelination. Consistent with this, immunofluorescence analysis showed a reduction in myelin area, suggesting a potential link between Bcas1 and myelin in TDP-43A315T mice. Further Study: More behavioral assessments and histologcial analysis need to be performed after the treatment of blebbistatin to confirm its influences. To further validate myelin changes, EM and MRI analysis will be performed. Finally, we plan western blot analysis of *Bcas1* and other myelin-related proteins to confirm mRNA-protein correlation.

Keywords : TDP-43, Frontotemporal dementia, Myelin reduction, Cognitive dysfunction

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P-581

Protein denitration by tyrosine-containing peptides is a new strategy to treat intractable diseases.

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Studies have frequently reported that key regulatory proteins lose their functions in many intractable diseases because of tyrosine (Tyr, Y) nitration, which can cause other diseases or worsen the existing disease. Many attempts have been made to identify druggable substances to restore Y-nitrated proteins to denitrated forms and thus produce active proteins, but no remarkable results have been found. Based upon our recent findings that chronic stress decreased glutamine synthetase (GS) activity via Y-nitration and that Y supplementation restored its activity, we determined whether Y and Y-containing peptides had a denitration effect on several regulatory proteins, including GS, manganese-superoxide dismutase, copper/zinc superoxide dismutase, catalase, and HSP60. After confirming the denitration effect of Y and Y-containing peptides, we evaluated the

clinical availability using well-established intractable disease mouse models of depression, mild cognitive impairment, epilepsy, hyperammonemia, and acute kidney injury. Interestingly, Y or tyrosyl glutamine (YQ) treatment showed remarkable therapeutic effects on each disease. Although the disease-causing nitrated proteins were different for each disease, Y or YQ treatment showed denitrative effects on such proteins and activated enzymes, resulting in therapeutic efficacy. These results, to the best of our knowledge, are for the first time in drug development history and will make the way to overcome intractable diseases.

Keywords : protein denitration, tyrosine peptide, intractable disease, enzyme activation, tyrosine

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P-582

Screening of bioactive flavonoids with anti-Alzheimer's potential from *Cirsium japonicum*

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder associated with oxidative stress, inflammation, and amyloid-beta (Aβ) accumulation. *Cirsium japonicum* has been reported to exhibit anti-inflammatory, hepatoprotective, and neuroprotective activities. Nevertheless, comprehensive studies identifying the specific flavonoid constituents responsible for these effects and delineating their differential efficacy remain scarce. This study screened the neuroprotective potential of five *Cirsium japonicum*-derived flavonoids (i.e. cirsimarin, cirsimaritin, pectolinarin, pectolinarigenin, and hispidulin) by evaluating their antioxidant and anti-inflammatory activities *in vitro* antioxidant assays and H_2O_2-treated HMC-3 microglial cell. The antioxidant capacity of the flavonoids was first evaluated via ABTS, DPPH, and FRAP assays. HMC-3 cells were exposed to H_2O_2 to induce cytotoxicity, followed by treatment with each compound (1–10 μM). MTT and LDH assays were used to assess cell viability and cytotoxicity. Hispidulin, selected based on its superior efficacy, was further analyzed by western blot to assess its effects on inflammation-related markers (inducible nitric oxide synthase, cyclooxygenase-2, nuclear factor kappa B); apoptotic regulators (B-cell lymphoma 2 (Bcl-2), Bcl-2-associated X protein); amyloidogenic pathway proteins (beta-site APP cleaving enzyme 1, presenilin-1, presenilin-2); and antioxidant enzymes (nuclear factor erythroid 2–related factor 2 (Nrf2), heme oxygenase-1 (HO-1), superoxide dismutase). Hispidulin significantly improved cell viability and reduced LDH leakage in H_2O_2-treated HMC-3 cells. It downregulated pro-inflammatory and pro-apoptotic factors, suppressed amyloidogenic pathway activation, and upregulated antioxidant defenses via Nrf2/HO-1 signaling. These results highlight hispidulin as the most effective among the tested *Cirsium japonicum*-derived flavones, suggesting its therapeutic potential for AD.

Keywords : Cirsium japonicum, Hispidulin, Alzheimer's disease, Neuroinflammation, Hydrogen peroxide

P-583

Neuroprotective effects of *Cirsium japonicum* var. *maackii* flower in oxidative and cognitive impairment models

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Cognitive impairment is a hallmark of various neurodegenerative diseases, characterized by deficits in learning, memory, and attention. *Cirsium japonicum var. maackii* (CJM) is known for its anti-inflammatory, hepatoprotective, and neuroprotective effects. However, the neuroprotective properties of CJM flower (CJMF) remains underexplored. This study investigated the antioxidant and neuroprotective effects of the ethanol extract of CJMF (ECJMF) against oxidative stress in SH-SY5Y cells and cognitive deficits in scopolamine-induced ICR mice. The antioxidant capacity of ECJMF was assessed by measuring its flavonoid and polyphenol contents. ECJMF exhibited dose-dependent acetylcholinesterase inhibition, suggesting enhanced cholinergic activity. It significantly improved viability in H_2O_2-treated SH-SY5Y cells, as confirmed by MTT and LDH assays. *In vivo*, scopolamine-induced cognitive impairment in mice was mitigated by ECJMF administration, evaluated through T-maze, novel object recognition, passive avoidance, and Morris water maze tests. Western blot analysis demonstrated that ECJMF upregulated synaptic and cholinergic proteins, increased neurotrophic and antioxidant factors, and reduced inflammatory markers. Additionally, it promoted anti-apoptotic signaling by increasing the Bcl-2/Bax ratio and activating the PI3K/AKT pathway. These results indicate that ECJMF has multifaceted neuroprotective effects and may be a valuable functional food ingredient to prevent cognitive decline.

Keywords : Cirsium japonicum var. maackii flower, Cognitive impairment, Oxidative stress, Scopolamine, Behavioral test

P-584

The minimum effective dose of $_L$YQ as an antidepressant and a new antidepressive effect of D-tyrosine ($_D$Y), an enantiomer of $_L$Y

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Major depressive disorder (MDD) is a common mood disorder and can contribute to suicide. Recently, we reported that L-tyrosine (LY) and L-tyrosylglutamine (LYQ) have antidepressant properties on chronic immobilization stress (CIS)-induced depressive mice via activation of glutamine synthetase (GS) in the medial prefrontal cortex (mPFC). The activation of GS is achieved by denitration from 3-nitrotyrosine with LYQ dietary supplementation. In this study, we tried to find the minimum effective dose of LYQ for the CIS-induced depression mouse model. A half or quarter doses of LYQ from the previous study was

fed to mice throughout the experimental period. As a result, a half dose of LYQ showed similar antidepressant properties to the previous results, including changes in behaviors, stress-related biomarkers, and GS activity. Additionally, we tested whether D-tyrosine (DY) has antidepressive properties through denitration of GS. Mice were subjected to the CIS regimen and divided into two groups, and one group fed with DY-supplemented diet and the other with a normal diet. Interestingly, six-day DY supplementation after the CIS regimen was enough to restore the CIS-evoked phenotypes such as depressiveness, elevated levels of corticosterone and ROS/RNS, and decreased GS activity. From this result, it is suggested that DY does work in the denitration process rather than the inhibition of tyrosine nitration of GS. In further study, we will evaluate whether DYQ containing DY has antidepressive and denitrative effects in CIS-induced mice to discover more stable antidepressant candidate *in vivo*.

Keywords : Depression, Glutamine synthetase, Tyrosylglutamine, Denitration, Tyrosine nitration

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P-585

Tonic GABA and H_2O_2 production via the astrocytic glucocorticoid receptor activation pathway causes memory deficits in the Cushing's disease model.

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Cushing's disease is a rare endocrine disorder characterized by a persistent elevation of glucocorticoids. It is linked not only to significant endocrine and metabolic disruptions, such as insulin resistance, dyslipidemia, and fat redistribution, but also to notable psychiatric symptoms like depression and memory problems. Importantly, even after patients achieve remission, psychiatric effects can persist, significantly reducing quality of life. Despite the disease's impact on the central nervous system, especially on astrocytes, research on how astrocytes respond and the mechanisms involved remains limited. Our study established a chronic corticosterone exposure (CCE) model in mice, where corticosterone was administered in their drinking water for 21 days to mimic Cushing's disease. This model exhibited depressive behaviors, memory deficits, and various physiological changes. Electrophysiological and immunohistochemical analyses showed increased tonic GABA in the hippocampus, decreased synaptic transmission, astrocytic atrophy, and elevated levels of proteins involved in GABA synthesis. Additionally, using a gene knockdown approach, we found that astrocytic glucocorticoid receptor (GR) is essential for the corticosterone-induced increase in tonic inhibition. Moreover, after 3 hours of corticosterone treatment, there was no increase in tonic inhibition in Maob or Best1 knockout (KO) mice. We also observed real-time production of hydrogen peroxide (H_2O_2) under corticosterone treatment *ex vivo*, using the oROS-G sensor. Administration of MAO-B inhibitor KDS2010 or H_2O_2-decomposing enhancer KDS12025 improved memory and reduced depressive-like symptoms in the CCE model. These findings suggest that long-term corticosterone exposure causes astrocytic GR-mediated structural changes and increases GABA and H_2O_2 production, impairing hippocampal functions and offering insights into the neurobiological mechanisms underlying stress-related cognitive and mood disorders.

Keywords : Cushing's disease, Tonic GABA, H_2O_2, Corticosterone, Glucocorticoid receptor

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P-586

Early Olfactory Dysfunction and Immune Alterations in the Olfactory Epithelium of 5xFAD Mice

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Olfactory dysfunction is an established early symptom of Alzheimer's disease (AD), but its underlying mechanisms are not fully understood. In the central olfactory pathway, early AD-related pathologies such as amyloid-beta and tau accumulation have been identified in regions like the olfactory bulb, piriform cortex, and frontal cortex. In the peripheral olfactory system, previous studies have reported reduced numbers of olfactory sensory neurons, diminished olfactory receptor expression, and impaired epithelial regeneration in the olfactory epithelium (OE). However, how these early peripheral changes relate to central nervous system (CNS) pathology remains unclear. Recent research has also shown that aging impairs nasopharyngeal lymphatic drainage, potentially disturbing local immune homeostasis in the OE. Based on this, we hypothesized that immune dysregulation in the OE contributes to early olfactory deficits and may interact with AD pathogenesis. To investigate this, we used 5-month-old male 5xFAD transgenic mice, a widely used AD model at a stage preceding cognitive decline. Behavioral analyses included the Y-maze test for spatial working memory and the peanut butter (PB) preference test for olfaction, quantified as the PB/non-PB exploration ratio. While Y-maze performance showed no significant differences, 5xFAD mice exhibited a significantly lower PB/non-PB ratio, indicating early olfactory impairment. Single-cell RNA sequencing (scRNA-seq) of $CD45^+$ immune cells from the OE revealed altered immune cell composition and increased expression of pro-inflammatory cytokines in several immune subsets. These results indicate that olfactory dysfunction precedes cognitive symptoms in AD model mice and coincides with immune alterations in the OE. Although a causal link remains to be confirmed, our findings suggest that peripheral immune dysregulation may contribute to early olfactory symptoms in AD and may represent a novel diagnostic or therapeutic target.

Keywords : Alzheimer's disease, Olfactory dysfunction, Immune dysregulation, Single cell rna sequencing, Olfactory epithelium

P-587

Posterior parietal cortex dysfunction underlies sensory deficits in the *Shank3*$^{\Delta 14-16}$ mice

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Sensory processing disorder (SPD) is commonly observed in patients with autism spectrum disorder (ASD). Deletion of the *Shank3* gene is well-established cause of autistic phenotypes in both humans and mouse models. However, whether and how *Shank3* deficiency alters anatomical and functional connectivity in cortical areas involved in sensory processing remains unclear. In this study, we investigated behavioral sensitivity and cortical responses to visual and auditory stimuli in *Shank3*-deleted (*Shank3*$^{\Delta 14-16}$) mice. Using wide-field calcium imaging, we found that *Shank3*$^{\Delta 14-16}$ mice exhibited abnormal sensory processing, with decreased calcium activity in response to visual stimuli. In addition, they showed significantly reduced responses to audiovisual stimuli in the posterior parietal cortex (PPC), a key region for multisensory integration. Anatomical and functional connectivity confirmed that cortical inputs to the PPC were significantly reduced in *Shank3*$^{\Delta 14-16}$ mice. Furthermore, *Shank3*$^{\Delta 14-16}$ mice exhibited deficits in multisensory integration behaviors, supporting the idea that the Shank3 deletion weakens cortico-parietal integration. Interestingly, inactivation of the PPC in wild-type mice elicited "following" behavior during direct social interaction test, which is also observed in *Shank3*$^{\Delta 14-16}$ mice. Collectively, our findings suggest that Shank3-deficient mice experience sensory imbalance at both neural and behavioral levels, potentially due to weakened anatomical and functional connectivity in the posterior parietal cortex, which can lead to changes in social behaviors.

Keywords : Autism, Shank3, Sensory processing, Hypersensitivity, Multisensory integration

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P-588

BNIP3L/NIX-Mitophagy Sustains Astrocytic Neuroprotection Against Chronic Glucocorticoid-Induced Aging

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Introduction: Chronic exposure to elevated glucocorticoid (GC) levels and sustained hypercortisolism (HCM) has been associated with hippocampal shrinkage, impaired cognitive functions, and a heightened susceptibility to age-related neurodegenerative diseases (NDDs). However, the exact cellular pathways through which GC-induced stress leads to mitophagy dysfunction and neurotoxicity in NDD-relevant brain cells remain poorly understood. In this study, we explore how prolonged HCM interferes with BNIP3L/NIX-mediated mitophagy in both neurons and glial cells, contributing to neurodegeneration. Method: Using a human mini-brain-on-a-chip model spanning 1 to 9 weeks, we examine how GC-induced cortisol excess—frequently observed in Alzheimer's disease (AD)—modulates mitophagy-related mechanisms and amplifies NDD markers. Result: Prolonged HCM was found to suppress NIX-dependent mitophagy in neurons, increase mitochondrial reactive oxygen species (ROS), deplete ATP, and impair synaptic signaling, ultimately triggering tau pathology. While astrocytes initially responded with protective, anti-inflammatory activity, chronic HCM exposure led to impaired mitophagy, cytokine-driven neuroinflammation, and disturbed calcium balance. Similarly, microglia exposed to sustained HCM showed disrupted chemokine signaling, reduced phagocytic ability, and an accumulation of Aβ oligomers and alpha-synuclein aggregates in a tri-culture system. These findings highlight the critical role of mitochondrial activity and the therapeutic potential of mitophagy enhancement to counter NDD progression and promote healthy brain aging. Keywords: Mitophagy, Glucocorticoid, Neurodegeneration, Neuroprotection, Alzheimer's disease, BNIP3L/NIX, Mitochondrial dysfunction, Neurons, Astrocytes, Microglia, Tau pathology, mini-brain model.

Keywords : Glucocorticoid, BNIP3L/NIX Mitophagy, Neuroprotection, Neurodegeneration, , mini-brain model

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P-589

Integrative single-cell multi-omics analysis of epigenetic markers during the transition from impulsive to compulsive use of drug

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Significant differences in neural circuitry and molecular-level changes in the brain exist between the early stages of drug use (impulsive use), when drugs are used lightly for pleasure, recreation, etc., and the later stages of drug use (compulsive use), when drugs are used consistently and in large quantities. However, the transcriptomic and epigenomic mechanisms underlying these differences remain unclear, and new analytical methods are needed to assess transcriptomic and epigenomic changes at each stage and in specific brain reward regions. While single-cell multi-omics technologies have advanced, integrated research is still limited, and most existing analyses only scratch the surface of the molecular and neural changes involved. This study aims to establish a standardized big data analysis platform to analyze epigenetic changes by addiction stage and brain region, assess individual differences, and evaluate addiction harm. Using a mouse drug self-administration model covering both impulsive and compulsive use, we conducted behavioral analyses and collected tissue from key reward areas for advanced single-cell multi-omics profiling. Through behavioral and molecular profiling, we established an animal model that distinguishes between high craving, low craving, and compulsive use groups. Single-cell multi-omics revealed stage-specific epigenetic changes and identified novel candidate biomarkers

for addiction progression. In summary, this study demonstrates that single-cell multi-omics enables precise, standardized assessment of addiction harm and the discovery of stage-specific biomarkers for early diagnosis and personalized treatment. The resulting data and analytical tools are expected to contribute to addiction prevention, policy, and drug development, with broad applications in biomedical research and public health.

Keywords : Compulsive use, Drug addiction, Impulsive use, Self-administration, Single-cell multi-omics analysis

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P-590

Biobehavioral sequelae of an animal model of cannabinoid oral self-administration

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Cannabis, including both natural and synthetic cannabinoids, is among the most widely used psychoactive substances worldwide. These compounds often exhibit stronger affinity for cannabinoid receptors and have been associated with unpredictable and severe adverse outcomes, including psychosis, cardiovascular events, and death. Despite the growing public health impact, including increased incidence of cannabis-related mental health issues and greater healthcare utilization, our understanding of the long-term biobehavioral effects of both natural and synthetic cannabinoids remains limited. Importantly, cannabis use can lead to both physical and psychological dependence. Notably, cannabis is typically consumed via inhalation rather than intravenous (IV) injection in humans—a distinction that emphasizes the need for more translationally valid animal models. However, a robust model of voluntary cannabis intake has yet to be established, significantly hindering progress in elucidating the neurobiological mechanisms of cannabis addiction and the chronic effects of cannabinoid exposure. In this study, to complement the limitations of existing methods, we used a chocolate-flavored nutritional shake formulated in gelatin form to induce chronic voluntary oral intake of three cannabinoids—THC (Δ^9-tetrahydrocannabinol), CBN (cannabinol), and ADB-BUTINACA. Mice were given chocolate gel with cannabinoids added in a dose-dependent manner for 2 hours/day, 5 days/week, for 2 weeks. Gel intake, body weight, and body temperature of each individual were measured. The effect of cannabinoids on behavior was evaluated through open field, elevated plus maze, and Y-maze at 2 days and 2 weeks after intake. As a result, alterations in physiology and behavior were observed by cannabinoids. Future studies should investigate changes in systemic metabolite and brain neurophysiological changes in this mouse model of chronic voluntary oral cannabinoid intake.

Keywords : Cannabinoid, Oral self-administration, THC, CBN, ADB-BUTINACA

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P-591

Cell type specific striatal neuronal ensemble dynamic alteration in Parkinsonian state

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Objective and Background: Cholinergic interneurons account for a small fraction of striatal neurons, they play a pivotal role in encoding movement-related signals and mediating value-based learning in response to motivational and salient cues. Yet, how their spatiotemporal activity patterns are altered in parkinsonism is not well defined. This study therefore set out to delineate the changes in cholinergic interneuron dynamics between healthy and 6-OHDA–lesioned parkinsonian mice to uncover their underlying network mechanisms. Methods: Mice, injected AAV-GCaMP8f into the DS, performed open-field exploration while undergoing in vivo single-photon calcium imaging. Finally, we applied closed-loop optogenetic inhibition (CLOI)—triggered by real-time detection of the stop phase—to silence ChAT neurons and measured effects on locomotor velocity. Results: In parkinsonian ChAT-cre mice (n = 6), 6-OHDA caused marked degeneration of dopaminergic terminals and motor deficits. Across all sessions we recorded 881 D1, 1,255 A2a, 47 ChAT, and 11 PV neurons. D1, A2a, and ChAT populations exhibited robust encoding of mobility, immobility, and movement initiation, whereas PV cells did not deactivate during immobility. Baseline cholinergic ensembles displayed higher pairwise coactivity than D1/A2a neurons ($p < 0.05$) and reduced coactivity during movement. In the parkinsonian state, coactivity dropped further in immobility but remained unchanged during movement. Both baseline and parkinsonian mice showed increased cholinergic firing at movement onset ($p < 0.05$), yet during stops only the baseline group exhibited a significant activity drop—the parkinsonian group sustained elevated firing. Spatial correlation was unrelated to distance in baseline mice but became negatively correlated with distance during immobility in parkinsonian mice. CLOI timed to stop onset significantly enhanced locomotor speed versus baseline-off trials ($p = 0.045$), whereas random inhibition yielded no benefit.

Keywords : Striatal cholinergic interneurons, Parkinsonism, Cholinergic ensembles, Striatal neuronal ensemble dynamic, Spatiotemporal activity patterns

P-592

Modulation of Insular Cortex Neurons Alleviates Motor Symptoms and Gut Dysfunction in Parkinson's Disease

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Parkinson's disease (PD) is the most common neurodegenerative movement disorder, often accompanied by non-motor symptoms such as gastrointestinal (GI) dysfunction. The insular cortex (IC), a central

hub for interoception, modulates gut-related signaling and immune responses, suggesting that targeting IC activity could influence gut health in PD. However, its specific contribution to PD pathogenesis remains poorly understood. In this study, we aimed to elucidate the causal role of PD-activated neurons in the IC using TRAP2 (Fos-iCreERT2) mice. Chemogenetic inhibition of these activated neurons alleviated motor symptoms and protected dopaminergic neurons. Given that glutamatergic neurons are predominant in the IC, we selectively targeted this population through chemogenetic manipulation, which resulted in significant anti-parkinsonian effects. Immunofluorescence analysis revealed that inhibition of insular glutamatergic neurons attenuated MPTP-induced reactive astrogliosis in both the striatum and substantia nigra pars compacta. Furthermore, this intervention downregulated pro-inflammatory cytokine expression, preserved the expression of intestinal tight junction proteins, and mitigated gut inflammation. Taken together, this study demonstrates that chemogenetic modulation of IC neurons effectively ameliorates both motor deficits and GI dysfunction in a PD model. These findings suggest a novel role of the IC in PD pathogenesis and may provide a new direction for PD treatment, particularly targeting the gut-brain axis.

Keywords : Parkinson's disease, Insular cortex, Chemogenetics, Gut–brain axis, Neuroinflammation

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P-593

Cerebellar Activation Differences in Major Depressive Disorder and Controls During Emotional Music and Non-Music Stimuli: An fMRI Study

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In recent years, cerebellum is increasingly being recognized for its role in cognition, emotion, and higher order brain functions. This study aimed to compare the cerebellum activation patterns in control and MDD subjects using data from the ds000171 dataset. First level analysis was conducted by extracting trial-wise cerebellar activation from BOLD signals within a probabilistic cerebellum atlas ROI, followed by motion related noise correction. Mean activation during each trial's onset and duration was computed for positive and negative music and non-music stimuli. In the second-level analysis cerebellar activation was compared between control and MDD groups using two-sample t-tests separately for each emotion condition ($p < 0.05$). The results showed significant difference for positive non-music trials, where 'Control subjects' had higher cerebellar activation than 'MDD subjects' Further exploring this result, it was found that Control participants showed higher activation in Crus I and II regions, whereas MDD participants had greater activation in lobules VII and X for the stimuli of positive non music. By focusing on the cerebellum, current study found that music-emotion processing differs between control and MDD groups.

Keywords : Emotion, Music, Cerebellum

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P-594

Slc45a1-Htr2a axis as a regulator of female-biased neurodevelopmental disorder

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Slc45a1, a proton-coupled glucose transporter, has recently been associated with neurodevelopmental disorders (NDDs) through a few human genetic studies. However, the underlying neurobiological mechanisms remain poorly understood. To address this, we developed a Slc45a1-knockout (KO) mouse and discovered sex-dimorphic behavioral phenotypes resembling core features of neurodevelopmental disorders, such as reduced social preference, impulsivity, inattention, anxiety, and hyperactivity. The behavioral alterations were accompanied by neurophysiological changes including E/I imbalance and altered intrinsic action potential properties in the medial prefrontal cortex (mPFC). Slc45a1-KO cells showed an increased pH both in vitro and ex vivo, compared to WT. To understand how an alkalized intracellular environment could contribute to these alterations, we performed a bulk RNA-sequencing and observed a significant upregulation of Htr2a, serotonin receptor 2a (5-HT2A) specifically in female KO mice, which was also confirmed by qRT-PCR. Furthermore, we found that treatment with volinanserin, a 5-HT2A antagonist, ameliorated several NDD-like behavioral phenotypes of female Slc45a1-KO mice, including inattention, reduced social preference, and hyperactivity, while impulsivity remained unaffected.Taken together, our findings suggest that Slc45a1 deficiency causes female-biased neurodevelopmental disorder traits through pH dysregulation and heightened serotonergic signaling. Moreover, our study highlights the Slc45a1-Htr2a axis as a critical regulator of NDD phenotypes in female mice.

Keywords : Slc45a1, Neurodevelopmental disorder, Sex-specific phenotype, pH dysregulation, Serotonin receptor

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P-595

MLC1 deficiency alters microglial phenotype and disrupts homeostasis of adult neural stem cells

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Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a neurodevelopmental disorder primarily attributed to astrocytic and oligodendrocytic dysfunction. However, the role of microglia remains unclear. To investigate microglial involvement, we used 2-month-old MLC1 knockout (KO) mice and first validated MLC1 deletion by qPCR, along with astrocytic hypertrophy confirmed by immunohistochemistry (IHC). We observed a significant reduction in IBA1+ immunoreactive area in the hippocampus of MLC1 KO mice, accompanied by decreased

RNA expression of *Aif1*, suggesting diminished microglial presence. However, Toll-like receptor expression (*Tlr2*, *Tlr4*, *Tlr7*, and *Tlr9*) was unchanged, indicating preserved innate immune recognition in microglia. In contrast, the complement system showed distinct alterations as the expression of *C3*, which is primarily derived from astrocytes and involved in opsonization, was increased, whereas *CD11b* and *ITGB2*, which are components of complement receptor 3, and *C1qa* and *C1qb*, which are predominantly expressed by microglia and initiate the complement cascade, were downregulated. Additionally, hippocampal expression of *Cxcl12* and *Il4* was significantly reduced in MLC1 KO mice, suggesting impaired chemotactic and anti-inflammatory signaling. Given the role of microglia in adult neurogenesis, we further examined Ki67 expression and found an increase in the number of Ki67+ cells in the subgranular zone of MLC1 KO mice. However, cleaved caspase-3 staining revealed no difference in apoptosis between MLC1 wild-type and KO mice. Collectively, these results suggest that MLC1 deficiency not only affects astrocytes and oligodendrocytes but also involves microglial dysregulation, which can impact adult stem cell homeostasis. A comprehensive understanding of MLC pathophysiology requires consideration of all major glial cell types.

Keywords : Megalencephalic leukoencephalopathy with subcortical cysts (MLC), Microglia, Adult hippocampal neural stem cell, Complement system, Neurodevelopmental disorder

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P-596

Astrocyte-derived extracellular vesicles induced by glutamate suppress glioblastoma growth

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Glioblastoma (GBM), the most prevalent and aggressive primary brain tumor, presents formidable therapeutic challenges, with limited advancements in treatment improving patient outcomes. Extracellular vesicles (EVs), lipid bilayer-enclosed particles secreted by various cell types, facilitate intercellular communication through the transfer of bioactive molecules, including nucleic acids and proteins. EVs are increasingly recognized for their role in brain tumor progression and their potential utility as diagnostic and therapeutic agents. Our previous findings reveal that glutamate restricts GBM growth and promotes the formation of astrocytic barriers by upregulating astrocytic monoamine oxidase-B (MAO-B) activity and facilitating the deposition of chondroitin sulfate proteoglycans (CSPGs). However, the biological function of glutamate-induced astrocyte-derived extracellular vesicles (AEVs) influence glioblastoma growth remain largely unknown. Here, we identify a previously unrecognized function of glutamate-induced AEVs in suppressing the GBM. We further demonstrate that EVs derived from reactive astrogliosis exert tumor-suppressive effects, characterized by increased EV release and cargo modifications in response to glutamate. To elucidate the functional significance of reactive astrogliosis-derived EVs in GBM, we aim to identify key molecular cargo enriched within these vesicles. Our findings provide in-depth insights into the specialized roles of AEVs and the glutamate-mediated alterations in their nucleic acid and protein composition. These results suggest that glutamate-induced AEVs could serve as a foundation for their targeted regulation and potential application as therapeutic tools in reactive astrogliosis-associated brain diseases.

Keywords : Glioblastoma, Astrocyte-derived extracellular vesicles, Glutamate signaling, Reactive astrogliosis, Cancer suppression

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P-597

Dose-Dependent Inversion of LSD-Induced Behavior Suggests β-arrestin2-Mediated Addiction Potential at Ultra-Low Concentrations

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Lysergic acid diethylamide (LSD) is a classical serotonergic hallucinogen with high affinity for the 5-HT_2A receptor, a GPCR that initiates downstream signaling via both Gq proteins and β-arrestin2. Gq signaling has been linked to synaptic plasticity and neuroprotective effects, while β-arrestin2 mediates hallucinogenic responses. Although LSD has been widely regarded as non-addictive, our intravenous self-administration (SA) study in mice revealed unexpected operant drug-seeking behavior at ultra-low doses (0.0005 and 0.00005 mg/kg), whereas no such behavior was observed at higher doses (0.05 and 0.1 mg/kg). This paradox suggests that LSD may trigger reinforcement behavior via β-arrestin2-biased signaling at specific low concentrations. Given that β-arrestin2 is also involved in addiction pathways of opioids and stimulants, we propose that the addictive potential of LSD is dose- and location-dependent. The concept of location bias—where LSD activates distinct intracellular pathways depending on receptor localization (plasma membrane vs. endosome)—may explain this inversion (Dong et al., *Science*, 2023). This finding challenges the conventional view of LSD's abuse liability and provides a novel framework for its therapeutic application. Further validation will include dose-dependent analysis of BDNF signaling and 5-HT_2A receptor localization using Western blotting and confocal imaging.

Keywords : LSD, Beta-arrestine2, BDNF, Gq signaling, drug addiction

P-598

PLXDC2 fine-tunes microglial inflammatory and phagocytic responses in Alzheimer's disease

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Microglia are central orchestrators of neuroinflammation in Alzheimer's disease (AD), yet the molecular cues that define their pathogenic states remain incompletely resolved. By integrating bulk and single-nucleus RNA-sequencing data with brain and cerebrospinal-

fluid (CSF) proteomic meta-analyses, we pinpoint plexin-domain-containing protein 2 (PLXDC2) as the only molecule consistently up-regulated at both transcript and protein levels across AD-vulnerable brain regions and CSF. Single-cell resolution mapping further confines PLXDC2 expression to microglial subclusters enriched for inflammatory, phagocytic, and lipid-processing signatures closely associated with amyloid-β (Aβ) plaques. Despite this prominent enrichment, the functional role of PLXDC2 in microglia has been unexplored. Here we demonstrate that PLXDC2 overexpression in BV2 microglia triggers a transient, biphasic cytokine profile—early (6 h) suppression of IL-6 followed by later (24 h) attenuation of IL-1β—while leaving TNF-α unchanged. PLXDC2 also attenuates bulk particle phagocytosis, evidenced by reduced uptake of pHrodo-zymosan and Aβ fibril, yet does not affect synaptic debris clearance or lipid-droplet accumulation. These findings indicate that PLXDC2 selectively fine-tunes discrete microglial effector functions, dampening pro-inflammatory signaling and non-specific phagocytosis without impairing synaptic pruning or lipid metabolism. Together, our multi-omics discovery and mechanistic validation establish PLXDC2 as a previously unrecognized immunoregulatory receptor that shapes key facets of microglial activation in AD. Modulating PLXDC2 activity may therefore recalibrate microglial responses toward neuroprotection and offer a novel therapeutic strategy for mitigating AD progression.

Keywords : Alzheimer's disease, Microglia, Neuroinflammation

P-599

Microglial extracellular vesicle biomolecule tracking system (micEV-BTS) for prediction of microglia-neuron intercellular communications

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Intercellular communications between microglia and neurons are crucial for synaptic functioning including brain electric oscillation, synaptic transmission, axonal growth, and ion fluxes. Microglial extracellular vesicles (micEVs) have emerged as essential intermediates for microglia-neuron bidirectional communication; however, accurately quantifying micEVs from living cells in real-time has proven to be a significant challenge. In this study, we introduce a new platform that can quantify and track microglia-derived EVs in real-time. We deliver lentiviral vectors (CD81-pmiRFP670, pLenti-DsRed_IRES_SNCA:EGFP) into microglial cells and create a new analytic platform to tag microglia-derived EVs (RFP670 tagged CD81) and intravesicle-alpha-synuclein (EGFP tagged) simultaneously by via co-transduction method. We quantify the amount of monomeric alpha-synuclein or preformed fibrils in EVs using fluorescence correlation spectroscopy. Finally, we track and quantify micEVs and alpha-synuclein in real-time by our platform called Microglial Extracellular Vesicle Biomolecule Tracking System (micEV-BTS). Our platform can also contribute as a clinical application to predict or prevent neurological diseases and track disease progression.

Keywords : Parkinson's Disease, microglia, Exosome, Fluorescence Correlation Spectroscopy(FCS), Transduction

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P-600

Primary visual cortex dysfunction underlies visual learning deficits in a *Grin2b*$^{C456Y/+}$ mouse model of ASD

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Atypical sensory processing is a diagnostic feature of autism spectrum disorders (ASD), and sensory processing deficits are both diverse and commonly observed in individuals with ASD. One well-known ASD risk gene is *GRIN2B*, which encodes the GluN2B subunit of the ionotropic glutamate NMDA receptor. Although *Grin2b*-mutant mice showed hypersensitivity to somatosensory stimuli, other sensory abnormalities poorly understood. In this study, we identified abnormal visual processing in *Grin2b*-mutant mice carrying the heterozygous ASD-risk C456Y mutation (*Grin2b*$^{C456Y/+}$). *Grin2b*-mutant mice exhibited delayed learning in an orientation discrimination task, despite having normal optokinetic responses. Using *in vivo* two-photon calcium imaging, we found that neurons in the primary visual cortex (V1) of *Grin2b*-mutant mice exhibited increased spontaneous and stimulus-evoked activity, as well as broader orientation tuning. Moreover, V1 neurons in *Grin2b*-mutant mice failed to develop learning-dependent changes, such as sparser and stronger responses to the reward-associated stimulus following learning, that are observed in wild-type mice. Together, our findings provide new evidence that *Grin2b*$^{C456Y/+}$ mice exhibit impaired visual processing in V1, which may contribute to broader sensory deficits associated with *GRIN2B* mutations in ASD.

Keywords : Autism spectrum disorders, Grin2b, Visual processing, Perceptual learning, In vivo two photon imaging

Acknowledgements : This work has been supported by grants to S.H.L. from the Institute for Basic Science (IBS-R002-A2).

P-601

Female-specific role of basolateral amygdala endocannabinoid signaling in an animal model of depression

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Depression is more prevalent in females than males, yet the underlying metabolic mechanisms contributing to this disparity remain poorly understood. The sub-chronic variable stress (SCVS) protocol has recently been proposed as a model of female-specific stress vulnerability. Using this model, we performed non-targeted metabolomics analysisand found elevated arachidonic acid (AA) levels in stressed females but decreased levels in stressed males.

However, direct administration of AA to females induced no behavioral changes, suggesting that downstream metabolites, rather than AA itself, may mediate depressive behaviors. Thus, we reprogrammed AA metabolism by inhibiting key enzymes: fatty acid amide hydrolase (FAAH) with URB597, Monoacylglycerol lipase(MAGL) with JZL184, and phospholipase A2 (PLA2) with quinacrine. Only FAAH inhibition alleviated depressive-like behaviors in stressed females. URB597 also normalized increased spontaneous excitatory postsynaptic currents (sEPSCs) in the basolateral amygdala (BLA). This effect was blocked by CB1 receptor antagonist, AM251, indicating that anandamide (AEA) may play a role. To directly test the role of BLA, we infused URB597 via intra-BLA cannulation. Surprisingly, this exacerbated depressive-like behaviors in stressed females. This paradoxical effect suggests that AEA elevation within the BLA engages region-specific mechanisms that may promote, rather than buffer, stress response in females. Our findings revela a complex, region-dependent role of endocannabinoid signaling in female depression and suggest that therapeutic strategies may require targeted modulation of brain circuits

Keywords : Sex difference, Endocannabinoid, Anandamide(AEA), BLA, Depression

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P-602

A homozygous missense of TTYH3, a volume-regulated anion channel(VRAC), links lysosomal dysregulation to Autism spectrum disorder

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Autism spectrum disorders (ASDs) are common neurodevelopmental conditions that typically arise in early childhood and are thought to result from a complex interplay between genetic and environmental factors. A recent clinical study has reported an ASD patient with a missense mutation in TTYH3, a potential regulator of lysosomal osmolarity that acts as a lysosomal volume-regulated anion channel (Lyso-VRAC) to maintain lysosomal homeostasis. Based on this, we successfully generated a mouse model carrying a TTYH3 V349M mutation, which recapitulates the genetic defect and associated phenotype observed in patients, including impaired social interactions and obsessive-compulsive behaviors. Recent studies have reported elevated levels of lysosomal-associated membrane protein 1 (LAMP1) in various genetic animal models of ASD, suggesting that abnormal lysosomal function is involved in ASD. However, the underlying mechanisms linking lysosomal dysfunction to ASD remain poorly understood. We hypothesize the contribution of TTYH3 V349M mutation to lysosomal regulation and its role in ASD pathogenesis caused by upregulated TTYH3 expression in lysosomes. To investigate this possibility, we aim to confirm altered subcellular localization of TTYH3 in human induced pluripotent stem cell(hiPSC) derived astrocyte with V349M mutation introduced by CRISPR system. To further elucidate the role of TTYH3 point mutations in brain function, we plan to demonstrate altered astrocytic autophagy and lysosomal activity. We next sought to assess neuronal activity through whole-cell patch clamp to determine the potential effect of astrocyte-autophagy dysregulation on neuronal activity. Finally, we will test whether the targeted inhibition of lysosomal autophagy within astrocytes can restore neuronal function and lead to ASD-like behavioral rescue. Our work suggests that targeting TTYH3 and its associated pathways could represent a therapeutic strategy, addressing lysosomal dysfunction in ASD.

Keywords : Autism spectrum disorder, TTYH3, Lyso-VRAC

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P-603

Subunit-selective BK channel modulation rescues behavioral and electrophysiological deficits in Angelman syndrome.

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Angelman syndrome (AS) is a severe neurodevelopmental disorder caused by the loss of function of the UBE3A gene inherited from the mother. AS results in intellectual disability, motor dysfunction, and intractable epilepsy. Current treatments are largely symptomatic and there are no targeted therapeutics available. Previously, we demonstrated that upregulating calcium-activated large-conductance potassium (BK) channels induces neuronal hyperexcitability in AS using induced neurons derived from human pluripotent stem cells (hPSCs) and a mouse model of AS. BK channels play a central role in regulating action potential repolarization and firing frequency. These channels comprise a pore-forming alpha subunit (BKα) and various modulatory beta (BKβ) subunits. The β4 subunit is highly enriched in the brain and imparts distinct gating properties in neurons of the central nervous system (CNS). Here, we report the discovery of a first brain-selective modulator of the BK channels composed of BKαβ4, identified through a high-throughput functional screen. In vitro electrophysiological recordings of human induced neurons derived from hPSCs confirmed that this modulator significantly reduced action potential firing rates. Treatment with this modulator rescues seizure severity in chemoconvulsant-induced seizures in AS mice without causing observable motor or behavioral side effects. These findings establish BKαβ4 modulation as a promising precision therapeutic strategy for AS and potentially for other neurodevelopmental disorders.

Keywords : Angelman syndrome, BK channels, Neuronal hyperexcitability, CNS-selective inhibitors, Epilepsy therapeutics

P-604

Comparative Analysis of Subcortical Diffusion Metrics in 3T and 7T MRI: Implications for Parkinson's Disease Imaging Using Lead-DBS and HCP D

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Accurate imaging of subcortical structures is essential in studying

neurodegenerative diseases such as Parkinson's disease (PD), where dopaminergic neuron loss in the substantia nigra (SN) disrupts motor circuitry. This study compares diffusion MRI measures between 3T and 7T field strengths in subcortical regions relevant to PD. Using data from 49 healthy female subjects from the Human Connectome Project (HCP), we employed Lead-DBS for automated segmentation of 11 subcortical structures and DSI Studio for reconstructing diffusion connectomes and extracting key metrics: fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). Images were preprocessed with the HCP pipeline, and we standardized spatial resolution to 1.25 mm while excluding b = 3000 shells from 3T data. Statistical comparisons using FDR-corrected t-tests revealed significantly higher FA, MD, and RD in the left SN at 3T; higher MD and RD in the right amygdala; higher AD in the right red nucleus; and higher MD and AD in the right SN and subthalamic nucleus (STN). Connectivity analysis showed that over 85% of significant differences in FA, MD, and QA also favored 3T. Despite the spatial resolution advantages of 7T, our results indicate that 3T may provide more stable diffusion metrics due to reduced susceptibility to signal distortion and acquisition variability. These findings highlight the importance of acquisition protocol selection in diffusion MRI analysis of subcortical structures and support the use of Lead-DBS and DSI Studio as a reliable and largely automated pipeline for PD-related diffusion studies.

Keywords : Parkinson's disease, Diffusion MRI, Subcortical structures, 3T and 7T MRI, Lead-DBS

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P-605

Scn2a-linked myelination deficits and synaptic plasticity alterations drive auditory processing disorders in an ASD mouse model

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by complex sensory processing deficits, which continue to elude comprehensive mechanistic understanding. A key unresolved question is how alterations in neural connectivity and communication translate into the behavioral manifestations seen in ASD. Here, we investigate how oligodendrocyte dysfunction alters myelin plasticity and neuronal activity, leading to auditory processing disorder associated with ASD. We focus on the *SCN2A* gene, an ASD-risk factor, to understand its role in myelination and neural processing within the auditory nervous system. Transcriptional profiling suggests alterations in the expression of myelin-associated genes in *Scn2a* conditional knockout mice, highlighting the cellular consequences engendered by *Scn2a* deletion in oligodendrocytes. The results reveal a nuanced interplay between oligodendrocytes and axons, where *Scn2a* deletion causes alterations in the intricate process of myelination. This disruption instigates changes in axonal properties, presynaptic excitability, and synaptic plasticity at the single cell level. Furthermore, oligodendrocyte-specific *Scn2a* deletion compromises the integrity of neural circuitry within auditory pathways, leading to auditory hypersensitivity. Our findings reveal a pathway linking myelin deficits to synaptic activity and sensory abnormalities in ASD.

Keywords : Scn2a, Autism, Sodium Channel 1.2, Oligodendrocyte, Myelin

P-606

Endothelial DR6 Mediates Blood-Brain Barrier Dysfunction in Alzheimer's Disease

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Impairment of the blood-brain barrier (BBB), primarily composed of brain endothelial cells (BECs), is increasingly recognized as a key factor in the early pathogenesis of Alzheimer's disease (AD). Death receptor 6 (DR6) is highly expressed in BECs and acts as downstream of the Wnt/β-catenin pathway to promote BBB formation during development. Using an easy-to-perform method that we developed specifically for microvessel isolation and primary brain endothelial cell culture, we found that brain endothelial DR6 levels were significantly reduced in AD mouse model (APPswe/PS1dE9) at the onset of amyloid-β (Aβ) accumulation. This reduction was recapitulated in cultured BECs treated with toxic $A\beta_{25-35}$ oligomers. We further showed that suppressing DR6 exacerbated BBB dysfunction in the presence of $A\beta_{25-35}$ oligomers, while overexpressing DR6 enhanced the level of BBB functional proteins by activating both Wnt/β-catenin and JNK pathways. In conclusion, our findings provide new insight into the role of endothelial DR6 in AD pathogenesis, highlighting its potential as a therapeutic target to rescue BBB dysfunction in early-stage AD.

Keywords : Death receptor 6, Brain endothelial cells, Blood-brain barrier, Alzheimer's Disease

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P-607

Chemical A ameliorates cognitive impairment and neuroinflammation in a mouse model of Alzheimer's Disease

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Alzheimer's disease (AD) is a neurodegenerative disorder defined by progressive memory loss and cognitive decline. Although its pathological mechanisms are not fully understood, recent studies suggest a key role of neuroinflammation and metabolic dysregulation in disease progression. Chemical A is a small-molecule activator of a specific deacetylase known to modulate inflammatory and metabolic pathways. Based on these properties, we evaluated the therapeutic potential of Chemical A in a mouse model of AD. 5xfad mice are a transgenic model carrying five human mutations (APP: Swedish, Florida, London; PSEN1: M146L, L286V) that cause early and

aggressive amyloid pathology and cognitive impairment. Chemical A was administered through the standard diet. Behavioral assessments showed that Chemical A significantly improved memory performance. In the forced Y-maze test (FYMT) and the novel object recognition test (NOR), treated mice showed recovery of short-term and recognition memory. In the Morris water maze test (MWM), Chemical A reduced escape latency and promoted hippocampus-dependent search strategies. The open field test (OFT) revealed no alterations in locomotor function, and the elevated plus maze test (EPM) showed that disinhibition-like behavior remained unaffected by Chemical A. Immunofluorescence analysis demonstrated that Chemical A reduced amyloid-β accumulation and attenuated neuroinflammation, as indicated by reduced GFAP and Iba-1 signal intensities in hippocampal and cortical areas. These findings suggest that Chemical A improves learning and memory in 5xfad mice, independently of disinhibition-like behavior, and may have therapeutic potential for Alzheimer's disease.

Keywords : Alzheimer's disease, 5xfad, Chemical A, Behavioral tests, Neuroinflammation

P-608

Tiny monkey astronauts: A Feasibility validation of Marmoset-based realtime monitoring technology for space station brain networks

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Microgravity, circadian rhythm disruptions, and high-energy radiation in space significantly impact brain structure and function. However, no real-time technology currently exists in space laboratories for continuous long-term on-orbit monitoring of experimental animals' brain structure and function.This study established a ground-based validation system to assess the feasibility of marmoset-based real-time monitoring technology for long-term on-orbit monitoring of space station brain networks. Key developments include a custom marmoset carrier table and an animal centrifuge, designed to enable animal immobilization, vibration damping, and environmental conditioning. Using the centrifuge and a vibration table, we simulated the overload conditions and random vibrations experienced during the spacecraft ascent phase, respectively.Results showed that marmosets adapted well to these simulated overload and vibration environments, with notable changes observed in certain cytokines, such as interleukin 6 and interleukin 1-ß. Additionally, a multi-channel electrophysiological recording system and single-photon calcium imaging were used to synchronously monitor neuronal activity in the marmosets' primary motor cortex (M1). This work marks the first observation of space-specific environmental effects on M1 neuronal activity, laying a robust theoretical foundation for future efforts to safeguard astronauts' brain function and health.

Keywords : Common marmoset, Acceleration overload, Random vibration, Multichannel electrophysiology , Motor cortex

P-609

Acupuncture modulates the expression of circadian clock genes in a Parkinson's disease mouse model

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Circadian rhythm dysfunction is a common non-motor symptom of Parkinson's disease (PD). Although acupuncture has shown potential to modulate circadian rhythms, its effects in PD remain unclear. Here, we administered acupuncture at KI6 and BL62 acupoints for 12 days in an MPTP-induced PD mouse model to evaluate its therapeutic effects. Acupuncture restored disrupted sleep patterns to a state similar to controls and showed a tendency to improve motor deficits, along with increased tyrosine hydroxylase expression in the striatum. Rhythmic expression of dopamine synthesis-related genes (Th, Ddc, Dat) and core clock genes (Clock, Bmal1, Per1, Per2, Cry1) was also recovered. Furthermore, expression patterns of Pmch and Mchr1, regulators of the sleep-wake cycle, were normalized. These findings suggest that acupuncture may alleviate circadian rhythm disturbances in PD by modulating MCH neuronal activity and circadian gene expression, providing a potential therapeutic strategy for managing non-motor symptoms in PD.

Keywords : Parkinson's disease, Circadian rhythm, Non-motor symptoms, Acupuncture

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P-610

Glial-Mediated Neuroinflammation in Chronic Stress: A Molecular Link to Brain Disorders

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Chronic stress plays a huge role in the physical and mental health. Numerous studies show that chronic stress has a huge negative impact on the human body (Maximilian Seitz, 2025). Over an extended period of time, the unresolved chronic stress can induce neuroinflammation by the activation of the hypothalamic–pituitary–adrenal axis, which leads to the release of glucocorticoids (Ioulia Kokka;, 2023). Glial cells like microglia and astrocytes are also stimulated by prolonged stress, which sets off neuroinflammatory cascades that disrupt neuronal function and can act as a contributing factor in the development of neurodegenerative and mental health conditions (Sameer Hassamal, 2023). The prolonged effect of chronic stress can cause neuroinflammation, which plays a pivotal role in the onset of brain disorders such as depression, anxiety, schizophrenia, and chronic pain (Diana I Lurie, 2018). With a focus on finding early biomarkers and potential therapeutic targets, this study attempts to investigate the molecular and cellular pathways by which glia-mediated neuroinflammation is induced by chronic stress. In order to investigate glial responses to chronic stress exposure, we performed an integrative literature analysis and examined publicly available transcriptome datasets. Our study offers a more comprehensive, integrative viewpoint that emphasizes glial cells as a key connection between chronic stress and neuropathology, whereas other research

has concentrated on discrete elements of stress-related pathology.

Keywords : Chronic Stress, Neuroinflammation, Glial Cells, Transcriptomics, Brain Disorders

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P-611

Hippo kinases MST1/2 (STK4/3) regulate microglial homeostasis and inflammation in the CNS

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Background: The Hippo signaling pathway is a crucial regulator of immune responses, with MST1/2 (STK4/3) kinases serving as key upstream regulators in both innate and adaptive immunity. While their function in immune cell homeostasis and function is well established, their role in microglia—the resident macrophages of the central nervous system (CNS)—remains unclear. Aim: This study investigates the role of MST1/2 in microglial function and explores their potential as therapeutic targets for modulating microglial activity in CNS inflammation. Method: To elucidate the role of MST1/2 in microglia, we generated Cx3cr1-CreER x Mst1/2flox/flox mice for microglia-specific MST1/2 deletion. Microglial number, activation, and morphology were analyzed by flow cytometry and immunofluorescence. Mitochondrial structure and function were assessed via MitoTracker, TMRM, and electron microscopy. Cytokine/chemokine production was evaluated using multiplex arrays. Inflammatory responses and microglia–vascular interactions were further characterized using peripheral LPS challenge model. Result: MST1/2-deficient microglia exhibit disrupted homeostasis characterized by paradoxical increases in both proliferation and apoptosis. Deletion of MST1/2 induces mitochondrial hyper-fusion, accompanied by a metabolic shift toward glycolysis and elevated autophagic activity. Functionally, these microglia become hyper-reactive to inflammatory stimuli and secrete excessive proinflammatory cytokines. Moreover, MST1/2 deletion compromises microglial perivascular positioning, impairs vascular integrity, and facilitates increased leukocyte infiltration into the CNS parenchyma under systemic inflammatory challenge. Conclusions: MST1/2 are critical regulators of microglial homeostasis, immune reactivity, and vascular interactions. These findings underscore the importance of the Hippo pathway in CNS immune regulation and suggest MST1/2 as potential therapeutic targets for neuroinflammatory diseases.

Keywords : Microglia, Hippo signaling pathway, MST1/2 (STK4/3), Immunometabolism, Neuroinflammation

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P-612

Novel Intranasal Delivery of Sihosogansan Demonstrates Rapid Antidepressant Activity via GABAergic and BDNF/TrkB Pathways

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Background: Sihosogansan (SHSGS) is a traditional medicine used to treat depression. However, conventional oral administration requires high doses and prolonged treatment periods. This study aimed to investigate the rapid antidepressant effects of intranasal SHSGS and to identify its Q-markers. Methods: In zebrafish, SHSGS effects were evaluated in an MK-801-induced anxiety model using electroencephalogram (EEG) recordings. In mice, the rapid effects of intranasal versus oral SHSGS were compared through the open field and tail suspension tests. Mechanistic investigations combined computational network analysis with molecular studies of hippocampal tissue and primary neurons. Q-markers were identified through the integrative analysis of gas chromatography-mass spectrometry data, molecular docking, and experimental validation in behavioral and cellular models. Results: SHSGS normalized MK-801-induced EEG abnormalities within 30 minutes in zebrafish, particularly restoring delta/beta and theta/beta ratios. In mice, intranasal SHSGS showed rapid anxiolytic and antidepressant effects at 30 minutes post-administration, whereas oral administration had no significant effect. Mechanistically, the extract enhanced gamma-aminobutyric acid (GABA)ergic signaling by increasing hippocampal GABA type B receptor subunit 1, glutamate decarboxylase 67, and GABA levels, while activating the brain-derived neurotrophic factor/tropomyosin receptor kinase B/extracellular signal-regulated protein kinase (BDNF/TrkB/ERK) pathways. Through comprehensive analysis, three compounds - terpinen-4-ol, α-terpineol, and (-)-β-pinene - were identified as Q-markers, exhibiting mechanism-based activities comparable to the total extract. Conclusion: These findings demonstrate that intranasal SHSGS acts rapidly against depression through the GABAergic and BDNF/TrkB/ERK pathways, with identified Q-markers providing a foundation for optimization of quality.

Keywords : Sihosogansan, rapid-acting antidepressant, intranasal administration, neuritogenesis, Q-marker

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P-613

CREB2 as a Key Mediator of Oxidative Glutamate Toxicity in Neurons: Implications for Microglia-Induced Neuroinflammation

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Background: CREB2 (also known as ATF4) is a stress-responsive transcription factor implicated in diverse cellular responses, including

oxidative stress and neuronal injury. While glutamate-induced oxidative cytotoxicity is a well-established mechanism in neurodegeneration, the regulatory role of CREB2 in this process remains incompletely understood. Methods: To examine the specific contribution of CREB2, we first treated HT22 hippocampal neuronal cells with exogenous glutamate and assessed intracellular ROS levels, CREB2 protein expression, and cell viability. To investigate endogenous sources of glutamate, we stimulated BV2 microglial cells with lipopolysaccharide (LPS) and analyzed glutamate release and CREB2 expression in neurons treated with LPS-conditioned media (LPS-CM). The antioxidant N-acetyl-cysteine (NAC) was used to evaluate the ROS dependency of CREB2 activation. Results: Glutamate-treated HT22 neurons exhibited robust increases in ROS and CREB2 protein levels, accompanied by neuronal death. LPS-CM also elevated CREB2 expression and induced neurotoxicity, mimicking the effect of exogenous glutamate. Importantly, NAC co-treatment inhibited CREB2 upregulation and attenuated cell death in both glutamate- and LPS-CM-treated neurons, indicating ROS-dependent activation of CREB2. Conclusion: These findings identify CREB2 as a critical mediator of oxidative glutamate toxicity and suggest that microglia-derived glutamate contributes to non-cell-autonomous neuronal death via ROS–CREB2 signaling. Our results provide novel insight into the role of CREB2 in neuroinflammation and highlight it as a potential therapeutic target for glutamate-mediated neuronal damage.

Keywords : CREB2, glutamate, HT22, LPS, ATF4

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P-614

Neural precursor cells restore cognition and attenuate neuroinflammation by modulating autophagic mechanisms in Alzheimer's disease models

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by extracellular amyloid-β (Aβ) plaques, intracellular hyperphosphorylated tau tangles, synaptic dysfunction, and chronic neuroinflammation, ultimately leading to neuronal loss and cognitive decline. Due to the multifactorial AD pathology, recent studies have explored stem cell therapies, especially neural precursor cells (NPCs), to restore neural function, reduce pathology, and modulate neuroinflammation. The therapeutic potential of neural precursor cells (NPCs) derived from human pluripotent stem cells was assessed following intracerebroventricular (ICV) administration in two AD mouse models: an $A\beta_{1-42}$ injection model and the APP/PS1 transgenic mice. NPC transplantation enhanced hippocampal neurogenesis and significantly led to robust improvements in learning and memory deficits, as demonstrated by behavioral assessments. NPC-treated mice showed increased Aβ clearance (6E10, $p<0.05$ in hippocampus; $p<0.001$ in cortex; Thioflavin-S, $p<0.01$ in hippocampus; $p<0.001$ in cortex), attenuated neuroinflammation (TLR4, $p<0.01$ in both regions), and reduced activation of inflammasome signaling (NLRP3, $p<0.01$ in both regions). In addition, administration of NPCs also led to reduced levels of phosphorylated tau and diminished accumulation of autophagy-related substrates, indicating modulation of key pathological hallmarks implicated in AD progression. Furthermore, restoration of autophagic flux was accompanied by dampened immune responses surrounding protein aggregates, suggesting that NPC transplantation confers neuroprotection, at least in part, through modulating innate immune activity and promoting lysosomal function. Taken together, these findings demonstrate that transplantation of NPCs exerts both neuroprotective and immunomodulatory effects in the AD brain, underscoring their promise as a multifaceted therapeutic strategy for Alzheimer's disease.

Keywords : Alzheimer's disease, Neural precursor cells, Amyloid-β clearance, Autophagic flux, Tau pathology

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P-615

Synaptic ultrastructural alterations in human focal cortical dysplasia: insights from volume electron microscopy

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Focal cortical dysplasia (FCD) is a developmental disorder of the cerebral cortex and a leading cause of intractable epilepsy in children. A disrupted excitation-inhibition balance is a hallmark of neuronal hyperexcitability in FCD, yet the underlying ultrastructural mechanisms remain poorly understood. Using volume electron microscopy, we performed a morphological assessment of synapses and organelle distribution in the temporal cortical layer III of an FCD patient. Notably, the dysplastic region displayed fewer excitatory synapses but contained extra-large synapses with more synaptic vesicles. Additionally, inhibitory synapses were located further away from the nearest excitatory synapses, possibly weakening the effectiveness of inhibition in the dysplastic area. There was an increase in mitochondrial density and altered mitochondrial morphology within presynaptic boutons, along with a reduced proportion of postsynaptic protrusions containing a spine apparatus, indicating deficits in intracellular calcium handling and synaptic plasticity. These findings suggest that synaptic architectural modifications may contribute to neuronal hyperexcitability associated with epilepsy in FCD.

Keywords : Cortex, Epilepsy, Hyperexcitability, Synapse, Mitochondria

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P-616

Distribution of ChAT-Positive Neurons in the DMV of a Primate Parkinsonism Model

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The dorsal motor nucleus of the vagus (DMV) is a key cholinergic center within the vagal parasympathetic pathway. It contains large populations of cholinergic neurons expressing choline acetyltransferase (ChAT), a critical enzyme for acetylcholine synthesis and a common marker of cholinergic integrity. These neurons regulate visceral autonomic functions and may be involved early in Parkinson's disease (PD), particularly related to non-motor symptoms. However, DMV pathology remains undercharacterized in nonhuman primates (NHPs). In this study, we analyzed the spatial distribution of ChAT-positive neurons in the DMV following unilateral intracarotid artery administration of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in cynomolgus monkeys. ChAT-positive cells were visualized using DAB-based immunohistochemistry, and adjacent sections were Nissl-stained to delineate DMV cytoarchitecture. No statistically significant or consistent asymmetry was observed between hemispheres. However, minor differences in local cell density or spatial distribution could not be ruled out. These results suggest that DMV cholinergic neurons may be relatively preserved in early-stage MPTP-induced parkinsonism. This preservation, along with the chronic-phase features of the model, may reflect limited vulnerability or compensatory mechanisms. Nonetheless, subtle topographic or subcellular alterations may exist but remain undetected without higher-resolution spatial or functional analysis. This study provides a histological reference for future assessments of DMV pathology in NHP models and raises the possibility that this region contributes to early autonomic dysfunctions in PD. High-resolution mapping and physiological evaluations are warranted to clarify the relevance of these early cholinergic changes.

Keywords : Dorsal motor nucleus of the vagus (DMV), Parkinson's disease, Cholinergic neurons, Nonhuman primates (NHP), MPTP model

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P-617

Exploring Brain-Heart Interaction in Cognitive Function: The Roles of Heart Rate Variability and Sex Differences

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The heart and brain are intricately connected through a bidirectional regulatory system, influencing with each other to ensure adaptive responses to internal and environmental stimuli. This dynamic interaction, refer to as the brain-heart axis, plays a vital role in human well-being. Heart rate variability (HRV), a widely recognized indicator of the autonomic nervous system (ANS), has emerged as a key parameter for assessing brain-heart interaction. Recent research based on the close link between ANS function and brain activity has revealed significant associations between HRV metrics and brain function indices, highlighting the potential of HRV in the early detection and management of neurodegenerative diseases. Furthermore, sex differences have been shown to modulate brain-heart interactions across the lifespan. For instance, women display distinct patterns of cognitive decline related to vascular factors. While active research is underway in the field of neurocardiology, the diverse parameters of HRV measurement make it difficult to draw comprehensive conclusions. In particular, the influence of sex and gender on the relationship between HRV and cognitive function remains underexplored. This review systematically elucidates existing literature on HRV and cognitive function, identifies the HRV analysis methods most closely associated with cognitive decline, and summarizes the current status and study results related to sex and gender differences in heart-brain interactions. Studies published within the last 15 years were reviewed using key search terms including "HRV (heart rate variability, electrocardiography)", "brain (brain/cognitive function)", and "brain-heart (brain-heart axis/interaction)", and related terms. By identifying gaps in current research, this review provides a foundation for future studies aimed at refining HRV- based assessments of cognitive health and better understanding sex- and gender- specific mechanisms in the brain-heart axis.

Keywords : brain-heart axis, Heart rate variability, Brain, Cognitive function, Sex difference

P-618

Hippocampal Microstructural and Proteomic Changes in Pilocarpine-induced Temporal Lobe Epilepsy Model

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This study examined seizure mechanisms in a temporal lobe epilepsy (TLE) model by analyzing microstructural and proteomic changes in hippocampal regions following localized pilocarpine injection into the right hippocampus of Sprague–Dawley rats. Spontaneous recurrent seizure (SRS) duration and severity were assessed at 4 and 8 weeks

after status epilepticus (SE), both of which significantly increased at 4 weeks and remained elevated at 8 weeks. Behavioral tests (open field, elevated plus maze, forced swim) showed anxiety- and depression-like behaviors, with a marked increase at 8 weeks. Proteomic analysis of ipsilateral and contralateral hippocampi from control, 4-week, and 8-week models identified significant proteins (FDR < 0.1, fold change > 1.5). Ipsilaterally, 220 proteins were upregulated and 29 downregulated; upregulated proteins were associated with cell adhesion, neurogenesis, glial activation, and inflammation (e.g., IGBP1, SLC12A9), while downregulated proteins related to trans-synaptic and calcium signaling (e.g., MAPT, ATP2B2). Contralaterally, 108 proteins including Cav1 and PFN1 were upregulated, while 29 including Dlgap2 and Syngap1 were downregulated. Immunohistochemistry with NeuN, Iba-1, GFAP, c-FOS, and GAD showed decreased NeuN in CA1/CA3, Iba-1 elevation in CA3 at 8 weeks, GFAP increase in CA1 at 4 weeks, c-FOS upregulation, and GAD reduction across regions. Transmission electron microscopy revealed reduced excitatory synapse density in DG and CA1, decreased density in the inner molecular layer of DG, increased postsynaptic density length in most subregions, and irregular thickened myelin in CA1. These findings demonstrate that pilocarpine-induced seizures lead to neuronal loss, glial proliferation, and synaptic/myelin remodeling, contributing to hippocampal hyperexcitability. This highlights the utility of integrated structural, molecular, and behavioral analyses to elucidate TLE pathophysiology and identify therapeutic targets.

Keywords : Temporal lobe epilepsy, Seizure, Proteomics, TEM, Hippocampus

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P-619

Estrogen deficiency induces anxiety and depression-like behaviors via caspase-1-mediated neuroinflammation

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Background: The high risk of depressive disorders in postmenopausal women is an emerging medical issue, but no pathophysiological mechanism remains largely unknown. Based on the hypothesis that caspase-1, activated by inflammasome complexes after estrogen production decreases, affects anxiety and depressive behaviors, we investigated the effects and underlying mechanisms of caspase-1 using an ovariectomized (OVX)-induced mouse model. Along with changes in estrogen receptors (ERα and β) expressions from 4 to 12 weeks after OVX, behavior tests (anxiety and depression), microglia, and astrocytes were measured in brain regions. *Results & Conclusion*: OVX-induced wild-type (WT) mice exhibited overexpression of caspase-1 in brain regions, which induced anxiety- and depression-like behaviors (open field, forced swimming, tail suspension, and rota-rod tests); these behavioral alterations have been linked to a suppression in the expression of ERβ. While loss of caspase-1 expression in Caspase-1−/− knockout mice no showed these behaviors. The decreased ERβ expression induced microglial-derived neuroinflammation, as indicated by notable activations of ionized calcium-binding adapter molecule 1 and interleukin-1 beta. These behavioral alterations were associated with caspase-1-mediated neuroinflammation via microglia and astrocyte over-activation, as evidenced by CX3CR1/Iba-1 and GFAP/LCN2 double-positive signals in the hippocampus. Our study suggests evidence shedding light on the fact that caspase-1 activation is a key mediator of depression in women after menopause.

Keywords : Menopause, depression, Neuroinflammation, Microglia, Estrogen

P-620

Protective effects of *Dioscorea bulbifera* and *Zingiber officinale* mixed extracts against glutam

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This study aimed to evaluate the neuroprotective effects of mixed extracts from *Dioscorea bulbifera* and *Zingiber officinale* (DBZO) against glutamate-induced excitotoxicity in HT-22 cells and to elucidate the associated molecular mechanisms. Neurotoxicity and protective effects were assessed using MTT and LDH assays, while cellular morphology was analyzed via microscopy. DBZO extract significantly restored axonal integrity disrupted by glutamate exposure. A DCFDA assay confirmed that DBZO reduced reactive oxygen species (ROS) generation in a concentration-dependent manner, underscoring its antioxidant capacity. Western blot analysis demonstrated that DBZO markedly decreased glutamate-induced neuronal death at 0.25 and 0.5 mg/mL. The observed neuroprotection was associated with the inhibition of the MAPK signaling cascade and the downregulation of apoptotic markers, including Caspase-3 and PARP. Moreover, DBZO activated the PI3K/Akt/mTOR survival pathway, enhancing neuronal viability. It also boosted antioxidant defenses by modulating Keap1 and NQO1 expression, thereby reducing oxidative damage. Collectively, these findings suggest that DBZO confers neuroprotection by regulating oxidative stress and apoptosis through NRf2/NQO-1 signaling. Due to its strong antioxidant and antiapoptotic properties.

Keywords : Dioscorea bulbifer, Zingiber officinale, HT-22, Glutamate, Neuroprotection

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P-621

Time-dependent mitochondrial fission through Calpain-2/CDK5/p25 and Drp1 signal pathway in MPTP-induced cynomolgus monkey model of Parkinson's disease

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Parkinson's disease (PD) is characterized by progressive loss of dopaminergic neurons. Using a cynomolgus monkey model of MPTP-

induced PD, we examined the temporal progression of neuropathological features, including dopaminergic neuronal loss, neuroinflammatory responses, mitochondrial alterations, and related signaling pathways. Monkeys received repeated MPTP injections until peak motor deficits were observed (designated as week 0; 0W), followed by analyses at 1, 12, and 48 weeks post-symptom stabilization. Immunoblotting and immunofluorescence analyses revealed a sustained reduction in tyrosine hydroxylase (TH) expression and TH-positive neurons in the substantia nigra (SN) from 1W onward. Concurrently, neuroinflammatory markers GFAP and Iba1 showed dynamic but persistent elevation, indicating astrocytic and microglial activation. Mitochondrial morphology in TH-positive neurons shifted from elongated, interconnected structures to fragmented, punctate forms by 1W, with decreased mitochondrial length and altered perinuclear distribution maintained through 48W. Western blot analysis demonstrated an early peak in Drp1(S616) phosphorylation at 1W, suggesting mitochondrial fission occurs early during disease stabilization. Moreover, the Calpain-2/CDK5/p25 signaling axis was dynamically regulated, with Calpain-2 peaking at 1W and again at 48W, while p25 levels increased progressively over time. These findings highlight that mitochondrial dysfunction and neuroinflammation are early and persistent features of MPTP-induced parkinsonism in cynomolgus monkey, and implicate the Drp1 and Calpain-2/CDK5/p25 pathways in the pathogenesis of PD. This model provides valuable insights into disease progression and potential therapeutic targets for early-stage intervention.

Keywords : Parkinson's disease, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), cynomolgus monkey, mitochondrial dynamics, calpain-2

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Molecular and Cellular Neuroscience P-622~P-706

P-622

Paradoxical Modulation of cAMP level by hM4Di

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Chemogenetics using designer receptors exclusively activated by designer drugs (DREADDs) has become one of the most advantageous tools for understanding neural circuits. The inhibitory DREADD hM4Di is widely used to suppress neuronal activity through Gi/o-coupled signaling, which is expected to reduce intracellular cyclic-AMP (cAMP) levels. On the contrary to the orthodox expectation, here we show that hM4Di activation does not consistently decrease cAMP levels or CREB phosphorylation but instead paradoxically increases them, particularly at high agonist doses, in contrast to another Gi-DREADD, KORD. This unexpected effect is consistently observed across multiple cell lines, including HEK293T cells, neurons, and astrocytes. Our loss-of-function study of GNAO1 (encoding Gαo) and GNAS (encoding Gαs), combined with a G-protein coupling assay, reveals that this unexpected cAMP elevation arises from hM4Di's unintended binding to Gαo. These findings uncover the molecular basis of the atypical signaling of hM4Di and raise critical considerations for its application in neuroscience research.

Keywords : Designer receptors exclusively activated by designer drugs (DREADDs), hM4Di, GNAO1, cyclic-AMP, CREB phosphorylation

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P-623

Astragalus mongholicus and Scutellaria baicalensis Extracts Mixture as a potential therapeutic against inflammation and Pyroptosis in ischemic stroke

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Ischemic stroke is a major cause of morbidity and mortality worldwide, primarily due to the limited availability of effective therapies. While tissue plasminogen activator (tPA) remains the only FDA-approved thrombolytic treatment, it is constrained by a narrow therapeutic time window and an increased risk of hemorrhagic complications. Post-stroke neuroinflammation and pyroptosis—a form of programmed necrotic cell death mediated by inflammasome activation—are recognized as major contributors to secondary brain injury. The NLRP3 inflammasome, in particular, plays a pivotal role in amplifying inflammatory cascades and promoting neuronal damage following ischemic insult. In this study, we investigated the therapeutic potential of a combination of Astragalus mongholicus and Scutellaria baicalensis (AM-SB), two traditional herbal extracts with known anti-inflammatory and antioxidant properties. Using a transient middle cerebral artery occlusion (tMCAO) mouse model, we observed that AM-SB treatment significantly increased survival rate and reduced infarct volume, as confirmed by TTC staining and MRI. Functional improvements were evident through better performance in neurological severity scoring, rotarod testing, novel object recognition, and passive avoidance behavior. Mechanistically, AM-SB attenuated glial activation and reduced the expression of inflammatory cytokines such as TNF-α and IL-1β. Furthermore, AM-SB effectively suppressed pyroptosis by downregulating NLRP3, ASC, cleaved caspase-1, and GSDMD protein levels. Collectively, these findings suggest that AM-SB exerts robust neuroprotective effects through dual modulation of inflammatory and pyroptotic pathways, offering a promising adjunct or alternative strategy for ischemic stroke treatment.

Keywords : tMCAO, ischemic stroke, Astragalus mongholicus, Scutellaria baicalensis, pyroptosis

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P-624

Ginsenoside Rk1 Induces ER Stress–Mediated Apoptosis via Caspase-12 Activation in Human Brain Cancer Cells

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Brain tumors such as neuroblastoma and glioblastoma represent two of the most common and aggressive forms of central nervous system malignancies, characterized by poor prognosis and limited treatment options. Although ginsenoside Rk1, a pharmacologically active compound derived from Panax ginseng, has demonstrated antitumor activity in various cancers, its precise mechanisms of action against brain cancer cells remain incompletely understood. In this study, we investigated the therapeutic potential of Rk1 using human neuroblastoma (SH-SY5Y) and glioblastoma (U87MG) cell lines. Treatment with Rk1 resulted in significant suppression of cell viability and induction of apoptosis in a dose-dependent manner. Apoptotic cell death was confirmed by increased expression of pro-apoptotic proteins, including Bak, caspase-9, cleaved caspase-3 (C-casp3), and cleaved PARP (C-PARP), accompanied by downregulation of the anti-apoptotic protein Bcl-2. Mechanistically, Rk1 disrupted mitochondrial membrane potential (MMP) and significantly elevated intracellular Ca^{2+} concentrations, thereby activating endoplasmic reticulum (ER) stress pathways. This was evidenced by enhanced expression of ER stress markers such as CHOP, BiP, and caspase-12, indicating activation of a mitochondria-mediated intrinsic apoptotic pathway in conjunction with ER stress–induced signaling. Furthermore, Rk1 inhibited epithelial–mesenchymal transition (EMT)–associated markers, suggesting additional anti-metastatic properties. Collectively, our findings demonstrate that ginsenoside Rk1 induces apoptosis in neural-derived tumor cells via dual activation of the mitochondrial apoptotic cascade and ER stress–dependent mechanisms. These results support the potential use of Rk1 as a promising therapeutic agent for the treatment of malignant brain tumors.

Keywords : Brain cancer cells, ER stress, Caspase-12, RK-1, Apoptosis

P-625

Neuropathic Pain from Corneal Nerve Damage: Ultrastructural and Histological Characterization of the Trigeminal Ganglion and Brain

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Peripheral neuropathic pain (PNP) is a chronic condition arising from damage to peripheral nerves. Corneal nerve injury provides a clinically relevant model due to its dense sensory innervation and link to central pain pathways. Yet, the mechanisms by which such injury leads to persistent pain remain poorly defined. The trigeminal ganglion (TG), as the primary relay for corneal sensory input, plays a crucial role in transmitting nociceptive signals to the brain. While prior studies have explored molecular and electrophysiological changes, the histopathological and ultrastructural alterations in the TG following corneal nerve injury remain underexplored. In this study, we used a pulled nerve model in adult mice to simulate corneal neuropathic pain. We examined the TG and associated brain areas using immunofluorescence (IF) and transmission electron microscopy (TEM) to assess neuroinflammation, neuronal integrity, and synaptic organization. IF staining revealed reduced neuronal density and signs of neuroinflammation in the TG of neuropathic mice compared to controls. TEM analysis further showed axonal degeneration, thinning of myelin sheaths, and depletion of synaptic vesicles, indicating impaired neuronal communication and ongoing degeneration. These findings highlight the TG as a key site of pathological remodeling in corneal neuropathic pain. Structural changes, including glial activation and synaptic disruption, support a model of maladaptive plasticity contributing to chronic pain. Our use of both IF and TEM provides a multi-scale view of the pathology, offering insights into the cellular basis of pain chronification. This work sets the foundation for future studies aimed at identifying therapeutic targets and molecular biomarkers in PNP.

Keywords : Neuropathic Corneal Pain, Trigeminal Ganglion, Ultrastructural Analysis, Transmission Electron Microscopy, Neuroinflammation

P-626

Molecular basis of PIP_2 regulation in L-type 1.2 Ca^{2+} channel

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Voltage-gated calcium channels (VGCCs) are essential ion channels that facilitate the transport of extracellular Ca^{2+} ions into the cytosol in response to changes in membrane voltage, crucial for Ca^{2+}-mediated cellular activities. Phosphatidylinositol 4,5-bisphosphate (PIP_2) plays a significant role in regulating the expression and functions of VGCCs. However, the molecular mechanisms underlying PIP_2 regulation in the L-type $Ca_V1.2$ Ca^{2+} channel, a subtype of VGCCs, remain unclear. We found that neutralization of four basic residues—R507, R508, R511, and R514—located in the C-terminal I-II loop ($S0_{II}$) of the α1C subunit, a mutant referred to as AAAA, resulted in dramatic changes in channel properties and PIP_2 sensitivity. The AAAA mutant exhibited decreased current density, shifted activation curve, slowed current decay, and a loss of PIP_2 sensitivity. Based on recent research in *Nature*, we tried to identify specific PIP_2 regulation residues, distinct from those affecting channel expression through previously reported cryo-EM structures. R514 (XXXA) emerged as a critical residue for PIP_2 regulation, exhibiting similar changes in channel properties as the AAAA mutant, although PIP_2 sensitivity was only slightly retained. Additional mutation of R507 (AXXA) resulted in a complete loss of PIP_2 sensitivity and similar channel properties to the AAAA mutant. R507 and R508 (XAXX, AAXX) showed less or no changes, although R511 (XXAX) exhibited similar PIP_2 sensitivity yet a shift of activation curve in opposite way. In contrast to the N-type $Ca_V2.2$, $Ca_V1.2$ showed no PIP_2 interaction at $S4_{II}$, the voltage sensor of domain II in the α1C. Thus, it can be concluded that the $Ca_V1.2$ channel is primarily regulated by PIP_2 at the I-II loop of the α1C, predominantly at R514 and to a lesser extent at R507. This study highlights the distinct regulatory mechanisms of PIP_2 in VGCC subfamilies, suggesting that PIP_2 regulation should be considered differently across these channels.

Keywords : CaV1.2 Ca^{2+} channel, PIP_2, PIP_2 binding site, Dr-VSP, PIP_2 sensitivity

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P-627

Characterization of TRPA and TRPV orthologs in the gastropod mollusk Pacific abalone

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TRPA and TRPV are an evolutionarily conserved group of ion channels found in invertebrates such as arthropods and nematodes, as well as in vertebrates such as teleost fish and mammals. In bilaterian animals, TRPA1 and TRPV are activated by temperature fluctuation and channel-specific ligands, and are mainly expressed in nociceptive sensory neurons. Although their sequences are similar to one another, little is known about the responsiveness of molluscan TRPA1 and TRPV to ligands and temperature. In this study, we used sequence-based clustering and phylogenetic analysis to identify TRPA1- and TRPV-like orthologs in the Pacific abalone (*Haliotis discus hannai,* Hdh). A total of eight subtypes of TRPA1-likes have been identified, which have been named Hdh-TRPA1-like-1 to -8. In addition, eleven subtypes of TRPV-likes have been identified, which have been named Hdh-TRPV-like-1 to -11. We identified Hdh-TRPA1-like-1, -3, -6, -8, and Hdh-TRPV-like-3 as putative TRP channels to respond to water temperature change by examination of gene expression profiles generated by RNA sequencing and quantitative PCR in the sensory tissues such as eyes and tentacles. We further characterized the effects of several compounds on Hdh-TRPA1-like-1 and Hdh-TRPV-like-6 channels using intracellular Ca2+ imaging. The mammalian TRPA1 electrophilic activator allyl isothiocyanate (AITC) activated both Hdh-TRPA1-like-1 and Hdh-TRPV-like-6 in the heterologous expression system HEK-293 cells. In this study, we have shown that Hdh-TRPA1-like-1 and Hdh-TRPV-like-4 are functional TRP channels in Pacific abalone. As TRPA1 and TRPV1 thermal sensitivity varied among vertebrate species, our findings are helpful to understand the evolutionary route that contributed to diversification of thermal and ligand sensory perception of TRP channels in marine mollusks.

Keywords : TRPA1-like channels, TRPV-like channels, Pacific abalone, Temperature, AITC

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P-628

The Role of ITPKB in Regulating Calcium Homeostasis in Dopaminergic Neurons and Astrocytes in Parkinson's Disease

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The regulation of calcium homeostasis is essential for maintaining neuronal function, and its significance becomes even more pronounced in neurodegenerative diseases such as Parkinson's disease (PD). In this study, we aimed to identify ITPKB as a key gene that regulates calcium homeostasis in pathological conditions similar to PD. When toxic proteins such as α-synuclein accumulate, intracellular calcium levels increase, leading to heightened calcium toxicity in neurons and reactive gliosis in astrocytes, which subsequently induces neuroinflammatory responses and neuronal death. Our study confirmed that ITPKB expression is upregulated to compensate for this calcium imbalance, suggesting a potential protective mechanism for maintaining calcium homeostasis in both neurons and astrocytes. However, in contrast, silencing ITPKB resulted in increased calcium levels in both neurons and astrocytes, leading to neuronal death and astrocyte reactivity. These changes ultimately exacerbated PD-like pathological alterations, worsening disease progression. Through this study, we demonstrated that ITPKB is an essential gene for maintaining calcium homeostasis and plays a critical role in dopaminergic neurons and astrocytes. These findings suggest that ITPKB may serve as a potential therapeutic target for PD and other neurodegenerative diseases associated with calcium dysregulation.

Keywords : Parkinson's disease, Calcium homeostasis, Neuron, Astrocyte, ITPKB

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P-629

Dopamine D2 receptor antagonists promotes primary cilia elongation and induce ER-stress mediated apoptosis in brain cancer cells

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Primary cilia are microtubule-based sensory organelles essential for detecting extracellular signals, and their role in cancer pathophysiology is increasingly recognized. Although several antipsychotic drugs have shown anticancer potential through drug repurposing, the effects of dopamine D2 receptor (D2R) antagonists in brain tumors remain insufficiently understood. In this study, we demonstrate that D2R antagonists—haloperidol and L-741,626—significantly induce primary cilia elongation in human neuroblastoma (SH-SY5Y) and glioblastoma (U87-MG) cells. This elongation correlates with activation of endoplasmic reticulum (ER) stress pathways, evidenced by upregulation of CHOP and BiP, and enhanced apoptosis as indicated by caspase-3 activation. Notably, siRNA-mediated knockdown of ciliary structural proteins (IFT88 or KIF3A) abolished both ER stress and apoptotic responses, confirming the cilia-dependent nature of this mechanism. Furthermore, intraperitoneal administration of haloperidol (10 mg/kg) significantly suppressed tumor growth in a neuroblastoma xenograft mouse model. These findings reveal a previously unrecognized mechanism by which D2R antagonists exert anticancer effects through primary cilia–mediated ER stress signaling and highlight the potential of targeting cilia-dependent pathways as a therapeutic strategy for neural tumors.

Keywords : Brain cancer cells, Dopamine D2 antagonist, Primary cilia, ER stress, Apoptosis

P-631

Poster Award Candidate

Functional specialization of border-associated macrophages is defined by niche-specific transcriptomic and ultrastructural profiles in mouse and human

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Border-associated macrophages (BAMs) are a specialized population of tissue-resident macrophages at interfaces between the central nervous system and the periphery, including the meninges, choroid plexus, and perivascular spaces. Meningeal macrophages are categorized into dural and leptomeningeal types, which differ both anatomically and transcriptomically. Differential expression of MHC Class II (MHCII) and Lyve1 is a hallmark of this heterogeneity. We conducted a multi-modal investigation to 1) validate these transcriptomic distinctions, 2) determine if they translate to protein and ultrastructural features, and 3) assess their conservation in humans. By integrating single-cell RNA sequencing datasets from mice and humans, we confirmed regional heterogeneity of BAMs. Dural macrophages were predominantly MHCII-high, while leptomeningeal and perivascular macrophages were Lyve1-high. Within MHCII-high dural cells, we identified a subtype with monocyte-like transcriptomic features and low expression of canonical BAM genes, distinct from another subtype resembling differentiated, tissue-resident macrophages. Lyve1$^+$ BAMs contained abundant phagocytic inclusions, autophagosomes, and lipid droplets, consistent with roles in phagocytosis and metabolic support. In contrast, MHCII$^+$ BAMs exhibited a well-developed endoplasmic reticulum, typical of antigen-presenting cells. We also identified a novel BAM subpopulation with low MHCII and Lyve1 expression, enriched for interferon (IFN)-responsive genes. Human single-cell data showed a conserved specialization pattern, including segregation of MHCII$^+$ and Lyve1$^+$ BAMs and an IFN-responsive cluster. Histological analysis of postmortem human brain confirmed spatial localization of these subtypes. Our study provides a multi-modal atlas of BAMs, demonstrating that their functional specialization is closely linked to anatomical niches and defined by distinct transcriptomic and ultrastructural features.

Keywords : Border-associated macrophage, Correlative light and electron microscopy and immuno-electron microscopy, Transcriptome, Meninges, MHCII

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P-632

Poster Award Candidate

Harnessing theta-gamma coupled brainwaves using ultrasound for spinal astrocyte revitalization and sustained neuropathic pain relief

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Ultrasound stimulation is a promising non-invasive strategy for neuropathic pain, yet its sustained effects and underlying mechanisms remain poorly understood. We investigated brainwave-patterned low-intensity continuous theta-burst ultrasound stimulation (LI-cTBUS) in a mouse model of partial sciatic nerve crush injury (PCI). LI-cTBUS substantially alleviated mechanical allodynia during and after treatment. Mechanistically, PCI upregulated brain-derived neurotrophic factor (BDNF)/tropomyosin receptor kinase B (TrkB) signaling, while LI-cTBUS enhanced extracellular BDNF uptake by spinal astrocytes, thereby normalizing the BDNF/TrkB pathway and restoring potassium chloride cotransporter 2 (KCC2) function. Furthermore, LI-cTBUS attenuated reactive astrogliosis via activation of the transient receptor potential ankyrin 1 (TRPA1) channel, indicating a glial mechanism for ultrasound-induced analgesia. Transcriptomic profiling revealed that PCI altered the spinal transcriptome, whereas LI-cTBUS reversed inflammatory signatures, corrected aberrant BDNF/TrkB signaling, and restored GABAergic transmission. Collectively, these findings demonstrate that LI-cTBUS reprograms reactive astrocytes, suppresses nociceptive signaling, and provides sustained relief from neuropathic pain, underscoring its therapeutic potential for non-invasive spinal neuromodulation.

Keywords : ultrasound neuromodulation, BDNF/KCC2, reactive astrocytes, TRPA1, neuropathic pain

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P-633

Structure Studies of the Neuroinflammatory Lcn2–Slc22a17 Complex

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Lipocalin-2 (Lcn2, also known as NGAL) is a pro-inflammatory glycoprotein

that plays a pivotal role in the regulation of neuroinflammatory processes and has been implicated in several neurological disorders(Suk, K. *Progress in neurobiology*). Its transmembrane receptor, Slc22a17, mediates cellular uptake of Lcn2 and propagates downstream signaling events. Despite its biological relevance, structural and functional understanding of the Lcn2–Slc22a17 interaction remains elusive(Jung, BK et al. *Experimental & molecular medicine*). Thus, we aimed to determine the structure of the Lcn2–Slc22a17 complex using cryo-electron microscopy (cryo-EM). We successfully cloned and expressed both Lcn2 and its receptor proteins in HEK293 GnTI$^-$ cells. His-tagged Lcn2 and Flag tagged Lcn2-receptor were purified using affinity chromatography and size-exclusion chromatography. To solve the structure of both the Lcn2–receptor complex and Apo-receptor, we screened a range of cryo-EM imaging conditions. From over 2,500 EM-micrographs, we were able to reconstruct a rough 3D map of Apo-Lcn2 receptor. However, the resolution was insufficient for atomic-level modeling. Currently, we are optimizing sample conditions such as incorporating lipid nanodiscs to improve particle stability and orientation, aiming to achieve high-resolution structural determination of the Lcn2–Slc22a17 complex.

Keywords : neuroinflammation, Structure, cryo-EM

P-634

A Journey Structural Determination of Human MLC1

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MLC1 is a membrane protein with eight transmembrane domains and is mainly expressed in astrocytes (J Hwang et al., *Open Biology*, 2021). Genetic mutants on Mlc1 are associated with an early-onset rare genetic neurological disease called Megalencephalic Leukoencephalopathy with Subcortical Cysts (MLC), which leads to progressive neurodegeneration. MLC typically presents with infantile macrocephaly, followed by progressive gait disturbances and cognitive impairment. However, the structure and function of MLC1 have not been fully understood. Thus, we aimed to determine a 3D-structure of human MLC1 protein using cryo-EM technique. We successfully expressed MLC1 proteins, in HEK293S GnTI- cells and purified them for cryo-EM microscopic imaging. We have obtained ~3.3 Å dataset, though the orientation preference in the EM-grid hinder fine structural determination. Currently, we have been screening various conditions to identify an optimal condition for overcoming orientation preference. The addition of 0.0005~0.001% CTAB to the MLC1 in LMNG micelle showed improved cryograph. In addition, reconstitution of MLC1 protein into PE/PC/PG lipid nanodisc with membrane scaffold protein (MSP) 1E3 belt protein increase orientation diversity.

Keywords : Cryo-EM, membrane protein, purification, structure

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P-635

Structural and functional modulation of human BEST1 channel by an amino acid metabolic enzyme

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Bestrophin (BEST) channels, including human BEST1 (hBEST1), are calcium-activated chloride (Cl^-) channels that respond to intracellular [Ca^{2+}] elevations. Recently, we identified human PYCR3, an enzyme in proline metabolism, as a novel binding partner of hBEST1 through IP-MS. The interaction between hBEST1 and hPYCR3 was confirmed via Co-IP and SEC, where the two proteins co-migrated, indicating a direct interaction. To investigate effect of hPYCR3 on hBEST1 channels, we performed whole-cell recordings. We found that hPYCR3 overexpression increased hBEST1 current density in HEK293T cells, whereas PYCR3 knockdown significantly reduced it. Furthermore, co-expression of hBEST1 and hPYCR3 in hPYCR3 knockout HEK293T cells augmented hBEST1 current levels, underscoring hPYCR3's critical role in modulating hBEST1 activity. Functional analysis of the enzymatically inactive hPYCR3 G252V mutant revealed no enhancement of hBEST1 current density. This result highlights that hPYCR3 enzymatic activity is essential for hBEST1 modulation. Additionally, treatments with proline and cofactors further supported a mechanistic link between hPYCR3-mediated proline metabolism and hBEST1 activity. These findings identify hPYCR3 as a key enzymatic regulator of hBEST1. We aim to investigate whether the effects of hBEST1 and hPYCR3 observed in vitro are recapitulated in vivo using retinal pigment epithelial (RPE) cells, where hBEST1 is highly expressed, to explore their physiological relevance. Additionally, we aim to resolve the complex structure of hBEST1 and hPYCR3 to elucidate the mechanisms underlying their structural modulation. Ongoing studies aim to elucidate the structural and functional mechanisms underlying hPYCR3-dependent modulation of hBEST1, offering new insights into the interplay between proline metabolism and ion channel regulation.

Keywords : BEST1, PYCR3, Cryo-EM complex structure, whole-cell patch-clamp, Co-Immunoprecipitation

P-636

Structural studies on the microglia TREM2-DAP12 complex

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Triggering Receptor Expressed on Myeloid cells 2 (TREM2) is a transmembrane protein specifically expressed in the microglia of the brain. TREM2 is an immune receptor that binds anionic ligands. Ligand binding induces phosphorylation of the immunoreceptor tyrosine-based activation motif (ITAM) within the intracellular domain of its adaptor protein DNAX activation protein 12 (DAP12), thereby activating downstream signaling pathways that regulate microglial survival, proliferation, phagocytosis, and motility. Among the risk factors of Alzheimer's disease (AD) found to date, the TREM2 rare variants

are one of the most dangerous factors for AD development. TREM2 signaling stimulate microglial Aβ plaque clearing in the early-stage AD. However, over-activated TREM2 signaling can induces in uncontrolled neuronal death in the late-stage AD. Although the extracellular domain structure was revealed by X-ray crystallography, the structure of full length TREM2 and DAP12 protein complex remain to be elucidated. We have successfully expressed TREM2 and DAP12 proteins in Hi5 insect cell infected with baculovirus, and purified human TREM2 and TREM2/DAP12 protein. Interestingly, When TREM2 was separated from Superdex 200 column using size-exclusion chromatography, TREM2 peak could be observed at about 13 mL, indicating that TREM2 should be assembled in a certain oligomeric state. Indeed, 2D classification of Cryo-EM imaging showed that TREM2 may form a dimeric architecture. However, the orientation of TREM2 particles observed in Cryo-EM imaging does not seem to be diverse, so to overcome this, we plan to increase the diversity of orientation by binding DAP12 and antibodies to TREM2 or making it in a lipid nanodisc state.

Keywords : Alzheimer's Disease, Microglia, TREM2, Cryo-EM

P-637

Hypoxia induces immediate awakenings in Drosophila melanogaster

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Adequate oxygenation is crucial for cellular function in all living organisms. Hypoxia, characterized by reduced oxygen availability, can result from factors such as snoring, sleep apnea, high altitudes, and strokes. Although the effects of hypoxia on various physiological processes are well-known, its impact on sleep patterns is less understood. In this study, we show that hypoxia leads to immediate awakenings in Drosophila melanogaster, disrupting sleep due to reduced oxygen levels. Wild-type fruit flies exposed to hypoxic conditions (2% oxygen) showed increased locomotor activity compared to those in normal atmospheric oxygen (21%). We assessed sleep parameters with the Drosophila Activity Monitor (DAM) and found that hypoxia significantly increased awakenings and fragmented sleep. Additionally, we examined how hypoxia-sensing neurons interact with clock neurons to trigger awakenings during low oxygen levels. These findings highlight the neurological effects of hypoxia-induced sleep disturbances and enhance our understanding of sleep disorders related to oxygen deficiency.

Keywords : Hypoxia, Hypoxia-sensing neuron, Clock neuron

P-638

Impact of dysregulated miR-204 on NPTX1 expression and neurodegeneration in Alzheimer's disease

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MicroRNAs (miRNAs) are a class of small, endogenous, non-coding RNAs, typically 18~25 nucleotides in length, that regulate gene expression at the post-transcriptional level by binding to complementary sequences within 3'untranslated regions (3'UTR) of target messenger RNAs (mRNAs). These regulatory molecules are involved in a wide range of physiological processes. Alzheimer's disease (AD) is the most common form of dementia and a progressive neurodegenerative disorder characterized by the extracellular accumulation of amyloid-β(Aβ) plaques and the intracellular aggregation of hyperphosphorylated tau protein into neurofibrillary tangles. Recent studies have identified several miRNAs with altered expression profiled in AD patients and transgenic animal models, suggesting that miRNAs may play critical regulatory roles in disease onset and progression. In this study, we performed miRNA expression profiling of hippocampal tissues from 4-month-old 5xFAD mice. Among several differentially expressed miRNAs, miR-204 was significantly down-regulated compared to controls. To explore the downstream effects of miR-204 dysregulation, we conducted target prediction using multiple miRNA databases, which identified neuronal pentraxin 1 (NPTX1) as a high-confidence target. NPTX1 is known to be involved in synaptic pruning, glutamate excitotoxicity, and neuronal apoptosis. To validate this regulatory relationship, we transfected primary rat neurons and assessed NPTX1 protein expression levels and associated cellular outcomes. Suppression of miR-204 led to an upregulation of NPTX1 and was accompanied by increased markers of neuronal apoptosis and cell death. In contrast, treatment with miRNA-204 mimic reduced NPTX1 expression and rescued neurons from apoptosis. Collectively, our findings demonstrate that the downregulation of miR-204 contributes to increased NPTX1 expression and neuronal vulnerability, suggesting a previously unrecognized mechanism underlying AD-related neurodegeneration

Keywords : microRNA, NPTX1, Alzheimer's disease, Apoptosis

P-639

Non-invasive ultrasound treatment induces neuroprotective astrocytes

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Ultrasound stimulation is emerging as a promising non-invasive therapeutic approach for various neurological disorders; however, its underlying cellular and molecular mechanisms remain poorly understood. Astrocytes, multifunctional glial cells known for regulating neuronal health, synaptic remodeling, cerebral blood flow, and maintenance of brain homeostasis, represent compelling targets for ultrasound-based therapies. To cope with physiological challenges such as inflammation or ischemia, astrocytes undergo reactive transformation characterized by distinct molecular profiles: the neuroinflammatory A1 phenotype, induced by pro-inflammatory factors, promotes neuronal damage, whereas the neuroprotective A2 phenotype, activated by cytokines and growth, enhances neuronal survival and repair. Here, we explored whether low-intensity pulsed ultrasound could preferentially induce beneficial astrocytic responses in primary cortical astrocyte

cultures. RNA sequencing and immunocytochemical analyses revealed that ultrasound stimulation triggered significant transcriptional shifts toward a neuroprotective A2-like profile, characterized by increased expression of genes related to neuronal support, tissue repair, and activation of neuroprotective signaling pathways, without inducing markers associated with the neurotoxic A1 phenotype. Cell viability and apoptosis assays confirmed ultrasound stimulation did not cause cytotoxic effects. Our findings highlight astrocytes as key mediators of ultrasound's therapeutic effects and suggest ultrasound-induced astrocytic modulation as a novel, safe, and effective approach to enhance neuroprotection in brain disorders.

Keywords : Astrocyte, Ultrasound stimulation , Neuroprotection

P-640

Discovery of TRPV1-selective inhibitory peptides via phage display screening for non-opioid pain modulation

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Transient receptor potential vanilloid 1 (TRPV1) is a nonselective cation channel expressed in peripheral sensory neurons, which plays a key role in detecting noxious stimuli such as heat, capsaicin, and inflammatory mediators. TRPV1 plays a crucial role in pain transmission and hypersensitivity, and has attracted much attention as a promising therapeutic target for the treatment of chronic, neuropathic, and inflammatory pain. However, the development of TRPV1 inhibitors has been limited due to side effects such as thermoregulation disorders. In this study, we aimed to discover novel TRPV1-selective inhibitory peptides using phage display screening. Using this method, two candidate peptides (peptide 1 and peptide 2) were selected and synthesized, and their functions were evaluated in HEK293T cells stably expressing TRPV1. Functional evaluations were performed using Fura-2 AM-based calcium imaging and whole-cell patch clamp electrophysiology. Calcium imaging results showed that peptide 2 significantly inhibited 100 nM capsaicin-induced calcium influx at the same concentration (100 nM). Peptide 1 also showed an inhibitory trend, but the effect was weaker and less consistent than that of peptide 2. Notably, peptide 2 also showed potent TRPV1 inhibitory activity in mouse dorsal root ganglion (DRG) neurons, confirming its efficacy under physiologically more relevant conditions. These results suggest that phage display-based screening is an effective strategy for discovering functional TRPV1 inhibitory peptides. In particular, peptide 2 shows strong potential as a novel analgesic candidate. Future studies will focus on optimizing the potency and biocompatibility of the peptide and evaluating its analgesic effects in animal models of chronic pain.

Keywords : TRPV1, Phage Display, Inhibitory Peptide, Calcium Imaging, Pain Modulation

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P-641

Neuroprotective and anti-depressant effects of Tenebrio Molitor hydrolysate in LPS-induced neuroinflammation models

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Introduction : Environmental pollution caused by synthetic drugs contradicts the Sustainable Development Goals(SDGs), and their modest efficacy and frequent side-effects leave major gaps in mood-disorder care. Among edible insects, Tenebrio molitor(TM) larvae have been reported to possess various health benefits, including anti-inflammatory, antioxidant, and anti-hyperglycemic effects. Recent studies suggest that enzymatic hydrolysis of it's proteins can further enhance their bioactivities by improving digestibility and releasing bioactive peptides. Therefore, using TM hydrolysates(TMH) may evaluated for its protective effects against lipopolysaccharide(LPS)-induced neuroinflammation. Methods : TMH(≤0.5 mg/mL), generated using Alcalase®, was applied to PC-12 cells 24 h prior to LPS(5 μg/mL) treatment. The most effective dose(0.125 mg/mL) was then administered intracerebroventricularly to ICR mice, followed by intraperitoneal injection of LPS(0.083 mg/mL). After 24 h, behavioral assessments including open field test(OFT), tail suspension test(TST), as well as measurements of body weight and hippocampal cytokine mRNA expression, were conducted. Results : In vitro, TMH significantly prevented LPS-induced reductions in cell viability, LDH release, activation of caspase-9/cleaved-caspase-3, and upregulation of IL-1β, NF-κB, and p-JNK (all $p < 0.05$). In vivo, LPS increased immobility in both OFT and TST without affecting locomotion or body weight; these effects were normalized by TMH treatment. TMH also reduced hippocampal IL-1β and IL-6 mRNA levels, with a downward trend observed for IL-10. Conclusion : TMH mitigates both neurotoxic and depressive-like effects of systemic LPS in complementary cell and animal models, supporting its potential development as an eco-friendly, non-synthetic therapeutic agent for neuroinflammatory mood disorders.

Keywords : Anti-neuroinflammation, Neuroprotection, Hippocampus, Edible insects, Hydrolysates

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P-642

Short-chain fatty acids-induced cholecystokinin secretion leading to neuroprotective anti-inflammation in gut–blood–brain model

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The gut–brain axis is increasingly recognized as a critical regulatory pathway in neurodegenerative diseases, while short-chain fatty acids (SCFAs) emerging as key microbial metabolites involved in host–neuroimmune signaling. In Parkinson's disease (PD), SCFA levels are consistently reduced in fecal and serum, yet the underlying mechanisms leading to this dysregulation and its consequences on brain pathology remain poorly understood. To investigate this, we developed a compartmentalized

microfluidic gut–blood–brain platform that enables the mechanistic dissection of how gut microbial metabolites influence neuroinflammatory states and α-synuclein accumulation in the central nervous system. First, we reconstructed a physiologically relevant gut epithelial barrier incorporating enteroendocrine cells and showed that SCFA treatment activated TRPA1-mediated Ca^{2+} influx, which in turn promoted the secretion of the neuroactive gut hormone cholecystokinin (CCK). Second, we demonstrated that CCK traversed a dynamic, selective permeable blood–brain barrier and successfully reached a 3D human brain module composed of astrocytes, microglia, and neurons. Third, we found that CCK stimulation induced anti-inflammatory polarization of glial cells and enhanced microglial phagocytic activity, indicating a shift toward a neuroprotective environment. In parallel, we observed a marked reduction in intracellular α-synuclein accumulation within neurons, supporting the functional relevance of this signaling axis. These findings reveal the link of gut microbial activity to neuroimmune modulation and provide biological insight into how intestinal metabolic cues may attenuate PD-related synucleinopathy.

Keywords : Gut-Brain Axis, SCFA, Cholecystokinin, Parkinson's Disease, Microfluidic chips

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P-643

Human iPSC-derived microglia provide a platform for neuroimmunology research

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Microglia is a tissue-resident macrophage in the central nervous system (CNS). Microglia is involved not only in immune responses in the CNS, but also in the development and functional regulation of neurons and other glia cells. In contrast to peripheral blood mononuclear cells, microglia is inherently difficult to isolate in a stable and reproducible manner. Microglia derived from animal model or immortalized cell lines capture only partial aspects of human microglia identity due to genetic divergence. Conversely, human iPSC-derived microglia provide a reliable and renewable source that recapitulates of microglia development through primitive hematopoiesis. Therefore, we generated mature microglia from human iPSCs and confirmed functional properties. Initially, embryonic bodies (EBs) were generated from human iPSCs using SCF, BMP4, VEGF, and Y-27632. To differentiate the primitive macrophage progenitor (PMP) using IL-3 and M-CSF. PMP cells were expressed myeloid immune cell markers (CD11b, CD14, CD45). For microglia maturation, PMP cells were cultured with IL-34 along with low concentrations of GM-CSF and M-CSF. After maturation step, cells express typical microglia markers (IBA-1, CX3CR1, TMEM119, P2RY12). In the phagocytosis assay, we observed that iPSC-derived microglia internalized fluorescence latex beads in a time dependent manner. Furthermore, LPS treatment induced an inflammatory phenotype in microglia, characterized by increased expression of M1-associated markers and inflammatory cytokines. Lastly, iPSC-derived microglia exhibited in vivo-like morphological characteristics, including the formation of branched structures in a 3D matrigel environment. Taken together, we established iPSC-derived microglia exhibiting functional characteristics, and these microglia is expected to be applicable to the study of microglia function and role in neuroimmunology research.

Keywords : Stem cell, iPSC, Differentiation, Microglia, Neuroimmunology

P-644

Diosgenin alleviates pain by preserving mitochondrial and endoplasmic reticulum function in a sciatic nerve injury model

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This study aimed to elucidate the molecular mechanisms by which diosgenin alleviates neuropathic pain and motor dysfunction by protecting mitochondrial and endoplasmic reticulum (ER) function. Neuropathic pain was induced using the chronic constriction injury (CCI) model in mice. Animals were divided into four groups: normal control, CCI, and CCI treated with diosgenin at 50 or 100 mg/kg (CCI+D50 and CCI+D100). Pain behaviors were assessed using von Frey and Hargreaves tests, while motor function was evaluated through open field and rotarod tests. To investigate underlying mechanisms, qRT-PCR and Western blot analyses were performed on spinal cord tissue to assess neuroinflammatory markers, mitochondrial function, and ER stress. Diosgenin treatment gradually alleviated mechanical allodynia, thermal hyperalgesia, and motor impairment compared to the untreated CCI group. Furthermore, diosgenin significantly reduced the expression of proinflammatory cytokines (IL-1β, IL-6, TNF-α), mitochondrial apoptosis-related proteins (Cytochrome C, Apaf-1), and ER stress markers (GRP78, CHOP) in the spinal cord tissue. These findings suggest that diosgenin effectively attenuates pain hypersensitivity and motor dysfunction after peripheral nerve injury by ameliorating neuroinflammation, mitochondrial dysfunction, and ER stress in the spinal cord, indicating its potential as a therapeutic candidate for neuropathic pain.

Keywords : Diosgenin, Neuropathic pain, Mitochondrial Apoptosis, Endoplasmic reticulum stress, Mice

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P-645

Analysis of Cardiac Changes Under Diverse Physiological Conditions in *Drosophila melanogaster* Using High-Frequency Ultrasound Imaging

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Cardiovascular diseases remain a leading cause of mortality worldwide, underscoring the need for in-depth insight into cardiac physiology to improve therapeutic interventions and clinical outcomes. Various physiological and genetic factors, such as oxygen deprivation and disruptions in circadian rhythm or sleep regulation, can profoundly influence cardiac function. *Drosophila melanogaster* offers a valuable

model system due to its conserved pathways, including hypoxia-responsive mechanisms like the HIF pathway, and its amenability to genetic manipulation and cardiac functional analysis. Nonetheless, the small size of *Drosophila* poses significant challenges for direct visualization of cardiac contractions and hemolymph circulation. To overcome this, we utilized the Vevo F2 LT high-frequency ultrasound imaging platform, which provides higher resolution than conventional imaging methods, to noninvasively capture real-time heartbeats and hemolymph flow dynamics in *Drosophila*. Using this system, we assessed cardiac alterations not only in response to hypoxic stress (0.4% oxygen exposure for 3 hours) but also across circadian rhythm and sleep-related genetic mutants. This comprehensive approach allows us to elucidate how diverse physiological and genetic perturbations affect cardiac performance and morphology in *Drosophila*. Our study establishes a robust methodology for functional cardiac imaging in this model organism, advancing our understanding of heart physiology under multiple experimental conditions and laying groundwork for future investigations into cardiovascular regulation.

Keywords : Drosophila, Heart, Ultrasound imaging system

Acknowledgements : The adult *Drosophila melanogaster* has a body length of ~3 mm and an open circulatory system. Its heart is a tube-like structure along the dorsal midline, forming part of the dorsal vessel. The posterior region acts as the contractile heart, and the anterior region forms the non-contractile aorta. It pumps hemolymph, *Drosophila*'s blood.

P-646

A cardiac steroid digoxin induces pro-regenerative macrophages to promote axon growth

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The dorsal root ganglion (DRG) relays sensory signals from the periphery to the central nervous system. While central DRG axons exhibit limited regeneration, their peripheral counterparts regenerate robustly. Our previous research demonstrated that DRG macrophages play a key role in promoting sensory axon regeneration following peripheral nerve injury. However, the molecular signatures defining this pro-regenerative macrophage phenotype remain unclear. Using an in vitro neuron–macrophage co-culture model, we recapitulated this phenotype, as evidenced by significant neurite outgrowth activity in macrophage-conditioned media (CM). To uncover the underlying molecular mechanisms, we performed bulk RNA sequencing on macrophages and employed the Connectivity Map (CMAP), a database linking gene expression patterns to small molecule perturbagens. This allowed us to predict small molecule compounds capable of inducing gene expression pattern similar to that of pro-regenerative macrophages. The top 10 candidates with the highest CMAP scores were evaluated for their ability to promote neurite outgrowth via macrophage-CM. Systematic, unbiased quantification using high-content imaging identified two hit compounds that significantly enhanced neurite outgrowth. Notably, digoxin, a cardiac steroid, emerged as the most promising candidate for inducing the pro-regenerative macrophage phenotype. Validation experiments confirmed that CM obtained from macrophages treated with digoxin markedly increased neurite elongation in cultured DRG neurons. This approach establishes a platform for identifying small molecules capable of reprogramming macrophages to exert pro-regenerative effects on neurons in various neural injuries and diseases.

Keywords : macrophage, dorsal root ganglion, axon regeneration , connectivity map, cardiac steroid

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P-647

Role of Shank2 in human neuron development and function

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The importance of chemical neurotransmission in human behaviour control cannot be understated, and its formation is dependent on the precise synapse assembly involving the timed recruitment of a myriad of presynaptic and postsynaptic protein molecules into defined synaptic sites. Among the different postsynaptic density (PSD) proteins, the Shank family of proteins have attracted much attention for its role as the central regulator of excitatory synapse development and function. Despite redundancy and importance of Shank2 in the synaptic assembly and potential non-neuron function-specific effects, there is a lack of understanding of the fundamental role of Shank2 in synaptic and neuronal functions. Given the inherent differences between rodent models and actual human physiology, a consolidated understanding of Shank2's function in the human neuronal system is lacking. In this study, we sought to elucidate the role of Shank2 in human neuron function in a human embryonic stem cell (hESC)-derived cortical neuron model. An examination of the impact of Shank2 ablation on functional synaptic neurotransmission through standard electrophysiological methods suggests its involvement in the modulation of N-methyl-D-aspartate receptor (NMDAR) response in human neurons. There is a concomitant alteration in the action potential (AP) waveform as a reduction in the AP and the afterhyperpolarization (AHP) duration and an increase in tertiary neurite growth. Bulk RNA sequencing and proteomics suggested that the Shank2-specific changes are due to a global gene expression and cell differentiation dysregulation. Using an alternative chemical-derived human neuron model that recapitulates specific stages of neurogenesis provided further evidence for the impact of Shank2 ablation in neuronal differentiation. The findings in this study highlight the NMDAR-specific impact of Shank2 in the human neuron system and a previously unknown and potential role of Shank2 in neuronal fate determination.

Keywords : Human neuron, Synapse, Neurophysiology, PSD proteins

P-648

Translatome Profiling of Perisynaptic Astrocytic Processes in the Spinal Cord After Nerve Injury

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Perisynaptic astrocytic process(PAP) of the tripartite synapse is important structure in regulating synaptic transmission. As PAP is the compartment of astrocyte closest to the synapse, it is able to respond to local stimuli separately to the soma area. Recently, importance of local translation of PAP in tripartite synapse has been reported. However, the profile of PAP in nerve injury models is remain unknown. In this study, we investigated how nerve injury affects the translation of PAPs in mouse spinal cord. To obtain translatome of PAP, we isolated synaptosomes from spinal cord of L5 sciatic nerve transection(SNT) model. In this experiments, RioboTag mice were used to selectively label ribosomes in GFAP positive cells with hemagglutinin(HA) epitope. HA-tagged ribosomes were magnetically immunoprecipitated with translating RNAs. To identify translatomic difference between sham and SNT model, we performed RNA sequencing. Through data analysis, we identified P2ry14 and Has3 as notable candidates. We further confirmed that two candidates are differentially expressed in astrocytic processes. Among the two genes, Has3 encodes hyaluronan synthase, an protein that produces hyaluronan in the extracellular matrix. Hyaluronan is a polysaccharide found in the extracellular matrix, responsible for maintaining tissue structure and mediating cell signaling. In a previous study, hyaluronan produced by hyaluronan synthase in astrocytes facilitates the accumulation of glutamate transporters to transport glutamate at specific domains of the astrocyte membrane. However, the precise role of Has3 in nerve injury model remains unclear. To investigate this, we examine the recruitment of the glutamate transporter GLT-1 around synapses and observed significant reduction in the SNT model compared to the sham. Our findings suggest that Has3 expression in PAP is critical for regulating neural transmission following nerve injury.

Keywords : Astrocyte, Neuropathic pain, Synapse, Perisynaptic astrocytic process

P-649

Astrocytic OAT Tunes Tonic E/I Balance to regulate synaptic plasticity and Hippocampal Memory

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Maintaining the balance between excitatory and inhibitory (E/I) transmissions is crucial for normal brain function. Astrocytes have emerged as a hidden puppet master for regulating E/I balance to tune the synaptic transmission and plasticity by tonically releasing gliotransmitters such as glutamate and GABA. However, the molecular mechanisms regulating the balance of excitatory and inhibitory gliotransmitter synthesis in astrocytes remain unclear. Here, we identify the astrocytic enzyme ornithine aminotransferase (OAT) as a key modulator of tonic astrocyte-to-neuron communication. Specifically, OAT catalyzes the conversion of ornithine to glutamate, thereby reducing the pool of ornithine available for GABA synthesis. Astrocyte-specific gene-silencing of OAT in the dorsal hippocampus led to a significant increase in tonic $GABA_AR$ current and a concurrent decrease in tonic NMDAR current, whereas OAT overexpression showed the opposite effect. Moreover, TFLLR-induced astrocytic transmitter release differentially affected subsequent fEPSP and long-term potentiation (LTP). Specifically, astrocytic OAT gene-silencing led to reduced fEPSP, likely due to a shift towards predominant astrocytic GABA release, which failed to induce LTP by a sub-threshold 40 Hz stimulation. Conversely, TFLLR treatment in OAT-overexpressing astrocytes increased fEPSP, suggesting a shift towards greater astrocytic glutamate release, which consequently facilitated LTP induction by the 40 Hz stimulation. In addition, astrocytic OAT gene-silencing showed a marked trend of deficits in hippocampal memory function. Collectively, these findings highlight astrocytic OAT as a crucial regulator of tonic E/I balance by modulating astrocytic gliotransmitter synthesis, critical for hippocampal memory.

Keywords : Astrocytes, Tonic gliotransmission, Ornithine aminotransferase (OAT), Tonic E/I balance, Synaptic plasticity

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P-650

New small molecule probe for visualizing choroid plexus

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The choroid plexus (ChP) is a key structure in the brain responsible for producing and regulating cerebrospinal fluid (CSF), as well as contributing to neurogenesis and central nervous system immunity. Despite its importance, the ChP remains poorly understood, particularly in terms of its development and regulation. In this study, we report the development of a fluorescent small-molecule probe capable of selectively labeling ChP epithelial cells in both mouse models and human brain organoids. The probe was initially tested on mouse primary glial cultures and tissue sections to confirm its specificity, followed by colocalization studies using established ChP markers such as TTR and AQP1. In 3D ChP explant cultures, we demonstrated that inhibition of specific SLC transporters disrupted probe labeling, suggesting a transporter-mediated mechanism of uptake. Notably, the probe enabled live imaging of ChP structures in human neural organoids after ~35 days of differentiation. This advancement provides a key platform for observing the ChP in real time, facilitating deeper investigation into its physiological and pathological dynamics.

Keywords : Choroid plexus, Small molecule probe, 3D culture, Human brain organoid, Real-time visualization

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P-651

Profiling diuretic hormone 44 (DH44) neurons as internal nutrient sensors in the *Drosophila* brain

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Diuretic hormone 44 (DH44) neurons in the *Drosophila* brain function as internal nutrient sensors, modulating behavior in response to metabolic cues. In this study, we characterize the molecular identity and signaling mechanisms of DH44 neurons located in the pars intercerebralis (PI) region. DH44-PI neurons secrete the DH44 peptide and are distinct from insulin-producing cells and classical neurotransmitter-expressing (GABAergic or cholinergic) cells. These neurons are activated by nutritive sugars, primarily through voltage-gated calcium channels. We also found evidence that a subset of these neurons express KATP channels, linking intracellular ATP levels to neuronal excitability. Furthermore, DH44 receptor 1 (DH44-R1) is expressed in dopaminergic neurons and is likely involved in mediating downstream hedonic feeding behavior. Together, our findings highlight DH44-PI neurons as a unique neuroendocrine population that integrates metabolic signals to regulate behavioral responses.

Keywords : DH44 neurons, KATP channel, Voltage-gated calcium channel, Dopamine

P-652

State-Dependent Retrieval of Sodium-Associated Flavor Memory in Mice

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Sodium chloride (NaCl) elicits concentration-dependent taste preferences in animals: low concentrations are typically attractive, while high concentrations are aversive. However, when internal sodium levels are depleted, animals show a different preference, favoring high NaCl concentrations over low. This bidirectional modulation provides a unique model for studying how internal physiological states regulate memory retrieval. In this study, we examined whether mice could form a salt-flavor associative memory, and its expression depends on the internal sodium state. Mice were trained using a two-bottle protocol with cherry-flavored water and grape-flavored 500 mM NaCl. Following conditioning, they were injected with furosemide and assigned to either normal or sodium-deficient diets. When tested with flavor-only solutions, sodium-depleted mice preferred grape, while controls preferred cherry. Since high NaCl activates both low-salt and high-salt pathways, we examined them separately. For low-salt association, 50 mM NaCl was paired with grape; for high-salt, 500 mM NaCl was combined with amiloride to block low-salt sensing. Mice trained with low salt preferred grape under sodium depletion but showed no preference under normal conditions. Those trained with amiloride-treated high salt preferred cherry on a normal diet and consumed both flavors equally when sodium-depleted. Equal intake in both cases indicates absence of retrievable salt-associated memory. These findings suggest that memory valence depends on the sensory pathway engaged during training and is expressed in a state-dependent manner.

Keywords : Sodium appetite, Salt taste pathways, State-dependent memory, Engram

P-653

Tweety-homolog (TTYH) family is stretch-sensitive anion channel regulating astrocytic volume

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Brain volume regulation is a vital homeostatic process that maintains ionic and osmotic balance, essential for the proper function and health of the nervous system. Astrocytes play a central role in this process by utilizing a variety of ion channels, transporters, and abundant water channels. Despite their importance, the molecular mechanisms by which astrocytes sense and regulate volume changes remain poorly understood. In this study, we identify the Tweety-homologs (TTYH1, TTYH2, TTYH3) as the pore-forming subunits of stretch-activated anion channels in astrocytes. Through electrophysiological recordings and FRET-based biosensor imaging, we demonstrated that positive pressure applied via patch pipette induces Cl- currents that are temporally synchronized with membrane stretch. Gene silencing of *Ttyh1/2/3* abolishes both swelling-induced Cl- conductance and cell swelling, underscoring their essential role in astrocyte volume regulation. Cryo-electron microscopy shows that TTYH proteins form dimeric complexes in the plasma membrane. Each TTYH subunit contains five transmembrane domains, and we elucidate the ion permeation pathway by identifying a conserved positively charged arginine residue at position 213 in TTYH1 that is critical for pressure-induced Cl- conductance. Under resting conditions, cholesterol binding inhibits this conductance; however, positive-pressure displaces cholesterol from the channel, thereby activating Cl- flux. These findings are supported by single-channel recordings of hTTYH1 reconstituted into lipoproteins, confirming the TTYH family as bona fide mechano-sensitive anion channels. Together, our results provide new insights into the molecular mechanisms governing astrocyte volume regulation.

Keywords : Astrocyte volume regulation, Mechanosensitive anion channels, Cholesterol-dependent gating

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P-654

Poster Award Candidate

Astrocyte-specific deletion of TTYH1 enhances neuronal excitability and long-term memory persistence

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Astrocytes regulate neuronal excitability and cognition through ionic buffering, metabolic support, and gliotransmitter signaling. Tweety homolog 1 (TTYH1), an astrocyte-enriched membrane protein, has been proposed either as a swelling-activated chloride channel or as a lipid-transporter, but its physiological role remains largely unknown.

To investigate its function, we generated inducible astrocyte-specific TTYH1 knockout mice (hGFAP-CreER^{T2}; TTYH1-fl/fl, TTYH1-aKO) and confirmed the selective deletion of TTYH1 in hippocampal astrocytes via immunostaining. To determine whether astrocytic TTYH1 influences hippocampal function, we performed electrophysiological recordings in CA1 pyramidal neurons. Neurons from TTYH1-aKO mice exhibited increased excitability, reduced action potential threshold, and enhanced evoked excitatory postsynaptic currents, without changes in paired-pulse ratio. Notably, Tonic N-methyl-D-aspartate receptor currents were significantly reduced, suggesting altered postsynaptic signaling. Behaviorally, TTYH1-aKO mice displayed normal locomotion, anxiety-like behavior, and sociability, but exhibited enhanced long-term memory retention in multiple T-maze tests at 30- and 90-days post-training. These findings reveal that astrocytic TTYH1 plays a critical role in regulating hippocampal excitability and memory persistence, highlighting its importance in astrocyte–neuron interactions and hippocampus-dependent cognition.

Keywords : Astrocyte-neuron interaction, TTYH1 , Neuronal excitability, Memory persistence

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P-655

Microbial conversion of MSG to GABA enhances sleep via gut-brain signaling in *Drosophila*

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GABA acts as a major inhibitory neurotransmitter in the brain, suppressing neural excitation and inducing calming effects. Elevated GABA levels improve sleep onset, duration, and quality through sleep-promoting neural circuits. Previous studies have demonstrated that oral intake of GABA can increase sleep duration, yet the pathways by which gut-absorbed GABA reaches the brain remain unclear. Notably, a strain of *Lactobacillus plantarumKS* (*LPKS*), originally isolated from kimchi, has been reported to produce GABA using monosodium glutamate (MSG), a common artificial flavor enhancer, as a substrate. This suggests kimchi ingestion could introduce *LPKS* into the gut, where it might use dietary MSG to synthesize GABA and modulate behavior. To investigate this possibility, we employed a *Drosophila* model system. Flies were fed *LPKS* with MSG, and compared to controls fed only *LPKS*. Remarkably, flies co-exposed to *LPKS* and MSG exhibited increased sleep duration, closely resembling the sleep patterns observed in flies directly fed GABA. This suggests that elevated internal GABA levels which is made by microbial species contribute to the observed sleep changes. We examined how gut-derived GABA reaches the brain. Previous research and our studies show dietary GABA increases sleep in Drosophila, implying a route for brain access. Given that GABA may poorly penetrate the *Drosophila* blood-brain barrier, we hypothesize that vagal afferents neurons expressing GABA receptors might relay GABAergic signals to the brain, thereby altering sleep regulation. In this study, feeding MSG to microbe-exposed flies significantly increased sleep duration, mimicking direct GABA feeding. These findings collectively provide experimental evidence that gut microbes can generate neuroactive metabolites from dietary components and influence sleep behavior, potentially through neural pathways connecting the gut and brain.

Keywords : Gut-brain axis, GABA, Microbiome, Sleep regulation, Drosophila

P-656

Reactive astrocytes exacerbate tau pathology via impaired autophagy and elevated MAO-B under neuroinflammatory conditions

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Reactive astrocytes, early pathological hallmarks of Alzheimer's disease, have been implicated in tau pathology through interactions with amyloid plaques. However, their involvement in neurofibrillary tangle formation and cognitive decline remains unclear, and it is still debated whether astrogliosis drives or merely follows tau pathology. We hypothesized that reactive astrocytes contribute to tau pathology via impaired autophagic flux and dysregulated monoamine oxidase-B (MAO-B) activity. We confirmed that neuronal overexpression of three-repeat (3R) tau alone was insufficient to induce pathological features of tauopathies. However, combining with inflammation-induced astrocytic activation, hTau3R expression increased NFT accumulation and memory deficits. Additionally, adenovirus-induced reactive astrocytes showed autophagic dysfunction. Next, we observed that astrocyte specific ATG5 knockdown exacerbated tau-associated pathology in hTau3R-overexpressing mice, accompanied by elevated MAO-B expression. Notably, astrocytic MAO-B inhibition reduced tau pathology. Together, these findings establish a causal role for reactive astrocytes in driving tau pathology through dysregulation of autophagic flux and MAO-B activity.

Keywords : Alzheimer's disease, Reactive astrocyte, Tauopathy, Astrocytic autophagy, Astrocytic MAO-B

P-657

Physiopathological role of astrocytic DNAJC6 in Parkinson's disease

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DNAJC6, which encodes the co-chaperone auxilin, plays a role in endocytosis and intracellular vesicle trafficking. Given its physiological function, we hypothesized that its dysfunction may also contribute to pathogenesis of adult-onset PD, beyond its established role in juvenile-onset parkinsonism, where loss-of-function mutations in DNAJC6 have been identified as a genetic cause. Supporting this hypothesis,

DNAJC6 expression was decreased in postmortem brain tissues and transcriptome datasets from patients with late-onset PD. In our mechanistic studies, α-synuclein preformed fibrils (α-syn PFF) treatment reduced the expression level of the transcription factor nuclear receptor related 1 (Nurr1) and Forkhead box protein A2 (Foxa2), which were bound to the DNAJC6 promotor, leading to decreased DNAJC6 mRNA expression in human embryonic stem cell (hESC)-derived midbrain cultures. Additionally, phosphorylation of Leucine-rich repeat kinase 2 (LRRK2) and physical interaction between LRRK2 and DNAJC6 were increased by α-syn treatment, promoting phosphorylation-dependent degradation of DNAJC6 in human midbrain cultures. Based on these findings, we further investigated the role of astrocytic DNAJC6 in both in vitro and in vivo models of PD. Genetic ablation of DNAJC6 in hESC-derived astrocytes using the CRISPR-Cas13d system (CasRx) induced mitochondrial and lysosomal dysfunction in physiological level. Consistently, DNAJC6 Knockdown exacerbated synucleinopathy whereas CRISPR-mediated overexpression of DNAJC6 rescued α-syn PFF-induced pathology in human midbrain tri-cultures. In a mouse PD model generated by combined α-syn PFF and AAV-mediated α-syn overexpression, upregulation of DNAJC6 rescued behavioral deficits and histopathological alterations. These findings highlight a physiopathological role of astrocytic DNAJC6 in PD and support its potential as a therapeutic target.

Keywords : Parkinson's disease, α-Synuclein, DNAJC6, Astrocyte

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P-658

Lysophosphatidylcholine-induced mitochondrial stress and MAO-B–driven oligodendrocyte inflammation promote demyelination in Multiple Sclerosis

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Understanding the cellular mechanisms of myelination and demyelination is crucial for unraveling the pathology of Multiple Sclerosis (MS). However, accurately replicating human MS pathologic hallmarks and the contribution of oligodendrocytes (OLs) presents a significant challenge due to the complex pathology of demyelination. Here, we establish an in vitro model of demyelination using nanofiber-supported OL cultures treated with lysophosphatidylcholine (LPC), mimicking acute and chronic MS-like pathology. We cultured human OL cells (MO3.13) on aligned laminin-coated electrospun nanofibers to effectively replicate axonal topography, promote robust cell attachment, and facilitate myelination, as evidenced by the expression of Myelin basic protein (MBP) and Proteolipid protein (PLP), comparable to coculture models with Neurons on the chip. Then, we treated Oligodendrocytes with lysophosphatidylcholine at 10–50 μg/mL for 24 h and up to 10 days. Results revealed a dose- and time-dependent shift in the oligodendrocyte stress response, characterized by increased reactive oxygen species (ROS) production, mitochondrial dysfunction (MAO-B), antioxidant depletion (Nrf2), and elevated extracellular hydrogen peroxide (H_2O_2). These changes marked a "tipping point" where acute, manageable stress transitioned into chronic inflammation, correlating with myelin fragmentation and OL death. This nanofiber model offers a tractable platform for studying OL behavior, mapping demyelination thresholds, and supporting drug screening for remyelination and antioxidant therapies.

Keywords : Demyelination in Multiple Sclerosis, Oligodendrocyte Inflammation, Lysophosphatidylcholine, Nanofiber In Vitro Model, Mitochondrial Dysfunction

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P-659

MSG's Effects on Neural Stem Cells and Hippocampal Neurogenesis

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Monosodium glutamate (MSG), a common food additive known for enhancing umami flavor, is generally regarded as safe in most countries, with few regulatory restrictions. While previous research on MSG's neurotoxicity has primarily focused on neurons, its potential effects on neural stem cells (NSCs) have been largely overlooked. This study aimed to assess MSG's neurotoxicity in NSCs and hippocampal neurogenesis. In vitro experiments showed that MSG induced cytotoxicity in primary neuron cultures but did not appear to affect NSCs. In vivo, 4-week-old male C57BL/6 mice were treated with MSG or sodium chloride (NaCl) for two weeks. The results revealed that neither substance influenced the expression of neuronal markers or glutamate receptors in the hippocampus. Moreover, no significant differences were observed in NSC proliferation, survival, or neuronal differentiation in the MSG-treated group. Neurobehavioral assessments, including the Morris water maze test, also showed that MSG had no effect on spatial learning or memory. These findings provide the first comprehensive evaluation of MSG's effects on NSCs, suggesting that MSG does not exhibit neurotoxic effects on hippocampal neurogenesis or cognitive functions at typical dietary intake levels.

Keywords : Monosodium glutamate, Neurotoxicity, Neuron, Neural stem cell, Hippocampal neurogenesis

Acknowledgements : MSG compound that widely recognized as a flavor enhancer that provides anumami taste. Adult hippocampal neurogenesis has been observed in the human hippocampus, leading to the generation of functional neurons from neural stemcells (NSCs). This process contributes to structural and functional plasticity in the subgranularzone(SGZ) of the hippocampus.

P-660

Generation of Neurosupportive Active Astrocytes Induced by Single-Cell Nanoencapsulation

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Astrocytes are bewilderingly heterogeneous in function and state. Many states of astrocytes, such as reactive, active, and stressed, have been proposed, but their functions and origins are still remaining unresolved. Herein, we report a chemical approach, called single-cell nanoencapsulation (SCNE), for the in-vitro induction of neurosupportive active astrocytes. TiO_2 SCNE irreversibly stimulates astrocytes towards active astrocytes, and they assist primary hippocampal neurons in the development of neurites and mature synapses. Moreover, they express unique phosphorylation pattern of signal transducer and activator of transcription 3 (STAT3) and have high BDNF level and cAMP base level, indicating differentiation toward the active astrocytes with neurosupportive functions, by upregulated cAMP-PKA-CREB pathway. Even after the implantation, the active astrocyte features remained. The findings suggest a new target for cell therapy after central nervous system injury by providing an unconventional chemical approach to brain-cell manipulation.

Keywords : Astrocyte, Nanoparticle, Encapsulation, Active astrocytes

P-661

PLCγ1 dependent neural plasticity is required for dynamic hippocampal CA2 network processing social memory in mice

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A growing body of evidence suggests that the hippocampal CA2 region plays a critical role in social memory, including the detection of novelty, recognition, and the association of valence with social identity. While discrimination between familiar and novel conspecifics by CA2 ensembles has been well characterized, how these ensembles evolve during the gradual transition from novelty to familiarity remains largely unexplored. To address this, we performed *in vivo* calcium imaging in wild-type (WT) and CA2-specific Plcg1 conditional knockout (cKO) mice, tracking single-cell and population-level CA2 activity during repeated exposures to the same novel conspecific. We observed that a subset of CA2 neurons displayed stable social tuning across exposures, while population-level activity became progressively growing in the extent of dynamicity, suggesting ensemble-level reorganization of CA2 network during familiarization. These processes were significantly blunted in Plcg1 cKO mice, where both tuning stability and population dynamics plasticity were impaired. At the synaptic level, we found that PLCγ1 is required for theta-burst stimulation-induced long-term potentiation (LTP) at entorhinal cortex–CA2 synapses, suggesting a mechanism by which PLCγ1 supports both stable social representations and ensemble dynamics during familiarization. Together, these findings indicate that CA2 encodes the transition from novelty to familiarity via ensemble dynamics and tuning stability, and that this process is critically dependent on PLCγ1-mediated synaptic mechanisms.

Keywords : CA2, Social memory, learning, social novelty

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P-662

Human brain and organoid transcriptomes reveal key receptor tyrosine kinase pathways and genetic signatures in Alzheimer's disease

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by transcriptomic alterations affecting multiple genes. Many researchers have tried to predict major hallmarks AD pathogenesis for diagnosis but the association between receptor tyrosine kinase (RTK) pathways and AD diagnosis is still unclear. This study aims to identify RTK-associated gene signatures crucial to AD pathogenesis and assess their potential as diagnostic biomarkers for AD. The study investigated changes in RTK pathway gene expression related to AD by analyzing brain transcriptome data from two independent public datasets (GSE84422, GSE109887). Differentially expressed genes (DEGs) were analyzed from the GSE84422 and GSE109887 datasets and overlapping genes (oDEGs) were identified. RTK-related genes (ooDEGs) were subsequently selected through functional enrichment analysis. These were further refined into AD-related genes (DAGs) through protein-protein interaction (PPI) network analysis. Logistic regression and receiver operating characteristic (ROC) analyses were conducted on the selected DAGs to evaluate their diagnostic potential, with additional gene expression validation performed in brain organoids and primary neurons. A total of 145 genes were identified as oDEGs in the above two datasets, and 18 genes were selected as ooDEGs. Six DAGs (*ITGB1*, *AXL*, *GFAP*, *NRG1*, *CAV1*, and *RHOA*) were selected. The diagnostic powers of the six DAGs for AD were 0.825 (GSE84422) and 0.884 (GSE109887). Human brain organoids and primary neuronal models were used to validate the biological relevance of these findings. *AXL* and *ITGB1* were finally selected as key genes for RTKs pathway in AD and were significantly increased in AD.

Keywords : Alzheimer's disease, receptor tyrosine kinase, transcriptome, AXL, ITGB1

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P-663

Single nucleotide differences in *Gpr151* functional RNA 5'UTR sequence changes axon regenerative potential in CAST/EiJ mice

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For successful nerve regeneration following injury, neurons undergo

dynamic transcriptomic changes. *Gpr151* is one of the injury-responsive genes and has a significant role at the RNA level rather than the protein level. Our previous research has demonstrated that the 5'UTR RNA sequence of *Gpr151* contributes to axon regeneration by direct binding with CSDE1 protein and altering its coordinating RNA pool. Here, we discovered a distinct SNP within this functional *Gpr151* RNA in CAST/EiJ mice, known for their high neuronal regenerative potential, resulting in structural differences. The 5'UTR sequence of *Gpr151* in CAST/EiJ mice significantly enhances axon regeneration compared to that of C57BL/6 mice. Additionally, differences are noted in the respective binding proteins. Our studies aim to deepen the understanding of the functional RNA and the impact of its SNP.

Keywords : Regeneration, axon, RNA, SNP

P-664

Modulation of gating kinetics by β subunits in N-type calcium channel

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The N-type voltage-gated calcium channel ($Ca_V2.2$) regulates synaptic transmission by controlling calcium influx under depolarization. β subunits act as modulators for the gating properties of various calcium channels. However, the mechanisms by β2 splice variants differentially regulate $Ca_V2.2$ current kinetics remain unclear. Here, we elucidate how β2a and β2c subunits distinctly regulate $Ca_V2.2$ current kinetics. Using whole-cell voltage-clamp in HEK293T, we analyzed current decay with a double exponential function model. During a 1 s pulse, the current decayed much more slowly in $Ca_V2.2$ with β2a compared with β2c. Fitting model uncovered β subunit-dependent patterns in amplitude components (A and B) and time constants (τ_A and τ_B). $Ca_V2.2$ with β2a showed a dominant slow component ($A \approx 0.78$, $\tau_A \approx 1.64$ s) and a minor fast component ($B \approx 0.22$, $\tau_B \approx 80$ ms). In contrast, $Ca_V2.2$ with β2c displayed a predominant fast component ($A \approx 0.78$, $\tau_A \approx 93$ ms) and a minor slow component ($B \approx 0.22$, $\tau_B \approx 0.36$ s). We hypothesize that components A and B represent voltage-dependent inactivation and deactivation, respectively, under sustained depolarization. β2a induces rapid channel deactivation, allowing the current to reach equilibrium between activation and deactivation quickly with slow inactivation. Conversely, β2c promotes rapid overall current decay primarily through accelerated inactivation, overshadowing the gradual deactivation process. In addition, our results from N-terminal manipulation of β subunits support that localization of β subunits determines the dominant pathway involved in current decay and deactivation. Our findings demonstrate a significant functional divergence between membrane-anchored (β2a) and cytosolic (β2c) subunits within the β2 family, highlighting the critical role of β subunit localization in fine-tuning channel function. This study will provide novel insights into the molecular basis of calcium signaling in neurons.

Keywords : N-type calcium channels, β subunits, Current decay & Deactivation, Ca2+ signaling

P-665

NS1 Binding Protein Regulates Stress Granules via p62 Ubiquitination and GABARAP Recruitment in ALS

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The NS1 binding protein, known for interacting with the influenza A virus protein, is involved in RNA processing, cancer, and nerve cell growth regulation. However, its role in stress response independent of viral infections remains unclear. This study investigates the NS1 binding protein's function in regulating stress granules during oxidative stress through interactions with GABARAP subfamily proteins. We find that NS1 binding protein localizes to stress granules, interacting with core components, GABARAP proteins, and p62, a protein involved in autophagy. In cells lacking NS1 binding protein, stress granule dynamics are altered, and p62 ubiquitination is increased, suggesting impaired stress granule degradation. Overexpression of NS1 binding protein reduces p62 ubiquitination. In amyotrophic lateral sclerosis patient-derived neurons, reduced NS1 binding protein and p62 disrupt stress granule morphology. We have also performed LC-MS analysis to identify novel NS1 binding protein-interacting proteins, and will present preliminary functional insights into these candidates. Together, these findings identify the NS1 binding protein as a negative regulator of p62 ubiquitination and a facilitator of GABARAP recruitment to stress granules, implicating it in the regulation of stress granules and the pathogenesis of ALS.

Keywords : stress granule, als, autophagy, p62, ns1-bp

P-666

Activating Odorant Receptors in Hypothalamic Astrocytes Sex-differentially Regulates High-fat-diet induced Obesity

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We previously elucidated that $GABRA5^+$ neurons in the lateral hypothalamic area (LHA) project to adipose tissues and inhibit fat accumulation. In obese mice, these neurons show reduced firing due to tonic inhibition by astrocytic GABA synthesized via MAOB: silencing astrocytic MAOB or pharmacologically inhibiting it with KDS2010 restores neuronal activity. This promotes thermogenesis and reduces weight gain without affecting food intake. These findings suggest astrocytic GABA as a promising target for obesity treatment. However, the molecular and cellular mechanisms of disrupted fatty acid metabolism in obesity remain unclear. Here, we found that a few of the extra-nasal odorant receptors (ORs), the largest subfamily of G protein-coupled receptors, are sensitive to medium-chain fatty acid (MCFA) and

lactone analogues in astrocytes. We propose that odorant receptors (ORs), OlfrY and OlfrZ, in hypothalamic astrocytes are expressed sex-differentially. We hypothesize that the hypothalamic astrocytic OlfrY, OlfrZ and heterodimer of OlfrY/Z differentially regulate GABA signaling and astrocytic reactivity, thereby mitigating or exacerbating obesity. These findings suggest a physiological function for astrocytic ORs in the biphasic regulation of obesity and highlight their potential as a therapeutic target for sex-dependent obesity-related treatment.

Keywords : Astrocytes, GPCR, Odorant receptors, Obesity

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P-667

PDGF-BB Treatment Activating pCREB to Restore Gliovascular Unit in a Parkinson's Disease Model

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Platelet-derived growth factor-BB (PDGF-BB) has been reported to ameliorate synucleinopathy, a key pathological hallmark of Parkinson's disease (PD). However, its role in modulating gliovascular interactions remains unexplored. In this study, we established a three-dimensional human gliovascular model composed of astrocytes and endothelial cells, recapitulating essential features of the glial limitans and the blood-brain barrier (BBB). We constructed a PD-like model with treatment of preformed fibril alpha-synuclein (PFF), which led to disrupted gliovascular interactions characterized by diminished VE-cadherin expression and the loss of AQP4 polarization at astrocytic endfeet, alongside endothelial activation and A1-like reactive astrocyte conversion. PDGF-BB treatment restored vascular stability by reducing inflammatory markers such as nitric oxide and ICAM-1 and enhancing the localization of junction proteins through pCREB activation. Furthermore, AQP4 function was rescued, as demonstrated by increased expression and re-polarization at astrocytic endfeet following PDGF-BB treatment. These findings suggest that PDGF-BB promotes gliovascular clearance mechanisms and may represent a promising therapeutic strategy for restoring neurovascular function in Parkinson's disease.

Keywords : PDGF-BB, pCREB, Gliovascular unit, Parkinson's disease

P-668

Temporal Remodeling of Collagen fibers After Spinal Cord and Peripheral Nerve Injuries

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Fibrotic scarring is a key barrier to axonal regeneration following central and peripheral nerve injuries. Among extracellular matrix (ECM) components, collagens type I and III are central to scar architecture but their spatiotemporal dynamics remain incompletely understood. This study investigated how collagen I/III deposition evolves over time following spinal cord injury (SCI) and peripheral nerve injury (PNI), with implications for the regenerative microenvironment. Using a thoracic contusion SCI model and a sciatic nerve compression model in rats, tissue samples were collected at defined intervals (1 day, 3 days, 1 week, 4 weeks, and 8 weeks post-injury). Immunohistochemical analysis of longitudinal sections was performed to quantify and localize collagen I and III deposition. The distribution patterns were analyzed in both acute and chronic phases, focusing on scar density and ECM remodeling. In the SCI model, collagen I gradually increased over time and dominated the ECM in the chronic phase. Collagen III appeared at 3 days post-injury, peaked at 1 week, and remained high through weeks 4 and 8, forming dense fibrosis around the lesion. In the PNI model, collagen I was highest at day 1, then steadily declined. Collagen III was broadly expressed from day 1 to 1 week, with widespread localization near the lesion. These results show a temporal and structural transition from early ECM deposition to chronic fibrotic scarring. While functional tests were not included, mature collagen-rich scars likely create an inhibitory ECM that negatively correlates with axonal regeneration. This study provides temporal-morphological evidence that collagen I and III undergo distinct phase-dependent remodeling after SCI and PNI. The chronic accumulation of collagen I may represent a key constraint to axonal regrowth. Targeting specific phases of ECM remodeling could be a promising strategy to modulate fibrosis and promote recovery after neural injury.

Keywords : Spinal cord injury, Sciatic nerve injury, Extracellular matrix remodeling, Fibrotic scar, Collagen

P-669

Age-dependent effects of HDAC4 haploinsufficiency on sleep and cognitive function

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Aging disrupts sleep architecture, notably by reducing slow-wave sleep and increasing non-rapid eye movement (NREM) sleep fragmentation. These changes are linked to neurodegenerative diseases such as Alzheimer's disease (AD), characterized by β-amyloid accumulation and sleep disturbances. While clinical studies suggest an association between sleep and dementia, the underlying molecular mechanisms remain unclear. Recent studies have identified the SIK3-HDAC4 signaling axis as a key molecular pathway regulating sleep. Phosphorylation of HDAC4 by SIK3 is linked to NREM sleep modulation, and HDAC4 haploinsufficiency is associated with persistent hypersomnia. In this study, we performed EEG/EMG-based sleep scoring across different age groups and evaluated anxiety and spatial memory using open field and object location tests. To examine changes under pathological conditions, we also analyzed sleep architecture and cognitive function in HDAC4 mutants crossed with AD model mice. We will show differences in sleep patterns between normal and hypersomnia-related aging, highlighting not only sleep duration but also fragmentation and delta power as indicators of sleep quality. We will also examine how hypersomnia, when combined with AD pathology,

exacerbates the deficit in cognitive performance. These findings are expected to support the hypothesis that the HDAC4 signaling pathway mediates the impact of sleep on aging-related neurodegeneration. Our work provides molecular-level insights into how sleep abnormalities contribute to the pathogenesis of AD and highlights the pathway as a potential therapeutic target for early diagnosis and intervention in aging-associated neurodegenerative disorders.

Keywords : Sleep architecture, Aging, HDAC4, Alzheimer's disease

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P-670

Polarization of microglia on nanopatterned titanium

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Microglia, the resident immune cells of the central nervous system, play a key role in neuroinflammatory processes. Recent advances in biomaterials suggest that surface nanotopography can modulate immune cell function; however, its effects on microglial activation remain underexplored. In this study, we investigated the effects of nanopatterned titanium on microglial polarization using both BV2 cell lines and primary microglia. Cells cultured on nanopatterned titanium exhibited distinct morphological changes and alignment, as observed through scanning electron microscopy (SEM) and immunocytochemistry. Importantly, pro-inflammatory markers were significantly downregulated at both the mRNA and protein levels in microglia grown on nanopatterned surfaces. Furthermore, Quant-Seq 3' mRNA sequencing revealed broad suppression of inflammatory gene expression, including genes involved in TNF and NF-κB signaling pathways, indicating attenuation of pro-inflammatory signaling cascades. These findings suggest that nanopatterned titanium surfaces can shift microglial polarization toward a less inflammatory phenotype, highlighting their potential as promising biomaterials for neuroinflammation modulation and central nervous system applications.

Keywords : Microglia, Nanopatterned titanium, Nanotopography, microglial polarization, pro-inflammatory response

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P-671

Depth of anesthesia alters surgery-induced neuroinflammation and microglia activity in young mice

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Postoperative delirium (POD) is a serious complication contributing to cognitive dysfunction after surgery across all age groups, but elderly patients are particularly susceptible. Perioperative stress from surgical trauma and anesthesia can trigger systemic inflammation and neuroimmune responses. Emerging evidence suggests that microglial activation and neuroinflammation may play a key mediator in POD pathogenesis. Recent studies also indicate that deep anesthesia is associated with a higher risk of POD. Therefore, we further examined the potential for neuroinflammation in adult mice that underwent exploratory laparotomy depending on the depth of anesthesia. Male mice (8 weeks old) received simple laparotomy under general anesthesia for 2 hours via endotracheal intubation. General anesthesia was administered at two different concentrations of sevoflurane: a high dose (2.6%) associated with burst suppression in EEG monitoring (Deep Anesthesia group), and a lower dose (1.8%) without burst suppression (Light Anesthesia group). Surgical procedures were performed within 15 minutes. Mice that received light anesthesia showed significant increases in the expression of inflammatory cytokine and chemokine genes from 0 to 72 hours post-surgery. In contrast, the mice in the deep anesthesia group exhibited a markedly attenuated inflammatory response, with lower expression levels or fewer upregulated genes. To assess whether this reduced inflammation was associated with changes in microglial activation, we examined microglial synaptic engulfment. LAMP1 was significantly upregulated at both 24 and 72 hours in the Low Anesthesia group (24hr: P=0.0003; 72hr: P=0.0002), and Homer1 also increased significantly at 24 hours (P=0.029). In the Deep Anesthesia group, no significant changes were observed at 24 hours, although LAMP1 showed a delayed increase at 72 hours (P=0.0133). These results suggest the need for further studies on anesthesia depth and surgery-induced neuroinflammation.

Keywords : Postoperative delirium, General anestheisa, Neuroinflammation, Microglia

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P-672

Examination of the contribution of Nodal Modulator 1 (Nomo1) in neuronal function and the development of autism spectrum disorder

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Withdrawn

Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder characterized by social interaction deficits, restricted interests, and repetitive behaviors. Recent studies suggest Nomo1, located at 16p13.11 chromosomal region - a CNV hotspot linked to ASD and other neurodevelopmental disorders - as a potential regulator of ASD. Although Nomo1 is primarily associated with the maintenance of endoplasmic reticulum structure, it has been shown to regulate the Nodal signaling pathway, suggesting its broader role in neurodevelopment and maturation. In this study, we sought to explore Nomo1's role in neuronal maturation and function. We observed the expression of Nomo1 across numerous brain regions, including the cortex, involved in the regulation

of high-order cognitive function. Cultured primary neurons derived from Nomo1-floxed mice brain tissue are transfected with AAV-Cre vectors to induce Nomo2 gene deletion in vitro. With the Nomo1-knockout neurons alongside classic methods for neurophysiological examinations (biochemistry and electrophysiology), we will evaluate the impact of Nomo1 ablation on the morphological and functional outcome of cortical and cerebellar neurons. This study aims to uncover the role of Nomo1 in brain development and ASD-related behaviors, providing insights into ASD pathophysiology and potential therapeutic targets.

Keywords : Autism spectrum disorder, Neurodevelopment, Neurophysiology

P-673

The effects and mechanism of virgin coconut oil on learning and memory impairment and amyloid precursor protein processing pathway in aging mice

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Objectives: To investigate the protective effects and underlying mechanisms of Virgin Coconut Oil (VCO) against learning and memory impairment, as well as its influence on the amyloid precursor protein (APP) processing pathway in aging mice. Methods: Fifty 2-month-old male Kunming mice were randomly assigned to five groups: normal control, aging model, aging + low-dose VCO, aging + medium-dose VCO, and aging + high-dose VCO. The aging model was induced by subcutaneous injection of D-galactose at the nape of the neck for 90 consecutive days. Learning and memory capabilities were evaluated using the Morris water maze test. Enzyme-linked immunosorbent assay (ELISA) was performed to measure the content of α/β/γ-secretases, $A\beta_{1\text{-}40}$ acetylcholinesterase (AChE), and 5-hydroxytryptamine (5-HT). Western blotting was used to detect the expression of ADAM10, BACE1, and PS1.Results: Behavioral tests demonstrated that VCO dose-dependently improved learning and memory in aging mice and reversed memory impairment. Biochemical analyses revealed that, compared with the aging model group, each VCO-treated group (low, medium, and high-dose) enhanced α-secretase content, inhibited β- and γ-secretase contents, reduced $A\beta_{1\text{-}40}$ content, decreased acetylcholinesterase (AChE) content, and increased 5-hydroxytryptamine (5-HT) content in brain tissue. Western blotting results showed that the aging model group exhibited downregulated ADAM10 expression and upregulated BACE1 expression relative to the normal control group. In contrast, VCO-treated groups displayed significantly increased ADAM10 expression and decreased BACE1 and PS1 expression levels compared with the aging model group. Conclusion: Virgin Coconut Oil exerts a protective effect on APP processing and ameliorates learning and memory deficits in aged mice, suggesting its potential as a therapeutic agent for age-related cognitive decline.

Keywords : MCFAs, APP Proteolytic Pathway, Aβ1-40, Aging, Learning and memory

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P-674

ATP-sensitive potassium channel–dependent inhibition of hypothalamic MC4R neurons underlies atypical antipsychotic–induced hyperphagia

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Atypical antipsychotics (AAPs), such as risperidone and olanzapine, are widely prescribed for neuropsychiatric disorders but are frequently associated with adverse metabolic effects, including hyperphagia and obesity. Given the critical role of melanocortin-4 receptor (MC4R)–expressing neurons in the paraventricular nucleus of the hypothalamus (PVH) in regulating appetite and energy balance, this study investigated the cellular mechanisms by which AAPs inhibit MC4RPVH neuronal activity. Using whole-cell patch-clamp recordings in *Mc4r*-Cre;*Ai14* mice, we found that acute application of risperidone and olanzapine induced membrane hyperpolarization of MC4RPVH neurons via activation of ATP-sensitive potassium (KATP) channels, an effect abolished by either glibenclamide or PKA inhibition. To assess chronic effects, we performed cell-attached and voltage-clamp recordings in female mice fed risperidone- or olanzapine-containing diets. Chronic risperidone exposure significantly decreased firing frequency of MC4RPVH neurons, whereas olanzapine reduced the proportion of active neurons without affecting their firing rates. Together, these findings demonstrate that KATP channel–dependent suppression of MC4RPVH neuron excitability contributes to AAP-induced hyperphagia, and further suggest that KATP channels may represent a promising therapeutic target for mitigating the metabolic side effects of AAP treatment.

Keywords : atypical antipsychotics, melanocortin-4 receptor, hyperphagia, patch-clamp experiment, ATP-sensitive potassium channels

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P-675

In Vivo CRISPR/Cas9 Screening Identifies Subunit-Specific Roles of proprioceptor ENaC in gait behavior

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Proprioception is essential for coordinated motor behavior, yet its complete molecular basis remains unknown. To identify ion channels in the peripheral nervous system that contribute to proprioception, we developed a panel of adeno-associated virus (AAV) for CRISPR-Cas9 screening. Based on previous studies, we build a candidate list of ion channels enriched in the peripheral sensory neurons in addition to mechanosensitive ion channels. Then, we designed and validated single guide RNAs (sgRNAs) *in vitro* targeting each candidate channels. AAVs carrying sgRNAs were systemically delivered via neonatal intracerebroventricular (ICV) injection into PV-IRES-Cre; LSL-Cas9 mice, enabling selective gene knockout in PV(+) proprioceptive neurons in the dorsal root ganglion(DRG). We then

assessed the motor function of AAV-infected mice using grip strength test, CatWalk-XT, balance beam, and Treadmill walking. The validity of the screening approach was confirmed by replicating known motor deficits in sgPiezo2 knockout model. Among the candidate genes, disruption of the *Scnn1* gene, which encodes subunits of the epithelial sodium channel (ENaC), induced marked motor impairments. Notably, *Scnn1b* and *Scnn1g* knockouts exhibited inconsistent gait patterns and abnormal joint kinematics during locomotion. The distinct phenotypes associated with individual subunit deletions likely reflect the heteromeric composition and functional diversity of ENaC complexes. Collectively, our findings identify ENaC subunits as critical regulators of gait behavior and demonstrate the effectiveness of our AAV CRISPR-Cas9 panel in elucidating the molecular mechanisms underlying proprioception.

Keywords : Proprioception, Mechanosensation, Proprioceptive channels, CRISPR-Cas9, Sensory neurons

P-676

BMDA prevents dopaminergic neuron loss by attenuation of astrocyte-mediated neuroinflammation in Parkinson's Disease

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Parkinson's disease (PD) is a neurodegenerative disorder marked by the progressive loss of dopaminergic neurons, leading to motor dysfunction. While current treatments primarily focus on preserving dopamine, targeting neuroinflammation is emerging as a potential therapeutic approach. BMDA (N-benzyl-N-methyl-dodecan-1-amine), a garlic-derived compound, has gained attention for its diverse pharmacological properties, including antioxidant, neuroprotective, anti-inflammatory, and anticancer effects. This study investigates the neuroprotective potential of BMDA in the context of PD, focusing on its impact on glial cell activation, dopaminergic neuron survival, and neuroinflammation. Mice were pretreated with BMDA (20 mg/kg, p.o.) for seven days before being administered MPTP (20 mg/kg, i.p.) four times at two-hour intervals. The results showed that BMDA improved motor function, protected dopaminergic neurons in the substantia nigra (SN) and striatum (STR), and reduced astrocyte activation. Furthermore, in vitro studies using primary astrocytes revealed that BMDA reduced GFAP expression and inhibited NF-κB signaling, leading to decreased production of pro-inflammatory cytokines. These findings suggest that BMDA could be a promising therapeutic agent for Parkinson's disease. By modulating astrocyte-driven neuroinflammation in addition to protecting dopaminergic neurons, BMDA offers a potential treatment strategy beyond current dopamine-preserving therapies, making it a promising candidate for future PD management.

Keywords : Parkinson's disease, neuroprotection, neuroinflammation, MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), garlic extracted compound

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P-677

Dysregulation of MeCP2 contributes to cognitive impairment in noise induced hearing loss models

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According to "World Report on Hearing" published by the World Health Organization, about 430 million people are currently suffering from hearing loss. Even it is expected that by 2050 1 in 4 individuals will have hearing problems. Hearing loss has three different types noise-induced hearing loss, age-related hearing loss, and sudden sensorineural hearing loss. Among them, noise-induced hearing loss frequently occurs in teenager and young adults who use electronic devices such as earphones and headsets, and it is gradually increasing. Unfortunately, hearing loss does not only mean the loss of auditory function. Numerous studies have shown a correlation between hearing loss and cognitive dysfunction. Thus, the risk of developing dementia increases 1.55 times compared to people with normal hearing. However, the exact molecular mechanism underlying cognitive dysfunction and hearing loss has not been studied. Meanwhile, MeCP2 (Methyl-CpG Binding Protein 2) an epigenetic regulator involved in synaptic plasticity and neural activity, is linked to disorders like Rett Syndrome and Alzheimer's disease, which exhibit both hearing loss and cognitive decline. We confirmed whether noise causes hearing loss and then cognitive decline by making a noise-induced hearing loss–cognitive impairment model through noise stress. One week (acute) and three months (chronic) after noise stress, we confirmed impairment to auditory function. Also we found that cognitive function was decreased compared to the control group in behavior test such as Novel Object Recognition (NOR), Passive Avoidance (PA), and the Y-maze test.

Keywords : Hearing Loss, Cognitive decline, MeCP2(Methyl-CpG Binding Protein 2), Noise exposure

P-678

Prion infection in a 3D spheroid culture system for antiprion drug screening

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Prion diseases are transmissible and fatal neurodegenerative disorders characterized by the accumulation of misfolded prion protein (PrPSc) in the central nervous system. Although various in vitro models, such as 2D cultures, have been utilized to study prion replication, they often fail to replicate the structural and cellular complexity of the brain. 3D models such as brain organoids have shown promise in mimicking the architecture of brain tissue but are limited by variability and the infection protocols for long-term studies. Here, we present a novel 3D spheroid model of neurons and astrocytes derived from mouse neural stem cells (NSCs), to study the pathogenesis of prion diseases. This model was generated by inducing spheroid formation from NSCs followed by infection with Rocky Mountain Laboratory (RML) prion strains. RML infection-3D spherical models with neurons and astrocytes generated apoptosis and gliosis resembling a neural microenvironment for prion propagation and neurodegenerative processes. Additionally, the ability

to support long-term prion transmission, secondary infection, and cryopreservation has been demonstrated. This innovative model enables long-term studies of prion dynamics and the evaluation of therapeutic interventions, bridging the gap between simple in vitro systems and in vivo models. Our findings demonstrate the utility of this 3D model as a valuable tool in prion research.

Keywords : 3D spheroid, Prion disease, Neural stem cells, Drug screening, Culture system

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P-679

A transcriptomic analysis of gyrencephalic cortex development in the miniature pig

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The swine's central nervous system (CNS) has anatomical features similar to the human brain. In particular, swine have a gyrencephalic brain, mainly composed of gyrus and sulcus with a developmental stage similar to humans. In particular, swine has a gyrencephalic brain, mainly composed of white and gray matter with developmental stages similar to humans. To understand gyrencephalic cortex development, we analyzed the gene expression by scRNA sequencing using 12 Yucatan miniature pig embryos between 4 weeks of fertilization and postnatal day 0. We identified significant subtypes of 10 progenitors and 7 neurons in the PFC region and revealed the specific gene expression similar to human development at the single-cell resolution. And it was confirmed that the gyrencephalic brain structure of the cerebral cortex is very similar to the developing human brain. Especially, it was confirmed that the inner subventricular zone (iSVZ) and the outer subventricular zone (oSVZ) are similar to developing human brains, and the neuronal differentiation is very active in the early stage of cortex with the gyrus and sulcus formation. Thus, the cortical structure, gene expression, and cell types and functions were similar to the human brain, thereby verifying the possibility of a neurodevelopmental research model.

Keywords : miniature pig, gyrencephalic cortex

P-680

Correlation between anesthesia-induced tonic inhibition mediated by astrocytic γ-aminobutyric acid and cognitive dysfunction

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Postoperative Cognitive Decline (POCD) occurs following anesthesia with surgery, and certain anesthetics are known to target inhibitory extrasynaptic γ-aminobutyric acid type A (GABAA) receptors mediated by glial GABA. However, the role of tonic inhibition mediated by glial GABA in the development of POCD remains unclear. This study aimed to evaluate whether tonic inhibition mediated by astrocytic GABA contributes to the emergence of POCD. Based on a previous study, we discovered that MAO-B, the major enzyme of the astrocytic GABA synthesis pathway, partially mediated immobility and hypnosis effects of inhaled anesthetics. Thus, we observed effects of potent inhaled anesthetics isoflurane, sevoflurane, and desflurane on MAO-B related effects in young 8 wk old B6 mice. Isoflurane and sevoflurane significantly enhanced tonic GABA currents in the hippocampus and increased astrocytic GABA levels and α5 GABAA receptor activity in the hippocampus during anesthesia, persisting 24 h after anesthesia. Enzymes responsible for GABA synthesis in astrocytes were also observed through IHC in the cortex, hippocampus, thalamus, and hypothalamus, regions previously linked to anesthetic effects. Significant changes were not observed, though isoflurane and sevoflurane induced upward trends in MAO-B expression levels directly after treatment, reverting 24 h after anesthesia. Tonic GABA currents, astrocytic GABA levels, and α5 GABAA receptor activity in the hippocampus were not significantly changed by desflurane during anesthesia or 24 h after anesthesia. In aged mice (~2 yr old), effects of sevoflurane were observed and we discovered that cognitive deficits emerged 1 month after anesthesia, resembling the effects of POCD. These results suggest that astrocytic GABA significantly mediates anesthetic-mediated POCD in the hippocampus for certain inhaled anesthetics in aged mice.

Keywords : Astrocytes, POCD, Anesthesia, MAO-B, Aging

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P-681

Microglial apolipoprotein E genotype regulates PI3K-Akt signaling pathway in brain assembloids

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Background: Apolipoprotein E4 (APOE4) is the strongest genetic risk factor for late-onset Alzheimer's disease (AD). However, the molecular mechanisms underlying the interaction between APOE4 and microglia, the brain's resident immune cells, remain largely unknown. Methods: We generated human iPSC-derived microglia with APOE3/3 or APOE4/4 genotypes using CRISPR-Cas9 editing and integrated them with brain organoids to construct a brain-microglia assembloid model. Single-cell RNA sequencing (scRNA-seq) was performed to analyze transcriptional changes across diverse cell types within the assembloids. Results: APOE4 microglia upregulated six genes involved in the PI3K-Akt signaling pathway, primarily within oligodendrocyte progenitor cells (OPCs). Gene interaction analysis revealed that differentially expressed genes (DEGs) in APOE4 microglia influenced the expression of these PI3K-Akt–related genes in the brain organoid context. A similar transcriptional pattern was observed in post-mortem brain transcriptomic data from AD patients. Furthermore, we experimentally validated the altered expression of these genes in the OPCs of assembloids containing

APOE4 microglia. Conclusion: Our findings suggest that the APOE genotype of microglia modulates PI3K-Akt signaling in oligodendrocyte lineage cells, leading to functional changes in OPCs. These microglia–oligodendrocyte interaction may represent a novel mechanism and potential therapeutic target for APOE4-associated Alzheimer's disease.

Keywords : APOE4, Microglia, Brain Organoid, Single-cell RNA sequencing (scRNA-seq), Alzheimer's disease

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P-682

Novel neuroprotective drug development strategy targeting tau hyperphosphorylation in AD

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Excessive phosphorylation and tau protein aggregation into neurofibrillary tangles are central contributors to the memory deficits observed in Alzheimer's disease (AD). A key mediator of this pathological tau modification is the enzyme GSK3β, whose dysregulated activity has led to the development of various inhibitors as potential AD therapeutics. However, many of these inhibitors also interfere with the enzyme's essential physiological functions, resulting in adverse effects. To address this, we previously engineered a novel GSK3β inhibitory peptide (GIP) by combining the phosphorylatable PPPSPxS motif from the Wnt co-receptor LRP6 with the Akt-responsive RxRxxS motif from GSK3β. Designed to be activated only under Akt-active conditions, GIP suppressed GSK3β-mediated tau phosphorylation in hippocampal extracts and mitigated Aβ-induced tau pathology and cytotoxicity in human neuroblastoma cells. In vivo studies showed that intravenous GIP administration significantly reduced hippocampal tau phosphorylation in 3×Tg-AD mice, without affecting Aβ plaque levels or neuroinflammation and ameliorated memory defects. These findings suggest that GIP serves as a promising therapeutic strategy for targeting tau pathology through Akt-dependent inhibition of GSK3β.

Keywords : GSK3β, Tau phosphorylation, Akt, Alzheimer's disease

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P-683

Multiplex imaging of ATP and Ado dynamics in vivo with an expanded toolbox of GRAB sensors

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Purinergic transmitters, including extracellular ATP, ADP, adenosine (Ado), play essential roles in both the peripheral and central nervous systems by interacting with specific purinergic receptors on different cell types. These extracellular purines can also undergo conversions, such as ATP degrading into adenosine, which regulates sleep, motion and neuroimmune interactions. Due to the complex nature of purinergic signaling, developing tools for concurrent monitoring with high molecular specificity and spatiotemporal resolution is essential. In this study, we present a series of optimized GPCR-Activation-Based (GRAB) sensors capable of detecting various purinergic transmitters. These sensors show good plasma membrane localizations, high sensitivity, and notably, high selectivity in distinguishing different purinergic transmitters. We showcase a novel GRAB-Ado sensor with faster kinetics, enabling detailed monitoring of Ado fluctuations during sleep-wake cycles. Furthermore, the development of red-shifted purinergic GRAB sensors enables dual-color imaging of distinct neurochemicals. We successfully applied these sensors to simultaneously record Ado and ATP dynamics in cultured neurons and mice in vivo. Leveraging high spatial resolution, we observed localized purinergic transmitter release in response to epileptic events using widefield and two-photon imaging in vivo. Taken together, the expanded toolbox offers a powerful approach for dissecting purinergic signaling in diverse biological contexts. It paves the way for a deeper understanding of the dynamic regulation of the purinergic system in health and disease.

Keywords : Fluorescent sensor, G-protein coupled receptor, Adenosine, ATP, Purinergic transmission

P-684

Functional role of EBP1 in MFN2-mediated mitochondrial fusion and mitophagy under Aβ-induced stress

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ErbB3-binding protein 1 (EBP1), a member of the PA2G4 family, is a conserved and ubiquitously expressed protein involved in various cellular processes, including proliferation. Recent studies have shown that EBP1 promotes mitophagy in an ischemia-reperfusion (IR) injury model. Specifically, Parkin-mediated ubiquitination at lysine 376 (K376) enables EBP1 to recruit the mitophagy adaptor protein p62, thereby facilitating mitophagosome formation. However, the impact of EBP1 depletion and the resulting mitochondrial dysfunction remains poorly understood. Here, we demonstrate that EBP1 is essential for maintaining mitochondrial integrity by regulating both mitophagy and mitochondrial dynamics. In EBP1-deficient mouse embryonic fibroblasts (MEFs), mitochondria exhibited a fragmented morphology and impaired function. Protein–protein interaction assays revealed that EBP1 binds to mitofusin 2 (MFN2), a key mediator of mitochondrial fusion, and domain mapping identified the 205–394 amino acid region of EBP1 as critical for this interaction. Given recent reports that EBP1 is cleaved in Alzheimer's disease (AD) and that its loss of function promotes Aβ production, we further investigated the relationship between EBP1 and mitochondrial function in 5xFAD mice. Interestingly, in 5xFAD mice, although overall EBP1 expression declined with age, its interaction with MFN2 was increased. Moreover, in cells transfected with mitochondria-targeted Aβ, the 205–394 amino acid fragment of EBP1 induced mitophagy more effectively than the full-length protein. Collectively, these findings suggest that EBP1 supports mitochondrial homeostasis by interacting with MFN2 and promoting mitochondrial fusion. Under mitochondrial

stress conditions such as Aβ accumulation, EBP1—particularly through its 205–394 region—facilitates the mitophagic clearance of damaged mitochondria, thereby preserving cellular function.

Keywords : EBP1, MFN2, Mitochondria, 5xFAD, Aβ

P-685

A NanoLuciferase-based reporter system for screening GCase-enhancing CPPs in Parkinson's disease

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Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons and the pathological aggregation of α-synuclein. Among known genetic risk factors of PD, mutations in GBA1, encoding the lysosomal enzyme glucocerebrosidase (GCase), are the most common. Importantly, reduced GCase activity is also observed in idiopathic PD and aging brains, suggesting its broader pathological relevance. GCase deficiency leads to the accumulation of its lipid substrate glucosylceramide (GlcCer), which promotes α-synuclein aggregation and contributes to neuronal toxicity. To identify peptide-based strategies that restore GCase function, we developed a GBA1-HiBiT knock-in HEK293T reporter system. This NanoLuciferase-based platform enables real-time, quantitative monitoring of endogenous GCase expression. Through the screening of 18 leech-derived peptides, we identified Hirunipin 4, a cell-penetrating peptide(CPP), as a potent modulator of GCase activity. Hirunipin 4 significantly increased GCase protein levels and enzymatic activity, and reduced α-synuclein aggregation and cytotoxicity in both SH-SY5Y cells and primary cortical neurons treated with α-synuclein preformed fibrils (PFFs). Mechanistically, Hirunipin 4 promoted nuclear translocation of TFEB, a master transcriptional regulator of lysosomal biogenesis, and enhanced GBA1 protein stability, suggesting effects on both transcriptional and post-translational regulation. Furthermore, it alleviated PFF-induced GlcCer accumulation and restore lysosomal homeostasis. Collectively, these findings identify Hirunipin 4 as a promising therapeutic candidate for PD and demonstrate the utility of our NanoLuciferase-based GBA1 reporter system as a novel platform for peptide-screening of GCase modulators.

Keywords : Parkinson's disease, GBA1, NanoLuc Binary technology-based luminescence assay, α-synuclein, Cell penetrating peptide

P-687

Effects of co-administration of aripiprazole and fluoxetine on mossy and granule cell activity in a mouse model of depression

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Neurotransmitters and neuropeptides regulate brain function and behavior. Major Depressive Disorder (MDD) has become a serious social issue, but the mechanisms of its onset and treatment have not yet been identified. Antidepressant drugs that target serotonin, such as Fluoxetine, are the most commonly used treatment for MDD. Recently, drugs targeting dopamine, norepinephrine, and other neurotransmitters are also being used and research on them is actively being conducted. Aripiprazole is a drug with relatively few side effects and is well known for its role as a dopamine-system stabilizer (DSS). While it was initially used to treat schizophrenia, it is now widely used for depression and has been reported to accelerate the antidepressant effects of selective serotonin reuptake inhibitors (SSRIs), such as Fluoxetine. Previous studies have reported that the co-administration of Aripiprazole and Fluoxetine improves antidepressant effects at the behavioral level. However, the cellular and molecular mechanisms are still not well understood, which may provide crucial insights into the onset and reversal of depression. Thus, we examined the reversal effects of pharmacological treatments on the hippocampus by assessing c-Fos expression in a Chronic Unpredictable Stress (CUS) mouse model. The results indicate that the observed effects are associated with mossy cells in the dorsal-medial areas of hippocampus, but not in the ventral areas. c-Fos+ neurons that were downregulated by CUS in the dorsal-medial areas were upregulated toward normal levels. Future research aim to focus on identifying critical factors underlying depression, including specific neurotransmitters and neural circuits, by targeting mossy cells and the hilus region of the hippocampus. Based on these findings, we seek to design a new mechanism-based therapeutic approach for depression.

Keywords : Aripiprazole, Fluoxetine, Hippocampus, Dopamine-system stabilizer, Chronic Unpredictable Stress

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P-688

Monitoring the dynamics of Alzheimer's Disease biomarkers and the *APOE*–tau axis via human cerebral organoids with immuno-SERS

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Non-invasive tracking of Alzheimer's disease (AD) biomarkers is critical for early detection and evaluating therapeutic responses. Despite the significance of tau protein as a hallmark of AD, its non-invasive monitoring across developmental timelines, age-associated variations, and apolipoprotein E (APOE) interactions remains unachieved. In this study, we demonstrate a label-free, non-invasive approach for tracking dynamic changes in multiple tau isoforms across developmental phases, aging-related changes, and various isogenic APOE genotypes using human cerebral organoids (hCOs) analyzed with surface-enhanced Raman spectroscopy (SERS). Principal component analysis (PCA) of the SERS spectra distinguishes four developmental stages of hCOs—embryoid body formation, neuronal induction, maturation, and maintenance. Time-dependent secretion patterns of tau variants, reflecting AD-like features, are detected and found to be modulated by astrocytic influence. Additionally, PCA of SERS data highlights genotype-specific clustering, showing a progressive increase in tau secretion from APOE2/E2 to APOE4/E4, elucidating the APOE–tau interaction in AD pathogenesis. This work offers a pioneering platform for non-invasive clinical investigation of AD progression, tau dynamics, and APOE-related risk profiling.

Keywords : Alzheimer's disease, cerebral organoids , Tau, APOE

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P-689

Deficiency of Chi3L1 promotes schizophrenia-like phenotypes by lowering BDNF levels

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Chitinase-3-like protein 1 (Chi3L1) is widely recognized as one of the major genes linked to neurodegenerative conditions. Schizophrenia (SCH) is a severe mental illness characterized by potential progressive brain alterations and cognitive impairment. Alterations in brain-derived neurotrophic factor (BDNF) have been implicated as key contributors to SCH pathology. Our investigation revealed that Chi3L1 expression was notably elevated in the brains of SCH patients, whereas BDNF levels were markedly reduced. To better understand the link between Chi3L1 and SCH, a series of behavioral assessments were conducted using Chi3L1 knockout (KO) and Chi3L1 wild-type (WT) transgenic mice. In vitro, Chi3L1 silencing in PC12 cells was accomplished through siRNA transfection. Subsequent neurite extension and BDNF production following NGF stimulation were evaluated. Chi3L1 KO mice demonstrated heightened anxiety-like responses and impaired sensorimotor gating. Mechanistically, both BDNF protein and mRNA expression, along with markers of neural plasticity, were diminished in the prefrontal cortex of Chi3L1 KO mice. Consistent with BDNF downregulation, intracellular calcium levels and expression of calcium signaling-related proteins (phospho-Akt and calpain-1) were decreased. Likewise, Chi3L1 knockdown in PC12 cells significantly lowered BDNF levels, neurite elongation, and calcium signaling via reduced p-Akt and calpain-1 expression. Application of LY294002 (a PI3K/Akt pathway inhibitor) or EGTA (a calcium chelator) suppressed neurite formation in PC12 cells, but these inhibitory effects were reversed upon BDNF supplementation. Collectively, these findings indicate that Chi3L1 may contribute to the pathogenesis of SCH by modulating BDNF expression.

Keywords : Chi3L1, schizophrenia, BDNF, prefrontal cortex , calcium

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P-690

Desensitization of TRPA1 by dimethyl itaconate attenuates acute and chronic pain in mice

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Chronic pain, affecting over 20% of the global population, remains a significant clinical challenge due to the limited efficacy of current analgesics. Dimethyl itaconate (DMI), a cell-permeable derivative of itaconate with known anti-inflammatory and immunomodulatory properties, has recently shown promise in alleviating pain symptoms. However, the mechanisms by which DMI modulates acute and chronic pain remain unclear. We investigated the interaction between DMI and the transient receptor potential ankyrin 1 (TRPA1) channel, a calcium-permeable ion channel implicated in various pain states. Molecular docking analysis revealed covalent interactions between DMI and key TRPA1 residues (Cys621). Functional assays using calcium imaging demonstrated that DMI directly activates TRPA1, whereas repeated exposure induces channel desensitization. To explore the physiological significance of these findings, we performed behavioral assessments in mice. Single plantar injection of DMI induced mechanical hypersensitivity in a dose-dependent manner, while repeated injections significantly attenuated pain responses. Furthermore, repeated intraperitoneal administration of DMI alleviated pain behaviors, motor dysfunction, and anxiety-like phenotypes in a variety of acute and chronic pain models, including DSS-induced colitis, CFA-induced inflammatory pain, AITC- and formalin-induced nociception, and oxaliplatin-induced neuropathic pain. Our findings demonstrate that DMI modulates TRPA1 activity through both activation and desensitization mechanisms, and highlight TRPA1 desensitization as a potential therapeutic strategy for the treatment of acute and chronic pain.

Keywords : Dimethyl Itaconate, TRPA1, Desensitization, Pain

P-691

Cell-type-resolved mosaicism decodes clonal architectures of the human forebrain

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The anatomical origins of specific brain cell subtypes and their lineage relationships within the human forebrain remain a topic of ongoing debate. To gain a comprehensive understanding of the brain's structural organization and cellular origins, direct observation in the mature human brain is essential. In this study, we leverage somatic mosaic variants within defined cell types as unique clonal markers—a strategy we term cell-type-specific mosaic variant barcode analysis. Using brain tissue from four hemispheres of two neurotypical human donors, we identified 287 and 780 mosaic variants, respectively, which enabled reconstruction of clonal dynamics. Analysis of clonal dispersion and variant allele fractions revealed that excitatory neurons in the hippocampus exhibit more restricted lineage patterns compared to excitatory neurons in the neocortex or GABAergic inhibitory neurons in the basal ganglia. Moreover, integrated genome and transcriptome analyses at both the single-cell and cell-type levels indicate that a subset of DLX1^{+} inhibitory neurons shares a dorsal neocortical origin with excitatory neurons and disperses radially. Finally, mapping mosaic variants across 17 regions of a single parietal lobe showed that clonal restriction along the anterior–posterior axis occurs earlier than along the dorsal–ventral axis in both excitatory and inhibitory neurons. These findings demonstrate that cell-type-resolved somatic mosaicism can reveal lineage trajectories underlying human forebrain development.

Keywords : Mosaicism, Clone, Development, Inhibitory neuron, Forebrain

P-692

Taurine inhibited astrocyte-mediated neuroinflammation and dopaminergic neuron loss in the PD mouse model

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Parkinson's disease (PD) is a neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons, primarily due to oxidative stress and inflammation. Targeting these pathological mechanisms presents a promising approach to slowing PD progression. Taurine, a naturally occurring amino sulfonic acid, has demonstrated potent antioxidant properties and neuroprotective effects, effectively preventing neuronal cell death. While taurine has been investigated for its role in mitigating microglial activation and restraining Alzheimer's disease progression, its effects on astrocyte activation in PD models remain largely unexplored. In this study, we found that taurine significantly attenuates astroglial activation in MPP^+-treated primary astrocytes by inhibiting the NF-κB pathway and mitochondrial superoxide. Furthermore, in vivo experiments using MPTP-induced PD models in male C57BL/6 mice revealed that taurine improved motor function, protected dopaminergic neurons, and reduced glial activation in both the striatum and substantia nigra. These findings underscore the anti-inflammatory effects of taurine, particularly through the suppression of astroglial activation, and support its potential as a therapeutic candidate for PD.

Keywords : Taurine, Astrocyte, Parkinson's Disease, MPTP(1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), Neuroinflammation

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P-693

Host longevity promoting bacterial genes protect dopaminergic neurons in *Caenorhabditis elegans*

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Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the selective loss of dopaminergic neurons in the substantia nigra and the accumulation of α-synuclein (α-syn) aggregates. Recently, the gut-brain axis is increasingly implicated in the pathogenesis of PD by linking changes in the gut microbiota and their genes to neurodegeneration. In this line, our previous study demonstrated that *Δhns Escherichia coli* (*E. coli*), previously shown to extend the lifespan in *Caenorhabditis elegans* (*C. elegans*) (Shin et al, PNAS, 2020), also able to rescue dopaminergic neurodegeneration in *C. elegans* PD model. In this study, we hypothesized that other longevity-associated microbial genes might also influence dopaminergic neurodegeneration. To test this hypothesis, we fed *C. elegans* with *E. coli* strains carrying deletions of eight distinct longevity-associated genes and assessed their effects on dopaminergic neurodegeneration. Among these, the *ΔpabA*, the *ΔtolC* and the *ΔmodB* were found to restore dopaminergic neurodegeneration in the *C. elegans* expressing human α-syn in dopaminergic neurons, while the *ΔyjfF* was found to damage dopaminergic neurodegeneration in the same *C. elegans*. These findings suggest that microbial genes associated with host longevity may also play a protective role in dopaminergic neuron survival and could represent novel modulators of PD-related neurodegeneration.

Keywords : Parkinson's disease, Dopaminergic neurons, C. elegans, α-synuclein, Bacterial genes

P-694

Argonaute-mediated small RNA pathways mediate maternal age-dependent behavioral plasticity in *C. elegans*

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Parental age influences progeny fitness, yet the molecular mechanisms underlying these effects remain largely unknown. Previously, our lab has shown that *C. elegans* progeny from old mothers exhibit reduced avoidance behavior toward a pheromone ascaroside#3 (ascr#3). This maternal-age-dependent behavioral change is associated with decreased expression of the *eri-1* exoribonuclease gene in the AVH interneurons. These findings suggest that a small RNA pathway modulates maternal-age-dependent neural activity, ultimately modulating behavioral outcome. However, the molecular and neuronal mechanisms in which small RNA pathways coordinate these processes across generations remain to be uncovered. To investigate the roles of small RNA pathways underlying maternal age-dependent behavioral plasticity, we first sought to identify which Argonaute proteins, the core components of RNA-induced silencing complexes (RISC), mediate ascr#3 avoidance behavior. We tested 19 out of 27 Argonautes in *C. elegans*, and found that the mutants of *alg-3, alg-5, ergo-1,* and *wago-10* exhibited significantly reduced ascr#3 avoidance behavior. We then examined the expression patterns of these genes and found that *alg-3* was expressed in the pheromone-sensing ASI neurons, while *ergo-1* was predominantly expressed in the germline but also in unidentified head neurons or glia. We are currently performing rescue experiments to determine whether the expression of Argonaute genes restores ascr#3 avoidance defects. While *eri-1* expression in the AVH interneurons is influenced by maternal age, its role in AVH function and the associated regulatory networks remain unclear. To investigate this, we are currently performing TRAP-sequencing to identify upstream and downstream factors. This research will elucidate how small RNA pathways coordinate gene regulatory networks to mediate behavioral plasticity across generations.

Keywords : maternal age, small RNA, Argonaute, pheromone avoidance, behavioral plasticity

P-695

Targeting lipocalin-2 with a small-molecule inhibitor to suppress neuroinflammation

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Lipocalin-2 (LCN2) is a proinflammatory mediator highly expressed in astrocytes under central nervous system (CNS) inflammatory conditions. While its pathological role is well established, LCN2-targeted therapeutics remain undeveloped. GP1, a small-molecule LCN2 inhibitor, was previously evaluated for its antifibrotic effects in models of chronic kidney disease and myocardial infarction. We developed DN300653 from the GP1 scaffold, optimized for anti-neuroinflammatory activity. DN300653 reduced glial activation and inflammatory cytokine levels in both primary glial cultures stimulated with LCN2 and an LPS-induced neuroinflammation model. Furthermore, it successfully rescued LPS-induced cognitive deficits *in vivo*. These findings highlight the therapeutic potential of LCN2 inhibition in the context of neuroinflammation and related CNS disorders. Targeting LCN2 may provide a more selective means of modulating glial reactivity while preserving essential immune functions. The dual efficacy of DN300653 in suppressing neuroinflammation and rescuing behavioral impairments supports its promise as a novel therapeutic candidate for CNS disorders characterized by inflammatory glial activation.

Keywords : Lipocalin-2 , LCN2, Small molecule inhibitor, Astrocyte, neuroinflammation

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P-696

The mRNA translation initiation factor eIF4G1 controls mitochondrial oxidative phosphorylation, axonal morphogenesis, and memory

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Translation is a fundamental mechanism that regulates cellular function. In particular, protein synthesis in neurons is essential for maintaining cognitive functions such as synaptic plasticity and memory formation. Eukaryotic initiation factor (eIF) 4F is a cytoplasmic complex composed of three subunits: a cap-binding protein (eIF4E), a DEAD-box RNA helicase (eIF4A), and a large scaffolding protein (eIF4G). Among these, eIF4G1 is particularly important because it coordinates the assembly of the translation initiation complex and facilitates ribosome recruitment, making it essential for proper animal development. However, its specific role in learning and memory remains poorly understood. In this study, we investigated the contribution of eIF4G1 to cognitive function by analyzing its role in translational regulation using the eIF4G1 haploinsufficient (eIF4G1-1D) mouse model. This model harbors a premature termination codon in the eIF4G1 gene caused by a CRISPR/Cas9-generated one-nucleotide deletion resulting in a frameshift. Ribosome profiling revealed that translation of mRNAs involved in the mitochondrial oxidative phosphorylation (OXPHOS) was decreased in the eIF4G1-1D brains, and consistently reduced in eIF4G1-silenced cells. This reduction in OXPHOS gene translation led to a decrease in cellular ATP levels. Axonal branching of primary hippocampal neurons derived from eIF4G1-1D embryos was significantly disrupted. Furthermore, eIF4G1-1D mice are impaired in hippocampus-dependent learning and memory. These results suggest that eIF4G1-mediated mRNA translation is crucial for optimal cognitive function, which is dependent on OXPHOS and neuronal morphogenesis. (SH Kim *et al.*, *Proc. Natl. Acad. Sci. U. S. A.*, 120(25):e2300008120, 2023)

Keywords : Translational control, eIF4G1, Mitochondrial oxidative phosphorylation, Learning and memory

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P-697

2′-Fucosyllactose Mitigates Cognitive Deficits in Alzheimer Models: Targeting Amyloid Pathology, Oxidative Stress, and Synaptic Plasticity

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Background: The development of new drugs for Alzheimer's disease (AD) remains a major challenge due to its multifactorial nature. 2′-Fucosyllactose (2′-FL), a human milk oligosaccharide, has shown neuroprotective properties. However, its effects on AD-related cognitive decline remain unclear. This study aimed to investigate the therapeutic potential of 2′-FL in an aging AD mouse model and explore its underlying mechanisms. Methods: 5xFAD transgenic mice were treated with 2′-FL and assessed for cognitive function using Morris water maze and Y-maze tests. Immunohistochemistry was used to evaluate amyloid-beta (Aβ) and phosphorylated tau (p-tau) in brain tissue. Blood samples were analyzed to determine circulating cytokine levels. BV2 microglial cells and primary hippocampal neurons (PHNs) were used in vitro to investigate the effects of 2′-FL on neuroinflammation, oxidative stress, and synaptic plasticity. Results: 2′-FL (300–1,200 mg/kg) improved cognitive performance in 5xFAD mice by shortening escape latency in the water maze and restoring alternation behavior in the Y-maze test. It significantly reduced Aβ plaque accumulation in the hippocampus and cortex but did not significantly affect tau hyperphosphorylation. 2′-FL also lowered plasma tumor necrosis factor (TNF)-α and interleukin (IL)-6 levels. In BV2 cells, it suppressed d-galactose-induced neuroinflammation by inhibiting TNF-α and IL-6 and nuclear factor-κB signaling. In PHNs, 2′-FL reduced oxidative stress, restored mitochondrial function, and limited DNA damage. It also promoted neurite outgrowth, synaptic vesicle recycling, and upregulated synaptic markers, including BDNF, PSD-95, and

SV2. Conclusion: 2′-FL improved cognitive deficits, reduced Aβ plaque deposition and pro-inflammatory cytokine levels in vivo, and mitigated oxidative stress and synaptic dysfunction in cellular models. These findings indicate that 2′-FL modulates multiple pathological features relevant to AD in preclinical models.

Keywords : 2'-Fucosyllactose, Alzheimer's disease, Cognitive function, Oxidative stress, Synaptic plasticity

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P-698

Mechanisms underlying the segregation and intracellular sorting of synaptic vesicles and ATG9 vesicles

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ATG9A, the only transmembrane protein among the core autophagy machinery, localizes to small vesicles and is abundantly expressed in the central nervous system. Recent studies have identified its presence at presynaptic sites in neurons. In *C. elegans* nerve terminals, ATG-9 vesicles undergo activity-dependent exo- and endocytosis, suggesting dynamic roles in synaptic autophagy. However, whether ATG9A associates with synaptic vesicles or resides in distinct vesicle pools remains unclear. Using an ectopic expression system, we previously demonstrated that ATG9A vesicles form condensates when co-expressed with synapsin, a neuron-specific protein critical for synaptic vesicle clustering. These condensates exhibit liquid-like properties, indicative of liquid–liquid phase separation (LLPS). Interestingly, when ATG9A and synaptophysin are co-expressed with synapsin, the two proteins form distinct microdomains within the same synapsin condensates. Correlative light and electron microscopy further reveal that ATG9A-positive vesicles are slightly larger than synaptophysin-positive ones, consistent with their distinct identities and differential sorting mechanisms within cells. To gain further insight into the mechanism and timing of this segregation, we examined the localization of ATG9A and synaptophysin during their trafficking through the endocytic pathway by employing a Rab5 mutant that induces the formation of enlarged endosomes. Notably, ATG9A and synaptophysin were found to intermix completely and did not segregate on these giant endosomes. This suggests that the separation of ATG9A from synaptophysin is not driven solely by the intrinsic properties of the proteins, but likely involves other, yet unidentified, cellular factors. These findings imply that ATG9A vesicle sorting is regulated by distinct co-factors or specialized cellular processes. Our study offers new insights into the mechanisms underlying ATG9A vesicle identity and their functional role in presynapses.

Keywords : ATG9A, Synaptic vesicle, Presynapse, LLPS, Phase separation

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P-699

Age-dependent brain change depending on ApoE genotype

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Background & Objective: Alzheimer`s disease (AD) is the most common neurodegenerative disease characterized by cognitive impairments and impaired daily activities. For AD development, the apolipoprotein E4 (apoE4) allele is recognized as a risk factor, while aging is the most significant environmental factor. In this study, we investigated the interaction of apoE and age on the cognitive behavioral changes using human apoE knock-in (KI) and knock-out (KO) mice. Methods: Body weights were measured biweekly from 5 to 9 months of age. Motor activity and anxiety were evaluated using open-field, rotarod, limb clasping, and elevated plus maze tests. Spatial and cognitive memory were assessed using the Y-maze and novel object recognition tests. Behavioral tests were performed at 3-, 6-, and 9 months of age. After behavioral tests, mice were sacrificed, and their brain and serums were collected. Total cholesterol, triglyceride, HDL, and LDL were measured using serum. Results: ApoE4 KI and apoE KO mice exhibited higher body weight compared to apoE3 KI mice in both sexes. This difference persisted across age. Serum analysis revealed ApoE4-dependent dysregulation in lipid metabolism, with ApoE KO showing the most severe changes. Behavioral tests demonstrated reduced motor activity and increased anxiety-like behavior in apoE4 KI and apoE KO mice compared to apoE3 KI mice. Y-maze showed no significant differences, whereas novel object recognition revealed impaired recognition memory in apoE4 KI and apoE KO mice compared to apoE3 KI mice at 6 months of age. Conclusions: This study demonstrated ApoE4 and ApoE deficiency-related changes in body weights and behavioral performance with age and sex, summarizing AD-related phenotypes. Investigation of cholesterol-related protein expression and axonal compartment changes in neuronal cells using immunohistochemistry or western blotting are undergoing.

Keywords : Alzheimer's disease, Apolipoprotein E, Cholesterol, Aging

P-700

Central amygdala pathway mediates GLP-1-induced aversion

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Recent studies of glucagon-like peptide 1 (GLP-1) medications have highlighted their effectiveness in treating obesity and type 2 diabetes. However, the emotional and neurobiological mechanisms underlying GLP-1 medication effects remain largely unexplored. Emerging clinical reports suggest potential emotional complications of GLP-1 medications, such as depression and anxiety, emphasizing the critical need to understand the brain circuits mediating these emotional side effects. Here, we elucidate the role of GLP-1 receptor

(Glp1R)-expressing neurons in the central amygdala (CeA) as key mediators of aversive emotional effects of GLP-1 medications. Using optogenetics, we revealed that CeAGlp1R neurons mediate the reduction in feeding behavior, consistent with the GLP-1 drug effect. Furthermore, CeAGlp1R neurons encode negative valence and elicit negative facial expressions in mice, leading to food rejection behavior. Notably, the inhibition of CeAGlp1R neurons attenuates the encoding of negative valence. Using calcium imaging, we showed that CeAGlp1R neurons are dynamically activated during feeding and aversive emotional states. Whole-brain mapping further disclosed that CeAGlp1R neurons densely project to the lateral habenula (LHb) and substantia nigra (SNR). These findings uncover the neural mechanisms underlying GLP-1-induced aversion, contributing to maximizing the efficacy of GLP-1 medications and improving the treatment of obesity.

Keywords : Central Amygdala, GLP-1, GLP-1 receptor neuron, aversion, obesity

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P-701

Confirmation of curcumin-mediated inhibition of tau aggregation using a tau-NanoLuc assay system

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Tau aggregation is one of the pathological hallmarks in Alzheimer's disease (AD). As the development of therapeutic drugs targeting tauopathy remains challenging, screening effective drug candidates is needed. To monitor the tau aggregation in living cells, we developed the tau aggregation reporter system using split NanoLuc (NLuc) luciferase, which is used to detect protein-protein interaction. In this study, we conducted NLuc based tau aggregation assay system and developed by using organic compounds including CCM. Curcumin (CCM), recognized as a potential inhibitor of tau aggregation, is considered a promising therapeutic candidate for AD. However, the precise mechanism underlying tau aggregation is not fully understood. To investigate the mechanism of tau aggregation using our system, we employed wild-type tau along with aggregation-prone mutants such as S396/404E, P301L and microtubule binding domain (MTBR). The tau aggregation was reduced in all models of NLuc-tau assay system by curcumin treatment. And we observed that the reduction in tau aggregation was not due to degradation, but rather to inhibition of aggregation. Although hexahydrocurcumin (HHC) has more efficiet in the pass of blood-brain barrier than CCM, HHC did not show the reduction of tau aggregation. Taken together, we confirmed that the NLuc-tau aggregation assay system is effective in investigating the level of tau aggregation in living cells. Further studies are ongoing to elucidate the mechanism of curcumin-mediated inhibition of tau aggregation.

Keywords : NanoLuc, Tau aggregation, Alzheimer's Disease, Curcumin, Tauopathy

P-702

Investigation of the microenvironmental influence on glycoprotein secretion in blood–brain barrier protection

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The blood-brain barrier (BBB) regulates substance exchange between the central nervous system (CNS) and peripheral circulation, maintaining brain homeostasis and protecting against external insults. The BBB is composed of brain endothelial cells, astrocytes, the basement membrane, and pericytes. Tight junction proteins and transporters are essential for barrier integrity and function. Proteins exist in glycosylated forms, contributing to their functional activity, structural stability, and regulation of cellular physiology. Abnormal glycosylation has been reported to cause BBB leakage and contribute to the pathogenesis of various neurological disorders, including Alzheimer's disease and multiple sclerosis. However, the link between glycoprotein regulation and energy metabolism remains unclear. Our previous studies showed tight junction instability in endothelial-specific Crif1 (CR6-interacting factor 1) knockout mouse (TEKCRIF KO mouse). In this study, we investigated whether glycosylation affects glycoprotein expression and BBB stability. Crif1 was knocked down in bEnd.3 brain endothelial cells, followed by mitochondrial inhibitor treatment. This induced ATP depletion, reduced glycoprotein expression, and impaired tight junctions and cell viability. In vivo, brain microvessels isolated from TEKCRIF KO mouse were stained with vascular markers and glycan-binding lectins, revealing decreased microvessel density and structural abnormalities. These results suggest that Crif1-mediated mitochondrial function is critical for maintaining glycosylation in endothelial cells and that its disruption impairs glycoprotein expression and compromises BBB microenvironment stability.

Keywords : Blood-brain barrier, Glycosylation, Mitochondria, Glycoprotein, Endothelial cells

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P-703

A distinct isoform of the mechanosensitive channel PIEZO mediates mating behavior in *C. elegans*

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PIEZO mechanosensitive ion channels, including PIEZO1 and PIEZO2, detect mechanical stimuli and transduce them into biological activities (Coste et al., 2010). Notably, PIEZO2 has at least 16 splicing isoforms with distinct tissue expression, but their functional differences remain

unclear. The *C. elegans* genome encodes a single PIEZO gene, *pezo-1*, with 14 isoforms (Bai X et al., 2020), whose functions and evolutionary conservation are also unknown. To investigate isoform-specific roles, we sorted the 14 isoforms into four groups based on mRNA length and analyzed their expression. The p1 promoter drives the longest *g* isoform, which regulates food swallowing in the pharyngeal valve (Park YJ et al., 2024) and shows structural and functional conservation with the mammalian PIEZO1. In contrast, the p3 promoter drives the shorter *pezo-1 i* isoform in tail neurons, including the 6th ray neurons of *C. elegans* males. Ray 6 neurons harbor sensory endings that are not exposed to the external environment (Sulston et al., 1980), suggesting a distinct role in mechanotransduction during mating. *i* isoform-specific, but not *g* isoform-specific, *pezo-1* mutant males showed defects in contact response, the initial mating step (Liu et al., 1995), which were rescued by expressing either *g* or *i* isoform under the p3 promoter. AlphaFold3 modeling revealed that the *i* isoform has a truncated blade domain compared to the g isoform. These data indicate that *pezo-1* isoforms mediate mechanosensation through distinct mechanisms in context-dependent ways. We are currently analyzing the electrophysiological properties of these *pezo-1* isoforms and testing functional conservation across species.

Keywords : PIEZO, mechanosensation, C. elegans, isoforms

P-704

CNMa Shapes the Behavioral and Survival Response Pattern to Macronutrient Environments

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Feeding behavior is shaped by dietary macronutrient composition, and animals often adjust their intake strategy to maintain nutritional balance. In *Drosophila*, the neuropeptide CNMa and its receptor are known to mediate protein hunger, but whether they contribute to adaptive feeding strategies and long-term survival across nutrient conditions remains unclear. Here, we examined the role of CNMa signaling in coordinating feeding responses and lifespan under defined protein-to-carbohydrate (P:C) dietary environments. In control flies, we observed a shift in nutrient leverage: flies prioritized protein intake under low-protein conditions but switched to carbohydrate leverage as dietary protein increased. However, CNMa ligand and receptor mutants failed to exhibit this flexibility and maintained a fixed intake pattern regardless of diet. Notably, under high-protein, low-carbohydrate conditions, CNMa mutants showed significantly reduced survival compared to controls. This suggests that the inability to adapt feeding behavior to nutrient context compromises physiological homeostasis and longevity. Our findings identify CNMa signaling as a critical mediator of nutrient-dependent behavioral flexibility, linking macronutrient sensing to both feeding decisions and survival outcomes in *Drosophila*.

Keywords : CNMa, Nutrient sensing, Lifespan, Feeding behavior, Macronutrient composition

P-705

Sigma-1 receptors increase spinal peroxynitrite production after spinal cord injury in mice

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The sigma-1 receptor is recognized as a ligand-regulated chaperone protein involved in various physiological and pathological processes. We have previously demonstrated that the expression of sigma-1 receptor is increased in the lumbar spinal cord dorsal horn of spinal cord injury (SCI) mice, contributing to the development of below-level mechanical allodynia following thoracic spinal cord injury. Here, we aimed to demonstrate that sigma-1 receptor could regulate the production of peroxynitrite, which may ultimately contribute to the development of below-level mechanical allodynia following spinal cord injury. A thoracic spinal cord hemisection was performed and mechanical allodynia was assessed in the hind paws using a von Frey filament. Blockade of sigma-1 receptors with BD1047 reduced the production of peroxynitrite and the expression of nitric oxide synthase in the lumbar spinal cord dorsal horn of SCI mice. Intrathecal administration of the peroxynitrite scavenger, FeTPPS suppressed the SCI-induced below-level mechanical allodynia. These results suggest that the activation of sigma-1 receptor increases the production of peroxynitrite resulting in the development of below-level mechanical allodynia following SCI in mice.

Keywords : sigma-1 receptor, peroxynitrite, spinal cord injury, below-level mechanical allodynia, spinal cord

P-706

Structural and functional investigations on the voltage-dependent mechanism of a hyperpolarization-activated Cl^- channel, CLC-2<

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The CLC family proteins are essential for maintaining Cl^- homeostasis across biological membranes. Four CLCs (CLC-1, -2, -K1, and -K2) are classified into Cl^- channels, while others (CLC-3 to -7) are Cl^-/H^+ antiporters. Previous studies have shown that CLC channels respond differently to the transmembrane voltages: CLC-1 is activated by depolarization, CLC-2 is activated by hyperpolarization, CLC-K channels are voltage-insensitive. A conserved glutamate residue (Glu_{ex} or Glu_{gate}) has been suggested to confer the voltage-dependency of both channels. Recently, Cryo-EM structures of CLC-2 (hCLC-2) were solved in the absence or presence of antagonist, AK-42. However, the mechanism by which this glutamate residue senses transmembrane voltage in opposite directions remains largely unknown. To investigate the voltage-dependent mechanism of CLC channels, we examined the voltage-dependent activation of wild-type and mutants of CLC-2 by electrophysiological means. We discovered that mutations of the pore-lining residues significantly altered voltage- and pH-dependent gating with different degrees. Also, we determined the cryo-EM structure of

wild-type mCLC-2 at ~2.9 Å resolution in the detergent-solubilized condition. To better understand the voltage dependent mechanism of CLC-2, we are optimizing Cryo-EM conditions for liposome-reconstituted CLC-2 channels in the absence or presence of voltage stimuli.

Keywords : Cryo-EM, Electrophysiology, Liposome

Neuroengineering P-707~P-723

P-707

Engineering a light-activated dopamine receptor for precise control of GPCR signaling

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Dopaminergic neurotransmission plays a crucial role in motor function through the coordination of dopamine receptor (DRD) subtypes, thus the functional imbalance of these receptors can lead to Parkinson's disease. However, due to the complexity of dopaminergic circuits in the brain, it is limited to investigating the individual functions of each DRD subtype in specific brain regions. Here, we developed a light-responsive chimeric DRD2, OptoDRD2, which can selectively activate DRD2-like signaling pathways with spatiotemporal resolution. OptoDRD2 was designed to include the light-sensitive component of rhodopsin and the intracellular signaling domain of DRD2. We confirmed OptoDRD2 triggered diverse DRD2-like signaling pathways upon light illumination. To explore unknown roles of DRD2 in basal ganglia circuitry, OptoDRD2 was expressed in excitatory neurons in lateral globus pallidus (LGP). Optogenetic stimulation of OptoDRD2 in the LGP region affected a wide range of locomotion-related parameters, such as increased frequency of movement and decreased immobility time, resulting in the facilitation of motor function of living mice. Therefore, our findings indicate a potential novel role for DRD2 in the excitatory neurons of the LGP region, suggesting that OptoDRD2 can be a valuable tool enabling the investigation of unknown roles of DRD2 at specific cell types or brain regions. Based on our previous study, we are currently optimizing OptoB2AR through structure-based refinement to improve its signaling properties. Furthermore, we are now applying this strategy to other GPCRs—including DRD1—to increase the diversity of optogenetically controllable receptors for studying subtype-specific signaling across distinct brain regions and cell types.

Keywords : GPCR, Optogenetics, Dopamine, DRD2, β2AR

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P-708

Discovering GPCR Heterodimerization: functional dynamics and therapeutic Implications

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G protein-coupled receptors (GPCRs) are membrane proteins that regulate diverse physiological and pathological processes. Conventional GPCR research focused on monomers, recent studies highlight the importance of GPCR heteromerization in modulating receptor function and distinct signaling pathways. GPCR heteromers are distinct complexes exhibiting altered ligand binding, specific signaling, and changes in receptor trafficking, which differ in monomeric GPCRs. Dysregulation of these heteromers has been implicated in several diseases, including neurological and psychiatric disorders, making them a promising therapeutic target. For example, heteromerization between the Serotonin 2A receptor (5-HT2A) and Dopamine D2 receptor (D2) is associated with psychiatric conditions such as hallucinations and schizophrenia. While co-immunoprecipitation has demonstrated physical interactions between 5-HT2A and D2, assessing individual GPCR activity within these heteromers remains challenging due to the absence of appropriate GPCR sensors. To overcome these limitations, we applied circular permutated fluorescent protein (cp-FP)-based GPCR sensors, PsychLight2 and G-DRD2, which detect structural changes in GPCRs upon activation. Using these sensors, we monitored the real-time activities of 5-HT2A and D2 receptor in heteromer. Our findings revealed that the 5-HT2A receptor suppresses D2 activity, and this suppression is influenced by the activation of 5-HT2A receptor induced by its ligand. Notably, these results demonstrate that GPCR heteromerization alters the functional properties of individual GPCRs compared to their monomeric counterparts. Our approach suggests the utility of cp-FP-based sensors in elucidating GPCR heteromer functions and provides insights into how GPCR heteromerization contributes to receptor-specific regulation and activity. These findings highlight the potential of GPCR heteromers as novel therapeutic targets.

Keywords : GPCR, GPCR heteromer, Cp-based sensor, Serotonin, Dopamine

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P-709

Timed electrical stimulation training to change tingling to a natural-like pressure

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Electrical stimulation has emerged as a groundbreaking technology, offering effective sensory feedback in a wide range of therapeutic and

practical applications. In this study, we propose a novel approach to train the nervous system to adapt to artificially evoked afferent volleys, aiming to remap the perception of tingling sensations into natural sensations like pressure. Participants (n = 7) completed baseline tests, training, and post-training assessments on three consecutive days. Two gel electrodes were positioned on the dorsal extensor surface distal to the right olecranon, directly over the radial nerve (posterior interosseous branch). On Day 1, the 80 Hz stimulus current was titrated from 0 mA up to perception and discomfort thresholds; their midpoint was used as stimulation intensity for all trials. The training session then consisted of three 10-min blocks of the T-Rex game, separated by 1-min pauses; participants played with the right elbow where the stimulation was applied in sync with the press. Two distinct adaptation patterns emerged. Group A (n = 4) started with a mixed yet pressure-dominant percept (mean ± SEM = 3.17 ± 0.17) and, after training, climbed to 3.30 ± 0.16; their right-to-left elbow-force ratio fell from 0.72 ± 0.003 to 0.49 ± 0.004. Group B (n = 3) remained tingling-dominant (2.36 ± 0.16 → 2.47 ± 0.16) while their force ratio rose from 1.16 ± 0.008 to 1.60 ± 0.019. These preliminary findings suggest that pairing non-invasive 80 Hz stimulation with voluntary elbow presses can, in half of the users, re-map an artificially evoked tingling into a pressure-like sensation. Overall, the pressure-dominant shift observed in 4/7 of subjects supports our neuroplasticity-based strategy as a practical, non-invasive alternative for remapping artificial tingling to natural pressure.

Keywords : non-invasive electrical stimulation; neuroplasticity, sensory remapping; pressure perception, radial nerve

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P-710

Neural recording device capable of neurotransmitter monitoring according to deep brain stimulation in mouse brain model

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Deep brain stimulation (DBS) has emerged as an effective method for treating neurological disorders, but monitoring of neurotransmitter interactions during stimulation remains challenging. Here, we developed an advanced neural recording device capable of real-time neurotransmitter monitoring during DBS in a mouse brain model. The device integrates microelectrode-arrays (MEA) with functionalized electrodes to simultaneously record electrophysiological signals and electrochemically detect neurotransmitters, specifically dopamine and glutamate, in the target brain region. The device fabrication involves flexible electronics, incorporating SU-8 and parylene C layers, optimized for mechanical stability and biocompatibility. The device consist of molybdenum based interconnects and connection pads fabricated through pholithographic lift-off processes, ensuring robust adhesion and enhanced sensitivity. Microelectrode-array surfaces were modified with molybdenum compounds, such as molybdenum oxynitride, to improve electrochemical performance for neurotransmitter detection. In vivo validation was conducted in the striatum of mice undergoing DBS targeting the subthalamic nucleus (STN). The electrophysiological signals and neurotransmitter concentrations were continuously recorded the whole stimulation process. Results demonstrated significant, temporally correlated increases in dopamine and glutamate release during DBS, reflecting neural modulation by stimulation parameters. Additionally, electrophysiological activity showed concurrent alterations indicative of network modulation. Our research provides new insights into neurotransmitter interactions related with DBS, highlighting the interplay between neural stimulation and neurochemical signaling. This results not only advances basic science but also holds potential for clinical pathology contributing to therapeutic optimizations for neurological conditions such as Parkinson's disease and brain tumor.

Keywords : Deep brain stimulation, Neurotransmitter, Neural recording, Microelectrode-arrays, Flexible electronics

P-711

A miniaturized ultrasound stimulation system for wireless neuromodulation in freely moving mice

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Transcranial focused ultrasound stimulation is emerging as a promising neuromodulation technique, offering advantages such as noninvasiveness, precise spatial targeting, and the ability to reach deep brain regions. However, conventional ultrasound setups suffer from its bulkiness, restricting behavioral analysis especially in small, freely moving animals. While some efforts have been made to downsize the driving components for ultrasound transducers, miniaturized systems for freely moving mice remain scarce. In this work, we introduce a compact, wireless ultrasound stimulation device for behavioral modulation in freely moving mice. The system integrates an optimized class-E amplifier for efficient, high-power ultrasound delivery on a lightweight, flexible PCB. Additionally, a custom 3D-printed acoustic lens enables targeted stimulation of midline thalamic nuclei, which are implicated in locomotion, anxiety, and fear processing. Behavioral experiments reveal that ultrasound stimulation acutely reduces locomotion and induces anxiety-like behaviors. This miniaturized ultrasound stimulation system offers a practical, noninvasive solution for studying neuromodulation in freely behaving animals.

Keywords : Ultrasound stimulation, Wireless circuit, Locomotion, Freely moving, Deep brain stimulation

P-712

Tactile encoding in S1 and exploration of information expansion via patterned ICMS in monkeys

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Accurate decoding of tactile information from neural signals is critical for advancing sensory neuroprosthetics. This study investigated whether

neural activity recorded from the primary somatosensory cortex (S1) of a monkey could reliably distinguish between different tactile stimuli and related behavioral outcomes. The monkey was trained to perform a tactile discrimination task, identifying two vibratory stimuli (10 Hz vs. 5 Hz) applied to the palm and selecting the corresponding target (left or right) on a screen. Neural activity was recorded via chronically implanted Utah arrays in S1 during task performance. We classified each trial into one of four categories defined by stimulus type and behavioral correctness (correct vs. incorrect). The decoding analysis showed robust classification performance significantly above chance, particularly for stimulus type (F1-score > 95%). In contrast, decoding of behavioral correctness alone (correct vs. incorrect) remained near chance, suggesting that S1 activity predominantly reflects sensory input rather than decision accuracy. This indicates that incorrect behavioral responses likely result from downstream processing or decision errors, not from degraded sensory encoding in S1. To explore sensory feedback augmentation, we conducted sessions using patterned intracortical microstimulation (ICMS). The monkey discriminated between simple ICMS patterns (100 Hz, 100 μA vs. 40 μA) and temporally structured sequences (A–A vs. B–B with 450 ms pulses and a 100 ms gap), achieving over 80% accuracy. These results highlight the feasibility of using temporal ICMS patterns to encode richer tactile information, including potential combinations such as A–B or B–A. Overall, our findings demonstrate reliable tactile stimulus encoding in S1 and show that patterned ICMS can expand the bandwidth of artificial sensory feedback, supporting its potential for bidirectional neuroprosthetic applications.

Keywords : ICMS, Rhesus Macaque, Somatosensory Cortex, Neuroprosthetic, Tactile Stimulation

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P-713

Performance and safety evaluation of ultrasound device for blood-brain barrier opening in non-human primates

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The study aimed to evaluate the performance and safety of a focused ultrasound (FUS) device for blood-brain barrier opening (BBBO) in a non-human primate (NHP) model and to analyze the correlation between acoustic cavitation indicators and BBBO results to assess the suitability of real-time cavitation as a predictive indicator of BBBO. Additionally, the goal was to develop technology enabling safe and efficient BBBO using a real-time closed-loop feedback algorithm based on acoustic cavitation. A female cynomolgus monkey (4.8 kg) underwent four independent BBBO sessions using the NMS-01 FUS system (Neumous Inc., Republic of Korea), which integrates image registration for targeting, real-time acoustic cavitation monitoring, and a closed-loop acoustic power control algorithm. Eleven brain regions were sonicated with various ultrasound parameters. During each procedure, real-time cavitation signals were recorded to analyze the correlation between cavitation indicators and BBBO. After sonication, T1-weighted MR images confirmed the location, volume, and contrast enhancement of BBBO, while T2-weighted images assessed edema or hemorrhage in the targeted areas. All targeted areas showed successful recording of cavitation signals and BBBO without significant adverse effects. The linear relationship and correlation coefficient between cavitation indicators and BBBO volume were y = 1.16x + 36.69, (R = 0.94), and for contrast enhancement intensity, y = 1.28x + 67.49 (R = 0.93). The closed-loop algorithm maintained stable ultrasound output upon reaching the preset threshold. These results demonstrate that the NMS-01 FUS system reliably achieves safe BBBO by incorporating real-time cavitation monitoring and closed-loop control, and real-time acoustic cavitation can serve as a predictive indicator of BBBO. Furthermore, the closed-loop algorithm enables safe and personalized BBBO by automatically adjusting ultrasound output parameters.

Keywords : Focused Ultrasound, Blood-Brain Barrier, Non-Human Primates, Evaluation

P-714

Temperature-dependent modulation of visual behaviors in *Drosophila Melanogaster*

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In all organisms, maintaining an optimum body temperature is vital for their survival. However, small poikilothermic organisms, such as *Drosophila melanogaster*, lack internal temperature regulation and are therefore vulnerable to temperature fluctuations in their surrounding environments. Since extreme temperatures remarkably shorten their life span, they display a preference to certain temperature ranges. When flying, *Drosophila* perform a combination of straight-line flight, and turns. By prolonging periods of straight-line flight in regions of unfavorable temperature, they can more quickly escape. To help maintain straight-line flight in turbulent conditions, flies exhibit a reflexive visual-motor behavior called the optomotor stability reflex. This triggers corrective micro adjustments of flight direction, called saccades, in response to whole field optic flow. In hot conditions, this optomotor stability reflex is reinforced, suggesting it may be crucial for maintaining straight-line flight in adverse temperature conditions. In this study, we demonstrate how *Drosophila*'s temperature sensing modulates visuomotor responses through behavior experiments. Furthermore, we work to identify candidate neural circuits that intersect both the temperature sensing and visual systems in flies, using connectome analysis, and genetic silencing experiments. This study provides insight into how interactions between multiple senses drive behaviors that maximize survival. These insights can contribute to the development of algorithms for multi-sensory robotic systems through mathematical modeling of behavioral patterns.

Keywords : Drosophila melanogaster, Temperature-dependent modulation, Optomotor stability reflex

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P-715

Temporal modulation of early-stage organoid differentiation using precision ultrasound stimulation

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Organoids are rapidly emerging as a promising in vitro platform with the potential to replace in vivo animal experiments. Due to the inherent structural and functional complexity of organoids, controlling the precise timing of biosignaling cues has become critical for cellular development and therapeutic applications. Recently, direct stimulation modalities, such as electrical, optogenetic, and ultrasound stimulation, have been developed to overcome the limitations of conventional biochemical approaches. Ultrasound is particularly attractive due to its practically infinite range of waveform parameters that are modulated by the pulse repetition frequency (PRF) and acoustic intensity (I). However, there is still a lack of precision stimulation platforms and comprehensive biomarker assays for selective control of organoid development. Here, we propose a modular piezoelectric-based ultrasound stimulation platform integrated with conventional well-plates for PRF and intensity-dependent neuromodulation of midbrain organoids (mBOs). We demonstrate that specific ultrasound parameters enable safe modulation of the differentiation timing and maturation of mBOs. This work demonstrates the potential of focused ultrasound as a promising neurotool for precise control of organoid growth.

Keywords : Midbrain organoid, Ultrasound stimulation, Preclinical platform, Differentiation, Maturation

P-716

Patternable luminescent patch for selective, wide-field cortical stimulation

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Wide-field cortical stimulation has emerged as a promising, minimally invasive technique to modulate large-scale brain networks. However, the underlying circuit-level mechanisms and behavioral outcomes remain insufficiently delineated. To dissect these effects at a mechanistic level, optogenetic stimulation provides a suitable approach due to its cell-type specificity. Conventional approaches, including optical fiber bundles and LED-based systems, are limited by structural complexity and spatial inflexibility in the context of wide-field cortical stimulation. To overcome these constraints, we present a patternable luminescent patch (PLP) composed of microscale high-luminescence particles uniformly embedded within a flexible poly(methyl methacrylate) (PMMA) matrix. This patch offers diverse geometries and uniform conformity to the cortical surface, enabling wireless, region-specific optogenetic stimulation without restricting subject mobility. This system propose a novel platform to elucidate the biological and behavioral impact of wide-field cortical activation across brain-wide networks.

Keywords : Cortical stimulation, Optogenetics, Luminescent particles, Wireless neural stimulation, Behavioral neuroscience tool

P-717

A single, versatile algorithm for segmenting cells immunolabeled with diverse cell-type marker proteins from whole-brain images

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The brain is composed of heterogeneous types of cells. Whole-brain labeling using marker proteins (e.g., PV+, SOM+, GFAP+) combined with automatic image analysis enables unbiased assessment of cell type distributions throughout the brains in health and disease. However, automated identification of marker-positive cells remains challenging due to variability in labeling patterns, cell densities, morphologies, and subcellular localization of diverse marker proteins. Consequently, existing approaches often rely on AI models tailored to specific markers, which limits their scalability and general applicability. Here we present a versatile algorithm, termed ANYCELL, that can segment cells positive with diverse cell type markers from whole brain images without the need of marker-specific model customization. This pipeline supports high-throughput, reproducible, and standardized brain-wide cellular analysis, thereby broadening the scope of quantitative neuroanatomical studies.

Keywords : Whole brain imaging , 3D image analysis, Cell type

P-718

Combined 3D-CNN and 4D-Swin transformer on resting-state fMRI Using Multi-stage classification for cognitive dysfunction

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Withdrawn

[Introduction] Early detection of chronic neurodegenerative disorders, such as Alzheimer's Disease (AD), is crucial. Detecting early or subtle alterations requires resting-state fMRI (rs-fMRI) to observe temporal variability in brain regions of interest (ROIs). Existing approaches rely heavily on statistical time-series analyses or deep-learning frameworks based on image data, but they do not fully leverage high-dimensional information and offer limited explainability for clinical adoption. Therefore, we focus on maximizing the utility of 4D data while emphasizing clinical interpretability. [Methods] We introduce M4F3D-HDA (Multi-task 4D fMRI 3D-timeseries Hybrid Deep Architecture),

a dual-deep-branch framework designed to enhance clinical interpretability in resting-state fMRI analysis. The architecture captures spatiotemporal patterns by integrating voxel-wise representation from a 4D Swin Transformer and correlation-aware time-series features from a 3D Convolutional Neural Network. This design enables simultaneous classification of AD stages and regression of connectivity matrices. Standard rs-fMRI preprocessing is performed using FSL, followed by voxel-wise and temporal sub-windowing. We evaluate the performance of M4F3D-HDA on the Open Access Series of Imaging Studies (OASIS), Alzheimer's Disease Neuroimaging Initiative (ADNI), and UK Biobank (UKB) datasets. [Results] Our experiments demonstrate that M4F3D-HDA enables accurate multi-stage classification and effectively predicts functional connectivity patterns. These outcomes highlight the model's ability to deliver clinically interpretable results with strong performance across datasets. [Conclusion] M4F3D-HDA offers a novel perspective on explainable AI, addressing deep learning's inherent black-box challenge. By capturing spatiotemporal variability and predicting connectivity patterns associated with meaningful group differences, our model represents a promising step toward interpretable neuroimaging biomarkers.

Keywords : Multi-task Learning, Deep Learning, Resting-state fMRI, Cognitive Dysfunction, Explainable AI

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P-719

Improving B1 homogeneity in 7T MRI using high-dielectric pad: effects on T1 imaging, brain segmentation, and diffusion tensor metrics

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Ultra-high field magnetic resonance imaging (MRI) systems operating at 7 Tesla offer enhanced spatial resolution and signal-to-noise ratio (SNR), but are challenged by B1 field inhomogeneity. This study investigates the efficacy of a custom-designed high-dielectric pad ($\varepsilon r \approx 233$) in improving image quality and quantitative reliability in T1-weighted imaging, brain segmentation, and diffusion tensor imaging (DTI), with specific focus on the cerebellum, a region vulnerable to RF inhomogeneity. Four healthy volunteers were scanned using a 7T MRI system with and without the high-dielectric pad. T1-weighted images were acquired via MP2RAGE, and DTI data were collected with high b-value multiband EPI. Quantitative analyses included SNR measurements, FreeSurfer-based cerebellar segmentation, and DSI-Studio-based connectometry focusing on quantitative anisotropy (QA), mean diffusivity (MD), and fractional anisotropy (FA). The high-dielectric pad significantly enhanced tissue contrast and signal intensity in T1-weighted images without introducing distortions. The average SNR improved by 24.7% in T1-weighted and 50.2% in diffusion images. While cerebellar volume segmentation showed minimal volumetric changes, QA values in DTI increased dramatically—from an average of 430,100 without the pad to 1,473,803 with the pad. Tractography demonstrated enhanced fiber clarity, especially in cerebellar pathways. These findings suggest that high-dielectric pads offer a simple and effective passive shimming solution for improving B1 homogeneity in ultra-high field MRI. They particularly benefit diffusion imaging and could support more accurate neuroanatomical quantification, especially in lower brain regions. This work lays groundwork for further research into dielectric material optimization and its integration into clinical neuroimaging protocols.

Keywords : dielectric pad, Ultra-high field MRI , B1 field homogeneity, Diffusion tensor imaging , Brain segmentation

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P-720

3D bioprinted GelMA/TMP scaffold incorporating neural stem cell-derived EVs and NPCs for enhanced spinal cord injury repair

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Spinal cord injury (SCI) leads to irreversible neurological deficits due to the central nervous system's limited regenerative capacity and the absence of effective therapeutic strategies that promote true tissue repair. While various approaches such as biomaterial scaffolds, neural progenitor cells (NPCs), and extracellular vesicles (EVs) have demonstrated individual therapeutic benefits, each alone remains insufficient to fully address the complex and multifaceted pathology of SCI. Therefore, combinatorial strategies that integrate structural, cellular, and biochemical elements are needed to achieve more effective and comprehensive regeneration. Here, we developed a multifunctional 3D bioprinted hydrogel scaffold integrating neural stem cell-derived EVs (NSC-EVs) and NPCs within a gelatin methacryloyl (GelMA) and tetramethylpyrazine (TMP) matrix. NSC-EVs exhibited superior pro-angiogenic, neurotrophic, and immunomodulatory properties compared to adipose-derived EVs, enhancing endothelial tube formation and neuronal differentiation in vitro. The GelMA/TMP/NSC-EV/NPC scaffold further promoted NPC viability, neurogenesis, angiogenesis, and anti-inflammatory responses. In a rat complete transection SCI model, this scaffold preserved spinal cord tissue, restored vascular integrity and the blood–spinal cord barrier, and attenuated neuroinflammation and glial scarring. It also facilitated axonal regeneration and remyelination, leading to significant improvements in locomotor recovery by 28 days post-injury. These findings highlight the therapeutic potential of a multifunctional 3D bioprinted scaffold that delivers coordinated structural, cellular, and biochemical cues to overcome key regenerative barriers in SCI, offering a promising strategy for clinical translation.

Keywords : Spinal cord injury, Tissue engineering, 3D bioprinting, Neural progenitor cells, Extracellular vesicles

P-721

Effects of Chemogenetic Virus Injection and Clozapine Administration in Spinal Cord Injury

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Purpose: This study aimed to investigate the effects of chemogenetic modulation on nerve regeneration and functional recovery after acute spinal cord injury (SCI) using a rat model. A chemogenetic AAV virus (AAV5-hSyn-hM3Dq-eYFP) was injected at the injury site, followed by intraperitoneal administration of clozapine. Materials & Methods: Acute SCI was induced in 8-week-old male Sprague-Dawley rats by applying compression to the T9 vertebra for 30 seconds. Rats were divided into five groups: Sham, SCI, aSCI_Ctrl, aSCI_CS, and cSCI_CS, with virus and clozapine administered at different time points depending on the group. Weekly behavioral assessments were performed using the BBB locomotion test and ladder rung walking test. Immunohistochemistry (IHC) was conducted in four sets to evaluate neural regeneration. Western blotting was performed to assess the expression of pPLC-β, pPKC-γ, pAKT, Neurocan, PTP-Z, mGluR5, and BDNF. Inflammatory and immune responses were analyzed via qRT-PCR targeting iNOS, TNF-α, CD206, and IL-10. Statistical analyses were conducted using Prism 7.0. Results: Among the five groups, the aSCI_CS group showed the most significant improvements. Quantitative behavioral assessments demonstrated that the group receiving the virus one week after SCI and clozapine one week post-virus showed the highest functional recovery. Western blot results revealed the strongest expression of regeneration and calcium signaling markers in this group, while IHC showed the highest levels of neural marker expression. qRT-PCR results indicated elevated levels of M2 and anti-inflammatory markers in the aSCI_CS group. Conclusion: The aSCI_CS group demonstrated the greatest therapeutic effect in both behavioral and molecular analyses. These results suggest that sequential treatment with chemogenetic virus and clozapine significantly promotes nerve regeneration and motor function recovery following spinal cord injury.

Keywords : Chemogenetic Virus, Spinal cord Injury, AAV5-hSyn-hM3Dq-eYFP, Clozapine, DREADDs

P-722

Real-Time Induction of K-Complexes by NonInvasive DBS

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Although noninvasive deep brain stimulation (niDBS) has recently garnered significant interest, continuous induction of K-complexes using niDBS remains unreported in the literature. K-complex is a feature detected in sleep EEG and is a neural hallmark related to CSF clearance. Here, we introduced a new niDBS technique for inducing K-complexes continuously. Our niDBS technique involves impedance-matched microcurrent Radio Frequency Pulse (RFP) modulation to patch anodes. To observe the induced K-complexes, EEGs were measured using a 6-channel wireless EEG device with dry electrodes during microcurrent RFP modulation. We found that our microcurrent RFP modulation induced the canonical negative Kcomplex (n1–p1–n2) —a negative deflection less than 100 μV, followed by a slow positive complex and a terminal negative peak. Furthermore, the polarityreversed counterpart of the negative K-complex, the positive Kcomplex (p1–n1–p2) —a positive deflection over than 100 μV, was also observed. Especially, both the negative and the positive K-complexes were generated consistently. We artificially induced the negative and the positive Kcomplexes during the wake state. These findings suggest that our niDBS technique has the potential to precisely modulate CSF dynamics. Our niDBS technique induced sequential and repeated K-complexes, both negative and positive phases, during the wake state. These induced K-complexes suggest that our novel niDBS technique is presumably associated with sensory receptors, the RAS, CSF dynamics (production, circulation, and clearance mechanisms), the glymphatic system, and/or MLVs. This study highlights the potential for further investigations to validate the negative and the positive Kcomplexes induction mechanism via modulation of neuronal membrane potentials (tonic/phasic burst) that would mediate EPSPs (AMPA/NMDA) and IPSPs(GABA), voltagegated ion channels, and voltage-gated calcium channels.

Keywords : K-Complex, Non-Invasive Deep Brain Stimulation, RAS, CSF Dynamis, MLVs

P-723

Effects of long-term high-fat diet intake on inflammatory mediators and dopamine-related genes in the striatum

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Background: Previous studies have reported that prolonged intake of a high-fat diet leads to reduced physical activity, decreased dopamine D2 receptor binding in the brain, and increased inflammatory responses, ultimately impairing cognitive function in mice. However, the relationship between reduced physical activity and striatal inflammation or dopamine D2 receptor expression in obese mice remains unclear. Objective: This study aimed to investigate the impact of a high-fat diet on exercise motivation, focusing on the role of inflammatory cytokines and dopamine-related gene expression in the brain. Methods: Six-week-old male mice were randomly assigned to four groups: standard diet (ND), high-fat diet (HFD), ND + exercise, and HFD + exercise. The HFD group was fed Rodent TestDiet® 58Y1. Voluntary physical activity used as an indicator of exercise motivation, was measured daily for 12 weeks. After the experimental period, mice were fasted for 16 hours, followed by a glucose tolerance test. The striatum was then dissected for molecular analyses. Results: The HFD group exhibited decreased expression of the dopamine D2 receptor gene and increased expression of inflammatory cytokines in the striatum. These effects showed a tendency to be ameliorated by exercise intervention. Conclusion: Our findings suggest that reduced exercise motivation induced by a high-fat diet may be associated with increased midbrain inflammation and decreased expression of dopamine D2 receptor genes. Further studies are warranted to elucidate the relationship between inflammatory mediators and dopamine receptor gene expression in the midbrain.

Keywords : High fat diet, Exercise, Inflammatory, Dopamine

Others P-724~P-751

P-724

Screening of novel TMEM16C activators

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Lipid scrambling is a rapid process that dissipates the asymmetrical distribution of phospholipids in the plasma membrane. It is involved in various physiological functions such as blood coagulation and apoptosis. Many TMEM16 members are recognized as Ca^{2+} -activated phospholipid scramblases, which transport phospholipids between the two leaflets of the plasma membrane nonspecifically and bidirectionally; among these, TMEM16C is abundant in the brain, especially in neuronal cells. In previous study, we investigated the scrambling activity of three human TMEM16C isoforms. Among three isoforms, membrane localized TMEM16C isoforms1 and 3 could transport phosphatidylserine to the outer leaflet. After generating human TMEM16C isoform1-overexpressing cells, we screened new modulators for TMEM16C protein by using high content screening. We are currently testing whether these effects were observed only in TMEM16C protein or other TMEM16 family members, such as TMEM16A and TMEM16F.

Keywords : Lipid transport, Scramblase, TMEM16, Modulator, Screening

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P-725

Standardizing *C. elegans* as a NAMs platform to advance alternative neurotoxicity testing

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Increasing restrictions on animal testing have heightened the demand for scientifically validated new approach methodologies (NAMs) for neurotoxicity testing. Despite global efforts to advance alternative approaches, standardized and widely accepted protocols remain limited. This study aims to optimize *in vivo* NAMs for neurotoxicity testing by employing *Caenorhabditis elegans* (*C. elegans*) as a model organism to potentially replace conventional vertebrate-based models. We refined key experimental variables to enhance the model's applicability as an alternative methodology, using well-characterized neurotoxicants, and subsequently validated the protocol with additional test compounds. Our study encompasses six domains for neurotoxicity evaluation: (1) Oxidative stress analysis, through quantification of reactive oxygen species levels and antioxidant enzyme activities; (2) Neuroanatomical assessment, via detection of structural alterations via fluorescence imaging; (3) Neurophysiological evaluation, through analysis of neuronal activity and neurotransmitter signaling through molecular profiling and fluorescence imaging; (4) Cellular organelle dysfunction assessment, by analyzing mitochondrial, endoplasmic reticulum, and lysosomal function in relation to neuronal impairment; (5) Locomotion assessment, by measuring movement velocity, travel distance, and paralysis incidence using automated tracking systems; and (6) Behavioral analysis, by evaluating sensory response and memory. By integrating these multifaceted neurotoxicity indicators, which reflect both developmental and degenerative neurological processes, this study aims to contribute to the establishment of *C. elegans* as a scientifically validated and practically applicable NAMs platform for neurotoxicity testing.

Keywords : Alternative methodology, New approach methodologies, NAMs, Neurotoxicity

Acknowledgements : This study was supported by the A-STAAR (Advancing Standardized Toxicity Testing through Alternative Animal Model Resources) project from Ministry of Food and Drug Safety (RS-2024–00331685).

P-726

Establishment of Taste Bud Organoids from Anterior Lingual Mucosa

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Excessive salt intake is a major risk factor for various modern diseases. Salt perception is regulated by taste cells within taste buds, particularly those responsive to salty stimuli located in the fungiform papillae (FuP) of the anterior tongue. However, their limited number has made molecular and cellular analysis difficult. While many in vivo studies on taste have been conducted, suitable in vitro models remain scarce. Although organoid technology has been applied to mimic taste buds, all existing taste bud organoids have been derived from circumvallate papillae (CVP) in the posterior tongue. No model has been reported that recapitulates FuP-specific taste cells. Here, we successfully established culture conditions to generate anterior tongue-derived taste bud organoids (aTBOs) containing all major taste cell types. This represents the first in vitro model that mimics FuP taste cell biology. Our platform provides a valuable tool to investigate the mechanisms of salty taste perception and may contribute to developing strategies for regulating salt intake.

Keywords : Taste, Taste bud, Taste bud organoid, Salty taste

P-727

Evaluation of QT/QTc interval changes and proarrhythmic risk of five drugs of abuse using *in vitro* and *in vivo* approaches

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Some drugs with abuse potential have been linked to cardiovascular effects, but their direct impact on cardiac electrophysiology is not fully understood. In this study, we evaluated the integrated ion channel effects of five abuse-prone drugs using human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) and a multi-electrode array (MEA). Field potential duration corrected for beat rate (FPDc), beat period, and amplitude were recorded following acute drug exposure. Tested compounds included zolpidem, diazepam, diethylpropion, mazindol, and fentanyl. To simulate overdose, drugs were applied across concentrations from 0.1 to 100 times the reported human maximum plasma concen-

tration (C_{max}). Diazepam induced concentration-dependent reductions in FPDc (2.5%, 1.0%, −25.5%), beat period (−1.0%, −11.6%, −21.4%), and amplitude (−1.9%, −1.9%, −8.2%) at 0.111, 1.113, and 11.133 μM, respectively. At 111.3 μM (C_{max} ×100), beating was completely arrested. Fentanyl (0.237 μM) and zolpidem (14.054 μM) significantly increased FPDc. Notably, sildenafil, fentanyl, and zolpidem prolonged FPDc at 100× C_{max}, while diazepam decreased FPDc at 10× C_{max}. Diazepam also reduced beat period and amplitude from C_{max}, with arrest at 100× C_{max}. To complement in vitro data, *in vivo* ECG recordings were conducted in male Sprague-Dawley rats. Diazepam at 10× C_{max} showed a trend toward QT shortening, with statistically significant reduction. Fentanyl induced acute QT shortening after intravenous injection, followed by significant QT prolongation. Mazindol significantly prolonged QT interval at 100× C_{max}, possibly due to interspecies differences between humans and rodents. These findings suggest that several abuse-prone drugs may pose a proarrhythmic risk when used at supratherapeutic levels.

Keywords : Cardiac electrophysiology, hiPSC-CMs, MEA, QT interval prolongation

Acknowledgements : This research was supported by a grant (23211MFDS219) from Ministry of Food and Drug Safety in 2022-2024.

P-728

Discovery of a Potential Neuroprotective Agent Against Cerebral Ischemia/Reperfusion through Inhibiting CaMKIIα Autophosphorylation Overactivation

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Background: Stroke remains a leading cause of global disability and mortality, highlighting the critical need for timely neuroprotective therapies, particularly for cerebral ischemia. Despite extensive research, no neuroprotective agent has yet approved by FDA. Calcium/calmodulin-dependent protein kinase II alpha (CaMKIIα), a key mediator of calcium overload responses following stroke, presents a promising therapeutic target. In this study, we identified a novel compound targeting the CaMKIIα hub domain that effectively attenuates CaMKIIα autophosphorylation in a glutamate-stimulated primary neuron model, suggesting its potential as a therapeutic candidate for ischemic stroke. Methods and Results: We performed virtual screening of 1.6 million commercially available compounds to identify hits targeting the CaMKIIα hub domain using Schrödinger suite software. Candidate compounds were refined through molecular dynamics simulations and evaluated via MM/GB-SA binding free energy calculations. Surface plasmon resonance analysis identified 49 CaMKIIα-binding candidates, 17 of which exhibited micromolar affinity. Among these, one compound demonstrated significant neuroprotective effects in glutamate-stimulated primary neurons. Western blot analysis confirmed a moderate reduction in CaMKIIα phosphorylation following treatment compared to controls. Conclusion: This study reports the discovery of a novel polyheterocyclic amine-based compound that reduces neuronal injury in glutamate-stimulated models, potentially through selective inhibition of CaMKIIα autophosphorylation by interacting with its hub domain. These findings highlight its promise as a neuroprotective agent for ischemic stroke treatment.

Keywords : CaMKIIα, Calcium overload, Ischemic stroke, neuroprotective agents

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P-729

The effects of Glucagon-like peptide-1 receptor agonist in senescent microglia

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Microglia are the tissue-resident innate immune cells of the brain in supporting the central nervous system (CNS) environment and health. Aging is characterized by a progressive deterioration of physiological function. Aging is associated with cellular senescence and cellular senescence contributes to aging-associated disease such as Alzheimer's disease. Glucagon-like peptide-1 (GLP-1), an incretin hormone, show anti-diabetic effects. In addition, GLP-1 receptor (GLP-1R) activation play crucial roles in aging and modulates cellular senescence. And, GLP-1R activation can enhance learning, memory, neurogenesis, and neuroprotection beyond glycemic control. Interestingly, senescent microglia decreased the secretion of GLP-1 than young microglia. GLP-1R agonist treatment of senescent microglia significantly decreased the expression of p16 and p21 and reduced Bodipy intensity. Phagocytosis and oxygen consumption rate of senescent microglia by GLP-1R agonist was significantly improved in senescent microglia. And, senescence-associated beta-galactosidase $(SA\text{-}\beta\text{-}gal)^+$ cells were significantly decreased by GLP-1R agonist treatment *in vitro*. These results suggest that GLP-1R agonist has an important role in senotherapy. And, it suggests that modulation of senescent microglia-dependent neuroprotective pathways might be an important effect of GLP-1R agonist.

Keywords : microglia, glucagon-like peptide-1, aging, senescence, senotherapy

P-730

The Body-Brain axis mediating the responses to protein deprivation

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Balanced intake of macronutrients – protein, carbohydrate, and fat – is essential for the well-being of organisms. Adequate calorie intake but insufficient protein consumption leads to several ailments, including kwashiorkor. Here, we show that a microbiome–gut–brain axis in *Drosophila* mediates the detection of EAA deficiency and stimulation of a compensatory appetite for EAAs. We found that CNMamide (CNMa) neuropeptide was highly induced in enterocytes of the anterior midgut during protein deprivation. However, the mechanism by which

the gut CNMa influences the brain to promote EAAs consumption remains poorly understood. In our study, we identified distinct neuronal populations expressing CNMa receptor (CNMaR) that are critical for the protein appetite. Gut-derived CNMa activates enteric neurons and ellipsoid body neurons to promote the intake of EAAs. By contrast, CNMa inhibits the activity of sugar-sensing DH44 neurons, thereby reducing sugar intake and further enhancing the EAA appetite. Similarly, protein-deprived mice show increased EAA appetite, independent of hepatic *FGF21* and required spinal pathway. Together, we propose the fundamental mechanisms underlying the maintenance of EAA homeostasis across species.

Keywords : Essential amino acids, Nutrient-specific appetite, Gut-brain axis, Post-ingestive nutrient sensing, CNMa-CNMaR signaling

Acknowledgements : We thank Minsoo Kyung for MS analyses, Institue for Basic Science (IBS, Director: Eunjoon Kim) for two-photon imaging support, and Suh lab members for helpful discussions. This work was supported by the National Research Foundation of Korea (multiple grants), KAIST Chancellor's fund, and Samsung Science and Technology Foundation.

P-731

Geroprotection in female mouse brains by long-term MAOB inhibition

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Aging is the process of accumulating molecular damage in cells over time. This process causes the cells of a system to stop dividing and enter a stage called replicative senescence, defined by the inability to repair cellular damage, regenerate, and maintain biological homeostasis. The expression of mitochondrial enzyme monoamine oxidase B (MAO-B), encoded on the X-chromosome, has been known to increase with age in human brains. In astrocytes, this enzyme generates H_2O_2 as a byproduct, which can produce reactive oxygen species (ROS) - well-known key determinants of cellular fate during aging. Studies regarding the effect of MAOB inhibition on lifespan have been conducted in male animals, showing significant improvement, but not in females, who carry two copies of this gene. In this study, we find that long-term continuous administration of KDS2010, a novel and reversible MAO-B inhibitor, extends the lifespan as well as health span of female C57BL/6J mice by up to 5 months. Age-associated neurodegeneration, as well as astrocyte atrophy, is delayed in the hippocampus, which can be attributed to reduced astrocytic MAOB expression. We report that the brains of female and male mice age differently, and that MAOB-mediated H_2O_2 production likely accelerates aging of female brains, which can be rescued or delayed by KDS2010 administration.

Keywords : Aging, Astroycte, Sexual dimorphism, MAOB

Acknowledgements : This work was supported by the Institute for Basic Science (IBS), Center for Cognition and Sociality (IBS-R001-D2 to C.J.L.). We thank Dr Kiduk Park and his team at KIST for the timely provision of compounds used in this study. We acknowledge the support provided by the IBS Mouse facility in the care and monitoring of aging animals.

P-732

Glucose Sensor and Cholesterol Sensor for Diabetes Monitoring and Cardiovascular Disease Prevention

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Introduction: Cardiovascular disease (CVD), a major complication of diabetes, has led to a sharp increase in global mortality. Early diagnosis is limited by invasive procedures like blood sampling and reliance on enzyme-based glucose sensors, which are costly and unstable. Managing CVD requires monitoring multiple biomarkers, including glucose and cholesterol, highlighting the need for non-invasive and reliable diagnostics. To address this, we developed a sensitive, non-enzymatic metabolite sensor using a simple electrochemical deposition method that forms micro-nano hierarchical structures for efficient biomarker detection. Results, Conclusions, and Discussions: The glucose sensor based on copper-nickel porous foam demonstrated excellent electrocatalytic performance with high sensitivity, selectivity, and stability. The enlarged surface area from the micro-nano hierarchical structure significantly enhanced glucose oxidation without the need for enzymes. Similarly, the cholesterol sensor, utilizing GNP and NiO-modified electrodes, showed effective cholesterol detection with strong signal response and minimal interference from other substances. Both sensors enable non-invasive, real-time monitoring through saliva samples, eliminating the discomfort and inconvenience associated with blood sampling. This allows for more frequent, painless monitoring, improving patient comfort and adherence. The simplified, enzyme-free design not only reduces manufacturing costs but also enhances sensor stability and lifespan. Overall, this biosensing platform provides reliable and accurate detection of key cardiovascular risk factors, supporting early diagnosis and personalized management of diabetes and CVD. It is particularly beneficial for resource-limited settings and portable health monitoring devices. Ultimately, this approach has the potential to improve health outcomes by making continuous monitoring more accessible and convenient for patients at risk of chronic diseases.

Keywords : Cardiovascular Disease Prevention, Glucose Sensor, Cholesterol Sensor, Non-enzymatic sensor, Diabetes

Acknowledgements : [1] J. Zhang, M. D. Baró, E. Pellicer, J. Sort. Nanoscale, 2014, 6, 12490 (2014). [2] Nasir Rafique, Abdul Hannan Asif, Rajan Arjan Kalyan Hirani Hong Wua, Lei Shi, Shu Zhang, Hongqi Sun. Journal of Colloid and Interface Science. Journal of Colloid and Interface Science. 615, 865–875 (2022). [3] Vidya Raj, Ruiz Jaime, Didier Astruc, K. Sreenivasan, Volume 27, Issue 1 (2011)

P-733

Reproductive Experience Shapes Distinct Behavioral Profiles in Female Mice

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Reproduction is essential for the continuation of species, and the

brain plays a central role in optimizing reproductive fitness through hormonal modulation of neuronal circuits. In rodents, pregnancy induces a wide range of behavioral adaptations, including reduced anxiety, increased feeding, altered thermoregulation, enhanced nesting, and sleep changes, all of which reshape daily routines and social interactions. In this study, we investigated how reproductive experience influences exploratory and social behavior in female mice by comparing virgin, male-exposed, and pregnant groups. Pregnant females exhibited significantly increased approach time and frequency toward novel objects compared to other groups, suggesting heightened object-oriented motivation during pregnancy. In contrast, in a three-chamber social interaction test, virgin females showed a preference for the familiar mouse, whereas both male-exposed and pregnant mice preferred to interact with a novel conspecific, indicating a shift in social preference following male exposure or pregnancy. Additionally, we utilized custom MATLAB-based tracking algorithms to quantify movement and measure distances during behavioral assays, enabling precise analysis of exploratory patterns across groups. These findings highlight distinct behavioral shifts driven by reproductive experience, with object-related behaviors prominently altered in pregnant mice and social behaviors differing notably in virgins, providing insights into how pregnancy and prior social exposure modulate female behavioral strategies.

Keywords : Reproductive experience, Pregnancy, Social interaction, Female mouse, Mouse behavior

P-734

A multiplexed imaging workflow for spatial proteomic analysis of the mouse brain

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Understanding the spatial organization of various biomarkers within tissues is crucial for precision diagnostics, including companion diagnostics in oncology. Spatial proteomics enables the identification of biomarker co-expression patterns and their biological contexts, providing essential insights for therapeutic decision-making. Multiplexed imaging-based technologies including IMC and cyclic staining (e.g., t-CyCIF) are one of the most representative techniques for spatial proteomic research. IMC provides ultra-high multiplexing capacity using metal-conjugated antibody labeling with no spectral overlap. Cyclic staining-based techniques provides the usage of standard antibodies and reagents, ensuring high-resolution optical imaging and flexible panel design across multiple rounds. Here, we propose a multiplexed imaging workflow that enables the visualization of multiple proteins across the mouse brain. By optimizing staining methods, staining conditions, image processing, and data analysis, we demonstrate spatial proteomic analysis of various proteins in the mouse brain. Additionally, we present 3D multiplexed imaging from a brain section, followed by further analysis of the multiplexed image data.

Keywords : Multiplexed Imaging

P-735

Age- and disease-related dysfunction and compensation of neural oscillations during episodic memory retrieval

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Alzheimer's disease (AD) involves both age-related and pathological neurocognitive changes, making it difficult to predict its early progression based solely on behavior. To identify neural markers that differentiate normal aging from disease-related changes, we utilized a previously validated scene-based episodic memory across young adults, healthy older adults, mild cognitive decline patients, and AD patients, while recording EEG activity during memory retrieval. The patient group performed worse in spatiotemporal memory (the location of objects (where) or sequential order (when) of scenes) compared to object recognition memory (what). By comparing EEG activity across groups, we first identified age-related changes in theta oscillations. Young adults showed prominent posterior theta increases along with strong long-range coherence between posterior and anterior regions. In contrast, both healthy older adults and patients showed theta activity in lateral frontal regions, but the theta connectivity across regions was absent. These suggest that older adults relied more on frontal theta, potentially required to initiate memory reactivation, in response to reduced long-range coordination. Next, desynchronization during memory retrieval was prominent in the alpha band (8–12 Hz) for young adults, while a similar response was shifted to the beta band (15–20Hz) for older adults. Notably, older adults demonstrated significantly greater beta desynchronization during correct trials compared to incorrect ones. However, this effect diminished with the progression of AD, resulting in decreased episodic memory performance. Therefore, beta desynchronization may be a compensatory mechanism to support memory retrieval in healthy aging, which gradually deteriorates with disease progression. With both localized and distal connectivity measures, our study offers novel insight into the changes in neural activities underlying episodic memory performance in normal and pathological aging.

Keywords : EEG, Episodic Memory, Aging, Alzheimer's Disease

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P-736

Long-term bis (2-ethylhexyl) phthalate exposure changes subthreshold stress to be severe stress, evoking depressive behaviors

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Depression is a common psychiatric disorder, but it leads to suicide at

a high rate. A positive correlation between depression and exposure to bis(2-ethylhexyl) phthalate (DEHP) is suspected. In previous studies, it was reported that the long-term DEHP exposure caused depressive-like behaviors by inhibiting glutamatergic neurotransmission through disruption of glutamate (Glu)-glutamine (Gln) homeostasis in the medial prefrontal cortex (mPFC). These results are similar to the mechanism of chronic stress-induced depression. To investigate the association between long-term DEHP exposure and chronic stress in the occurrence of depression, a low level of DEHP was exposed to mice, and then some of them were subjected to a seven-day chronic immobilization stress (CIS) that did not cause depressive behaviors. As a result, depressive-like behaviors, including anxiety, despair, and anhedonia, were observed in DEHP and CIS double-exposed mice. In these mice, the stress-related biomarkers such as corticosterone and ROS/RNS increased, glutamine synthetase (GS) activity reduced, and tyrosine nitration on GS increased in mPFC. In addition, Glu and Gln decreased in the mPFC. However, depressive-like behaviors and biomarker changes were not found in DEHP or CIS single-exposed mice. In spontaneous excitatory postsynaptic current analysis, the activity of glutamatergic neurotransmission decreased in DEHP and CIS double-exposed mice. These results demonstrate that environmentally relevant DEHP can change the daily life with subthreshold stress into severe stressful life that evokes depressive behaviors. It is also announced that new approaches are needed for future studies about whether environmental pollutants affect human health.

Keywords : bis(2-ethylhexyl) phthalate, depression, chronic stress, glutamine synthetase, tyrosine nitration, glutamatergic signaling

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P-737

Effects of pulsed transcranial photobiomodulation of the prefrontal cortex on temporal credit assignment

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Real-world decisions often involve delayed outcomes, making it crucial to infer causal relationships between past actions and future consequences—a process known as temporal credit assignment. Deficits in this ability can lead to maladaptive behaviors in domains involving long-term consequences, such as health, finance, and substance use. Converging evidence from neuroimaging studies suggests that prefrontal cortex plays a key role in causal inference. Here, we investigated whether frontal transcranial photobiomodulation (tPBM) modulates higher-order cognition and influences performance on credit assignment tasks. Forty healthy adults (male/female = 20/20; age = 21.53 ± 3.10) were randomly assigned to receive 10 minutes of 850 nm LED tPBM at pulse frequencies of 10 Hz (n = 14), 20 Hz (n = 13), or 40 Hz (n = 13). Stimulation was applied once daily for three consecutive days at the same time each day. To assess temporal credit assignment performance, participants completed a probabilistic reward learning task both before the first and after the final stimulation session. In the task, participants made a series of choices between two options, learning their reward probabilities through trial and error. Critically, outcomes were delivered after variable delays sampled from a Poisson distribution, requiring inference of delayed causal relationships. Performance was quantified as the proportion of optimal choices. Our results showed that only participants who received 10 Hz pulsed tPBM showed a significant improvement in performance from pre- to post-intervention ($t(13) = 3.90$, $P = 0.0018$), whereas no such enhancement was observed in the 20Hz or 40 Hz groups. These results indicate that frontal tPBM, at specific pulse frequency, can modulate credit assignment ability. Our findings highlight the potential of non-invasive neuromodulatory interventions to enhance higher-order cognitive functions, with broad implications for understanding and addressing health-risk behaviors.

Keywords : reinforcement learning, credit assignment, non-invasive stimulation, photobiomodulation

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P-738

Behavioral and neural signatures during discriminating emotional valence in mice

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Empathy, the ability to recognize and understand the emotional states of others, is crucial for appropriate social interactions and often impaired in psychiatric disorders. While much research has focused on negative emotions, such as fear and pain, how animals recognize a broader range of emotions, including positive ones, remains unclear. Recent studies suggest that mice can distinguish between emotional states and neutral states and that the prefrontal cortex (PFC) is involved in discriminating emotional states. However, it remains unclear whether these responses are driven merely by the detection of emotionally salient cues or whether mice can actively differentiate the emotional valence (i.e., positive vs. negative) of social targets. To address this, we investigated whether mice can differentiate between emotional valences. Using a two-chamber test, we found that mice preferentially investigated conspecifics in stressed or relieved states over neutral ones, consistent with previous findings. Furthermore, when both stressed and relieved conspecifics were present, investigation time was significantly longer toward the stressed individuals. In addition, infralimbic cortex activity recorded via fiber photometry showed a trend towards increased responses to relieved compared to stressed conspecifics during emotional discrimination tasks. To assess brain-wide network changes, we measured c-Fos expression after social interaction, depending on the conspecific's emotional states. Interaction with stressed mice was associated with stronger connectivity in frontal cortical areas. These results suggest emotion-specific brain network recruitment during social affective recognition.

Keywords : Emotion discrimination, Social behavior, PFC

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P-739

Low-intensity ultrasound (LIUS) relives bladder dysfunction and pain in cyclophosphamide-induced cystitis mice models

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Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic inflammatory disease of the bladder that is characterized by suprapubic pain associated with bladder fullness, daytime urgency, nocturia, and urgency urination. The exact cause of the pain associated with BPS/IC is unclear, but one of the mechanisms is enhanced bladder afferent activity. Various neuromodulation techniques have been proposed for pain management in patients with IC/BPS who have failed medication. Sacral nerve stimulation and posterior tibial nerve stimulation has been reported to improve chronic pelvic pain, urgency, and control voiding patterns. However, current neuromodulation techniques are invasive and accompanied by discomfort. Low-intensity ultrasound (LIUS) is non-invasive neuromodulation method with no thermal effects or tissue damage. In this study, we investigated whether non-invasive ultrasound stimulation could alleviate pain by modulating afferent neural pathways in a CYP-induced cystitis model. Ultrasound stimulation was targeted to the L6-S1 spinal cord region or L6-S1 DRG region and given once a day for 10 days from the first day of CYP administration. The ultrasound protocol used the experiment was a continuous theta burst ultrasound (cTBUS) consisting of 200 Hz bursts of a 5 Hz (theta) train pattern, characterized by theta-gamma coupling. Chronic cystitis mice induced by CYP showed lowering thresholds for both mechanical and thermal stimulation compared to normal controls. LIUS stimulation at both L6-S1 spinal cord and DRG could effectively alleviate mechanical and thermal hyperalgesia in the cystitis mouse model. In addition, cystitis mice exhibited multiple small void spots, indicating symptoms of overactive bladder, but these were significantly reduced in the ultrasound stimulation groups. Neuromodulation with LIUS has been shown to be able to reverse lowered pain thresholds in chronic cystitis as well as alleviate abnormal voiding patterns.

Keywords : Pain, Neuromodulation, Ultrasound, Micturition, Dorsal root ganglion

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P-740

Immersive visual-thermal stimulation applied to a third person virtual avatar modulates upper limb skin temperature

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Immersive VR can evoke a sense of physical presence and realism. While visual-thermal cues on a first-person avatar influence thermal perception and skin temperature, it is unclear whether these effects stem from visual input alone or are mediated by self-identification. We examined this using a motion-mimicking third-person (3P) avatar and a VR mirror to manipulate self-identification. Two scenarios simulated cold or hot stimulation on the avatar's right arm with matching ambient lighting (blue/red). In the Sync condition, the avatar mirrored participant movement; in Async, it moved independently. Nine participants (5 female, M = 28.2 ± 5.6) took part. Skin temperature was measured at six sites on the arms and hands, and a 10-item questionnaire assessed presence, self-identification, and thermal experience. A reference session without visual input controlled for HMD-related temperature effects. Presence ratings (6.55 ± 0.21) were higher than the neutral rating (5.0). Self-identification scores were significantly higher in Sync than Async across both stimuli ($p < .001$). Participants perceived visual thermal cues as realistic (6.66 ± 0.37). Skin temperature increased in the cold condition ($\Delta T = +0.05°C$) and decreased in the hot condition ($\Delta T = –0.11°C$), regardless of synchrony. Paired t-tests showed significant differences between cold–sync and hot–sync ($p = .023$), and between cold–async and hot–async ($p = .007$), indicating cue polarity effects. Although differences between Sync and Async were observed (cold: $\Delta T = +0.05°C$; hot: $\Delta T = –0.02°C$), they were not statistically significant, likely due to the small sample size. These preliminary results suggest that visual thermal cues in VR can influence both subjective and physiological responses. While the role of self-identification did not reach significance, it remains a promising factor. Further data collection is planned to validate this possibility.

Keywords : Body Ownership, Self-Identification, Virtual Reality, Visual Thermal Illusion, Skin Temperature

P-741

TRPV1 expressed by melanocortin-4 receptor neurons regulate body weight

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It is well known that the melanocortin-4 receptors (MC4Rs) in the sympathetic nervous system play a role in energy metabolism regulation. Our previous study demonstrated that TRPV1 is responsible for the activation of sympathetic preganglionic neurons by MC4Rs. Thus, we hypothesized that TRPV1 expressed by MC4R neurons may also regulate energy expenditure. To knock out TRPV1 specifically in MC4R neurons, we generated conditional knockout mice ($Mc4r^{cre/+}$::$TRPV1^{f/f}$, referred to as TRPV1 CKO) using the Cre-LoxP system. Body weight and food intake were measured weekly from 4 to 20 weeks of age under *ad libitum* conditions on a normal chow diet. We found that TRPV1 CKO mice have increased body weight without changes in food intake on normal chow diet. We also noted that the increases in body weight was primarily due to increased fat mass, using nuclear magnetic resonance (NMR). Next, we measured metabolic parameters such as oxygen consumption (VO_2), carbon dioxide production (VCO_2), energy expenditure, and locomotor activity using an indirect calorimetry system. The results showed that VO_2 and VCO_2 levels were decreased, suggesting reduced energy expenditure, while the respiratory exchange ratio (RER) remained unchanged. There was no significant differences in the locomotor activity. Importantly, we also collected organs and both white adipose tissue (WAT) and brown adipose tissue (BAT) wet mass were increased in the TRPV1 CKO mice. H&E staining revealed enlarged white adipocytes and increased fat granules in brown

adipose tissue. On the other hand, the appetite-suppressing effects of MTII remained unchanged in the TRPV1 CKO mice. There were no significant differences in glucose tolerance tests (GTT) and insulin tolerance tests (ITT) results between the two groups. Our findings suggest that TRPV1 expressed by the MC4R neurons plays a crucial role in regulating energy expenditure and fat mass, independent of food intake.

Keywords : MC4R, TRPV1, Energy expenditure, Obesity, Sympathetic nervous system

P-742

Establishment of a treadmill-based training protocol for gait assessment in mini-pigs

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Introduction: Mini-pigs are important non-clinical models in orthopedics and neurosurgery due to their anatomical and physiological similarities to humans. Treadmill-based gait analysis is essential for assessing implant efficacy, such as artificial joints. This study aimed to establish a reliable gait training protocol using a mini-pig with weight similarities to Adult humans. Methods: A 59 kg, 24-month-old male KSP mini-pig housed at the Korea Research Institute of Bioscience and Biotechnology (KRIBB) was used. To encourage voluntary treadmill use, the animal underwent two weeks of treat-based acclimation. Training sessions occurred three times weekly between 2:00 and 4:00 p.m., with morning fasting to boost motivation. Outside training, the cage door remained open to allow free roaming and facilitate walking adaptation. Results: Training consisted of three cycles of 30 seconds walking followed by 1 minute rest. Treadmill speed was set at 2.62 cm/s. Over one month, walking durations gradually increased from 30 seconds to over 2 minutes. The mini-pig successfully achieved continuous treadmill walking for more than 2 minutes. Discussion: This protocol demonstrates that gait training is feasible in a 59 kg male mini-pig using human-grade equipment. Key success factors were treat-based reinforcement, a larger walking area, and voluntary movement outside formal sessions. Conclusion: A successful gait training protocol was established for a 59 kg male mini-pig using human-grade treadmill equipment. Treat-based reinforcement, ample walking space, and voluntary activity time were critical. This protocol provides a valuable preclinical reference for implant efficacy studies under physiologically relevant conditions.

Keywords : treadmill-based, gait assessment, minipigs, training protocol

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P-743

Identification and characterization of GAL4 drivers that mark distinct cell types and regions in the Drosophila adult gut

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The gastrointestinal tract in the adult Drosophila serves as a model system for exploring the mechanisms underlying digestion, absorption and excretion, stem cell plasticity, and inter-organ communication, particularly through the gut–brain axis. It is also useful for studying the cellular and adaptive responses to dietary changes, alterations in microbiota and immunity, and systematic and endocrine signals. Despite the various cell types and distinct regions in the gastrointestinal tract, few tools are available to target and manipulate the activity of each cell type and region, and their gene expression. Here, we report 353 GAL4 lines and several split-GAL4 lines that are expressed in enteric neurons (ENs), progenitors (ISCs and EBs), enterocytes (ECs), enteroendocrine cells (EEs), or/and other cell types that are yet to be identified in distinct regions of the gut. We had initially collected approximately 600 GAL4 lines that may be expressed in the gut based on RNA sequencing data, and then crossed them to UAS-GFP to perform immunohistochemistry to identify those that are expressed selectively in the gut. The cell types and regional expression patterns that are associated with the entire set of GAL4 drivers and split-GAL4 combinations are annotated online at http://kdrc.kr/index.php (K-Gut Project). This GAL4 resource can be used to target specific populations of distinct cell types in the fly gut, and therefore, should permit a more precise investigation of gut cells that regulate important biological processes.

Keywords : Drosophila gut, Gal4, Regional, Cell-type specificity, resource

P-744

Real-time decision making under uncertainty: An IRL-based analysis of naturalistic driving task

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Naturalistic tasks enable the study of complex and natural behaviors within controlled lab environments by providing expansive state-action spaces that reflect the real environment. This method addresses key limitations of conventional behavioral paradigms. In our previous study (Lee et al., 2024), we developed a naturalistic real-time driving task - the (static) highway task - and applied an inverse reinforcement learning (IRL) algorithm to model participants' behavior. We found that the reward functions inferred by IRL could serve as indicators of impulsivity. A subsequent fMRI study further revealed strong correlations between IRL

reward trajectories and neural activity in the reward circuitry, suggesting that they may reflect internal value representations in the brain. In the current study, we extended the task by incorporating environmental uncertainty through stochastic lane changes by non-player vehicles (*dynamic* highway task). Twenty-eight participants completed highway tasks in both static and dynamic versions of the task in a counterbalanced order. Behavioral analyses showed that both mean speed and mean reward significantly decreased in dynamic conditions, indicating behavioral adaptation under uncertainty. We examined IRL reward trajectories with a focus on two salient events: cut-ins and overtaking. Preliminary analyses showed that the IRL reward for higher speed in dynamic settings has decreased for all distance situations compared to static settings. Additionally, they suggest that the IRL reward trajectories may differ across impulsivity levels. During cut-in events, the high impulsivity group showed a steeper drop in IRL reward compared to the low impulsivity group. In overtaking situations, group differences appeared to diminish under dynamic conditions. In the further analyses, we aim to investigate how reward evaluation under uncertainty differs across individual traits, including impulsivity and anxiety.

Keywords : Naturalistic paradigm, Inverse reinforcement learning, Deep learning, Impulsivity

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P-745

Motion cues delivered via somatosensory inputs can increase or decrease the level of motion sickness caused by virtual-reality experience

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Simulator sickness is a multifaceted discomfort induced by sensory stimuli during virtual experiences. It is commonly explained by the sensory conflict theory, which attributes symptoms to mismatches between expected sensory feedback— shaped by both current and prior experience—and actual sensory feedback. Additional somatosensory cues have been proposed to mitigate simulator sickness by reducing sensory mismatch. However, some studies reported that additional somatosensory cues reduce simulator sickness, while others reported no effect or even suggested that they may exacerbate the sickness depending on the type and nature of the cues. This study aimed to examine how the additional somatosensory motion cues influence the experience of simulator sickness. 22 healthy young adults participated in a 129-second roller coaster simulation using a VR headset and a 3-DOF motion platform. Each participant experienced three conditions in a crossover design: (1) *V* (VR only), (2) *V+S* (VR+ motion cues), and (3) *S* (motion cues). Simulator sickness and related factors were evaluated with fNIRS and six other questionnaires include Simulator Sickness Questionnaire (SSQ). SSQ results revealed divergent responses 41% of participants exhibited an increase in simulator sickness from the *V* to *V+S* condition (M = 12.2 to 36.5), whereas another 41% showed a decrease (M = 50.5 to 24.8). These findings suggest that somatosensory motion cues may either exacerbate or reduce sensory conflict, depending on individual differences. Additionally, fNIRS results indicated significant changes in cortical activities associated with the simulator sickness. Overall, the data suggests that the traditional sensory conflict theory may need to be refined to better account for individual differences in simulator sickness responses to additional somatosensory motion cues. This also highlights the importance of personalized approaches in mitigating simulator sickness in a virtual-reality environment.

Keywords : Simulator sickness, Motion cues, Sensory conflict theory, Virtual Reality(VR), Functional Near-Infrared Spectroscopy (fNIRS)

Acknowledgements : This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (No. RS-2023-00209864) and the Korea Evaluation Institute of Industrial Technology (KEIT) funded by the Korean government (MOTIE)(No. RS-2025-04992970).

P-746

Brain-targeted delivery of fluoxetine via red blood cell membrane biomimetic nanocarriers with stiffness optimization to reverse depressive behavio

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Depression is a leading cause of disability and suicide. Conventional antidepressant therapies are challenged by inefficient drug delivery. This study investigates a red blood cell membrane-coated nanoparticle system to enhance BBB penetration and improve the therapeutic efficacy of fluoxetine, a common antidepressant. Two nanoparticles were designed: one containing a PLGA core (Flu-PRP) and the other composed solely of red blood cell membranes (Flu-RP). Both carriers were coated with erythrocyte membranes functionalized with brain-targeting peptides. The nanoparticles exhibited uniform particle sizes (100–200 nm), negative surface charges, and a maximum drug loading efficiency of 25%, with sustained drug release kinetics. Notably, nanoparticles with distinct mechanical properties demonstrated divergent biodistribution patterns: softer Flu-RP nanoparticles showed reduced hepatic accumulation and enhanced brain targeting efficiency, whereas stiffer Flu-PRP nanoparticles predominantly accumulated in the liver.In a mouse depression model established via the Chronic Unpredictable Mild Stress (CUMS) model, therapeutic outcomes were systematically evaluated. The Flu-RP treatment group achieved remission of depressive phenotypes, while conventional fluoxetine and Flu-PRP groups exhibited limited efficacy. Safety assessments confirmed no significant toxicity of either nanoparticle formulation, these findings highlight the critical influence of nanoparticle physical properties (e.g., stiffness) on in vivo behavior and therapeutic performance. The softer Flu-RP nanoparticles, owing to their reduced phago- cytosis by macrophages, demonstrated superior evasion of hepatic clearance and enhanced brain delivery.This drug delivery strategy, the physical characteristics of nanomaterials, provides a novel approach for treating depression and other central nervous system disorders, with potential to shorten therapeutic timelines and minimize systemic side effects.

Keywords : Depression, Deliver, Fluxetine, Nanoparticles

P-747

Study on the Effects of Alcohol Exposure on Learning and Memory in Mice and Its Underlying Mechanisms

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Alcohol stimulation, a common stressor in daily life, influences neuronal activity and thereby affects memory. A key controversy lies in the differential effects of alcohol exposure at various memory phases, with varying concentrations potentially exerting distinct impacts on neuronal function. We hypothesize that high concentrations of acute alcohol exposure during the memory consolidation phase alter neuronal activity and consequently impair memory. To test this, we employed behavioral paradigms including the novel object recognition (NOR) test, novel location recognition (NLR) test, and contextual fear conditioning (CFC) to evaluate the effects of alcohol exposure at different concentrations during the consolidation phase on memory performance in mice. Our findings indicate that in spatial memory tasks (NOR and NLR), memory encoding did not affect hippocampal CaMKII expression or phosphorylation; however, high-concentration alcohol exposure during consolidation significantly reduced hippocampal neuronal activity and induced memory deficits. In contrast, in the contextual fear conditioning paradigm assessing contextual memory, memory encoding enhanced hippocampal CaMKII phosphorylation, potentially facilitating long-term potentiation (LTP) to strengthen memory. This mechanism may partially compensate for alcohol-induced reductions in neuronal activity, resulting in no observable memory impairments following alcohol exposure during consolidation in this task. These results demonstrate that alcohol impacts memory by modulating neuronal activity and that acute high-dose alcohol exposure during memory consolidation alters neuronal function, thereby impairing memory. This study provides important experimental evidence elucidating how alcohol-induced changes in neuronal activity affect memory processes.

Keywords : Memory, Alcohol, Exposure, Consolidation

P-748

A neuropeptide signaling pathway mediates pheromone avoidance behavior in *C. elegans*

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Animals adjust their behavior to environmental changes to improve their chances of survival. Despite the crucial role of neuropeptides in modulating behavior, the neuronal and molecular mechanisms underlying neuropeptide mediated behavioral plasticity are not fully understood. *C. elegans* secretes a pheromone mixture called ascarosides. A specific pheromone component, ascr#3, elicits repulsion in wild-type hermaphrodites. This response is further modulated by sex, stress, and early experience (Jang et al., 2012, Hong et al., 2017, Ryu et al., 2018). Previously, we have shown that a *flp-26* regulates ascr#3 avoidance behavior (Hwang et al., in prep). To further understand the mechanism of *flp-26*-mediated avoidance, we first aim to identify its receptor(s). To this end, we compiled a list of 44 putative GPCR candidates of which expression in ADL was identified from the CENGEN database based on the gene expression levels of single-cell RNA-Seq data. We found that *npr-1, npr-20, npr-26, frpr-16,* and *frpr-18* mutants exhibit reduced avoidance. Next, we are currently investigating the expression pattern of these genes in order to determine expression in the ADL neurons.Additionaly, NPR-6, DMSR-1, and DMSR-7 were identified as FLP-26 receptors through in vitro studies (Isabel et al., 2023). We are currently investigating their roles in acute ascr#3 responses. Ultimately, these findings will help us understand the mechanism by which neuropeptides modulate pheromone avoidance at the molecular and neural circuit levels.

Keywords : Neuropeptide, ascarosides

P-749

Predictive coordinated eye and tail movements in response to periodic visual motion in goldfish

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Animals predict future events based on past experiences to compensate for sensorimotor delays. Eye movements represent such behavior capable of acquiring predictive control. The optokinetic response (OKR) stabilizes vision by rotating the eyes to follow wide-field visual motion. In goldfish, when the motion reverses periodically, a predictive form of OKR (pOKR) emerges, characterized by a deceleration of eye velocity prior to each reversal (Miki et al., 2018, 2020). Notably, these findings were obtained under conditions in which the head and trunk were fixated, leaving the functional significance of pOKR under more naturalistic conditions unclear. Visual stabilization can also be achieved through whole-body motion, known as the optomotor response (OMR). In nature, animals may rely on predictive OMR (pOMR), or a combination of pOMR and pOKR. In this study, we examined tail movements in goldfish (4–6 cm) under a semi-restrained condition, where only the head was fixed, allowing free tail movement. Vertical black-and-white stripes were presented around a transparent cylindrical tank (12 cm in diameter, 6 cm in height). During training, the stimulus rotated at 24°/s and reversed every 8 s for 1 h (225 cycles). In the subsequent test phase, reversals occurred every 16 s for 64 s (2 cycles), and the training-test sequence was repeated eight times. From the onset of training, the animals bent their tails in the direction of visual motion. After 2 h, clear pOKR was observed. In contrast, tail-bending behavior lagged behind the stimulus reversal by approx. 0.3 s. Nonetheless, during the test, tail bending consistently occurred for the first 8 s of each cycle and then gradually returned to the neutral position, even though the visual stimulus continued in the same direction. These results provide the first evidence of predictive tail movements in goldfish. The observed behavior suggests a form of pOMR that may operate in coordination with pOKR to stabilize vision in nature.

Keywords : OKR, Predictive control, OMR, Tail movement, free moving

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P-750

Self-powered neural modulation *via* cervical motion-induced bioelectrical harvesting in an implantable system

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Neuromodulation is a cutting-edge technique that selectively alters or regulates the function of the nervous system through electrical stimulation. It has shown therapeutic efficacy in treating drug-resistant neurological disorders such as epilepsy, depression, Parkinson's disease, and anxiety disorders. Representative modalities include vagus nerve stimulation (VNS), deep brain stimulation (DBS), and spinal cord stimulation (SCS), all of which deliver targeted electrical pulses to specific nerves or neural circuits. While these systems typically rely on primary batteries, recent advances have enabled the integration of rechargeable batteries in DBS and SCS systems. Triboelectric energy harvesting has emerged as a promising power source for self-sustainable implantable devices due to its material versatility, biocompatibility, and ability to convert subtle biomechanical movements into electrical energy. This approach enables the generation of physiologically relevant electrical pulses or the storage of harvested energy for subsequent use in neuromodulation systems. This study proposes a triboelectric nanogenerator (TENG) that can be implanted in the cervical region to generate electrical pulses triggered by natural neck motions such as nodding, swallowing, or rotation. The device architecture is based on a multilayered interdigitated electrode design, enhancing output performance through geometrical stacking. Experimental validation demonstrates that low-frequency biomechanical stimuli (0.1–1 Hz) can be effectively multiplied by increasing the number of electrode grids. The resulting pulse amplitude from a single actuation event varies from 5.11 mA to 0.045 mA, tunable via the capacitance of intermediate energy regulation circuits. These findings suggest the potential of implantable TENGs as both direct neuromodulation pulse generators and sustainable energy sources for powering conventional neuromodulation devices.

Keywords : Triboelectric nanogenerator, Energy Harvesting, Multi-layer, Implantable device, Neuromodulation

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P-751

Regulation mechanisms and functions of fast adenosine release in dorsal striatum

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The striatum is a critical brain region for motor control. In Parkinson's disease (PD), the degeneration of dopaminergic neurons severely impairs striatal function, leading to motor dysfunctions. Beyond the dopaminergic system, other neuromodulatory systems, such as the adenosine system, have also received attention for their potential role in alleviating PD symptoms. However, the cellular origin and exact role of adenosine in the striatum during motor control remains unclear. In this study, we characterized the release patterns of adenosine in the striatum during locomotion and explored the regulatory roles of local and long-range neural circuits on adenosine release. Furthermore, motor learning in mice was enhanced after knocking out adenosine receptors in striatum. Together, this study provides new insights into the role of adenosine in striatal function, which could contribute to the development of new strategies for managing the motor symptoms associated with Parkinson's disease.

Keywords : Adenosine, Dorsal Striatum, Motor Control, Neural Circuit

Synapses and Circuits P-752~P-776

P-752

Gene Therapy Targeting Synapses Through AAV9 Delivery Boosts Functional Recovery Following Spinal Cord Injury

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Spinal cord injury (SCI) triggers a cascade of neurodegenerative processes, including neuronal cell death, synaptic damage, and chronic neuroinflammation, which impede motor function recovery. Our previous research indicated that the expression of vesicular glutamate transporter 1 (VGLUT1) and leucine-rich glioma inactivator 1 (LGI1) is diminished following SCI, suggesting a potential mechanism for the impairment of excitatory synaptic signaling. VGLUT1 facilitates glutamate loading at presynaptic terminals, while LGI1 sustains the excitability and structural stability of postsynaptic neurons through interaction with ADAM22/23. To assess the therapeutic potential for synaptic function recovery, we employed adeno-associated virus serotype 9 (AAV9) vectors expressing VGLUT1, LGI1, or both in a moderate contusion SCI rat model. The vectors were administered adjacent to the injury site, and functional recovery was evaluated over a 12-week period. In vitro, we assessed neuronal survival and axonal regeneration through the conductivity of primary cortical neurons under oxidative stress. The expression of VGLUT1 and LGI1 enhanced neuronal survival and axonal growth under oxidative stress, with neurite lengths increased (VGLUT1: 228 ± 16.7 μm; LGI1: 238 ± 17.5 μm) compared to the damaged control (184 ± 29.6 μm) at MOI 5×10^4. In vivo, both therapies significantly reduced lesion cavity volume (Control: 2.05 mm^3; VGLUT1: 1.10 mm^3; LGI1: 1.27 mm^3) and ED1-positive cell infiltration (Control: 1,889.3; VGLUT1: 982.3; LGI1: 971.7), indicating reduced inflammation and tissue damage. Behavioral tests (BBB scale and horizontal ladder test) demonstrated improved motor recovery in all treatment groups, with LGI1 yielding superior outcomes compared to VGLUT1 or combination therapy. This study demonstrates that AAV9-mediated VGLUT1 and LGI1 gene delivery promotes functional recovery following SCI, supporting the potential for clinical translation of gene therapy for SCI treatment.

Keywords : Spinal cord injury, Gene therapy, Functional recovery, Neuroinflammation, Synaptic plasticity

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P-753

Poster Award Candidate

Encoding the Glucose Identity by Discrete Hypothalamic Neurons via the Gut-Brain Axis

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Animals need daily intakes of three macronutrients: sugar, protein and fat. Under fasted conditions, however, animals prioritize sugar as a primary source of energy. They must detect ingested sugar – specifically D-glucose – and quickly report its presence to the brain. Hypothalamic neurons that can respond to the caloric content in the gut regardless the identity of macronutrient have been identified, but until now, the existence of neurons that can encode the specific macronutrients remained unknown. We found that a subset of corticotropin-releasing factor (CRF)-expressing neurons in the hypothalamic paraventricular nucleus (CRF^{PVN}) respond specifically to D-glucose in the gut, separately from other macronutrients or sugars. CRF^{PVN} neuronal activity is essential for fasted mice to develop a preference for D-glucose. These responses of CRF^{PVN} neurons to intestinal D-glucose require a specific spinal gut-brain pathway including the dorsal lateral parabrachial nuclei. These findings reveal the neural circuit that encodes the identity of D-glucose.

Keywords : hypothalamic CRF neurons, glucose encoding, gut-brain axis

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P-754

Frontoparietal as well as cholinergic inputs are necessary for the activity of the posterior parietal cortex during short-term memory

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Working memory (WM), the transient storage and maintenance of information, is a fundamental cognitive process. While previous studies have highlighted the importance of long-range synaptic connections within the prefrontal cortex (PFC) and posterior parietal cortex (PPC), as well as the modulatory role of acetylcholine (ACh), it remains unclear how neuromodulatory signals and interareal connectivity cooperate to sustain neuronal activity during short-term memory (STM). In this study, we investigated the functional significance of frontoparietal synapses—specifically, PFC-driven inputs to the PPC—and examined how ongoing frontoparietal activity contributes to sustained PPC activity during STM. Our findings demonstrate that the PFC provides direct and robust excitatory input to the PPC, such that high-frequency PFC activity evokes membrane depolarization in PPC neurons via strong monosynaptic connections. Strikingly, we also found that cholinergic activation induces autonomous persistent firing in PPC neurons, with activity lasting for several seconds. To assess the behavioral relevance of these inputs, we used optogenetic inhibition of frontoparietal synapses and pharmacological blockade of muscarinic ACh receptors (mAChRs). Both manipulations significantly impaired performance on a delayed Y-maze task, which depends on intact STM. To further investigate the circuit mechanisms, we recorded PPC neural activity during a delayed Y-maze task. In correct trials, PPC neurons exhibited direction-selective firing during the delay period. However, inhibition of either frontal or cholinergic inputs led to a significant reduction in PPC delay activity and a marked decrease in direction-selective neural responses. Together, our findings suggest that inputs from the PFC and cholinergic systems are critical for sustaining direction-selective neural activity in the PPC, and that this frontoparietal–cholinergic interaction plays a vital role in supporting short-term memory.

Keywords : Prefrontal cortex, Posterior parietal cortex , Acetylcholine , short term memory, optogenetics

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P-755

Persistence of CTA Memory in PBN Ensembles Following Extinction

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Conditioned taste aversion (CTA) is a well-established paradigm for studying associative learning, yet the neural circuitry and molecular mechanisms underlying CTA extinction remain unclear. In this study, we combined targeted recombination in active populations (TRAP) with chemogenetic manipulation to demonstrate that the parabrachial nucleus (PBN) remains essential for CTA memory recall even after extinction. Using neural tracing, we identified PBN projections to the central amygdala (CeA) that mediate CTA memory retrieval and further revealed distinct upstream inputs to the CeA during retrieval versus extinction. Additionally, transcriptomic profiling of key brain regions uncovered molecular signatures differentiating CTA acquisition and extinction. Our findings indicate that extinguished CTA memories persist in a latent state and reveal distinct neural circuits and molecular mechanisms governing CTA memory formation and extinction.

Keywords : Conditioned taste aversion, Parabrachial nucleus, Central amygdala

P-756

Inhibitory Interneurons in the Mediodorsal Nucleus of the Thalamus and their Modulation and Termination of Short-Term Memory

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Short-term memory (STM), the ability to temporarily retain and manipulate information, relies on coordinated thalamofrontal dynamics. The mediodorsal nucleus of the thalamus (MD), through its reciprocal connections with the medial prefrontal cortex (mPFC), plays a key role in maintaining delay-period activity during STM tasks. Given the limited capacity of STM, unloading and refreshing the retained information after the need should be equally important. However, the mechanisms underlying the modulation and termination of STM remain unexplored. In this study, we identified a population of parvalbumin-expressing (PV^+) inhibitory interneurons within the MD and characterized their intrinsic electrophysiological properties using whole-cell patch-clamp recordings. MD inhibitory (MD_{IN}) neurons exhibited narrower and higher frequency action potential than MD excitatory (MD_{EX}) neurons and facilitated by high-frequency inputs from mPFC. Further, strong and reliable inhibitory synaptic inputs were found on the MD_{EX} neurons. In line with this, high-frequency activity of the mPFC afferents activated MD_{IN} neurons, which in turn inhibited nearby excitatory neurons. Despite the sparsity of the MD_{IN} neurons, this inhibition was achieved through robust and reliable synaptic connections, effectively suppressing excitatory activity within the MD. Synaptophysin-mRuby labeling revealed dendrodendritic synapses among MD_{IN} neurons, indicating local inhibitory interactions within the MD. These findings suggest that the MD_{IN} neurons regulate STM by responding selectively to sustained cortical input through feedforward dendrodendritic inhibition, thereby ensuring its timely termination by suppressing MD_{EX} neurons. Importantly, this study provides the first direct evidence of PV^+ inhibitory interneurons within the MD. Our findings suggested MD_{IN} neurons as a novel mechanism for controlling both the maintenance and termination of STM, offering a new perspective on thalamocortical dynamics.

Keywords : mediodorsal thalamus (MD), inhibitory interneuron, short-term memory, thalamofontal circuit, short-term plasticity

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P-757

Role of Basal Ganglia Network Regulation in ADHD-like phenotypes in mice

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Attention-deficit/hyperactivity disorder (ADHD) is characterized by impulsivity, inattention, and hyperactivity. Although neuromodulators such as dopamine and noradrenaline are implicated, the synaptic circuit-level mechanisms underlying the disorder remain unclear. Previously, we established a chronic dorsomedial striatum (DMS) activation model, characterized by altered bridging collaterals of D1 receptor-expressing medium spiny neurons (MSNs). This model recapitulates core ADHD-like behaviors, including impulsive decision-making and working memory deficits. Here, we investigated brain circuits of this ADHD model mice in three aspects. First, neuronal recording in the DMS during free behavior showed chronic DMS activation enhances the D2-MSNs mediated locomotor control. Second, we examined the connectivity between Arkypallidal neurons in the globus pallidus externa (GPe)—the principal target of bridging collaterals—and the dorsal striatum. GPe Arkypallidal neurons form topographically organized projections to the striatum, and ADHD model mice displayed increased synaptic strength between bridging collaterals and Arkypallidal neurons. Chemogenetic activation of Arkypallidal neurons partially rescued ADHD-like phenotypes in these model mice. Third, we observed presynaptic release probability at D1-MSN to substantia nigra pars reticulata (SNr) synapses was significantly decreased. Since SNr regulates the activity of substantia nigra pars compacta (SNc) dopaminergic neurons, dopamine system may contribute to this ADHD-like phenotypes. We tried to impair dopamine release from SNc neurons using a vesicular monoamine transporter 2 (VMAT2) shRNA in both control and ADHD mice. Both groups exhibited exacerbated impulsive behaviors, highlighting the crucial role of dopamine. In summary, our findings expand the understanding of ADHD-related neural circuits to include both the GPe and SN, providing new insight into the complex synaptic mechanisms underlying ADHD pathophysiology.

Keywords : Impulsivity, Attention deficit-hyperactivity disorder, Dorsomedial striatum, Globus pallidus pars externa, Substantia nigra

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P-758

Mitochondrial calcium modulates odor-mediated behavioral plasticity in *C. elegans*

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Despite growing understanding of the various roles mitochondria play in neurons, how they contribute to higher brain functions such as learning and memory remains underexplored. Here, using the nematode *Caenorhabditis elegans*, we found that the mitochondrial calcium uniporter (MCU) pore forming unit MCU-1 is required for aversive learning to specific odors sensed by a single sensory neuron, AWC^{ON}. MCU-1 expression is required in the sensory neuron at the time of odor conditioning for proper behavioral response to 60 min of prolonged odor exposure. Through genetic and pharmacological manipulation, we show that MCU in AWC is activated in response to prolonged odor conditioning, causing mtROS production, leading to NLP-1 secretion. Interestingly, not all neuropeptides were controlled by MCU, suggesting that there is selectivity for this mode of neuropeptide release. Finally, we show that the timing of MCU activation, calcium influx into the mitochondrial matrix, as well as neuropeptide release, correspond with the OFF-neuron properties of the AWC neuron, and occur when AWC is

activated upon odor removal. Overall, our results demonstrate that, by regulating mitochondrial calcium influx, mitochondria can modulate the synaptic response to incoming stimuli in the sensory neuron, resulting in learning and modified behavior. Our future goal is to find additional neuropeptides in other neurons whose release is mediated by MCU, to see whether this can serve as a general strategy to independently control the release of different neuropeptide populations within the same neuron. To this end, we are currently conducting a battery of behavioral assays using the *mcu-1* mutant and the neuronal rescue strain.

Keywords : Mitochondria, Caenorhabditis elegans, MCU, neuropeptide, neuronal plasticity

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P-759

Acetylcholine switches the frequency-dependent activity filtering of thalamofrontal synapses and activity loop in short-term memory

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Short-term memory is associated with persistent neuronal activity in the prefrontal cortex (PFC). Reciprocal excitation between the mediodorsal thalamus (MD) and PFC has been proposed as a key mechanism supporting this persistent activity. However, the exact neural circuit mechanisms underlying short-term memory remain poorly understood. Notably, thalamocortical synapses are known to exhibit strong short-term depression. In this study, we demonstrate that acetylcholine functions as a switch for the cortico-thalamocortical activity loop. Specifically, we show that the fidelity of thalamocortical transmission during high-frequency activity is significantly enhanced by carbachol, a muscarinic acetylcholine receptor (mAChR) agonist, both in vitro and in vivo. This enhancement is mediated by increased intrinsic excitability of PFC neurons. Conversely, blocking mAChRs with atropine, a competitive antagonist, impaired performance in a short-term memory task. High-density recordings during behavior identified three medial PFC (mPFC) neuron populations: neurons active only during the cue period, neurons with sustained activity from the late cue period through the delay, and neurons with biphasic activity—showing activation both during the cue and again at the end of the delay and into the response period. These populations likely serve different functional roles: encoding external cues, maintaining information across the delay, and integrating cue encoding with motor planning or retrieval, respectively. Importantly, we found that direction-selectivity of mPFC neuron activity increased during the delay period in correct trials, both at the single-cell and population levels but was significantly reduced in error trials and in trials with mAChR blockade. Our findings demonstrate that muscarinic receptor activation is essential for maintaining the cortico-thalamo-cortical activity loop and sustaining task-relevant mPFC activity underlying short-term memory.

Keywords : Short-term memory, Acetylcholine, Medial Prefrontal Cortex, Thalamocortical synapses, Neuropixels

P-760

Asymmetric co-transmission by VGluT3+ neurons in the anterior bed nucleus of the stria terminalis

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Co-transmission has emerged as a key mechanism for fine-tuning synaptic function and is observed across various brain regions. Vesicular glutamate transporter 3 (VGluT3) is co-expressed with other vesicular transporters such as acetylcholine, GABA, and serotonin in areas including the striatum, hippocampus, and Raphe nuclei. In the anterior bed nucleus of the stria terminalis (aBNST), VGluT3 is abundantly expressed; however, the nature and functional role of neurotransmission from VGluT3$^+$ neurons in this region remain poorly understood. Here, we examined the synaptic output of VGluT3$^+$ neurons using pharmacological and electrophysiological approaches. We found that these neurons also co-release GABA and glutamate onto projecting areas, including the BNST and the paraventricular nucleus (PVN). While GABAergic currents were predominant, glutamatergic currents exhibited delayed onset and accounted for a smaller proportion of the total synaptic response. Importantly, glutamate and GABA were released independently, with glutamate showing higher release probability at lower stimulus intensities. These observations reveal a distinct mode of co-transmission in VGluT3$^+$ neurons and underscore the functional relevance of glutamate release, offering new insights into both region-specific and brain-wide roles of VGluT3-expressing circuits.

Keywords : VGluT3, Co-transmission, aBNST

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P-761

Thalamic Spike Frequency Adaptation Enhance Feature Selectivity via Intrinsic and Synaptic Modulation

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Accurately discriminating and perceiving sensory features in dynamic environments is critical for survival. In the primary somatosensory cortex (S1), spike frequency adaptation (SFA) triggered by prolonged stimulation is known to suppress overall responsiveness, yet paradoxically, it enhances feature discriminability by sharpening neural selectivity. While cortical mechanisms have been widely studied, the role of subcortical structures in shaping this transformation remains largely unexplored. Here, we show that the thalamus—long considered a passive relay—engages in active sensory refinement during sustained stimulation. Repetitive whisker input induces robust SFA in thalamic neurons, leading to a significant increase in feature selectivity. This adaptation arises from local thalamic mechanisms rather than top-down modulation. Mechanistically, thalamic adaptation tightens the temporal integration window for spike initiation, in part through synergistic interactions with synaptic depression at lemniscal inputs. Crucially, we identify Anoctamin-2 (Ano2), a calcium- activated chloride channel, as a key molecular player in this adaptation process. Our findings position the

thalamus as an active computational hub, capable of reshaping sensory encoding to optimize discriminability under sustained stimulation —a role previously underestimated.

Keywords : Thalamus, Spike Frequeny Adaptation, Somatosensation, Sensory processing, Adaptation

P-762

Synapse-specific N-glycosylation by B3gnt2 is critical for synaptic function and learning and memory behavior.

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N-glycosylation is an abundant and essential post-translational modification that regulates protein folding, trafficking, and stability. Despite its importance, its specific role at the synapse remains poorly understood. Here, we found synapse-specific N-glycan structure through glycome analysis comparing synaptosomes, which isolate synaptic components, and whole brain tissue. We also identified B3gnt2, which is involved in the formation of synapse-specific N-glycan structure. B3gnt2 knockdown in cultured primary cortical neurons and mouse CA1 pyramidal neurons led to weakened synaptic function and reduced intrinsic excitability. To determine whether synaptic dysfunction in CA1 pyramidal neurons caused by B3gnt2 knockdown leads to cognitive deficits, we conducted learning and memory behavioral test, including NOR, NPR, spontaneous alternation and Novelty preference test. Knockdown mice showed significant impairment in spatial and recognition memory, as well as reduced novelty preference. Our results demonstrate that synapse-specific N-glycan structure formed by B3gnt2 are critical for maintaining synaptic function and contributing to learning and memory behavior.

Keywords : N-glycosylation, B3gnt2, Synapse, Synaptic function, hippocampus

P-763

Analysis of AMPA receptor GluA1 subunit distribution at excitatory synapses of mouse auditory cortex upon acute nicotine exposure.

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Auditory information processing is involved in a wide range of behaviors such as sound recognition and learning. Auditory attention involves the cholinergic regulation of auditory cortex (ACx). Nicotine is known to improve attention via its actions on nicotinic acetylcholine receptors (nAChRs), but how its actions affect neurons to improve attention remains unclear (Ananth et al., 2023). Previous studies using local field potential recordings and flavoprotein fluorescence imaging have demonstrated that systemic nicotine exposure enhanced auditory evoked responses in ACx (Kawai et al., 2011; Nakanishi et al., 2022) suggesting that higher auditory function is vulnerable to nicotine exposure during adolescence. Although nicotinic acetylcholine receptors (nAChRs. These data suggested that nicotine exposure affects synaptic function in the cortex. Here, we biochemically analyzed the changes in synaptic molecules with a focus on excitatory synapses. Using synaptoneurosome prepared from ACx of early adolescent female FVB mice which include both pre- and postsynaptic components along with dendritic structures, we found that intraperitoneal nicotine injection increased Ser845 phosphorylation of the AMPA receptor GluA1 subunit within 10 minutes, without changing total GluA1 protein levels. This phosphorylation did not require concurrent white noise stimulation, indicating that systemic nicotine alone was sufficient to induce the biochemical changes. Next, we purified the postsynaptic density (PSD) fraction and quantified both the total GluA1 subunit and Ser845 phosphorylation. Under nicotine conditions, Ser845 phosphorylation and GluA1 protein levels increased by approximately 2.5-fold and 1.7-fold, respectively. In addition, nicotine administration increased the optical density of PSD-95 and tublin-βIII—proteins known to be structural components of the PSD—by approximately 1.5-fold and 2-fold, respectively. These results suggest that nicotinic activation rapidly induces GluA1 phosphorylation and PSD localization of GluA1-containing AMPARs and may also promote structural remodeling of the excitatory synapse in ACx.

Keywords : Auditory cortex, Cholinergic, nAChR, LTP, PSD

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P-764

Adolescent social isolation alters social novelty preference and synaptic transmission in the lateral septum

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Adolescence is a critical period when social experience shapes brain and behavioral development. Social isolation during this window leads to long-term emotional and social deficits. The lateral septum (LS), a stress-responsive region involved in social behavior, is implicated in mediating these effects, yet its plasticity after adolescent isolation remains unclear. Using a post-weaning social isolation (PWSI) mouse model, we examined social behavior and synaptic function in the LS. In the five-trial social recognition test, PWSI mice showed increased investigation time regardless of intruder sex, suggesting an altered response to repeated social stimuli. In the three-chamber test, PWSI mice lacked social novelty preference toward male conspecifics. Novel object recognition remained intact, indicating that the social novelty deficit was not due to impaired memory. Whole-cell patch-clamp recordings in LS neurons showed no differences in spontaneous excitatory or inhibitory postsynaptic currents (sEPSCs, sIPSCs). However, the amplitude of evoked excitatory postsynaptic currents (eEPSCs) was increased in PWSI mice. These findings provide a framework for understanding how adolescent social experience shapes circuit-level plasticity in the LS.

Keywords : Adolescence, Social isolation, Social novelty, Lateral septum, Synaptic transmission

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P-765

Synaptic correlates of operant learning and memory encoding

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Operant learning allows animals to associate specific behaviors with rewarding outcomes, yet the underlying synaptic and cellular mechanisms that support memory encoding during this process remain incompletely understood. In this study, we developed a custom operant chamber to train freely moving mice in a visual-cue-guided nose-poke task. Mice successfully learned to associate specific visual stimuli with nose-poke responses to obtain rewards. To identify neural populations activated during learning, we performed c-Fos immunohistochemistry and compared expression levels between trained and control animals. Additionally, temporal dynamics of neural activation were assessed by comparing c-Fos expression on days 4 and 8 of training, revealing stage-dependent engagement of brain regions. To probe the functional consequences of learning at the synaptic level, we performed ex vivo whole-cell patch-clamp recordings in the NAc core, uncovering electrophysiological changes associated with learning. Finally, using Dual-eGRASP, we visualized synaptic contacts between behaviorally activated mPFC and NAc neurons, identifying structural synaptic correlates of memory encoding in this pathway.

Keywords : Synaptic plasticity, Memory, Operant learning

P-766

Chemogenetic activation at LI11 mitigates atopic dermatitis via the vagus nerve–spleen axis

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Atopic dermatitis (AD) is a chronic pruritic dermatosis driven by Th1/Th2 immune imbalance, yet circuit-based therapeutic interventions remain underdeveloped. In a murine AD model induced by topical MC903, we injected an AAVretro vector encoding the excitatory DREADD hM3Dq around the LI11 acupoint, thereby confining receptor expression to LI11-innervating afferents and enabling ligand-gated activation of this neuronal subset without the confounding mechanical input of needle acupuncture. Chemogenetic activation of the LI11 pathway markedly lowered scratching behavior and composite dermatitis scores, normalized epidermal thickness, and diminished mast-cell and eosinophil infiltration. Lesional skin exhibited reduced transcripts of canonical Th1- and Th2-signature cytokines, whereas splenic flow cytometry revealed an increase in Foxp3□ regulatory T cells accompanied by systemic immune rebalancing. Retrograde tracer injection into the spleen labeled neurons in the dorsal motor nucleus of the vagus that showed robust c-Fos expression after LI11 stimulation, implicating a cutaneous–visceromotor vagal route in the observed anti-inflammatory actions. Surgical interruption of either the vagus nerve or the spleen abolished all therapeutic benefits, underscoring the necessity of an intact neural–immune axis. Collectively, these data demonstrate that selective neuromodulation at a single acupoint can recalibrate peripheral immunity and ameliorate AD-like inflammation, thereby highlighting the translational promise of circuit-guided acupuncture mimetics for inflammatory skin disease.

Keywords : Atopic dermatitis, Acupuncture, LI11, Vagus nerve, Neuromodulation

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P-767

Hippocampal encoding of a sequence of reward journeys

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Place cells in the hippocampus are known to represent positions of the environment but are also believed critical to encode spatiotemporal sequences. How place and sequence information are multiplexed in the hippocampus is largely unknown. Here we performed silicon probe recordings of hippocampal CA1 cells as mice ran head-fixed on a treadmill belt enriched with visual-tactile cues and had to recall a sequence of journeys to rewards that spanned over several belt cycles. The belt was 2-meter-long and 3 reward locations were interspersed over a distance of 6-meters. Preliminary analyses indicate that individual CA1 cells encoded fixed positions with respect to either belt layout or reward sequence, with the mouse performance to recall the reward sequence correlating with the cell encoding of reward sequence

Keywords : Hippocampus, dorsal CA1, Place cell, Spatial navigation

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P-768

Stimulation of the STING–GATs signaling pathway improves the cognitive dysfunction in APP-PS1 mice

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Tonic $GABA_A$ inhibition is a key regulator of hippocampus-dependent learning and memory. Our recent findings demonstrate that STING and its downstream signaling molecules, TANK-binding kinase 1 (TBK1) and interferon regulatory factor 3 (IRF3), influence tonic $GABA_A$ inhibition by modulating the expression of GABA transporters (GATs) in the central nervous system, thereby contributing to the regulation of hippocampal learning and memory processes. In this study, we evaluated the effects of activating the STING-GATs pathway on cognitive dysfunction in the APP/PS1 mouse model of Alzheimer's disease (AD). In the present study, littermate control (WT) and APP/PS1 transgenic mice were subjected to systemic intraperitoneal administration of either saline or cGAMP (a STING agonist) for 14 days. cGAMP reduced the aberrant tonic $GABA_A$ inhibition of dentate gyrus granule cells (DGGCs) in APP/PS1 mice, while it did not affect normal tonic $GABA_A$ inhibition in WT mice. The phasic current properties shown by sIPSC frequency, amplitude, and decay time constants were not different before and

after cGAMP treatment in both WT and APP/PS1 mice. Along with diminishing the aberrant tonic $GABA_A$ inhibition, learning and memory dysfunction, assessed by the Y-maze test and Barnes maze test, were significantly improved by systemic injection of cGAMP in APP/PS1 mice. Meanwhile, cGAMP had minimal effects on learning and memory in WT mice. In addition, motor activity and motor learning, assessed by the open field test and rotarod test, were not affected by cGAMP treatment in both WT and APP/PS1 mice. Interestingly, cGAMP increased GATs expression along with p-TBK1 and p-IRF3 in the hippocampus of both WT and APP/PS1 mice. Overall, our findings demonstrate that activation of the STING-GATs pathway sufficiently improves cognitive deficits in AD model mice.

Keywords : Alzheimer's disease, STING, GATs, hippocampus, GABAA inhibition

P-769

Nicotinic regulation of thalamocortical inputs to fast-spiking interneurons in mouse primary auditory cortex

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Acute nicotine exposure induces sensory filtering in the auditory thalamocortical system, where lemniscal thalamocortical (TC) transmission and intracortical excitatory synaptic responses carrying specific frequency information are enhanced, while those carrying nonspecific information are suppressed in primary auditory cortex (A1). The mechanism underlying this nicotinic enhancement of TC transmission is thought to involve the synchronization of axonal excitability and subsequent early (<20 ms) intracortical activities. The mechanism underlying this intracortical modulation likely involves the feed-forward inhibition of thalamorecipient pyramidal neurons (PNs) by fast-spiking (FS) inhibitory interneurons. Here, we investigated how nicotinic activation regulates this mechanism in the mouse TC system. We prepared auditory TC slices and investigated monosynaptic EPSCs in FS cells located in thalamorecipient layers 3/4. Like PNs, the local application of nicotine to the superior thalamic radiation enhanced the success rate of axon-evoked monosynaptic EPSCs in FS cells. However, unlike PNs, the local application of nicotine to recording FS cells in A1 reduced the success rate. These effects were diminished by dihydro-β-erythroidine, a selective antagonist of α4β2*-nicotinic acetylcholine receptors. An analysis of the paired-pulse ratio of EPSCs revealed no significant changes during nicotine application, suggesting that nicotine does not alter presynaptic release mechanisms. Nicotine had no significant effect on the frequency of spontaneous EPSCs, suggesting that the reduction in success rate occurs specifically at TC terminals. Finally, nicotine did not significantly affect monosynaptic inhibitory postsynaptic currents (IPSCs) but reduced the frequency of spontaneous IPSCs in PNs. These results suggest that cortical nicotine exposure can enhance intracortical activities by reducing TC excitatory inputs to FS cells thereby reducing feed-forward inhibition to PNs.

Keywords : Thalamocortical system, Nicotinic acetylcholine receptor, Fast spiking inhibitory interneuron, Primary auditory cortex

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P-770

Effects of Gamma-Ray Irradiation-Induced Neurogenesis Reduction on Cognitive Function in Monkeys

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The dentate gyrus of the mammalian hippocampus continues to generate new neurons throughout adulthood. These adult-born neurons become functionally integrated into existing circuits and are believed to contribute to learning and memory, particularly during the maturation phase when the new born neurons exhibit heightened synaptic plasticity. While the relationship between decreased adult hippocampal neurogenesis and impaired cognitive function has been well-documented in rodents, it is not clear whether these findings generalize to non-human primates. In the current study, gamma-ray irradiation was used to reduce the population of adult-born neurons in adolescent monkeys, we examined if irradiation impairs cognitive performance in shape discrimination task. The discrimination task was consisted of three difficulty levels (Level 1 to 3) and various retrieval delay times, each requiring progressively finer discrimination between shape pairs. During the baseline measurement, monkeys exhibited a pronounced decline in performance at higher difficulty levels as the delay increased. After irradiation monkeys with reduced levels of adult hippocampal neurogenesis showed significant deficits in the discrimination index compared to the baseline measurement before irradiation when the task required higher level of pattern separation. Additionally, we employed diffusion tensor imaging (DTI) to longitudinally track structural changes in the brain including neuronal loss in the dentate gyrus (DG). Our analysis suggests an increase in fractional anisotropy (FA), indicating alterations in white matter microstructure that may associated with reduced neurogenesis in the hippocampus after irradiation. Together, these findings suggest that decreased adult hippocampal neurogenesis impairs congitive function, fine pattern separation, and is associated with structural changes detectable through DTI, underscores functional significance of adult-born neurons in cognitive processing.

Keywords : Adult hippocampal neurogenesis, Pattern separation, Diffusion tensor imaging

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P-771

Long-Range Brain Network Modulation via Functionally Targeted Ultrasound Stimulation

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Transcranial ultrasound stimulation (TUS) is a promising non-invasive neuromodulation technique with high spatial and temporal

resolution. However, delivering ultrasound to deep brain regions, such as the hippocampus, requires traversing overlying structures, raising concerns about unintended effects. While focal cortical stimulation (e.g., M1) can induce synaptic plasticity such as long-term potentiation (LTP) and depression (LTD), these effects may reflect only partial circuit activation, insufficient to reorganize large-scale networks. To address these limitations, a pathway-based approach was developed to induce long-range propagation of ultrasound-evoked activity through anatomically and functionally connected circuits. Rather than targeting deep structures directly, upstream cortical nodes with known projections were stimulated. The thalamus to ACC was selected to examine whether TUS could activate a defined network. To mimic neural communication and modulate plasticity, ultrasound was configured to couple theta (5 Hz) and high-gamma (100 Hz) oscillations. The cerebellum, known for high-frequency oscillations and theta resonance (~5–7 Hz), was used as a stimulation site. Ultrasound was applied to the left M1, and ECoG signals were recorded from the ACC, bilateral S1 and thalamus, and deep cerebellar nuclei (DCN) using screw electrodes. Stimulation of the DCN induced phase–amplitude coupling (PAC) across multiple regions, with strong theta–gamma coupling observed in the right thalamus and bilateral S1. Activation patterns remained consistent regardless of anesthesia duration, indicating robust responses. Ongoing experiments using tungsten electrodes aim to provide higher-resolution data from bilateral thalamic VPM, ACC, and DCN. These findings suggest that targeting functional pathways with ultrasound may enable effective, distributed modulation of brain networks, offering a novel strategy for deep brain stimulation without direct penetration.

Keywords : non-invasive stimulation, long-range propagation, brain oscillations, neural circuits, synaptic modulation

P-772

CXCL5-CXCR2 constitutively maintains $GABA_AR$ tonic inhibition restraining seizure-prone changes in the hippocampus

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γ-Aminobutyric acid (GABA) the main inhibitory neurotransmitter is crucial for maintaining excitatory and inhibitory (E/I) balance in the brain. Even minor disturbances in E/I balance including altered activity of extrasynaptic $GABA_ARs$ ($eGABA_ARs$) generating persistent tonic inhibitory currents (I_{tonic}) can cause serious pathological conditions including increased seizure susceptibility. Here, we report that a key inflammatory mediator, C-X-C motif chemokine ligand 5 (CXCL5) an important role in regulating I_{tonic} by modulating the activity of $GABA_AR$ and GABA transporter 1 (GAT1). Using electrophysiology, we found that the I_{tonic} in dentate gyrus granule cells (DGGCs) was significantly less in CXCL5 knock-out (KO) mice than in wild-type (WT) mice. Exogenous GABA failed to mask the attenuation of I_{tonic} in CXCL5 KO mice, suggesting CXCL5 KO attenuated $eGABA_ARs$ activity in DGGCs. In addition, the GAT1 inhibitor (NO-711) induced a larger inward shift of $I_{holding}$ of DGGCs in CXCL5 KO mice than in WT mice, representing that CXCL5 intrinsically suppresses the activity of GAT1 in the hippocampal circuit. Along with diminished I_{tonic}, the pharmacological inhibition of CXCR2 (SB225002) mimicked the effect of genetic deletion of CXCL5 inducing the seizure-prone state. Taken together, these results show that CXCL5-CXCR2 maintains tonic $GABA_A$ inhibition by modulating the activity of $GABA_AR$ and GAT1, proposing a novel therapeutic target against the seizure-prone state.

Keywords : Tonic GABAA inhibition, GABAARs, GATs, CXCL5, Seizure

P-773

Each component of glutamate-glutamine cycle within the medial prefrontal cortex works differently to keep homeostasis and normal emotional behavior

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The regulation of glutamate (Glu)-glutamine (Gln) homeostasis in the medial prefrontal cortex (mPFC) plays a vital role in regulating emotional behavior, and its disruption by chronic stress may contribute to depression. However, the specific roles of individual components within the Glu-Gln cycle in relation to depression-related behaviors remain incompletely understood. This study aims to elucidate the specific roles of each component by implementing a cell- and region-specific conditional knockout (cKO) strategy. The genes encoding glutamine synthetase (GS), glutamate transporter 1 (GLT-1), and sodium-coupled neutral amino acid transporters SNAT-3 and SNAT-5 were selectively deleted in astrocytes, while SNAT-1 and SNAT-2 were ablated in glutamatergic neurons. GS and GLT-1 cKO mice exhibited depressive-like behaviors accompanied by elevated reactive oxygen/nitrogen species (ROS/RNS) within the mPFC. Notably, only GS cKO mice showed a marked reduction in Glu-Gln concentrations. Conversely, mice with cKO for SNAT-1, SNAT-2, SNAT-3, or SNAT-5 led to no significant behavioral changes. However, combined deletion of either SNAT-1/SNAT-2 or SNAT-3/SNAT-5 resulted in both depressive behaviors and lowered Glu-Gln levels, indicating synergistic disruption of cycle homeostasis. No systemic stress-related alteration was found in any cKO mice. Administering Gln, which is acknowledged for its antidepressant properties, to GS cKO mice ameliorated depressive behaviors and Glu-Gln concentrations. These findings elucidate the distinct and synergistic roles for the proteins involved in the Glu-Gln cycle in upholding appropriate Glu-Gln levels and mitigating ROS/RNS within the mPFC.

Keywords : Glutamate-Glutamine cycle, glutamine synthetase, glutamate transporters, sodium-coupled neutral amino acid transporters, depressive behaviors

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P-774

Pre-Cerebellar Brainstem Nucleus as a Source of Internal Timing Signals for Predictive Eye Movements

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The optokinetic response (OKR) is a reflexive eye movement that stabilizes vision by rotating the eyes to follow large-field visual motion. In goldfish, repeated exposure to visual motion stimuli with predictable reversal timing induces a predictive form of OKR (pOKR) (Marsh & Baker, 1997). After training, the eyes decelerate in anticipation of the stimulus reversal, a phenomenon known as predictive deceleration. Even in complete darkness, trained fish exhibit periodic eye velocity oscillations at around the learned period, referred to as predictive oscillations (PO). The cerebellum is essential for both the acquisition and expression of pOKR: cerebellectomy prior to training prevents learning, and removal after training abolishes the predictive response (Miki et al., 2018). During PO, Purkinje cells in the vestibulocerebellum fire in synchrony with eye velocity, suggesting that the cerebellum contributes to generating oscillatory motor commands. However, the origin of the learned periodic signal that drives PO remains unclear. A likely candidate is Area II, a brainstem pre-cerebellar nucleus in goldfish functionally analogous to the nucleus prepositus hypoglossi in mammals (Beck et al., 2006). Area II neurons encode both eye and head velocity (Straka et al., 2006), making it a potential source of timing signals for PO observed in the cerebellum. In this study, we recorded single-unit activity from Area II neurons during pOKR in goldfish. We found that their firing rates modulated in synchrony with the oscillatory eye movements during PO, supporting the hypothesis that Area II provides the periodic timing signals observed in Purkinje cell activity. Taken together with previous behavioral, neurophysiological, and anatomical evidence, our findings suggest that the timing information required for pOKR is transmitted, at least partially, from Area II to the cerebellum, which in turn drives extraocular muscles via the vestibular nuclei and ocular motor neurons.

Keywords : Velocity Storage Mechanism, Predictive Motor Control, Multisensory Integration, Rhythm

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P-775

Analgesic Effect of Human Placenta hydrolysate on CFA-Induced Inflammatory Pain in Mice

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To evaluate the efficacy of human placenta hydrolysate (HPH) in a mice model of CFA-induced inflammatory pain. TNF-α, IL-1β, and IL-6 are key pro-inflammatory cytokine factors for relieving inflammatory pain. Therefore, this study investigate whether HPH suppresses CFA-induced pain and attenuates the inflammatory process by regulating cytokines. In addition, the relationship between neuropathic pain and HPH was established by staining GFAP and Iba1 in mice spinal cord tissues. This study was conducted for a total of day 28, and inflammatory pain was induced in mice by injecting CFA into the right paw at day 0 and day 14, respectively. 100 μL of 20% glucose and polydeoxyribonucleotide (PDRN), and 100, 200, 300 μL of HPH were administered intraperitoneally twice a week. In the CFA-induced group, cold and mechanical allodynia and pro-inflammatory cytokine factors in spinal cord and plantar tissue were significantly increased. The five groups of drugs evenly reduced pain and gene expression of inflammatory factors, and particularly excellent effects were confirmed in the HPH 200, 300 groups. Meanwhile, the expression of GFAP and Iba-1 in the spinal cord was increased by CFA administration, but decreased by HPH administration, which was confirmed to suppress damage to peripheral ganglia. The present study suggests that HPH attenuates CFA-induced inflammatory pain through inhibition of pro-inflammatory cytokine factors and protection of peripheral nerves.

Keywords : Human placenta hydrolysate, Inflammatory pain, Neuropathic pain, Pro-inflammatory cytokine, glial cell

P-776

Low frequency Electro-acupuncture Treatment alleviates STZ induced diabetic neuropathic pain through noradrenaline system modulation

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Diabetic neuropathic pain (DNP) is a debilitating complication of diabetes that significantly impairs patients' quality of life, often manifesting as allodynia and hyperalgesia. Currently used antidepressant medications, particularly serotonin–norepinephrine reuptake inhibitors (SNRIs), exert analgesic effects primarily by increasing spinal norepinephrine levels. However, their long-term use is limited by central nervous system-related side effects and potential nephrotoxicity. This study aimed to compare the analgesic effects of low-frequency (2 Hz) and high-frequency (120 Hz) electroacupuncture (EA) at the ST36 acupoint in a mouse model of diabetic neuropathy and to elucidate the involvement of the spinal noradrenergic system in the underlying mechanisms. Subsequently, EA was applied to the ST36 acupoint in mice with streptozotocin (STZ)-induced diabetes, followed by behavioral assessments of mechanical allodynia and cold allodynia. In addition, antagonists for α1- and α2-adrenergic receptors were used to assess the involvement of the spinal noradrenergic pathway. EA at 2 Hz significantly attenuated hyperalgesia compared to 120 Hz, which was associated with increased spinal noradrenaline levels and activation of α1-adrenergic receptors. Bioelectric field simulations predicted a broader and deeper distribution of stimulation at 2 Hz compared to 120 Hz, which corresponded with the observed behavioral effects. EA at the ST36 acupoint exhibited frequency-dependent analgesic effects in diabetic neuropathy, likely mediated through activation of the spinal noradrenergic pathway. This study suggests the potential of low-frequency EA as a non-pharmacological analgesic therapy and provides a basis for its future application as an alternative treatment strategy for diabetic neuropathy.

Keywords : Bioelectric field simulation, Diabetic neuropathic pain, Electroacupuncture, Noradrenaline, ST36 acupoint

Systems and Computational Neuroscience P-777~P-825

P-777

EEG decoding study on model-based transfer learning

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Living organisms excel at transfer learning, the ability to form internal cognitive maps through experience and flexibly apply them to novel environments. Understanding the neural mechanisms is crucial for uncovering the basis of higher intelligence. We designed a rule-dependent spatial mapping task to investigate how the human brain constructs and utilizes cognitive maps during transfer learning. Participants performed a spatial decision-making task while 64-channel electroencephalogram (EEG) data were recorded. In each trial, subjects fixated on a central point, briefly viewed an image, and selected its associated location from five options arranged in a pentagon. During an intermediate delay, a color cue (red, blue, or yellow) indicated the rule: red for standard mapping, blue for a 72-degree clockwise rotation, and yellow for a 144-degree rotation, necessitating flexible adjustment of learned spatial associations. Behavioral results showed initially low accuracy that improved significantly with practice, reflecting cognitive map formation. The introduction of a new rule (blue cue) temporarily reduced accuracy, followed by rapid recovery. Notably, when a third rule (yellow cue) was added, performance remained stable, suggesting successful generalization of prior knowledge to novel conditions. To identify neural correlates of these adaptive behaviors, we developed a spatial position classifier using support vector machines and applied it to EEG data. Temporal generalization analysis revealed that location-specific neural representations emerged after image presentation and were flexibly updated following rule cues. These findings demonstrate that participants formed stable image-location associations and dynamically transformed them according to rule changes, as evidenced by EEG activity patterns. This study provides novel insights into the cortical dynamics of model-based transfer learning and the neural basis of cognitive map formation and flexibility.

Keywords : Transfer learning, Electroencephalogram, Model-based learning, Support vector machine, Temporal generalization analysis

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P-778

Inhibitory threshold modulation in visual cortex explains expectation-driven enhancement of sensorimotor behavior

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Organisms continually use prior knowledge to navigate dynamic environments, particularly when sensory input is uncertain. Previous research has demonstrated that motion expectations sharpen population tuning in the middle temporal (MT) area, thereby enhancing smooth pursuit eye movements. While these behavioral benefits are most evident under ambiguous sensory conditions, the neural mechanisms driving this enhancement remain unclear. In this study, we employed a recurrent neural network (RNN) model to investigate how prior expectations improve behavioral performance by modulating population tuning. The model revealed that neurons with preferred directions differing from the expected direction exhibited elevated response thresholds, reflecting selective inhibition. This inhibition sharpened tuning near the expected direction and reduced trial-by-trial variability in eye movements, leading to more stable behavior. These effects were pronounced under low-contrast conditions, not high-contrast conditions. Notably, even in the absence of explicit stimuli, spontaneous noise-driven activity showed biased population responses toward the expected direction, corresponding to directionally biased and less variable eye movements. To test the model's prediction of selective inhibitory modulation, we recorded local field potentials (LFPs) from area MT as a proxy for neuronal membrane potential. Consistent with the model, delta-frequency LFP power decreased as the difference between a neuron's preferred and the expected direction increased, supporting the presence of threshold modulation via inhibition. Collectively, these findings propose that behavioral benefits of expectation are mediated by inhibitory modulation of neuronal thresholds in visual cortex. This work provides a mechanistic explanation for how expectations refine sensory representations and stabilize motor outputs, highlighting feedback inhibition as a central mechanism of expectation-driven neural computation.

Keywords : Recurrent neural network, Middle temporal area, Smooth pursuit eye movement, Prior expectation, Population tuning

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P-779

Unbiased Imitation Optimizes Group Behavior

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Cultural evolution refers to how non-genetic information—such as behaviors, skills, and social norms—is passed on and accumulated across generations within human and animal groups (Richerson, 2008). Prevailing theories emphasize payoff- or success-biased imitation as the key driver of this process (Bridges, 2024), reflecting Darwinian models in biological evolution that highlight selection-based copying mechanisms (Mesoudi, 2009). However, real-world observations suggest that individuals often engage in payoff-irrelevant imitation (Bentley et al., 2004), raising the question: Is strategic selection necessary for driving cultural evolution? Here, combining animal behavioral data, human social learning experiments, and computational simulations, we show that unbiased random imitation alone can drive adaptive cultural change, even without payoff-based selection. First, in a behavioral analysis of a primate group learning a novel fruit foraging task, individuals with the greatest payoff gains tended to rely

on random, payoff-irrelevant imitation at early stages. Next, in a human psychological experiment, participants consistently adopted frequency-based random imitation during early trials, before any reliable link between choices and outcomes could be learned. To explore the mechanism further, we built a multi-agent evolutionary model. Each agent, defined by a behavioral trait affecting energy efficiency, used one of three strategies—payoff-biased imitation, random imitation, or pure trial-and-error behavior—and was evaluated by how well it acquired and used resources. Contrary to prevailing assumptions, under realistic payoff uncertainty, random imitation led to more consistent convergence toward optimal behavior, while selective imitation often caused premature convergence on suboptimal traits. These findings challenge the view that strategic selection is essential, highlighting random imitation as a robust mechanism for cultural evolution.

Keywords : Cultural evolution, Random imitation, Selective imitation, Primate data analysis, Multi-agent simulation

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P-780

Conjunctive Representation of Value and Space in the retrosplenial cortex

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The granular retrosplenial cortex (gRSC), a hippocampus-connected subdivision of the retrosplenial cortex (RSC), is involved in diverse cognitive functions including spatial navigation, episodic memory, and value-based decision making. To probe the underlying neural mechanisms, we examined the effects of inactivation and neural activity in the gRSC of mice performing a dynamic foraging task on a figure-8-shaped maze. Bilateral inactivation of the gRSC using muscimol severely impaired the animals' choice behavior. Analyses using reinforcement learning models suggest that gRSC inactivation increases choice bias while reducing learning rate. In addition, optogenetic inhibition of the gRSC during the reward-to-delay period reduced the probability of rewarded trials and disrupted win–stay/lose–switch strategies, indicating a role for the gRSC in guiding future decisions. Imaging data revealed that gRSC neurons encoded a range of task-relevant signals, including robust representations of decision value before choice and chosen value after choice, alongside spatial information. Further analysis revealed a positive relationship between decision value signals and spatial information in neurons significantly tuned to decision value. Moreover, gRSC pyramidal neurons were modulated by hippocampal axonal inhibition during the task, implying that hippocampal inputs convey task-related information to the gRSC. These findings support the view that the gRSC integrates value and spatial signals under hippocampal influence to guide flexible decision making. Ongoing work aims to elucidate the circuit-level mechanisms underlying this integration.

Keywords : Retrosplenial cortex, Value-based decision making, Hippocampal-cortical interaction

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P-781

Neural dynamics of emergent social roles in collective foraging by mice

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This study explores how individual foraging roles emerge among mice cohabiting with a predatory robot in the context of collective action for public goods. In a naturalistic experimental setting, each mouse could choose to work or freeride to obtain food. Across five groups, roles became clearly differentiated: "workers" successfully retrieved food, "participants" engaged but failed, and "freeriders" did not participate at all. Over time, work effort became concentrated in a few individuals, with work rates increasing from 19.8% to 69.6%, and freeriding rates rising from 39.3% to 60.6%. This role differentiation could not be explained by innate traits such as social rank, cognitive capacity, or motor ability. However, roles could be quantitatively characterized through behavioral metrics such as spatial occupancy patterns, kinetic energy, and latency to act, as well as through neural activity. Specifically, workers exhibited distinct neural signatures, with increased β-band (24–32 Hz) and decreased γ-band (70–90 Hz) power in the medial prefrontal cortex (mPFC), nucleus accumbens (NAc), and basolateral amygdala (BLA), while freeriders showed elevated γ activity in the PFC. Phase lag analysis revealed that β bursts originated in the PFC and were directed toward the BLA. During group foraging, the behavioral and neural patterns of top workers became increasingly distinct, enabling role prediction through linear discriminant analysis (LDA). Furthermore, group reorganization confirmed that roles are not fixed individual attributes, but are shaped through social context. Moreover, this reorganization was also accompanied by corresponding changes in β-band activity. These findings suggest that roles are not fixed individual attributes but are flexibly constructed and maintained through dynamic, context-sensitive neural processes shaped by ongoing social interactions.

Keywords : Social behavior , Foraging , Beta frequency

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P-782

Temporal Expectation Modulates Directional Expectation Through Alpha Oscillations during Sensorymotor Processing

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Alpha oscillations (8–12 Hz) have been implicated in mediating various forms of attention, including temporal, spatial, and feature-

based mechanisms. Despite its broad functional association, the precise computational role of Alpha rhythms remains unclear. In the present study, we found that Alpha oscillations are involved in regulating directional expectation. Previous study has shown that temporal expectation modulates directional expectation by confirming that directional bias and reliability (sharpening), indicators of directional expectation, change as a function of subjective temporal expectation for each participant [P-053, 2024 KSBNS]. To probe the neural correlates of the effects in EEG data, neural bias and sharpening effects quantified as Euclidean distance between the expected and other direction conditions, and the sharpness of population response estimated from an inverted encoding model, respectively. They were significantly correlated with temporal expectation only in occipital regions, suggesting that modulation of directional expectation affects sensory processing. To isolate frequency-specific contributions to these effects, we conducted a frequency lesion analysis by selectively removing individual frequency band and repeating the analyses. Remarkably, both effects were abolished when the Alpha oscillations were removed, indicating the involvement of Alpha in regulating directional expectation. We also found a decrease in Alpha power when temporal expectation was high, exhibiting lateralized suppression toward the expected direction. Importantly, when the Alpha was maximally attenuated through the lesioning, we found that the overall effects were significantly enhanced relative to the unfiltered EEG data. These findings suggest that lateralized Alpha attenuation, a phenomenon previously linked to the conjunction of temporal and spatial attention, plays a functional role in modulating directional expectation.

Keywords : Expectation, Prediction, Alpha oscillations, Sensorimotor processing

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P-783

The Role of Hippocampal Backprojections to the Medial Entorhinal Cortex in Spatial Cognition

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The hippocampus and medial entorhinal cortex (MEC) are key regions supporting spatial navigation. While the hippocampus contains place cells, the MEC hosts a variety of spatially tuned neurons, including grid cells, head-direction cells, border cells, and speed cells. These regions are highly interconnected, yet most research has focused on MEC-to-hippocampus projections, while the hippocampal backprojections to MEC remain largely understudied. Previous studies suggest that the formation of grid cells in MEC requires input from hippocampal CA1, indicating a critical role for CA1-to-MEC projections in spatial cognition. However, the underlying mechanisms remain poorly understood. In this study, we combined one-photon calcium imaging and electrophysiological recordings to examine how CA1 backprojection affect MEC network dynamics and spatial representations. We found that MEC predominantly receives input from a subset of CA1 place cells with fewer and smaller place fields but higher spatial information content. Chemogenetic inhibition of dCA1-to-MEC neurons significantly reduced both the power and frequency of MEC theta oscillations and decreased theta phase locking in MEC neurons. Chemogenetic inhibition of dCA1-to-MEC neurons led to a partial disruption of the hexagonal firing pattern in grid cells and caused a significant reduction in the speed modulation of speed cells. These findings demonstrate that hippocampal backprojection plays an essential role in modulating spatial representations and rhythmic coordination in the MEC.

Keywords : Medial entorhinal cortex, Hippocampus, Backprojection, Spatial cognition

P-784

Inter-individual entrainment of respiratory rhythms induced by huddling during sleep in mice

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Withdrawn

Social animals often exhibit physiological coordination during active interactions (Lindenberger et al., 2009), yet it remains unclear whether such inter-individual synchrony can emerge during co-sleeping, when external drivers of coordination are minimal. To investigate this, we employed CBRAIN–a wireless neural recording system for social animal developed in our lab (Kim et al., 2020)–to record local field potentials in medial prefrontal cortex and electro-olfactogram (EOG) from freely behaving mice. Co-housed mice were monitored during natural sleep episodes, with sleep categorized as solitary or huddling based on physical contact. EOG signals were temporally segmented with inhalation and exhalation cycles, validated through concurrent recordings with a nasal thermistor. We observed that huddling mice often exhibit structured patterns of inter-individual respiration: periods of in-phase and anti-phase locked breathing emerge transiently, with anti-phasic coupling occurring more frequently. These findings suggest that respiration may be entrained cross individuals during co-sleep, even in the absence of active communication. While sleep-state classification is ongoing, we hypothesize that such inter-individual respiratory locking could serve as a scaffold for broader physiological or neural coordination during sleep. This study introduces a novel approach to measuring respiration-based entrainment in naturalistic social sleep and offers preliminary evidence that physical proximity during rest can shape shared physiological dynamics across individuals.

Keywords : Sleep, Inter-individual coupling, EEG, Respiration, Huddling

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P-785

Modeling human elbow joint operation under proprioceptive error: a comparison between reinforcement learning and inverse kinematics

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Motor rehabilitation is essential for improving quality of life, but current strategies often overlook individual variability, leading to prolonged treatment, and increased costs. To address this limitation, model-based digital twins have gained attention for personalized rehabilitation due to their ability to make predictions with limited data and provide interpretable outputs. Approaches to model human sensorimotor operation can be broadly categorized into two types. The first is based on inverse kinematics (IK), which mathematically computes the motor commands required to achieve a target state. The second is based on reinforcement learning (RL), which learns policies through trial and error. Previous studies have typically assumed minimal sensory error—conditions under which IK performance was satisfactory. However, human proprioception exhibits markedly larger error than most artificial sensors, highlighting the need to compare models under realistic biological conditions. In this study, we compared RL and IK models under proprioceptive error. First, we conducted an elbow joint matching experiment, where subjects were asked to report the elbow joint angle by word and the contralateral arm, to collect proprioceptive error and motor output. We then simulated IK and RL models based on the measured proprioceptive error, to compare the performance of the two models. Performance was evaluated based on the similarity between simulation and experiment results (i.e., similarity in elbow joint angle mismatch), and the computing efficiency (i.e., computing resource usage). Specifically, the similarity was assessed using accuracy, precision, nonoverlap ratio, Kullback–Leibler divergence, and Wasserstein distance, while computing efficiency was evaluated using computing memory usage and execution time. The RL model outperformed the IK model in all metrics, suggesting that RL model better anticipates human sensorimotor operation than IK model under proprioceptive error.

Keywords : Motor rehabilitation, Sensorimotor operation, Reinforcement learning, Inverse kinematics, Proprioceptive error

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P-786

Spectral TRF(sTRF) – Linear Regression model using spectral information of EEG

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For decades, EEG-based auditory research has relied on event-related potentials (ERPs), which involve repeatedly presenting identical auditory stimuli to participants and averaging the resulting neural responses. Although informative for studying basic auditory processing and cognitive functions, ERP paradigms are poorly suited to real-world listening situations, where speech is continuous. Over the past 15 years, analysis techniques based on the temporal response function (TRF) have gained traction as an alternative. TRF methods allow researchers to track how the brain continuously encodes naturalistic speech, offering deeper insights into auditory attention under ecologically valid conditions. Over time, TRF approaches have been extended to incorporate multiple features of the stimulus including spectral characteristics. Meanwhile, while numerous studies have implied that each EEG frequency band reflects distinct aspects of speech processing, few studies analyzing EEG responses to auditory stimuli have focused on aspects in the frequency domain. In this study, we introduce a linear regression model that maps the spectral features of EEG to the presented auditory stimulus. This frequency-domain approach allows us to identify various features that may not be captured through conventional TRF methods. For instance, previous TRF-based studies have distinguished phonemic, semantic, or other levels of auditory processing by examining the latency of EEG responses. Due to overlapping peak latency ranges and low-amplitude TRF responses, detecting distinct cognitive responses to various stimulus features in the time domain can be challenging. Building on prior studies that have linked specific EEG frequency bands to distinct aspects of auditory cognition, this new approach to modeling the spectral structure of EEG has the potential to more clearly dissociate the neural processes underlying the perception of different stimulus features.

Keywords : EEG, TRF, linear model, spectral features

P-787

Versatile visual stimulation for awake mice in ultra-high field fMRI reveals diverse patterns in visual cortex

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Functional magnetic resonance imaging (fMRI) enables non-invasive investigation of brain-wide neural dynamics. Awake mouse fMRI further allows the study of cognitive processes through manipulation techniques such as optogenetics. However, delivering controlled visual stimuli in awake setups is technically challenging, especially in ultra-high field MRI. To address this, we developed a pixel-level visual stimulation system optimized for awake mouse 15.2T fMRI. To prevent magnetic attraction and signal interference in fMRI, a beam projector is placed 2 meters from the fMRI coil. Due to this distance and the limited bore size, front-mounted displays were not feasible. To overcome this, visual stimuli are generated by the projector and delivered through the tube to the rear of the screen, ranging from flickers to naturalistic scenes. Using this system, we explored whole-brain responses to visual stimuli in awake, head-fixed mice. We presented flickering stimuli (5 Hz) and moving gratings at 0.5, 2, and 8 Hz. Consistent with prior research, activation in the visual areas peaked at 2 Hz. Additionally, most strongly activated regions varied by frequency: 8 Hz gratings primarily activated the superior colliculus, while 2 Hz stimuli elicited stronger responses

in the visual cortices. Flicker stimuli enhanced activation in the anterior cingulate cortex, demonstrating that the system effectively drives distinct, stimulus-dependent cortical activation patterns. We are further developing this platform for virtual navigation and naturalistic scene presentation. In addition, we have integrated a reward delivery system and behavioral monitoring components to enable precise behavioral tracking. Combined with these features, this system can be used to study complex visual paradigms related to associative learning, spatial navigation, and cognitive planning in awake mouse fMRI.

Keywords : Awake mouse 15.2T fMRI, Visual stimulation system, Rear projection

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P-788

Projection-specific diversity of dopaminergic activity under aversive situations

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Dopamine signals in the brain have been widely implicated in reinforcement learning, particularly through encoding reward prediction errors (RPEs) as formalized by temporal-difference (TD) learning models. Mesolimbic dopamine activity, such as that in the ventral striatum (VS), has been shown to conform to a derivative-like form of a value function in both rewarding and aversive contexts throughout experiments. Meanwhile, the tail of striatum (TS) is the region that is recently known to play an important role in threat prediction. However, the computational basis has yet to be fully understood. We designed an active avoidance task using virtual reality in which mice learned to avoid receiving an electric shock by running out of a specific zone. Fiber photometry recording from VS in the previous work revealed that dopamine signals decreased at the entrance of the aversive zone and increased after they got out of the zone (n = 14 mice). Our probe experiments, including speed gain changes or teleportation in a virtual linear track, supported the TD RPE hypothesis (n = 8 -13 mice). In contrast, TS dopamine signals exhibited a markedly distinct pattern: it showed gradual increase of dopamine signal at the entrance of the shock zone and dip down at the end of it (n = 5 mice). Each shock reliably induced a phasic excitation in TS dopamine levels. We next designed a bar-moving protocol, which shows a horizontal bar moving down from the top and the animal receiving electric shock when the bar reaches the end. The TS dopamine ramped up as the bar moved down to get closer to the aversive stimuli, resembling the VS dopamine getting closer to the reward (n = 4 mice). Together, our results highlight the regionally distinct pattern of striatal dopamine circuits in shaping adaptive behavior under aversive conditions, providing a further understanding of how the brain encodes negative value through dopaminergic pathways.

Keywords : Avoidance, Aversive learning, Tail of striatum, Dopamine, Ventral Striatum

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P-789

Behavioral Identification of Loss Perception

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Loss—defined as the disappearance of previously available outcome whose existence was recognized with certainty—is a universal experience that profoundly shapes emotions, memories, and future choices. Despite its profound impact on emotions, memory, and behavior, the process of perceiving losses remains poorly understood. To address this, we introduce a behavioral paradigm using custom operant chambers with dynamic reward schedules to induce unexpected loss magnitudes. We employ a pose estimation tool to quantify behavioral patterns in relation to task events and chamber landmarks (e.g., nose-poking hole and reward port). By systematically varying the magnitude and context of loss and analyzing the resulting high-resolution behavioral data, we identified quantifiable behavioral signatures specific to loss conditions. With the systemic response data for various losses, we built a prediction model that can infer the degree of subjective loss in various situations. This approach provides a highlight translational potentials.

Keywords : Behavior, Emotion, Loss

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P-790

Intermittent social isolation enhances social investigation but impairs social memory in adult mice

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Social isolation profoundly impacts motivated behavior and neural plasticity. While the effects of acute and chronic social isolation have been extensively studied, the consequences of intermittent isolation during adulthood, particularly relevant to modern lifestyles, remain poorly understood. This study investigated the impact of intermittent social isolation (ISI) on social behavior and brain activation in adult male mice. Compared to group-housed controls, ISI males exhibited heightened social investigation and increased social interaction, reminiscent of craving-like behaviors. Intriguingly, this enhanced social investigation was accompanied by impaired social recognition memory in a three-chamber sociability test. Furthermore, ISI induced distinct patterns of neural activation in brain regions governing social processing, including the paraventricular nucleus of the hypothalamus, the intermediate part of lateral septum, the paraventricular nucleus of the thalamus, and the thalamic periventricular gray. Notably, ISI did not affect anxiety-like behaviors or spatial memory, emphasizing its specific impact on social domains. These findings demonstrate that ISI during adulthood selectively enhances social investigation while disrupting social memory in male mice, possibly mediated by distinct neural circuits. Understanding the neurobiological mechanisms underlying

these effects may inform interventions for individuals experiencing social isolation, an increasingly prevalent phenomenon in modern society.

Keywords : Intermittent social isolation, Social investigation, Social interaction, Social memory , Stress

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P-791

Two-Stage Learning Framework for Cross-Subject and Real-Time Seizure Detection Using Domain Generalization and Source-Free Adaptation

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[Introduction] Timely and accurate seizure detection is vital for enhancing the safety and quality of life in epilepsy patients. While many automated EEG-based methods have been developed, significant inter-subject EEG variability hinders model generalization. To tackle this, we propose a two-stage framework, SeizureDG-SFDA, combining Domain Generalization (DG) and Source-Free Domain Adaptation (SFDA). This reflects real-world clinical settings: a generalized model is first trained on multiple source subjects, then adapted to each new subject using only a small amount of unlabeled target data. [Methods] We evaluated the framework using EEG/LFP recordings from four rat models with spontaneous recurrent seizures after pilocarpine or kainic acid injection to the unilateral hippocampus (totaling 111 seizure events) under a strict cross-subject validation setup. [Results] SeizureDG-SFDA significantly outperformed conventional baselines, achieving an average F1-score of 92.6% and AUROC of 93.2%. t-SNE visualization confirmed that the DG strategy effectively learned domain-invariant representations, forming well-separated seizure clusters across subjects. Confidence and reliability analyses further showed that the model produces well-calibrated outputs, with stable score distributions and low calibration error. We further assessed real-time detection performance under various alarm-triggering schemes, analyzing the trade-offs between detection latency, sensitivity, and false alarm rate in practical deployment scenarios. [Conclusion] Comparative analysis against representative architectures such as EEGNet and EEGWaveNet confirmed that SeizureDG-SFDA delivers superior detection performance. These findings underscore its capability for both robust generalization and subject-specific personalization, highlighting its promise for real-time, cross-subject seizure detection in clinical applications.

Keywords : Seizure Detection, Domain Generalization (DG), Source-Free Domain Adaptation (SFDA), Cross-Subject Generalization, Real-Time EEG Monitoring

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P-792

Stochastic Innovation and Imitation Enhance Coordination in Multi-Agent Systems

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Reinforcement learning has achieved human-level performance in various real-world tasks, primarily within single-agent frameworks. However, in multi-agent systems, competition often arises due to limited resources and dynamically changing environments, disrupting global system optimization. Prior studies in multi-agent deep reinforcement learning have leveraged real-time information to help agents adapt, but such approaches have limited scalability in complex systems, due to high computational costs and non-stationarity. Interestingly, in nature, social animals have been observed to cope with similar challenges through a combination of stochastic behavior and imitation. Inspired by these biological principles, we propose a decentralized strategy that integrates stochastic and imitative behavior to mitigate competition among agents. We implemented a multi-agent road traffic simulation in which all agents navigate toward a common destination. In scenarios where every agent adheres to the optimal path, congestion intensifies as the number of agents increases. To alleviate this congestion, we first introduced a subset of innovators — agents that randomly deviate from the optimal path and select alternative routes. While this strategy significantly reduced congestion, the optimal level of randomness varied depending on the system size. To further address the challenges of a non-stationary environment, we then introduced imitators — agents that follow the behavior of the agent ahead. Notably, the combination led to further improvements in traffic flow compared to using innovators alone. Moreover, the most effective configuration emerged when most agents were imitators with only a few innovators. In conclusion, our findings highlight the potential of biologically inspired, decentralized strategies for scalable coordination in multi-agent systems.

Keywords : Multi-agent, Collective behavior, Social learning, Stochasticity, Imitation

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P-793

Hierarchical dynamics of information processing during auditory reversal learning

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Cognitive flexibility, the ability to adapt behavior to changing environments, is essential for survival. Although distributed neural networks are involved in this process, the precise hierarchical dynamics and regional differences in information processing remain unclear. In this study, we trained mice using an auditory reversal learning paradigm and recorded neural activity from the orbitofrontal cortex (OFC), posterior parietal cortex (PPC), auditory cortex (AC), and inferior colliculus (IC), regions implicated in auditory decision-making. By comparing neuronal activity across task rules, we examined how these areas encode distinct task-relevant

information. We first observed the auditory encoding properties varied across regions: in the AC and IC, frequency-specific activity remained stable across rule changes, while in the OFC and PPC, stimulus-evoked activity changed significantly after rule reversal. Notably, these changes were biased toward the Go stimulus, suggesting that reward-associated stimuli are more strongly represented in frontal and association cortices than in the sensory areas. We also found robust outcome- and action-related signals across all recorded areas. Interestingly, these signals were stable across rules in the IC, AC, and PPC, but highly flexible in the OFC. Additionally, we identified rule-dependent networks of pre-stimulus activity specifically in the OFC, indicating that this region encodes task rules beyond trial-based sensory or motor information. Together, our findings demonstrate that encoding properties evolve hierarchically across brain regions. Higher-order cortical areas such as the OFC play a critical role in flexible updating of task-relevant information during auditory reversal learning, thereby supporting cognitive flexibility.

Keywords : Cognitive flexibility, Reversal learning, Orbitofrontal cortex, Posterior parietal cortex

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P-794

Coordinated multi-frequency oscillatory bursts enable time-structured dynamic information transfer

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Slower (e.g., beta) and faster (e.g., gamma) oscillatory bursts have been linked to multiplexed communication in the brain, conveying top-down expectations and bottom-up prediction errors across distinct cortical layers. However, this oscillatory multiplexing theory faces key challenges: rhythms are nonlinearly coupled, and slow-phase modulation may be too sluggish to influence fast-timescale processing. Then, what are the deeper computational advantages of multi-frequency bursting? We investigate information transfer between two neural circuits, such as distinct cortical layers, generating sparse and transient oscillatory bursts with different intrinsic frequencies. By systematically exploring parameter space and applying unsupervised classification, we uncover a rich landscape of Multi-Frequency Oscillatory Patterns (MFOPs). These patterns include states where each population oscillates at its natural frequency or exhibits simultaneous/sequential multi-frequency bursts. Using transfer entropy, we show that distinct MFOPs correspond to specific Information Routing Patterns (IRPs) that selectively boost or suppress directional information flow at precise times and forming temporal graph motifs. Remarkably, the slower population can transmit information within latencies shorter than a single fast oscillation cycle or influence multiple fast cycles within a single slow cycle dynamics incompatible with simple frequency-based multiplexing. We further demonstrate that IRPs regulate the responsiveness to spikes occurring at specific delays, dynamically weighting historical signals. These findings reveal that coordinated bursts across frequencies enable flexible, temporally-structured information exchange, modulating spike timing far beyond conventional one-frequency/one-direction schemes. Multi-frequency activity thus provides a self-organized substrate for rich, adaptive information routing in the brain.

Keywords : Neural oscillation, Communication, Multi-frequency, Information transmission

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P-795

Real-time and periodic individual identification in freely moving mice using a bit-based LED tagging system

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Accurate identification of individual animals is essential for studying social behavior in freely interacting animals. However, conventional methods—such as fur dyeing, tail markings, or ear punches—tend to degrade over time and are often hard to distinguish in recorded videos due to low resolution or poor camera angles. These issues limit their usefulness in long-term or naturalistic experiments. To overcome this, we developed a lightweight, programmable LED tagging system that supports both continuous and event-triggered individual identification. This system encodes metadata (e.g., sex, generation, ID) into temporal LED sequences via a flexible bit-wise encoding scheme. The device operates in two modes: a self-timed mode that emits LED sequences at regular intervals, and an event-triggered mode that activates the same sequence in response to an infrared (IR) signal. This dual-mode function supports both autonomous operation and behaviorally relevant intervention without manual switching. Predefined LED sequences are assigned to each animal and can be decoded post hoc from standard video recordings. The mapping between sequences and individuals is externally recorded by the experimenter. Weighing under 1.8 grams with a 30 mAh rechargeable battery, the system operates for over 200 hours at 1-minute intervals or up to 720 hours at 5-minute intervals. Its emitted LED signals are compatible with standard RGB video and can be synchronized with frame-based behavioral tracking tools like DeepLabCut. The system can complement zone-specific RFID or event-triggered paradigms by providing an independent LED signal for individual identification. Overall, this method offers a minimally invasive, scalable, and power-efficient solution for long-term identification of individuals in socially and ethologically relevant experiments. Its small form factor and compatibility with existing behavioral analysis pipelines make it a versatile tool for neuroscience research.

Keywords : LED tagging, bit-wise encoding, event-triggered tagging, individual identification

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P-796

Serial Dependence in Categorical Decision-Making on Human Faces and Biological Motion

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In a previous study, Lee et al. (2025) observed that in serial decision-making episodes, serial dependence increases as the number of choice options increases. They proposed that the decision variable is updated within an abstract decision space in a Bayesian fashion. In this space, a greater number of choice options leads to finer prior distributions, which in turn results in stronger serial dependence. Since Lee et al. examined only relative decision-making tasks, it remains an open question whether the same account could also apply to natural categorization tasks, such as gender categorization. We hypothesized that the abstract decision space proposed by Lee et al. also operates in categorical decision-making tasks. Based on this, we predicted that serial dependence would increase as the number of choice options increases in gender categorization. We recruited participants via the online platform Prolific. They made gender judgments about facial images using either a 2-level or 8-level gender rating scale. We utilized deep learning algorithms to generate natural-looking, controllable images that allowed fine modulation of gender representation. We found that serial dependence was indeed stronger when participants used the 8-level rating scale compared to the 2-level scale. To test whether the proposed decision space is truly abstract and generalizable, we conducted an additional experiment in which the type of stimulus alternated on a trial-by-trial basis. Participants made gender ratings on human faces and biological-motion animations, presented alternately. We observed similar results. These findings suggest the possible existence of an abstract decision space that underlies both relative and categorical decision-making, and is also generalizable across different types of stimuli.

[Reference] Lee, H., Lim, J., & Lee, S. H. (2025). Belief updating in decision-variable space: past decisions with finer granularity attract future ones more strongly. iScience.

Keywords : Decision-making, Gender recognition, Human face, Biological motion, Machine learning

P-797

Music Genre Similarity in Human Brain: Investigation of Genre Classification Regions Using fMRI Data and Comparison with Actual Classificat

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Human music perception engages a distributed network of cortical regions that support basic auditory analysis, sensorimotor integration, and affective evaluation. Using the OpenNeuro Music Genre fMRI dataset (Nakai et al., 2022), current study investigated the neural representation of music genre similarity in the brain. The dataset consists the functional MRI data from five subjects listening to 540 music pieces across 10 genres. In contrast the microscopic approach of original study, current study adopted standard macroscopic whole brain analysis, and contrasts each pair of the genres. At the individual level, genre-specific brain activations were observed in the sensorimotor cortex, occipital lobe, superior temporal gyrus (auditory cortex), and anterior cingulate cortex. The highest neural contrast was found between disco and jazz, while the lowest was between jazz and metal. Group-level analysis revealed consistent activation in the superior temporal gyrus and anterior cingulate cortex, suggesting these regions are non-genre-specific music processing areas. The neural representation similarity between genres was quantified using Pearson correlation of activation patterns, and normalized similarity matrix was generated. Blues and rock exhibited the highest neural similarity, while disco and country showed the lowest. To compare neural and musical similarities, a RDM analysis was conducted using a music similarity matrix by Brandl & Schedl (2021). The Spearman correlation between neural and musical RDMs was not statistically significant ($\rho = 0.0768$, $p = 0.616$), and couldn't find the similarity between macroscopic level brain activity and feature-based genre representations. This whole-brain contrast of genre pairs complements the original study's fine-grained, voxel-level work—showing that genre-specific representations emerge only at the microscopic scale, whereas our macroscopic analysis reveals the shared network underlying all music listening.

Keywords : Music Genres, Neuroimaging

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P-798

Roles of entorhinal cortex and anterior thalamic inputs in population-level representation of egocentric geometry in the retrosplenial cortex

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The retrosplenial cortex (RSC) plays a key role in integrating spatial information for navigation by transforming allocentric inputs into egocentric reference frames. While individual neurons in RSC are known to encode egocentric geometry—such as the angle and distance of walls and corners relative to the animal—less is known about how such representations emerge and are modulated at the population level. To investigate how egocentric geometry is encoded at the population level in the RSC, we investigated the population coding of egocentric geometry in the RSC and the contributions of two major input pathways: the medial entorhinal cortex (MEC) and the anterior thalamic nuclei (ATN). Using in vivo calcium imaging in freely moving mice, we recorded activity from excitatory RSC neurons under control conditions and during pathway-specific optogenetic inactivation (590 nm) of MEC or ATN projections. Population-level activity patterns revealed structured low-dimensional manifolds corresponding to distinct egocentric geometrical features. Dimensionality reduction using UMAP showed that MEC inactivation led to a degradation in the clustering of geometric representations without altering their overall topography, indicating a loss of precision in population coding. In contrast, ATN inactivation disrupted the organization of the representational space itself, suggesting a breakdown in the stability of egocentric tuning across the neuronal ensemble. These findings suggest that cortical and thalamic inputs play complementary roles in shaping population-level representations of egocentric geometry in the RSC. While MEC input may enhance the precision of such representations, ATN input appears to be important for

their stability. These results provide a circuit-level perspective on how egocentric spatial information is organized in the brain.

Keywords : Retrosplenial Cortex (RSC), Population Coding, Calcium Imaging, Egocentric Geometry

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P-799

Distributed neural dynamics underlying sensory-to-motor transformation during olfactory decision making

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Perceptual decision-making requires the transformation of sensory inputs into motor outputs through intermediate processes such as working memory and action planning. While higher-order areas are often emphasized in these processes, how these functions emerge across the brain during learning remains unclear. To address this, we combined acute and chronic Neuropixels recordings in mice performing an olfactory delayed match-to-sample task. In the acute experiments, we recorded dozens of brain areas spanning the full olfactory decision-making pathway—from early sensory regions to the hippocampal, frontal, and motor areas. Early olfactory sensory areas such as the anterior olfactory nucleus (AON) showed robust delay-period odor-selective activity and match/non-match category encoding, dissociable from licking direction. In contrast, the anterior-lateral motor cortex (ALM) encoded licking direction but not perceptual decision, while the orbitofrontal (OFC) and prefrontal (PFC) cortices carried mixed decision and motor representations. To examine how these representations develop with learning, we performed chronic Neuropixels recordings in the AON, OFC, and ALM, tracking the same neurons across weeks. Odor-selective delay activity in the AON increased with learning, and categorical decision- making signals became more prominent and stable. These learning-related changes were also observed in downstream areas, suggesting that task-relevant signals are increasingly transformed and utilized across regions. Together, our findings reveal a learning-dependent reorganization of decision-related neural activity across distributed brain regions, where early sensory areas not only maintain sensory information but also serve as critical hubs for initiating flexible, experience-driven sensorimotor transformations. This challenges classical hierarchical views and highlights the adaptive nature of brain-wide networks in linking sensation to action.

Keywords : Neuropixels, Decision making, Olfactory, Sensory

P-800

Natural image training enables robust generalization in visual number sense of deep neural networks

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Number sense—the ability to estimate the number of objects in a visual scene—has been observed across diverse animal species, including bees, chicks, and human infants. Such a widespread presence suggests an evolutionary origin and may further reflect an inductive bias toward forming abstract internal representation that facilitates generalization across various contexts. Yet it remains unclear how natural environmental experiences give rise to this capacity. To address this question, we use deep neural networks as a testbed to investigate whether training with naturalistic images fosters robust and generalizable visual number representations. We compare two convolutional neural networks: one pre-trained on object classification using natural images (with only the final layer fine-tuned) and the other trained *de novo* on dot-array-based number estimation task. Both models were trained with a set of dot arrays with specific number, size, and spacing, and their behavioral performance was tested on novel dot arrays in different ranges of numerical and non-numerical features. In all cases of such a generalization test, pre-trained models maintained robust performance while *de novo* models struggled to generalize under novel conditions. To elucidate the differences between networks, we analyze hidden-layer activations using principal component analysis. Both models exhibited an ordered number line aligned with the first principal component, with its explained variance increasing in deeper layers, indicating progressive disentanglement of numerical information from other visual features. Notably, pre-trained networks showed higher-dimensional and more distributed representations in intermediate layers, which may underlie its superior generalization ability. Together, our results suggest that statistical regularities in natural images serve as a powerful inductive bias, facilitating the emergence of robust visual number sense.

Keywords : Numerical cognition, Deep neural network, Generalization, Inductive bias

P-801

Dopaminergic activities in the striatal subregions show distinct representations but common learning mechanisms

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Dopamine (DA) is a key neuromodulator in associative learning. In the ventral striatum (VS), DA signals have been well-characterized as signed reward prediction errors (RPEs), exhibiting excitation and inhibition to positive and negative valence, respectively. In contrast, DA signals in the dorsal striatum (DS) are thought to encode unsigned RPEs (salience), responding with excitation regardless of valence direction. Here, we explored how dopaminergic systems process positive, negative, or the sum of the two valences when animals underwent associative learning between neutral visual cues and these outcomes. We found that DA responses in the DS (n=11 mice) were most strongly excited by the combined condition, supporting the idea that dorsal DA signals reflect the sum of the unsigned RPEs. We further investigated DA dynamics using a reversal learning task. Cues previously predicting rewards were changed to predict shocks, and vice versa. When the outcome is suddenly reversed, DA in VS (n=12) showed greater prediction error responses (e.g., greater excitation to reward; greater inhibition to shock), which can be explained by the RPE hypothesis. In DS (n=8), interestingly, while the magnitude of DA response to the reversed

outcomes is smaller, the responses are still well explained by prediction error based on unsigned signals. Finally, we introduced another neutral cue that randomly predicted reward (50%) or shock (50%). DA response to the cue in VS (n=8) is the average of the cue responses to the two opposite USs, expected by temporal-difference (TD) RPE learning model. In line with this, cue response in DS (n=6) is the average of the cue responses to the two USs, suggesting that DS cue response is a result of the TD 'unsigned' RPE model. These findings suggest that striatal DA signals encode opposite valences through distinct regional formats, yet share a unified learning mechanism that supports flexible adaptation to complex, mixed-valence environments.

Keywords : Mixed valence, Associative learning, Striatal Dopamine, Ambivalent inputs, RPE

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P-802

Multiple visual features in naturalistic environments shape steering responses in flying Drosophila

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Neuroscientists studying vision have focused on how neural circuits respond to individual visual patterns. In Drosophila melanogaster, circuits tuned to specific patterns—such as moving bars, spots, and gratings—have been identified. However, in naturalistic environments flies are exposed to rich visual scenes that include optic flow, a whole-field motion cue driven by self-motion, object motion with distinct dynamics, or both occurring simultaneously. To understand visual processing in response to naturalistic scenes, we measured behavioral and physiological responses of Drosophila to naturalistic videos and developed models that are designed to capture the underlying neural computations. First, we recorded wing responses of tethered flies to panoramic, naturalistic videos and found that steering behavior was more reproducible across trials and flies when the videos contained optic flow. This raised a key question: Does optic flow play a dominant role in shaping steering behavior in Drosophila? To address this, we built a model that predicts wing steering based on optic flow extracted from the videos. The model accurately predicted wing responses and performed especially well for videos with prominent optic flow, highlighting its significant contribution. To identify the physiological basis of this processing, we performed whole-cell patch-clamp recordings from Horizontal System cells, a well-known class of optic flow detectors. The neural responses aligned with our model's predictions, showing that lateral asymmetries in optic flow strongly correlated with steering signals. To account for visual features beyond optic flow, we extracted the positions of moving objects in the videos. Incorporating both object motion and optic flow as inputs improved model performance in predicting wing steering. Together, our study represents an important step toward understanding how multiple visual features orchestrate steering behavior in natural environments.

Keywords : Drosophila, Visual system, Naturalistic scene, Modeling

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P-803

Dopamine activity in the tail of striatum predicts avoidance behaviors in complex threatening situations

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Previous animal studies have commonly used discrete sensory cues to associate fear. However, in humans, fear memories are often triggered by complicated visual elements. To address this, we presented a visual pattern as a cue for the fearful event. A mouse was placed in a transparent chamber surrounded by computer monitors to present the patterns, with a foot-shock grid floor. The chamber was filmed with a top-view camera to quantify movement energy made by the mouse. We tested whether mice can actively run away from a visual pattern (conditioned stimulus, CS) to avoid an electric shock (unconditioned stimulus, US). We split the chamber into "shock zone" and "safe zone". Each zone was notified by distinct visual patterns on the screen. The position of the shock zone was randomly assigned on each trial based on the mouse's current position. If the mouse did not leave the shock zone for the period of CS presentation (7s), the animal received a US (0.2mA, 2s). Well-trained mice were able to distinguish the two patterns and run away towards the safe zone before the US, with a success rate of over 80% (n = 4 mice). During the task, dopaminergic activity in the ventral striatum (VS) and tail of the striatum (TS) was measured using fiber photometry. The activity in VS dropped at the onset of all types of CS including the "safety" pattern, indicating that it did not differentiate pattern types. However, dopaminergic responses in TS clearly reflected the meaning of each pattern. The level of response was stronger when the mouse confronted the "shock" pattern than the "safety" pattern. Furthermore, TS activity remained elevated throughout the CS period in trials where the mouse failed to avoid the shock, whereas in successful avoidance trials, it returned to baseline at the time of crossing. These observations indicate that the dopamine signals in TS may selectively encode threat-predicting stimuli, while VS dopamine may signal more general aversive motivations.

Keywords : Active avoidance, Fear memory, Striatum, Dopamine

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P-804

Neurodevelopment-inspired learning of abstract and compositional representations

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The brain's perceptual learning begins with degraded sensory abilities—poor acuity and limited color sensitivity—that gradually refine. Although early deficiencies appear as inevitable handicaps, studies of congenitally blind patients gaining sight later reveal that bypassing this immature phase causes persistent cognitive impairments. By contrast, AI systems typically train on fully detailed inputs from the outset, leading to shortcut learning and overfitting to task-irrelevant, spuriously correlated cues. Here, we propose a curriculum of gradually

increasing sensory detail—akin to biological maturation—to steer models toward abstract, generalizable representations. In bias-sensitive image classification tasks where relevant features and misleading biases correlate spuriously during training, we compare conventional models—trained on high-resolution, full-color images—with "human-inspired" models that first learn from low-resolution, grayscale inputs and gradually increase detail. When evaluated on samples with removed spurious correlations, conventional models fail to generalize, whereas human-inspired models remain robust, mirroring the bias-resistance of human psychophysical results. Analysis of internal representations shows that only human-inspired models form latent codes for task-relevant features; conventional models stay trapped by biased attributes. Moreover, visual reconstructions from the representation of human-inspired models flexibly generate novel combinations of intrinsic features and bias attributes, demonstrating their compositionality that is absent in conventional models. These findings suggest that early sensory immaturities are not mere developmental constraints but evolutionarily adopted guides for learning abstract, compositional representations. Our results offer an effective solution to shortcut learning in AI and provide insight into why patients who regain sight later often struggle with visual tasks despite restored acuity.

Keywords : Sensory maturation, Shortcut learning, Representation learning, Debiasing, Compositionality

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P-805

Cerebellar Cortical Initial Learning: A Strategy for Adaptation in Non-stationary Environments

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Cerebellar motor learning is mediated by a dual system: a complex, high-cost cerebellar cortex and a simple, low-cost cerebellar nuclei. Previous work has shown that memories are differentially transferred from cortex to nuclei based on task difficulty, governed by a normative principle optimizing a bias-variance-overhead trade-off. However, why learning consistently initiates in the high-cost complex system remains incompletely understood, especially in dynamic environments. We hypothesize that this initial reliance on the complex system is not merely for computational advantage in static tasks, but is a key strategy for rapid adaptability and resilience in unpredictable, non-stationary environments. To test this, we designed a 'Ground Truth Shift' simulation and compared the performance (Mean Integrated Squared Error; MISE) of a simple model (1-layer linear regression) against a complex model (4-layer multi-layer perceptron) whose learning was inspired by cerebellar plasticity, employing an online, error-driven update analogous to a delta rule. During the environmental shift, the complex model showed vastly superior adaptability with faster error reduction than the simple model. It also demonstrated greater resilience, recovering performance more effectively upon returning to the stable phase. Future work will apply this adaptability-focused principle to a cerebellum-mimicking dual-system model to further explore its implications for system cost and performance. These simulations will then guide the design of *in-vivo* experiments to validate the adaptive role of the cerebellar cortex. This research adds the critical dimension of environmental dynamics to the normative principles of cerebellar learning, offering a more comprehensive understanding of its functional architecture.

Keywords : Cerebellum, Dual learning system, Adaptation, Non-stationary environment, Computational neuroscience

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P-806

Accumbal Neuropeptide Y Neurons Promote Reward Learning through Value Updating for Palatable Food

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Past pleasurable experiences influence future eating behavior. However, the neural mechanisms of how past food values are encoded and guide future food preferences remain unclear. Here, we demonstrated that neuropeptide Y (NPY) neurons in the nucleus accumbens (NAc) update the encoding of food value and promote reward learning for palatable food. We demonstrated that NAc^{NPY} neurons selectively respond to palatable food and food-associated cues. We also revealed that subpopulations of NAc^{NPY} neurons specifically track changes in value representations via updating outcomes. We showed that NAc^{NPY} neurons bidirectionally facilitate overeating through repeated positive experiences. Also, these neurons are necessary and sufficient for the formation of reward memory, specifically for palatable food. Electrophysiological recordings and in-vivo two-color imaging indicated that NAc^{NPY} neurons are directly activated by dopamine. These findings uncover a crucial role of NAc^{NPY} neurons in reward learning for palatable food, offering new perspectives on the mechanisms underlying food addiction and obesity.

Keywords : Nucleus accumbens, Neuropeptide Y, Food addiction, Reward Learning, Dopamine

P-807

Connectome-GAN: A Generative Model for Transforming Resting-state Brain Networks to Task-specific States

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Predicting task-specific functional connectomes from resting-state fMRI is a low-burden alternative to resource-intensive task-fMRI, but prior linear approaches such as C2C models may be limited in capturing the complex, non-linear dynamics of brain network reorganization. To overcome this, we developed a GAN-based model

to accurately transform an individual's resting-state to a task-specific fMRI connectome. Our GAN architecture employs convolutional layers for spatial features and a structure-preserving loss that captures both global and local connectome patterns to maintain network topology and symmetry. The dataset comprised resting-state and seven task fMRI data from 316 HCP subjects. Both C2C and GAN models were trained and tested using leave-one-out cross-validation (LOOCV) to generate task-specific connectomes. Model performance was evaluated using three metrics: spatial correlation, MSE, and modularity. Furthermore, we validated behavioral relevance by predicting fluid intelligence using connectome-based predictive modeling (CPM) by 10-fold cross-validation (1000 iterations). Our GAN showed improved performance over C2C models, achieving higher spatial similarity (0.70-0.74 vs. 0.64-0.72) and lower MSE (0.0074-0.0088 vs. 0.0077-0.0094) to empirical connectomes. GAN-generated networks more closely matched empirical task connectomes compared to C2C models across all seven tasks. Lastly, for fluid intelligence prediction using CPM, GAN-generated connectomes (r=0.159-0.239) more closely approximated the predictive performance of empirical task connectomes compared to C2C models (r=0.158-0.212), with both transformation methods substantially outperforming empirical resting-state connectome (r=0.0741). This study demonstrates that our GAN-based model improves rest-to-task connectome prediction by effectively capturing non-linear brain dynamics

Keywords : Brain connectome, fMRI, GAN, AI model, Computational Neuroscience

P-808

Molecular and Functional Heterogeneity of CaMKIIα+ Neurons in the Lateral Hypothalamus: Encoding Appetitive Motivation Over Food Consumption&

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The lateral hypothalamus (LH) contains diverse neuronal populations with distinct roles in regulating eating. Calcium/Calmodulin-Dependent Protein Kinase II alpha (CaMKIIα+) has long been recognized as a marker for excitatory neurons. In the lateral hypothalamus (LH), these excitatory neurons are known to suppress eating behaviors. However, our interpretation of scRNA sequencing and MERFISH data reveals molecular heterogeneity within LH CaMKIIα+ neurons, encompassing Vglut2- positive, Vgat- positive, and non-canonical neuronal subtypes. In vivo fiber photometry and miniature endoscope imaging show that these neurons are sequentially activated during appetitive behaviors, such as food-seeking and operant tasks, but are suppressed upon food contact. The activation timing of each LH CaMKIIα+ neuron population was consistently preserved in the same sequence, regardless of the type of appetitive behavior. Interestingly, optogenetic activation of all LH CaMKIIα+ neurons suppresses food intake, while activation of LH CaMKIIα+ Vgat+ neurons increases both appetitive and consummatory behavior. Our study highlights the heterogeneity and specific activation patterns of LH CaMKIIα+ neurons, which primarily encode the appetitive phase of eating behavior.

Keywords : Lateral hypothalamus, Appetitive behavior, CaMKIIα+

P-809

Multi-modal gating of visual input tunes the *Drosophila* heading compass

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Navigation of animals is a complex behavior that enables movement from one location to another. To navigate efficiently, animals must continuously process dynamic sensory information from both the external environment and their internal states. In *Drosophila*, the central brain region for navigation receives visual position information through the well-characterized pathway called anterior visual pathway (AVP). The AVP consists of parallel channels and layers that transmit visual signals, but all of them end with a specific class of neurons known as ring neurons. If flies modulate their navigational sensory input based on internal and external conditions, ring neurons can be a key bottleneck for this modulation. To test this hypothesis, we analyzed the recently released full-brain connectome of *Drosophila* and identified a candidate neuron, AOTU046, which innervates most ring neurons in specific AVP channels. Using artificial activation of AOTU046, we found that it can suppress the visual position information conveyed by ring neurons. To determine the conditions under which AOTU046 is active, we performed whole-cell patch-clamp recordings and monitored its activity change under various given conditions. First, AOTU046 exhibited a distinctive receptive field optimized for detection of horizon shifts. Second, it showed an asymmetrical response to changes in brightness, but not to specific visual patterns. Finally, AOTU046 was most strongly activated when the fly was walking, compared to other conditions. These findings suggest that AOTU046 can dynamically modulate visual position information to the navigation center by sudden changes in the visual environment and the locomotion state. Further experiments will investigate whether AOTU046 directly influences or supports navigational behavior of flies. This research highlights the importance of modulatory signals that operate outside traditional feedforward sensory pathways.

Keywords : Navigation, Drosophila, Connectome, Visual processing, Behavioral genetics

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P-810

Parallel top-down projections from the posterior parietal cortex facilitate behavioral flexibility in auditory reversal learning</

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The ability to flexibly modify behavior in response to changing environmental contingencies is fundamental to adaptive decision-making. However, how distributed brain circuits coordinate rapid adaptation remains unclear. Here, we demonstrated that the posterior parietal cortex (PPC) orchestrates auditory reversal learning in mice

via parallel projections to the auditory cortex (AC) and inferior colliculus (IC). *In vivo* electrophysiology revealed hierarchical plasticity whereby AC neurons flexibly updated stimulus selectivity and enhanced discriminability after reversal, contrasting with stable representations of stimulus identity in IC. AC inactivation selectively impaired reversal learning by degrading performance after rule reversal, whereas IC inactivation disrupted stable auditory discrimination across task phases. Dual retrograde tracing revealed anatomically segregated PPC neurons projecting to the AC (PPC_{AC}) and IC (PPC_{IC}). Projection-specific calcium imaging showed that PPC_{AC} neurons flexibly reorganized their activity to encode both Go and No-go stimuli and associated outcomes during transition. In contrast, PPC_{IC} neurons maintained stable representations of response outcomes. Optogenetic inactivation of PPC_{AC} impaired contingency updating, while silencing PPC_{IC} disrupted consistent response execution after rule reversal. Taken together, these results establish a double dissociation in top-down circuit control, with parallel PPC projections coordinating dynamic rule updating and stable motor execution for rapid behavioral adaptation. This work identifies a circuit motif by which the association cortex balances plasticity and stability to support cognitive flexibility.

Keywords : Behavioral flexibility, Auditory processing, Posterior parietal cortex, Top-down projection

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P-811

Axially multifocal metalens for 3D volumetric photoacoustic imaging of neuromelanin in live brain organoid

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Optical resolution photoacoustic imaging of uneven samples without z-scanning is transformative for the fast analysis and diagnosis of diseases. However, current approaches to elongate the depth of field (DOF) typically imply cumbersome postprocessing procedures, bulky optical element ensembles, or substantial excitation beam side lobes. Metasurface technology allows for the phase modulation of light and the miniaturization of imaging systems to wavelength-size thickness. Here, we propose a metalens composed of submicrometer-thick titanium oxide nanopillars, which generates an elongated beam of diffraction-limited diameter with an aspect ratio of 286 and a uniform intensity throughout the DOF. The metalens enhances visualization of phantom samples with tilted surfaces compared to conventional lenses. Moreover, the volumetric imaging of neuromelanin is facilitated for depths of up to 500 micrometers within the human midbrain and forebrain organoids that are 3D biological models of human brain regions. This approach provides a miniaturized platform for neurodegenerative disease diagnosis and drug discovery.

Keywords : Organoid, Metalens, diagnosis, drug discovery

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P-812

Thalamocortical Neuropharmacology in Absence Epilepsy: A Computational Model of T-type Ca^{2+} and Na^{+} Channel Dynamics

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Introduction: Childhood Absence Epilepsy (CAE) is a generalized seizure disorder marked by transient loss of consciousness, arising from abnormal thalamocortical oscillations. These pathological rhythms are associated with thalamic burst firing and cortical hyperexcitability, mediated by T-type calcium and persistent sodium channels, respectively. To investigate how these intrinsic ion channel dynamics contribute to CAE, we applied Dynamic Causal Modeling (DCM) to EEG data acquired before and after pharmacological intervention. We focused on effective connectivity to the posterior cingulate cortex (PCC), a region linked to conscious awareness and frequently affected during absence seizures. Methods: We constructed a conductance-based thalamocortical model (TCM) incorporating six cortical populations (superficial and deep pyramidal cells, inhibitory interneurons, and spiny stellate cells) and two thalamic populations (relay and reticular neurons), with dynamics governed by differential equations describing synaptic and membrane conductances mediated by AMPA, NMDA, GABA-A, T-type Ca^{2+}, and Na^{+} currents. EEG data were recorded from a pediatric CAE patient before and after administration of ethosuximide (ETX), the first-line treatment for CAE. DCM for cross-spectral density was applied to estimate ion channel–specific excitability and effective connectivity targeting a region-of-interest in the PCC. Results & Discussion: ETX administration altered thalamocortical dynamics and intrinsic excitability within the PCC. DCM revealed changes in conductance parameters linked to T-type Ca^{2+} and Na^{+} channels, suggesting modulation of neuronal gain and connectivity. These changes suggest a shift toward more stable network interactions involving the PCC, potentially contributing to seizure suppression in CAE. This approach offers a mechanistic framework linking ion channel modulation to functional brain state changes.

Keywords : Neuropharmacology, Thalamocortical Model, Childhood Absence Epilepsy, Dynamic Causal Modeling

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P-813

Dopaminergic regulation of reward-associated social memory in the hippocampal CA1

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The ability to recognize social identity and associate it with relevant information is essential for adaptive social behavior. Our previous work demonstrated that the dorsal CA1 hippocampus plays a critical role in the long lasting associative memory between social identity and reward. However, the neuromodulatory mechanisms underlying this process remain unclear. Here, we provide evidence that dopaminergic signaling is crucial for this form of associative social memory. Using a head-fixed social discrimination task, in which mice discriminate between two equally familiar male stimulus mice based on reward contingency, we found that pharmacological inhibition of dopamine D1 receptors in dorsal CA1 significantly impairs task performance. This result indicates that dopaminergic signaling in dorsal CA1 is important for performing the associative social memory task. To further investigate the role of dopamine in associating social stimuli with reward, we recorded dopamine dynamics with a genetically encoded dopamine sensor using fiber photometry during both initial learning and reversal learning. Our preliminary results reveal that although dopamine signals in the dorsal CA1 are heterogenous, they are reliably different between reward and non-reward trials even during the reward expectation period. Together, these findings highlight the importance of dopaminergic signaling in the dorsal CA1 for encoding and updating reward-associated social memory.

Keywords : Social, Reward, Dopamine, Hippocampus, Associative memory

P-814

A sleep-active hippocampal interneuron for memory consolidation

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Sleep has been recognized as critical for memory. Research in recent decades has established that hippocampal memory replay during sharp-wave ripples is central to memory consolidation in sleep. However, the neural circuits that control ripple generation and memory consolidation remain poorly understood—particularly whether there are specialized cell types or dedicated neural circuits for this process. Here, we systematically investigated the involvement of specialized interneuron circuits for memory consolidation, as the interneurons are the fundamental building block of neural circuits that control hippocampal information processing. While the majority of hippocampus interneurons are more active during Wake or REM rather than NREM sleep—the primary state for memory consolidation, we identified a genetically defined interneuron population that is selectively active during NREM sleep and is essential for controlling ripple generation and memory consolidation.

Keywords : Memory Consolidation, Ripple, Hippocampus, Interneuron, NREM sleep-active

P-815

Map-like Representations of Interpersonal Relationships in the Human Hippocampus

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Recognizing social relationships is fundamental to our functioning within social networks in daily life. Our previous research identified two principal dimensions underlying interpersonal relationship recognition: Amity-Hostility (PC1) and Restrained Amity-Suppressive Hostility (PC2). These dimensions are processed in distinct cortical systems – the right posterior superior temporal sulcus (rpSTS) for PC1, and the right ventromedial prefrontal cortex (rvmPFC) for PC2. However, it remains unclear how the brain integrates these dimensions into a unified representation of specific relationships. In this study, we investigated whether the hippocampus processes interpersonal relational information within a representational space defined by the PC1 and PC2 dimensions, in a manner analogous to spatial mapping. To do this, we conducted an event-related functional magnetic resonance imaging (fMRI) experiment in which participants watched naturalistic movie clips and evaluated the social relationship between a designated actor and target character. Using representational similarity analysis (RSA) and support vector regression (SVR), we found that the hippocampus represents interpersonal relationships based on distances within a space defined by the PC1 and PC2 dimensions, while the rpSTS and rvmPFC selectively encode information specific to the PC1 and PC2 dimensions, respectively. Mediation analysis revealed that hippocampal representations reflect distinct inputs from the rpSTS and rvmPFC. Feature transfer analysis further showed that the hippocampus receives dimension-specific information from these cortical regions and, critically, that this transfer is unidirectional–from cortex to hippocampus–with no evidence of significant reverse transfer. Collectively, these findings suggest that the hippocampus integrates dimensionally distinct cortical inputs into a map-like representation of interpersonal relationships.

Keywords : Social Recognition, Hippocampus, Spatial Map, Place-like Representation, Human fMRI

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P-816

Development of an auditory feedback experiment for rats and its application for measuring vocalization-induced suppression.

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Interactions between the vocal-motor system and the auditory system in the brain (vocal-audio interactions) play critical roles in vocal communications and their dysfunctions are implicated in

neuropsychiatric disorders. Auditory feedback experiments have been a powerful approach for studying vocal-audio interaction. In the auditory feedback experiment, the subject voice is measured with a microphone and fed back to the subject with a headphone in real-time with or without modification of the feedback sound. This allows precise control of the auditory input and induction of an artificial mismatch between the prediction based on the vocal command and the actual auditory input. Methods for the auditory feedback experiment have been suggested for humans, monkeys, and birds. However, the method for rodents has not been established, despite their known usefulness for investigation of neural circuit mechanisms and pathomechanisms in the neuropsychiatric disorders. In this study, we aimed to develop an auditory feedback experiment for rats. To this end, we developed a behavioral task to induce 50-kHz ultrasonic vocalizations, which is related to positive emotion, in a head-fixed rat. We also constructed an auditory feedback system for ultrasonic vocalizations, consisting of an ultrasonic microphone, an ultrasonic speaker, and a real-time processor. Using the developed method, we successfully reproduced the vocalization-induced suppression of the auditory response, which is a neural signature of vocal-audio interaction, in rat's auditory cortex. The present result suggests potential usefulness of the rodent auditory feedback experiment for investigating neural mechanisms of vocal-audio interaction and pathomechanisms in the neuropsychiatric disorders.

Keywords : vocal-audio integration, auditory feedback experiment, vocalization induced suppression, auditory verbal hallucination

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P-817

Flexible sensorimotor associative learning in frontal motor cortical circuits

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Learning arbitrary associations between sensory stimuli and voluntary actions is crucial for behavioral flexibility in a changing environment. While the frontal motor cortex (FMC) is known to play an important role in directing actions based on sensory inputs, whether and how FMC circuit plasticity underlies flexible remapping of sensorimotor associations remain largely unknown. Here, we demonstrate that FMC exhibits representational plasticity critical for learning flexible sensorimotor mappings. We established a sound-action flexible association learning task in mice and determined the causal role of FMC during learning. Using in vivo two-photon imaging to longitudinally track the same FMC populations, we show that single-neuron encodings are dynamically reorganized to increasingly represent the target association. A biophysically constrained recurrent neural network incorporating spike timing-dependent plasticity and three-factor learning rules recapitulated these dynamics, highlighting the role of specific plasticity rules in shaping representational remodeling. These findings establish FMC as a critical locus for flexible sensorimotor associative learning and provide mechanistic insights into how dynamic neural representations enable adaptive behavior.

Keywords : Associative learning, longitudinal imaging, representation reorganization, spiking neural network, synaptic plasticity

P-818

Category-based generalization and underlying circuit mechanism

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A fundamental cognitive function of the brain is to form categories about the sensory world and apply this knowledge to novel sensory conditions. However, the neural mechanisms underlying category-based generalization remain largely unexplored. The posterior parietal cortex (PPC) has been implicated in representing sensory categories and guiding perceptual decision-making. A key question is whether and how PPC circuits perform computations that support category-based generalization. To address this, we developed a novel behavioral paradigm in which mice make flexible decisions by generalizing previously learned categories. Both muscimol and optogenetic inhibition of the PPC revealed its critical causal role in category-based generalization. Using two-photon imaging, we examined population activity in layer 2/3 neurons and dendritic integration at the single-neuron level in layer 5 neurons. Layer 2/3 neurons encode information about choice, reward, and category. Layer 5 soma encode both choice and reward, and their apical dendrites additionally represent trial history. These findings demonstrate the indispensable role of the PPC in category-based generalization and reveal the underlying neural mechanisms supporting this cognitive process.

Keywords : Generalization, Category, Decision-making, Posterior parietal cortex, Dendrites integration

P-819

The Cerebellar Variance Paradox: A Formal Proof for Why a Complex System Must Be Low-Variance

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Systems consolidation of motor memory involves a transfer from the cerebellar cortex to the deep cerebellar nuclei (DCN), but the computational principles governing this dynamic process remain unclear. To formalize these principles, we introduce a normative framework where the choice of pathway is guided by minimizing a total cost function, $C_i(n)=B_i^2+k_i/n+O_i$, composed of squared bias (B_i^2), variance ($V_i(n)=k_i/n$), and overhead (O_i). A key empirical constraint is the universal preference for the complex cortex during the initial, data-limited phase of learning. Our formal proof reveals that this early-phase primacy is only possible if the cortex has a strictly lower intrinsic variance coefficient than the simpler DCN pathway ($k_c< k_s$). This result establishes the "cerebellar variance paradox": how can the cortex, a system with vastly greater architectural complexity, be inherently more stable and less noisy? Furthermore, our framework predicts the entire consolidation trajectory. After extensive training ($n\to\infty$), the variance term vanishes, and a second principle emerges: the simpler DCN is preferred only if its bias penalty is less than the cortex's overhead cost ($\Delta B^2<\Delta O$). These two boundary conditions define a critical transition point, $n_{crt}=\Delta k/(\Delta O-\Delta B^2)$, which quantitatively predicts the speed of memory transfer. This formula shows that consolidation is rapid for easy tasks ($\Delta B^2\to 0$) but slows dramatically or never occurs for difficult tasks as $\Delta B^2\to\Delta O$. In summary, this work makes two

contributions: first, it uncovers a fundamental paradox regarding the biophysical properties of cerebellar circuits. Second, it offers a comprehensive, predictive theory for the full dynamics of memory consolidation. This provides a new theoretical lens and a set of concrete, falsifiable hypotheses for future investigation.

Keywords : cerebellum, memory transfer, memory consolidation, cerebellar variance paradox , neuroAI

P-820

Somatostatin-expressing interneurons encode a negative reward prediction error in the mouse primary visual cortex

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Somatostatin-expressing interneurons (SST^+ INs) play a key role in sensory gating by inhibiting nearby excitatory neurons. However, their activity and function during visual decision-making remain poorly understood. In this study, we measured the calcium activity of SST^+ INs in the primary visual cortex (V1) of freely moving mice engaged in a visually guided decision-making task. SST^+ INs exhibited transient peri-stimulus activity, as well as sustained activity following the omission of an expected reward after a choice. When mice entered the reward zone, SST^+ IN activity increased in response to reward omission, reflecting the encoding of negative reward prediction error. A generalized linear model (GLM) analysis confirmed that reward omission was a stronger predictor of post-choice SST^+ activity than other task- or movement-related factors. Consistently, optogenetic activation of SST^+ INs after post-correct choices in expert mice deterred performance improvement. Furthermore, elevated SST^+ activity in V1 following reward omission correlated with impaired performance in the subsequent trial. These findings suggest that SST^+ INs in V1 encode negative reward prediction error, and this signal disrupts ongoing visual discrimination performance. Such encoding may modulate visually driven activity in V1 and promote behavioral adaptation in dynamic visual environments.

Keywords : Somatostatin interneurons, Primary visual cortex, Negative reward prediction error, T-maze, Visual discrimination

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P-821

Closed-Form Brain–Plasma PK Solutions Coupled with an Optimization Algorithm for CNS Drug Regimens

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The blood–brain barrier (BBB) decouples plasma pharmacokinetics from neural exposure, so CNS dosing still relies on trial-and-error or opaque numerical simulators. This study derives a novel closed-form two-compartment model that couples plasma elimination (k_e) and bidirectional BBB flux (k_{12}, k_{21}) under cyclic bolus dosing. By Laplace transforming the Dirac comb of doses and integrating the resulting geometric series, the study obtains a formula for brain concentration $C_b(t)$ that is valid for any number of doses and mainly contains elementary functions. The algebraic solution serves as the engine for a lightweight optimisation routine. Also, the greedy local-search algorithm starts from an initial dose (D) and interval (τ), computes the largest deviation of $C_b(t)$ from a user-defined therapeutic window over *N* cycles, and then moves one step in the single direction (±D or ±τ) that most reduces that error. Iteration halts when the window is satisfied or no further improvement is possible. Furthermore, the optional genetic algorithm provides multi-objective refinement. Using literature parameters for memantine, the closed-form trace reproduces a high-precision SciPy ODE integration to < 1 % root-mean-square error. Here, the greedy routine identifies schedules that keep $C_b(t)$ between 0.5–2 μM in 0.2 s and requires ~100 times fewer evaluations than the GA while staying within 5 % of its optimum. Halving or doubling BBB permeability shifts the recommended interval by up to 40 %, an insight obtained instantly because the model is analytic. By replacing black-box simulations with transparent equations while retaining simulation-grade accuracy, this study supplies a reproducible, hardware-light framework for clinician-friendly optimisation of CNS regimens.

Keywords : Blood-Brain Barrier(BBB), Two-Compartment Pharmacokinetics, CNS(Central Nervous System) Drug Regimens, Closed-Form Solution, Dose-Interval Optimization

P-822

Towards a Novel Encoding Model of Striatal Medium Spiny Neurons: Multiplex and Heterogeneous Value Encoding Patterns

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The dorsal striatum integrates reward prediction with action initiation and is driven by midbrain dopamine. However, the activity of dopamine neurons often diverges from dopamine concentrations at striatal terminals, and the consequences of this mismatch remain largely unexplored. Whether models originally built on dopamine neurons, such as temporal-difference (TD) learning and adjusted net contingency for causal relations (ANCCR), fit to the receptor-specific medium spiny neurons (MSNs) has not been elucidated. Using endoscopic one-photon calcium microscopy, we recorded MSNs in D1-cre (n=3) and A2a-cre (n=2) mice during a head-fixed task with exponential interval rewards (mean 12 s). Locomotion, licking, and reward timing were recorded. TD- and ANCCR-derived expected values were computed in a -3 to +3s peri-reward window, and mixed-effects regression related per-neuron ΔF/F to reward, first lick, locomotion, and expected value. In D1-MSNs (n = 121), 23% encoded reward, 8% lick, and 29% locomotion; A2a-MSNs (n = 89) showed higher proportions, with 33% encoding reward, 13% lick, and 51% locomotion. Neural population encoding expected value (4% among total MSNs recorded, for both TD and ANCCR; $p<0.05$) were distinct across model. In D1-MSNs: 67% of value neurons followed either of model, and all A2a-MSNs that encoded value responded solely to TD. Multivariate coding was frequent—D1: 40% single, 13% dual, <1% triple, 49% silent; A2a:35% single, 29% dual, 3% triple, 35% silent. Our findings reveal a multiplexed encoding pattern of reward, locomotion, licking, and expected value in striatal D1 and A2a medium spiny neurons. The expected value encoding differed between the TD and ANCCR models and also varied between the direct and indirect

pathways. These results support the hypothesis that value encoding in neurons expressing dopamine receptors may differ from that of dopaminergic neurons and may require more nuanced computational models to fully capture their dynamics.

Keywords : Dorsal striatum, Medium spiny neurons, Value encoding, Dopamine model, Multiplexed neural coding

P-823

Dopaminergic signaling underlies reward devaluation by repetitive consumption

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Reward devaluation, the process by which a reward loses its subjective value, is a fundamental mechanism for adaptive behavior. A primary example of this phenomenon is “sensory-specific satiety,” where the recent consumption of a particular food decreases its pleasantness or palatability, while the appeal of other unconsumed foods remains relatively stable. Although sensory-specific satiety is a widely used experimental model for inducing reward devaluation, its underlying neural basis remains unclear. The mesolimbic dopamine system, which includes dopamine-producing neurons in the Ventral Tegmental Area (VTA) projecting to the Nucleus Accumbens (NAc), is a well-established hub for reward processing. However, the specific role this system plays in mediating reward devaluation following repeated consumption has not been fully elucidated. This study was designed to address this knowledge gap through a two-pronged approach. First, we conducted behavioral experiments in mice using different sucrose gels to systematically investigate how external variables - such as eating duration, delay, and food similarity - contribute to reward devaluation. Moreover, concurrent with these behavioral paradigms, we monitored real-time dopamine release in the nucleus accumbens core and shell using fiber photometry, allowing us to examine how dopamine signals change as reward devaluation progresses. The behavioral data and statistical analyses show that following repetitive consumption of the same gel, mice altered their preference and reduced their intake, confirming that the reward value of recently consumed gel declined. Crucially, the fiber photometry data revealed that dopamine release within the nucleus accumbens directly reflected these behavioral changes.

Keywords : Reward devaluation, Sensory-specific satiety, Dopamine, Nucleus Accumbens

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P-824

The Cortical Mechanism of Cooperative Choices in Social Decision-Making

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The majority of our real-world decisions are made in a social context, contrasting with the individual decision-making models typically used in experimental settings. We largely lack behavioral approaches to social decision-making and, thereby, its neural underpinnings. In our study, we designed a behavioral paradigm in which mice could freely choose between cooperative and individual actions to obtain a reward. This paradigm required two mice to press two levers within a specific timeframe to receive water. An ‘individual choice’ was categorized when one mouse pressed both levers by itself. If the two mice pressed the levers jointly, we classified this action as a ‘social choice’. We found that mice can learn to make social choices at a comparable rate to individual choices. Furthermore, the level of familiarity between the mice influenced these choices, indicating that social recognition plays a significant role in social decision-making behavior. We also discovered that when the cost of social choice increased or the benefit decreased, the social choice rate declined, suggesting that mice utilize a value-based decision-making strategy, adjusting their choices according to the perceived costs and benefits in a social context. Next, we investigated the neural substrates of this social decision-making behavior. By employing the Neuropixels system, a high-throughput neural recording technique, we revealed neural computation underlying planning and execution of individual versus social choices. This study highlights the neural mechanisms involved in social decision-making, particularly regarding cooperative and individual choices.

Keywords : social, decision-making, cooperation, prefrontal cortex

P-825

Layer-specific and temporally organized neural dynamics supporting working memory in the prefrontal cortex

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Working memory refers to the capacity to temporarily store and manipulate information, a function critical for higher-order cognition. To investigate the local circuit dynamics underlying working memory in the prefrontal cortex, we performed multi-laminar recordings using Neuropixels probes in the medial prefrontal cortex of mice engaged in a delayed response task. Neurons in deep layers showed strong target selectivity during the sample and early delay periods, whereas superficial layer neurons exhibited firing patterns that differentiated correct from error trials during the late delay period. Cross-correlation analysis revealed that inter-laminar connectivity strength varied by target location (ipsilateral versus contralateral) during the early delay period and by trial outcome (correct versus error) during the mid-to-late delay period. Notably, superficial-layer neurons with significant deep-to-superficial functional connectivity showed higher correct-error decoding accuracy than other superficial-layer neurons during the late delay period. Together, these findings uncover the temporally structured circuit dynamics of working memory, demonstrating how laminar-specific signal processing and inter-laminar interactions support working memory.

Keywords : Working memory, Prefrontal cortex, Laminar-specific dynamics, Inter-laminar connectivity, Neuropixels

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Translational and Clinical Neuroscience P-826~P-844

P-826

Gait analysis using supervised deep learning to evaluate chemogenetic neuromodulation in non-human primate stroke models

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Gait analysis in non-human primates (NHPs) is important for understanding neural mechanisms of locomotor control in quadrupedal animals. Typical methods rely on costly motion tracking systems with markers placed on bony landmarks, which may disturb natural locomotion. This study aimed to evaluate markerless deep learning for gait analysis using video in an NHP ischemic stroke model. Photothrombotic capsular lesioning was employed to selectively target and destroy the posterior limb of the internal capsule (PLIC), creating a precision model inducing persistent motor deficits. This model provides a robust platform for investigating post-stroke recovery mechanisms. Clozapine-induced chemogenetic neuromodulation targeting the sensory-parietal cortex was performed to improve motor recovery. To measure the motor recovery following chemogenentic neuromodulation, markerless deep learning software was utilized to track joint coordinates and analyze gait at three time points: pre-stroke, post-stroke, and post-chemogenetic therapy, over a 9-week period. Gait phases (swing/stance) were defined by right hindlimb contact and liftoff. To evaluate gait abnormalities, kinematic variables such as distance at hip, step length, hip height, joint angle, joint angular distance, and angle excursion were calculated. Results showed the most severe gait impairments at 1-week post-stroke, reflecting significant locomotor deficits (notably, knee angle range decreased from 120–80° to 90–70°). Partial recovery was observed at 3 weeks, suggesting natural recovery mechanisms. While clozapine administration demonstrated a tendency toward recovery in gait parameters, the changes were not statistically significant. This study established an NHP ischemic stroke model to advance stroke understanding and develop translatable treatments. It demonstrated the utility of a cost-efficient markerless deep learning approach for assessing gait abnormalities and evaluating locomotor disease treatments.

Keywords : Gait analysis, Markerless pose estimation, Non-human primate, Stroke, Chemogenetic neuromodulation

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P-827

Therapeutic Effects of Transcranial Ultrasound Pulsed at 40 Hz in Alzheimer's Disease Mouse Model: Focusing on Changes in Glial Cells

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Alzheimer`s disease (AD) is a major cause of dementia. Amyloid-beta (Aβ) accumulation is a hallmark and pathology of AD. In AD mouse model, GABA produced from astrocytes suppressed neuronal activity and impaired cognitive functions. Moreover, demyelination, loss of the myelin sheath, in the AD mouse model was reported. Recently, it has been known that gamma entrainment at 40 Hz reduced Aβ in the AD mouse model brain. Previous studies reported that ultrasound stimulation could induce neuronal firing and microglial activation. Therefore, we would examine whether transcranial ultrasound stimulation (tUS) pulsed at 40 Hz improves AD pathologies by gamma entrainment. We used 6-month-old 5xFAD. We implanted EEG electrodes at the frontal and parietal cortex to record the EEG. Mice got two-hour daily ultrasound stimulation (300k Hz) pulsed at 40 Hz for two weeks. We performed the EEG recording and behavioral test to measure the cognitive functions before and after the ultrasound stimulation. Aβ levels in the cortex and hippocampus were measured using the ELISA kit. Brain sections were stained Aβ, Iba1, GFAP, GABA, proBDNF, and oligodendrocytes using the free-floating immunohistochemistry method. tUS elevated the gamma oscillation power and brain connectivity. tUS reduced the Aβ pathologies in the cortex and hippocampus. Moreover, tUS increased the microglial activation and reduced the GABA+ astrocytes in the cortex and hippocampus. Additionally, tUS restored the demyelination to WT level in the cortex and hippocampus. We confirmed that tUS improved the cognitive deficits of the AD mouse model. tUS improved the AD pathologies and cognitive functions. Moreover, tUS modulated all types of glial cells. tUS could reduce the GABA+ reactive astrocytes and increase microglial activation, proBDNF+ astrocytes, and MBP+ area. Consequently, we suggest that tUS might have therapeutic effects on the mouse model of AD by modulating glia cells.

Keywords : Alzheimer's disease, Ultrasound stimulation, Microglia, Astrocytes, Oligodendrocytes

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P-828

REM sleep suppression during diazoxide-induced acute hyperglycemia in a non-diabetic mouse model

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Introduction: Sleep is critical for maintaining metabolic balance. Disruptions in sleep and circadian rhythms impair glucose regulation

and hormonal signaling, contributing to metabolic syndrome. In diabetes, sleep disturbances are common and often linked to secondary complications like nocturia. However, the frequent overlap of hyperglycemia and poor sleep suggests a more complex, bidirectional relationship. Although recent studies highlight the connection between metabolism and sleep, the direct effects of acute hyperglycemia on sleep architecture remain unclear. Methods: To model acute hyperglycemia, C57BL/6 mice were fasted for 8 hours, followed by intraperitoneal diazoxide injection (in DMSO) and oral glucose gavage, inducing transient hyperglycemia (≥200 mg/dL) lasting ~6 hours. EEG/EMG was recorded during this period; saline-treated mice served as controls. For LC activity monitoring, a 4-month-old female TH-Cre mouse received EEG/EMG implants and fiber photometry surgery. AAV(DJ)-EF1a-DIO-GCaMP6f (10^{13} GC/mL, 1,000 nL at 100 nL/min) was injected into the right LC (−0.85, −5.45, −3.75 mm), and a fiber was placed 0.15 mm above the site. Results: Hyperglycemia led to REM sleep suppression, with reduced REM percentage, shorter bout length, and decreased average REM duration. EEG analysis showed a significant reduction in absolute power across all vigilance states, particularly during wake and NREM, indicating suppressed cortical activity. LC fiber photometry revealed increased calcium activity of LC noradrenergic neurons during NREM following diazoxide injection, suggesting hyperactive LC neurons may inhibit REM sleep entry. Conclusion: These findings demonstrate that acute hyperglycemia directly alters sleep structure, notably suppressing REM sleep and dampening cortical activity. Enhanced LC activity may mediate these effects, revealing a mechanistic link between metabolic disturbances and sleep regulation.

Keywords : Absolute power, Acute hyperglycemia, REM sleep suppression, Locus coeruleus, LC hyperactivity

P-829

Structural Brain Volume Alterations Associated with Sleep Disturbance and Cognitive Impairment in Depression

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Purpose: Depression is commonly accompanied by both cognitive impairment and poor sleep quality, but their shared neural correlates remain unclear. This study aimed to investigate structural brain differences in individuals with depression and to examine how regional volume reduction relates to sleep latency and cognitive function. Methods: Thirty-nine healthy controls and twenty-five individuals with depression participated in the study. Structural T1-weighted MRI scans were processed using FreeSurfer to extract cortical volume measures from predefined regions of interest (ROIs). Subjective sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI), and cognitive performance was measured using the Seoul Verbal Learning Test (SVLT) and Stroop Color-Word Test. Group comparisons were conducted using ANCOVA controlling for age, sex, and education. Pearson correlation analysis was used to examine associations between ROI volumes, cognitive performance, and sleep quality. Results: Compared to the control group, the depression group showed significantly reduced volume in the left medial orbitofrontal cortex ($F(1,61)=4.25$, $p=0.044$, $\eta^2=0.067$) and the right rostral middle frontal gyrus ($F=6.75$, $p=0.012$, $\eta^2=0.103$). The left medial orbitofrontal volume was positively correlated with verbal recognition performance on the SVLT ($r = -.264$, $p = 0.035$). In addition, PSQI sleep latency was strongly associated with slower Stroop word reading speed ($r = -.460$, $p < 0.001$), suggesting that poor sleep may impair cognitive processing speed. Conclusion: These findings suggest that reduced volume in prefrontal regions—specifically the medial orbitofrontal and rostral middle frontal cortices—is associated with impaired memory and prolonged sleep latency in depression. This study highlights a possible shared structural basis for cognitive and sleep-related vulnerability in depression.

Keywords : Sleep, Depression, Cognitive, Brain

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P-830

Enhanced Neurogenesis and Therapeutic Effects of Aducanumab by Focused Ultrasound in Alzheimer's Disease

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Background: Aducanumab (Adu), a human IgG1 monoclonal antibody targeting oligomeric and fibrillar forms of beta-amyloid, has demonstrated reduced amyloid pathology and improved cognitive impairment at high doses (10 mg/kg) in Alzheimer's disease (AD) clinical trials. This study aimed to investigate the effects of a lower Adu dose (3 mg/kg) with enhanced delivery via focused ultrasound (FUS) in an AD mouse model. Methods: FUS with microbubbles was used to open the blood–brain barrier (BBB) of the hippocampus, facilitating Adu delivery. The combined FUS-Adu therapy was administered three times, biweekly. Cognitive function was assessed using the Y-maze test. BrdU labeling and immunohistochemistry were utilized to examine neurogenesis and amyloid pathology. RNA sequencing and ingenuity pathway analysis evaluated gene expression profiles in hippocampal tissues. Results: FUS-mediated BBB opening markedly increased Adu delivery into the brain (~8.1-fold). Combined therapy significantly mitigated cognitive decline and reduced amyloid plaque levels in the hippocampi of 5×FAD mice compared to either Adu or FUS alone. Furthermore, combined treatment activated phagocytic microglia and increased astrocyte numbers associated with amyloid plaques. RNA sequencing revealed alterations in four enriched canonical pathways: phagosome formation, neuroinflammation signaling, CREB signaling, and reelin signaling. Conclusion: Enhanced delivery of low-dose Adu (3 mg/kg) via FUS effectively reduced amyloid deposits and attenuated cognitive deficits. Additionally, FUS-mediated BBB opening promoted

adult hippocampal neurogenesis, highlighting its therapeutic potential in AD treatment.

Keywords : Focused ultrasound, Alzheimer's disease, Drug delivery, Aducanumab, Adult hippocampal neurogenesis

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P-831

High-beta band EEG network connectivity as a potential biomarker for differentiating PTSD from other anxiety disorders: a preliminary study

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Post-traumatic stress disorder (PTSD) and anxiety disorders exhibit high comorbidity and share overlapping symptomatology, yet may differ in their underlying neurophysiological mechanisms. Thus, identifying both their shared and distinct features is essential for improving diagnostic precision and treatment strategies. This study aimed to identify network-based EEG biomarkers capable of distinguishing PTSD from anxiety disorders and healthy controls. Resting-state EEG was recorded from patients with PTSD (N=18), panic disorders (N=15), other anxiety disorders (N=17), and healthy controls (N=8). Functional connectivity was estimated using the corrected imaginary phase-locking value (ciPLV) across all pairs of 21 EEG channels. For each of six frequency bands (delta, theta, alpha, low-beta, high-beta, gamma), 21x21 connectivity matrices were constructed and subjected to graph-theoretical analysis. Four global network metrics—strength, global efficiency, local efficiency, and characteristic path length—were calculated for each frequency band and one-way ANOVAs were conducted for each metric. Significant group differences emerged exclusively in the high-beta band. Post-hoc Tukey's HSD tests revealed that patients with PTSD consistently showed lower strength, global efficiency, and local efficiency compared to healthy controls, indicating a globally disrupted and inefficient functional brain network in this frequency band. Importantly, no significant differences were observed between healthy controls and other anxiety disorder groups. These findings suggest that high-beta band network connectivity may serve as a selective biomarker for PTSD, differentiating it from both healthy individuals and patients with anxiety disorders. This specificity underscores the potential clinical utility of high-beta EEG network metrics in supporting differential diagnosis and improving our neurophysiological understanding of PTSD.

Keywords : PTSD, anxiety disorder, EEG, high-beta, network

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P-832

Poster Award Candidate

Modulatory effects of transcranial photobiomodulation and vagus nerve stimulation on alcohol dependence and craving

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Alcohol use disorder (AUD) is a chronic condition increasingly recognized as a brain disorder, involving dysregulation in neural systems such as the prefrontal cortex and reward circuits. Previous studies have shown that transcranial photobiomodulation (tPBM) has positive effects in attenuating cravings for illicit substances (e.g., opioid) and associated symptoms. Here, we investigated the modulatory effects of tPBM on alcohol dependence and craving in individuals at low to moderate risk for AUD. Given previous studies showing significant reductions in alcohol craving following transcutaneous auricular vagus nerve stimulation (taVNS) in individuals with AUD, we additionally examined the effects of taVNS alone, as well as the simultaneous application of tPBM and taVNS. Participants (alcohol use disorder identification test (AUDIT) score between 3 and 20; N=29, age=27.59±5.26) were randomly assigned to one of three groups: tPBM-only, taVNS-only, or combined tPBM+taVNS. Each participant was provided with a home-based neuromodulation device (tPBM, taVNS, or both) and instructed to follow a structured five-week protocol—empirically derived from prior findings in substance users—, completing one 15-minute session per day, five days per week, with at least 12 hours between sessions. Intervention effects were assessed by comparing pre- and post-intervention self-reports of alcohol dependence and craving. Our preliminary analyses revealed that alcohol craving scores were significantly reduced in both the tPBM-only and tPBM+taVNS groups, while a significant attenuation in alcohol dependence was observed only in the tPBM+taVNS group. These findings suggest that simultaneous application of tPBM and taVNS may serve as an effective neuromodulatory treatment for reducing both alcohol dependence and craving.

Keywords : Alcohol use disorder, Non-invasive stimulation, Photobiomodulation, Vagus nerve stimulation

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P-833

Single-Cell Transcriptomics Reveals CCL7+ Microglia as Mediators of White Matter Damage in Renovascular Hypertensive Brain

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White matter hyperintensities (WMHs), a common MRI feature in elderly individuals, are associated with demyelination and axonal degeneration in the white matter. We have previously demonstrated that the induction of renovascular hypertension (RVHT) results in prominent white matter degeneration in a subset of animals. The present study aimed to investigate the cellular and molecular mechanisms driving WMH in a rat RVHT model. Animals were stratified into sham, WMH-negative, and WMH-positive groups based on MRI and histopathology. White matter regions containing the corpus callosum and cingulum areas were dissected and subjected to single-cell RNA sequencing (scRNA-seq). Bioinformatic analysis was focused on microglia and oligodendrocytes given their critical roles in neuroinflammation and myelin homeostasis. Clustering and sub-clustering analysis revealed multiple glial subpopulations enriched in WMH-positive rats. Among these, a "focal white matter injury" microglial subcluster exhibited significantly elevated expression of CCL7. Immunohistochemistry and double immunofluorescence confirmed CCL7 expression in WMH lesions and revealed spatial juxtaposition with CD11b+ microglia, indicating their origin. Sub-clustering of oligodendrocytes was performed to assess cell-specific marker gene expression. To explore glial communication, cell–cell interaction analysis was performed using LIANA, which revealed predicted interactions between the focal white matter injury microglial subcluster and oligodendrocyte subclusters. To functionally assess the role of CCL7, mature oligodendrocyte cultures were treated with recombinant CCL7 for 24 and 72 hours. While short-term exposure had no effect, 72-hour treatment induced dose-dependent cytotoxicity and reduced MBP immunoreactivity. These findings identify CCL7 as a microglia-derived inflammatory mediator that contributes to white matter degeneration in RVHT by promoting oligodendrocyte injury and demyelination.

Keywords : White Matter Hyperintensities, CCL7, Oligodendrocyte, Microglia, Single cell RNA seq

P-834

KBN2201 ameliorates amyloid pathology, neuroinflammation, neuronal degeneration, and neurogenesis deficits in 9-month-old 5xFAD mice

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Alzheimer's disease (AD) is a progressive and currently incurable neurodegenerative disorder that affects millions of people worldwide. In this study, we investigated the therapeutic potential of KBN2201 [2-hydroxy-4-(trifluoromethyl)benzoic acid] in 5xFAD mice, a widely used transgenic model of AD. Chronic oral administration of KBN2201 from 9 to 12 months of age significantly attenuated AD-related pathology. KBN2201 treatment reduced the expression levels of amyloid precursor protein (APP), APP C-terminal fragments (APP-CTFs), and BACE1, leading to a substantial decrease in the number and size of amyloid-β (Aβ) plaques in both the cortex and hippocampus. Moreover, structural integrity in the hippocampal CA1 region was preserved, and dendritic complexity in cortical and hippocampal neurons was maintained. KBN2201 also promoted adult neurogenesis in the subventricular zone (SVZ) and hippocampus, as demonstrated by increased DCX and Ki67 expression. Behavioral testing using the Y-maze revealed that KBN2201 improved memory performance in 5xFAD mice. Collectively, these findings indicate that KBN2201 exerts multifaceted therapeutic effects via anti-amyloidogenic, anti-inflammatory, neuroprotective, and neuroregenerative mechanisms, supporting its potential as a promising candidate for AD treatment.

Keywords : Alzheimer's disease (AD), 5xFAD mice, KBN2201, Multitarget drug

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P-835

A drug discrimination test of four stimulants in rats trained with methamphetamine and cocaine

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Stimulants are known to have physical and psychological effects, and some are used to treat attention-deficit/hyperactivity disorder (ADHD). Drug discrimination (DD) is a method used to assess the potential abuse liability of drugs *in vivo,* and we evaluated 3-fluorophenmetrazine (3-FPM), α-D2PV, mephtetramine, and DF-MDBP, which have only been subject to limited investigation. Male Sprague-Dawley rats were divided into two groups: one group was trained to discriminate between methamphetamine (METH; 0.5 mg/kg, i.p.) and saline, and the other group was trained to discriminate between cocaine (COC; 5.6 mg/kg, i.p.) and saline. Subsequently, four stimulants were tested for their ability to substitute for the discriminative effects of METH and COC. As a result, 3-FPM and α-D2PV generalized to both METH and COC, while mephtetramine and DF-MDBP showed partial generalization. Additionally, response rates following administration of mephtetramine and DF-MDBP were reduced in both METH- and COC-trained rat groups. Because the response rates of mephtetramine and DF-MDBP were low, higher concentrations were not tested. In conclusion, 3-FPM and α-D2PV closely mimic the discriminative stimulus effects of METH and COC, suggesting a potential for abuse.

Keywords : drug discrimination, 3-Fluorophenmetrazine, α-D2PV, mephtetramine, DF-MDBP

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P-836

The effects of Heart-tonification acupuncture on a Chronic Stress-induced Mouse model of Depression

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Depression is a chronic neurological disorder characterized by various

symptoms, including depressed mood, diminished interest, pain, fatigue, sleep disturbances, and appetite changes. In this study, we investigated the effects of Heart-tonification acupuncture on a chronic unpredictable mild stress (CUMS)-induced mouse model of depression. Mice were exposed to CUMS for 13 weeks, and acupuncture was treated at Heart-tonification acupuncture points (HT9•HT3•LR1•KI10) from weeks 10 to 13. Depressive-like behaviors were assessed using the open field test, the marble burying test, and the forced swimming test. Pain-like behavior was evaluated using the von Frey test, and food intake was measured to monitor appetite changes. Changes of tyrosine hydroxylase (TH) expression, as a marker of dopaminergic neurons, were analyzed in the substantia nigra, mediodorsal thalamus, and arcuate nucleus of the hypothalamus. Expression levels of glutamate receptor 4 (GluR4) and Ionized calcium-binding adapter molecule 1 (Iba-1) were observed in the hippocampus. In conclusion, Heart-tonification acupuncture alleviated depressive-like symptoms through regulation of TH, GluR4, and Iba-1 expression in CUMS mouse models. Further research is needed to elucidate the direct regulatory mechanisms of acupuncture within dopaminergic circuits across specific brain regions.

Keywords : Depression, Acupuncture, Chronic stress, Heart-tonification, Dopamine

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P-837

Crosstalk between sleep homeostasis and circadian rhythm: the implications of photobiomodulation

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The two-process model is a foundational mechanism for regulating sleep-wake cycles, representing a close interaction between sleep homeostasis (Process S) and the circadian clock (Process C). The Two-Process Model overlooks the crucial interaction between its two constituent processes. Photobiomodulation (PBM) is a therapeutic technique that uses red or near-infrared (NIR) light to stimulate or modulate cellular function. Recently, we found that the PBM increases NREM sleep with increased ATP and adenosine (data not published yet). However, PBM's impact on the interaction between sleep homeostasis and circadian rhythm is not clearly understood yet. Therefore, we aim to investigate the effects of PBM stimulation on the endogenous circadian rhythm. We investigated the spontaneous sleep-wake activity of C57BL/6J female mice. PBM (810 nm light, 12 mW/cm², 43.2 J/cm²) was applied during Zeitgeber Time (ZT) 23–24. Following PBM application, sleep-wake dynamics and spectral density were analyzed via electroencephalogram (EEG). Furthermore, wheel-running activity was recorded in 12:12 LD followed by constant dark (DD) conditions. On day 8 of DD, PBM was applied at 0, 10, 30, or 60 minutes from the onset time of the alpha phase. The DD recording was continued for 7 days after PBM. Following PBM exposure, we observed significant changes in spontaneous sleep-wake activity. Specifically, the relative power of delta waves in the EEG spectrum was significantly increased in the post-PBM period compared to pre-PBM measurements. Furthermore, the percentage of NREM sleep also showed an increase post-PBM, indicating enhanced sleep induction. Circadian phase changes, determined from wheel-running activity, varied with different PBM durations and their analyses are in progress. These findings suggest that PBM leads to increased sleep pressure and a modified circadian phase. We propose that PBM can be a non-invasive, effective neuromodulating method to adjust sleep and circadian rhythm.

Keywords : Photobiomodulation, Sleep pressure, Circadian rhythm

P-838

Neural Markers of Listening Effort: An EEG Framework for Clinical Assessment of Auditory Disorders

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Auditory processing disorders (APD), age-related hearing loss, and cognitive impairment often present overlapping symptoms, complicating diagnosis. Objective neural markers that distinguish sensory and cognitive contributions to listening difficulty are essential for clinical assessment. EEG-based auditory attention decoding (AAD) and Temporal Response Functions (TRFs), which quantify the brain's time-locked response to continuous speech, have emerged as promising biomarkers for speech intelligibility and attentional engagement. However, clinical translation is limited by two key gaps: (1) lack of consensus on the optimal auditory presentation paradigm (such as clean, dichotic, or diotic) for reliable TRF evaluation, and (2) uncertainty about which analytic features best capture clinically meaningful processing differences. To address these issues, we recorded EEG from healthy young adults listening to speech under clean, dichotic, and diotic conditions, and compared TRF features and model performance across paradigms. TRF peaks at ~100 ms and ~200 ms were increasingly delayed and amplified from clean to dichotic to diotic conditions, reflecting rising cognitive load. The diotic condition, lacking spatial cues, required effortful internal stream segregation and elicited the greatest top-down engagement. Encoder and decoder model performance correlated strongly with behavioral attention across conditions (clean: r = 0.834; dichotic: r = 0.801; diotic: r = 0.792) and showed moderate reliability across paradigms (encoder: r = 0.556; decoder: r = 0.634), suggesting partially shared but distinct neural mechanisms. These findings show how listening context shapes neural speech tracking and support paradigm-specific TRF protocols as sensitive tools for probing auditory-cognitive function. Our work proposes a theoretical framework integrating neural, sensory, and cognitive measures, providing practical guidance for EEG-based diagnostics in hearing and cognitive disorders.

Keywords : Auditory processing, Neural biomarkers, Clinical diagnostics, EEG, Attention decoding

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P-839

Development of a rapid response platform integrating AI-based CBRN detection and regenerative medicine technologies

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This study aims to develop an integrated platform for rapid and effective response to chemical, biological, radiological, and nuclear (CBRN) threats by converging artificial intelligence (AI), molecular and quantum mechanics-based simulation, and regenerative medicine, including stem cells, extracellular vesicles (EVs), and organoids. Moving beyond fragmented approaches, the platform covers the full response pipeline—from hazard detection and toxicity prediction to tissue injury assessment and personalized therapeutic intervention. AI models trained on Raman spectroscopic data predict the molecular structure and toxicity of novel CBRN agents, forming a real-time toxicity knowledge base. Concurrently, cell-, organoid-, and animal-based models are used to mimic organ-specific injuries caused by CBRN exposure. To identify injury mechanisms and therapeutic responses, multi-omics analyses are applied to identify damage-associated biomarkers and elucidate the efficacy of stem cell- and EV-based therapies. Therapeutic studies focus on mesenchymal stem cells and EVs for their immunomodulatory, anti-inflammatory, and regenerative effects. Formulations are optimized for stability, delivery, and scalability, and validated through clinically relevant protocols, including GMP-compliant production processes. Each component of this platform—including AI-driven toxicity modeling, sensitive detection tools, digital diagnostics, and personalized regenerative therapeutics—possesses strong potential for technology transfer and commercialization. Ultimately, this integrated system will enhance national preparedness, reduce the public health burden, and deliver precision medical care tailored precisely to the exposure route and injury phenotype of each affected individual, thereby setting a new paradigm for CBRN disaster medicine.

Keywords : CBRN Response, AI prediction, Regenerative Therapy

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P-840

Neuroimaging, psychopathology and cognitive features of impulsivity subtypes in adolescents: implications for transdiagnostic psychiatry

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Impulsivity is a heterogeneous trait linked to psychiatric vulnerability, yet its stratification, neurobiological underpinnings and clinical implications remain poorly understood. Using baseline and 2-year follow-up data from the Adolescent Brain Cognitive Development (ABCD) Study (N=9,078), we identified three distinct impulsivity subtypes through latent profile analysis and latent transition analysis: low impulsivity (baseline: 56.1%; follow-up: 48.9%), motivational impulsivity (high urgency and sensation seeking, baseline: 33.5%; follow-up: 43.6%), and executive impulsivity (low perseverance and premeditation, baseline: 10.4%; follow-up: 7.4%). Cross-sectionally, the executive subtype showed elevated risks for most psychiatric diagnoses and psychopathology symptoms, poorer cognitive tests performance and the motivational subtype also exhibited significant but milder effects. For the neuroimaging results, our analyses of surface area, cortical thickness and brain activation during task revealed different neural signatures: executive subtypes showed predominant deficits in temporal regions (the left superior temporal cortex and the left transverse temporal cortex), whereas motivational subtypes displayed primarily frontal abnormalities (left superior frontal cortex, left caudal middle frontal cortex and left precentral cortex). Longitudinally, the executive subtype predicted increased psychiatric diagnoses, worsening psychopathology and some cognitive tests over two years, though not in brain metrics. Notably, transitions between subtypes were linked to changes in psychopathology and cognitive performance, but not in brain metrics. Our findings reveal clinically meaningful impulsivity subtypes with distinct neurobiological underpinnings. These neural patterns cut across traditional diagnostic boundaries offers new opportunities for precision psychiaty, such as region-specific neuromodulation and early intervention guided by these biomarkers.

Keywords : Impulsivity subtypes, Psychiatry, Neuroimaging features, Magnetic Resonance Imaging, Adolescent development

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P-841

East Asian Traditional Medicine for attention-deficit hyperactivity disorder in children and adolescents: A scoping review

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Background: East Asian Traditional Medicine (EATM) offers various modalities—such as herbal medicine, acupuncture, and manual therapy—for managing attention-deficit hyperactivity disorder (ADHD) in children and adolescents. This scoping review aimed to identify the overall status and characteristics of EATM treatments for children and adolescents with ADHD. Methods: Following the Arksey and O'Malley framework, we searched 13 databases in English, Korean, Chinese, and Japanese. Articles evaluating the effectiveness and safety of EATM treatments for ADHD in children and adolescents aged < 18 years were included. EATM treatments were categorized into herbal medicine, acupuncture, manual therapy, miscellaneous modalities, and combined treatments. Results: A total of 198 studies were ultimately included in the review. When categorized by treatment method, most studies focused on herbal medicine (n = 104), followed by miscellaneous modalities (n = 41), acupuncture (n = 26), and combined treatments (n = 20), and manual therapy (n = 7). Most studies were conducted in China (78.3%) and published in Chinese (75.3%). Among these, 169 were randomised controlled trials, 19 were controlled clinical trials, and 10

were systematic reviews and/or meta-analyses. Among controlled trials, most studies reported positive effects in the experimental group (n = 101, 53.7%); however, > 50% of the studies did not report adverse events (n = 107, 56.9%). Conclusions: This comprehensive review provides an unprecedented overview of diverse EATM treatments for paediatric patients with ADHD, including herbal medicine, acupuncture, manual therapy, and miscellaneous modalities. Further studies should focus on methodological improvements, such as the use of standardised diagnostic criteria and systematic reporting of adverse reactions. This study provides foundational data for future research and clinical practice, including the development of research protocols and treatment guidelines.

Keywords : Attention-deficit hyperactivity disorder, ADHD, scoping review, East Asian traditional medicine, children

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P-842

Sex differences in the effects of sleep efficiency on brain structure and cognitive aging: Literature review

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Recent sleep studies highlight that sleep is a key modifiable factor in brain aging and cognition. However, the role of sex differences in this relationship remains underdetermined and sometimes inconsistent across studies. The primary objective of this review was to summarize findings from large-scale population-based studies and to elucidate how sex differences impact on the relationship between sleep and brain health. We also compared ethnic differences across study groups of included references. Studies have shown that poor sleep qualities are associated with higher-order cognitive processing related to the frontoparietal cortex, hippocampus, and basal ganglia , and that these associations are often stronger in women. Hormonal transitions across the lifespan have been suggested as a possible contributing factor. Some studies have found that sleep-related cortical thickness reduction in the default mode network better predicts memory decline in women, suggesting that sex differences should be considered when predicting cognitive decline based on sleep. While some studies report inconsistent sex differences, it is important to examine these sex-specific patterns due to the complex interplay of biological, hormonal, and sociocultural factors. Understanding sex differences in the relationship between sleep and the brain may help us develop more targeted sleep-based strategies to promote healthy brain aging.

Keywords : Sleep efficiency, Brain aging, Sex differences, Neuroimaging, Narrative review

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P-843

Evaluating Cognitive and Neural Changes in Mild Cognitive Impairment with Portable Prefrontal EEG

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Background: Mild cognitive impairment (MCI), a cognitive decline syndrome in the elderly is often a precursor to dementia. Its early detection is crucial for timely diagnosis and possible intervention from dementia. Electroencephalography (EEG), a recording of brain electrical activity is gaining wide attention for studying MCI due to its accessibility, non-invasiveness and relative affordability. However, early cognitive changes, particularly those detectable through portable devices that combine physiological and cognitive markers, are not well understood. This study examined cognitive and behavioral deficits in MCI using selective attention ERPs from a prefrontal two-channel EEG. Methods: A total of 407 cognitively normal (CN) adults and 160 MCI patients completed 5-minute auditory oddball ERP tasks. Cognitive status was assessed with the Seoul Neuropsychological Screening Battery (SNSB), including the Korean Mini-Mental State Examination (K-MMSE). Group differences were tested with independent t-tests; associations among neuropsychological, behavioral, and ERP measures were evaluated using Pearson's correlation and logistic regression. Results: MCI patients displayed slower information processing and poorer task performance, including lower accuracy, more errors, and greater response time variability, compared to their CN counterparts. Logistic regression identified specific ERP and behavioral measures as significant predictors of MCI status, independent of demographics and neuropsychological scores. Neuropsychological scores correlated with both ERP and behavioral measures. Discussion: Slowed information processing and reduced task performance in MCI could be indicative of early neurological and attentional deficits. Therefore, portable EEG measures of prefrontal ERPs, combined with behavioral assessment, may enhance early screening efforts for MCI and complement traditional neuropsychological screening.

Keywords : mild cognitive impairment, event-related potential, electroencephalography, behavioral measures, cognitive function

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P-844

An insight into aging breakpoints through multisystem biomarkers in the Korean population

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Aging is a continuous biological process which characterized by varying rates of physiological decline across the lifespan. Understanding aging breakpoints in several biomarkers, including the autonomic nervous system (ANS) biomarkers, which is specific age ranges when biological aging begins to accelerate, plays a critical role in physiological regulation. It is critical for guiding preventive health strategies and precision aging interventions. This study aimed to identify aging breakpoints in the Korean population from multisystem biomarker. A total of 7,805 individuals (69.3% women and 30.6% men), aged 18 to 84 years, were recruited. Variables selection was conducted by correlation analysis and comprehensive analysis. Cumulative distribution plot were used to estimate baseline trends. GAM were applied to derive the first derivative (dy/dx) which representing the rate of biomarker change with age, and the second derivative (d^2y/dx^2) which capturing the acceleration or deceleration of aging. Finally, segmented analysis will show the breakpoint of aging. Our findings revealed that several biomarker for ANS derived from heart rate variability (HRV) including low frequency (LF) and high frequency (HF), HRV index, and heart rate (HR), as well as the other multisystem biomarkers from basic anthropometric, biochemical, and bioimpedance including height, systolic and diastolic blood pressure, aspartate aminotransferase (AST), glucose, glomerular filtration rate estimated (GFRE), waist-to-hip ratio (WHR), percent body fat (PBF), bone mineral content (BMC), phase angle of the lower limb (PA-lower), and extracellular water in the lower limb (ECW-lower), exhibited distinct aging patterns, differing between men and women. These insights could contribute to refining age-specific health screening thresholds and inform more targeted, sex-sensitive interventions to support healthy aging in East Asian populations.

Keywords : Aging breakpoint, Biomarker, Healthy aging

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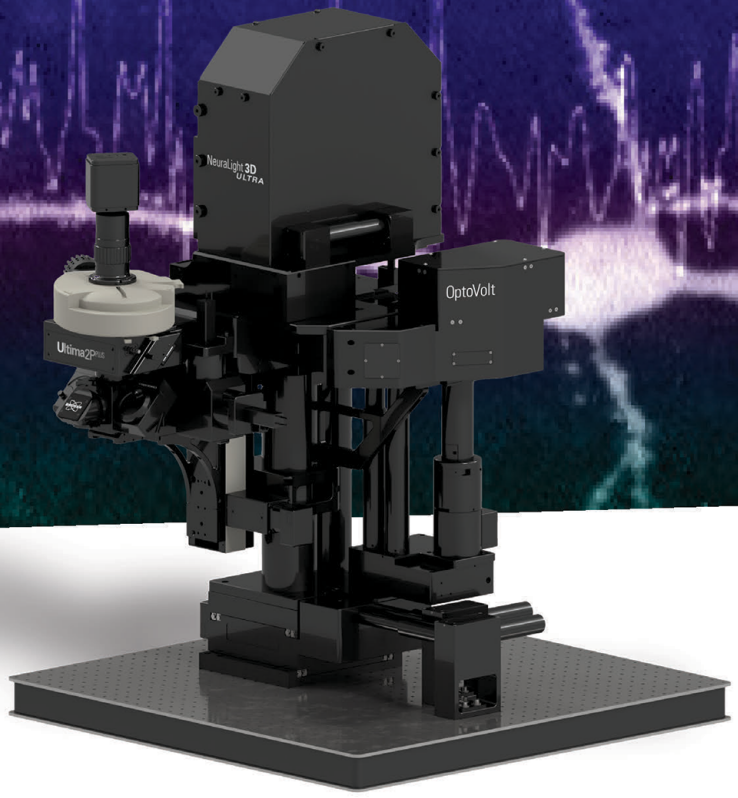

MULTIPHOTON MICROSCOPY

OptoVolt Module

High-Speed Voltage Imaging at Single Neuron Resolution

Bruker's OptoVolt™ Module for Ultima 2Pplus multiphoton microscopes delivers unprecedented kilohertz imaging rates to enable voltage imaging neural research.
It provides a significant improvement over standard imaging techniques by capturing electrical dynamics at up to 1000 frames per second and providing software-selectable multiplication modes well suited for imaging fast dynamics optimized for speed or field-of-view size. These accelerated imaging speeds allow neuroscientists to capture millisecond dynamics of cell-to-cell neural communication, and with the emergence of fluorescent voltage indicators, it is even possible to measure neural activity with higher temporal resolution than fluorescent calcium indicators have allowed.

INSCOPIX MINISCOPES nVista 2P

Two-Photon Brain Imaging in Freely-Behaving Animals

Enhanced Resolution Over One-Photon Technology
One-photon imaging can suffer from out-of-focus excitation that resuts in higher background noise and lower resolution (~4-5 microns) compared to its two-photon counterpart. The nVista 2P system can improve the ability to differentiate overlapping cells or accurately coregister the same cells across sessions. It offers reduced background, improved resolution (1.6 microns), and the ability to image densely-labeled or deep regions, such as the entorhinal cortex and hypothalamus, all during free behavior.

Improved Two-Photon Solution for Freely-Behaving Studies
Two-photon benchtop systems, where the animal is fixed, often require workarounds to recreate natural behaviors, using joystick and ball running. These paradigms demand extensive training and can lead to unrealistic behaviors (e.g., athlete-animal syndrome).

The nVista 2P system solves these issues by integrating and miniaturizing traditional benchtop fluorescence instrumentation into a well-balanced miniscope, enabling freely-behaving experiments without compromising the animal's ability to interact with its environment. When paired with the Inscopix nVision behavior recording system, scientists can now observe more natural behaviors, such as place preference and socialization.

바이러스를 다루는 최적의 파트너,
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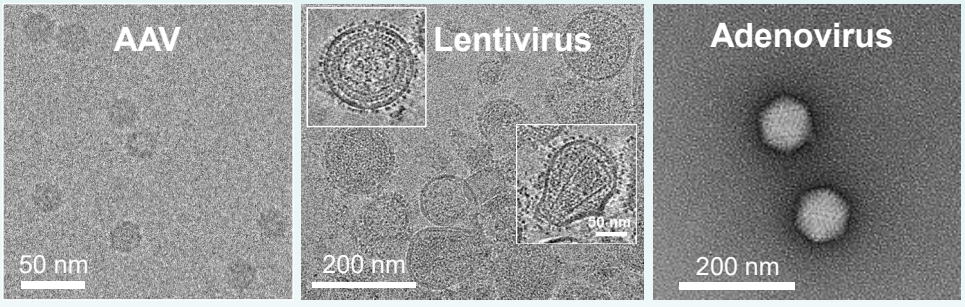


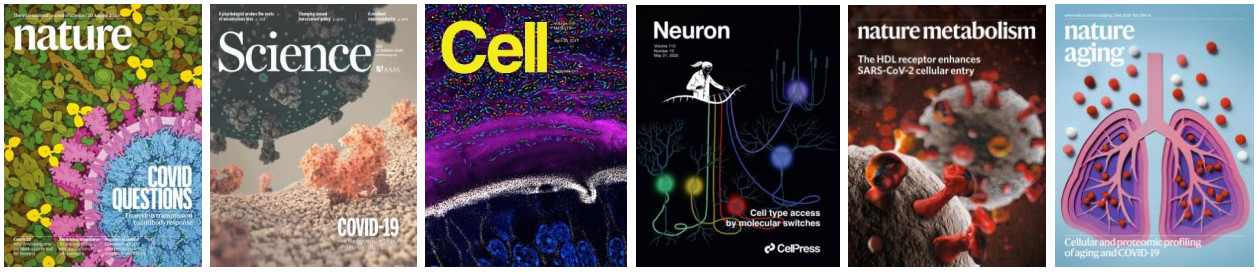
Cryo-TEM 이미지 **(KIST** 특성분석센터**)**

맞춤형 바이러스 제작

- AAV, Lentivirus, Adenovirus 등 고효율·고농도 제작
- Titer ≥ 10^{12} vg/mL

유전자 조절 벡터 설계

- Cre-lox 기반 Cre-On/Cre-Off shRNA library 지원
- Cell-type specific shRNA 제작



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문의: **selee@kist.re.kr, 02-958-6989**

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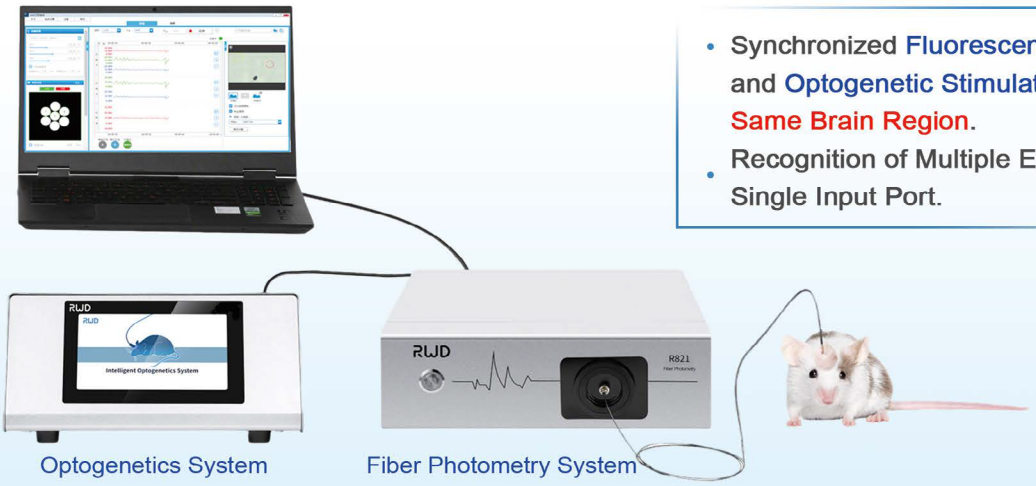
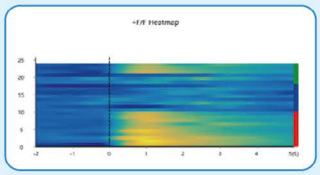
Multichannel Fiber Photometry

Compatible with 465/589/635 Optogenetics

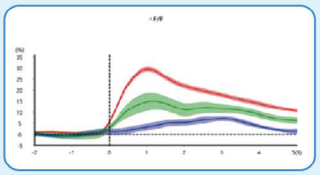


Optogenetics System　　Fiber Photometry System

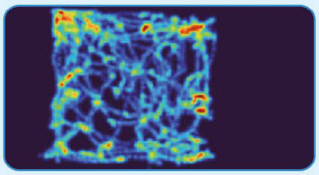
- Synchronized Fluorescence Recording and Optogenetic Stimulation in the Same Brain Region.
- Recognition of Multiple Events via a Single Input Port.



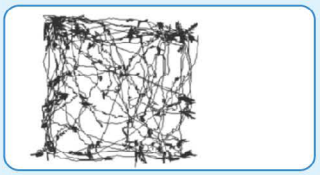
Fluorescence Heatmaps



Curve Graphs



Gaussian-smoothed Fluorescence Place Heat Map



Trajectory

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Including fluorescence heatmaps, curve graphs, animal trajectory graphs,etc.

Signal Acquisition Sensitivity

Meets the need for weak signal detection at the picowatt level (axons/glia).

Professional Data Analysis

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Wavelength of excitation light :

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Note: 640 nm light source (for four-color system) is available as an option

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라이브셀인스트루먼트(Live Cell Instrument, LCI)는 바이오 연구용 장비(Live Cell Imaging) 및 전용 소모품과 의료기기 장비를 전문적으로 제조, 판매 회사입니다.
이번 전시회를 통하여 QuadScan (Innovative Single Pinhole Molecular Confocal System)을 국내에 첫 선을 보이며, Nexcope(80년 역사의 현미경 제조사로서, Nikon, Leica 등의 주요 현미경 모델을 공급하는 실질적인 메이저 현미경 회사) 현미경 국내 총판 대리점으로서 주요 현미경을 선보입니다.

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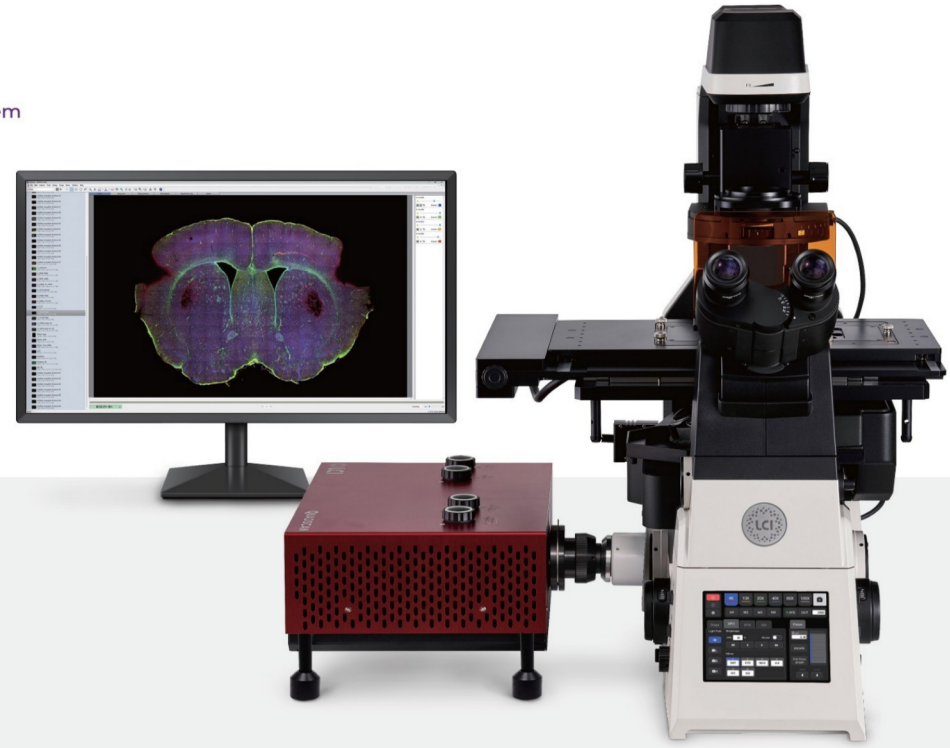

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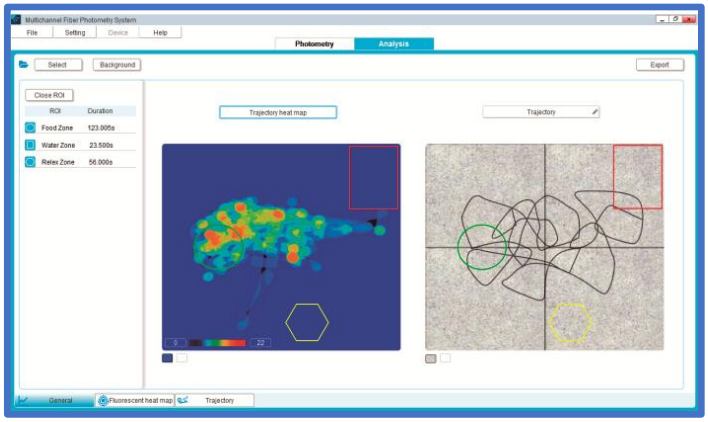

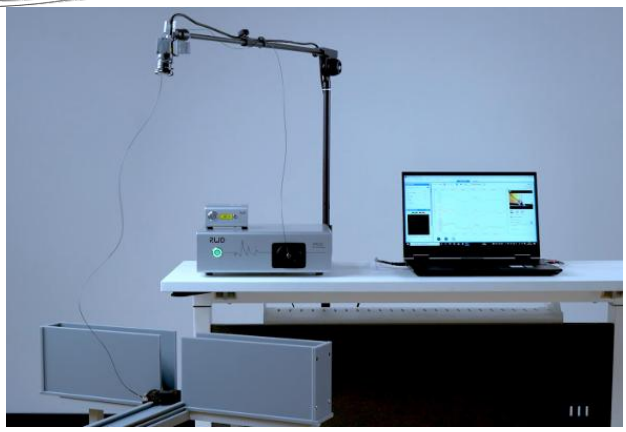

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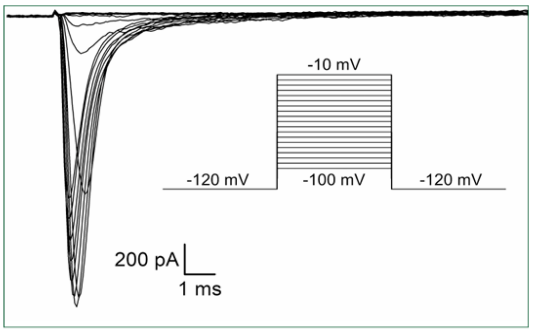

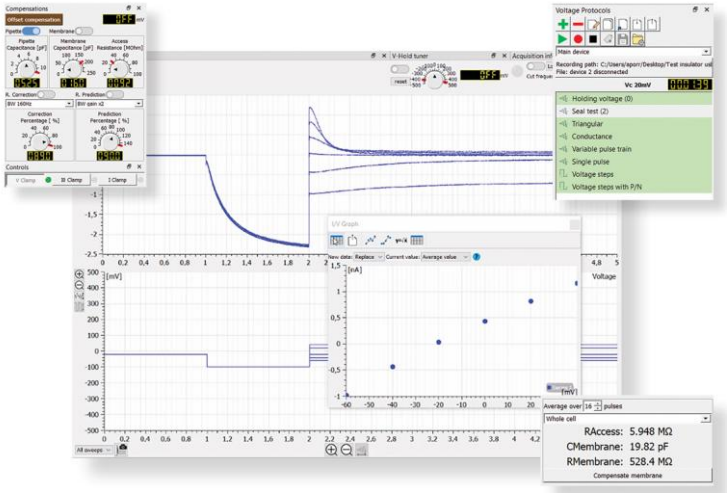

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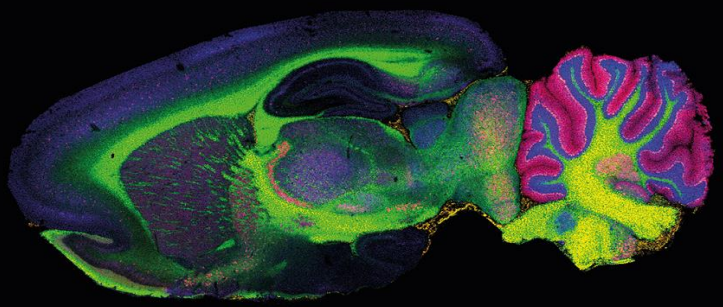

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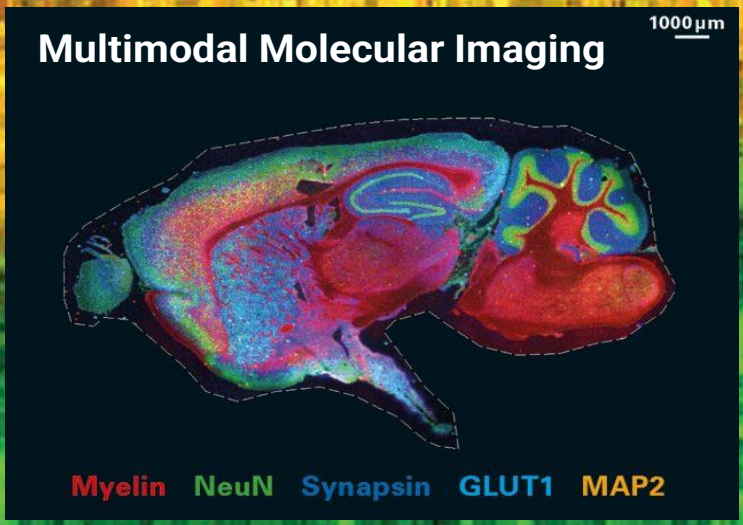

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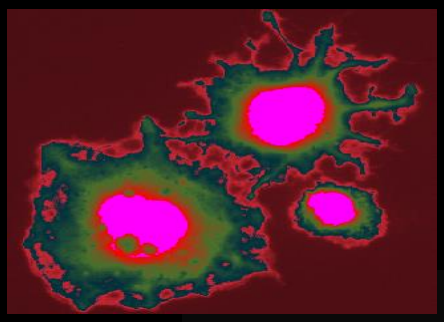

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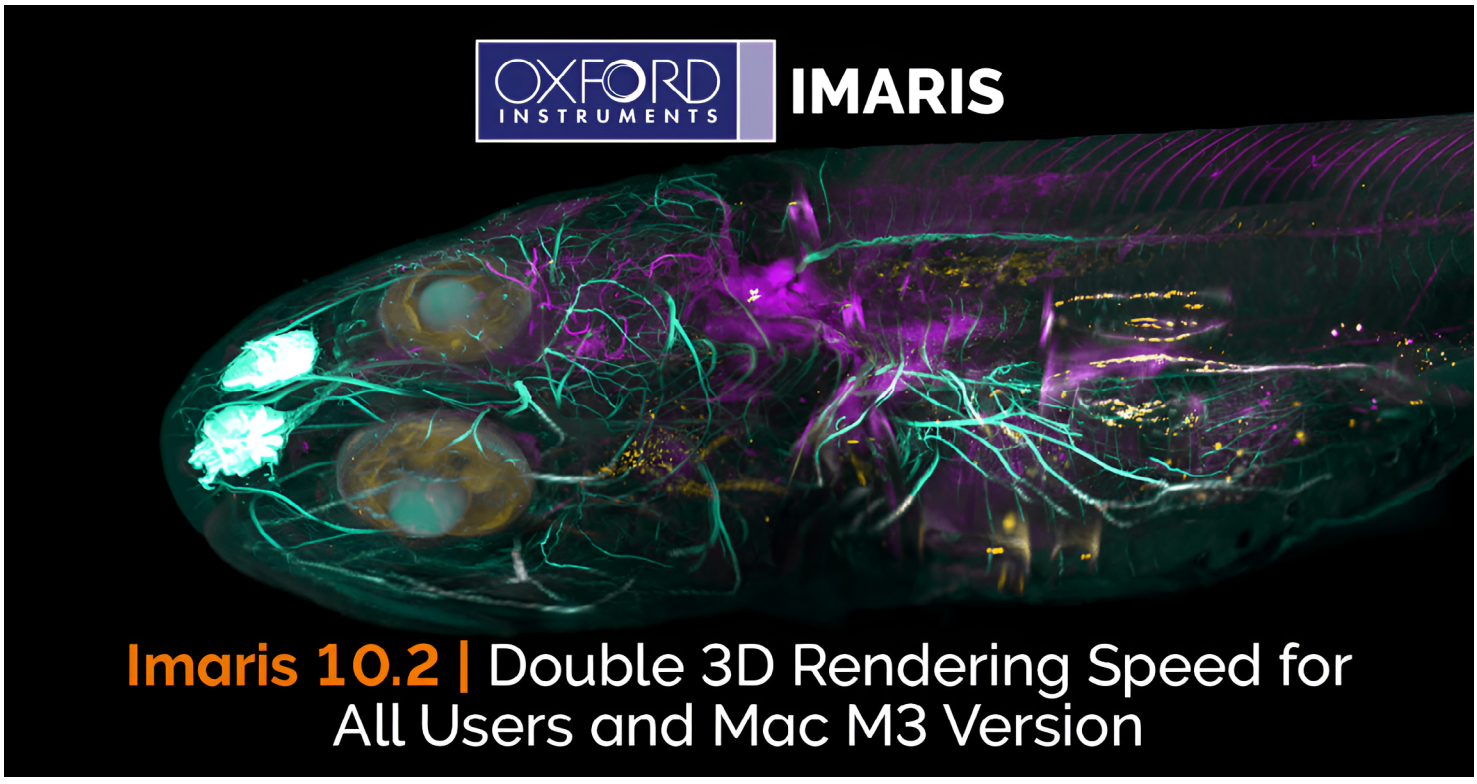

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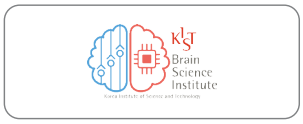
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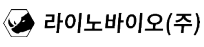
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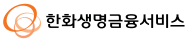
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한국과학기술연구원 뇌과학연구소	Korea Institute of Science and Technology BSI	오상록	02-958-5114	https://kist.re.kr/ko/index.do	종합출연연구소
JW중외제약	JW Pharmaceutical	신영섭	010-5142-6779	https://www.jw-pharma.co.kr/mobile/pharma/ko/main/m_main.jsp	제약
벡터빌더	VectorBuilder Inc.	Bruce Lahn	02-833-9631	www.vectorbuilder.com	클로닝, AAV, 렌티바이러스제작, IVT RNA, stable cell line 제작, Library, CRO, GMP plasmid, GMP 바이러스
(주) 우성크라이어텍	Woosung Cryotech Co,.LTD	정용주	031-732-2555	www.woo-sung.com	초저온 저장용기 도소매
Preclina Inc.	Preclina Inc.	강영모		www.preclina.com	Preclinical CRO
Chinese Neuroscience Society	Chinese Neuroscience Society			https://www.cns.org.cn/en/	Non-profit organization
Ecocell Co., Ltd	Ecocell Co., Ltd	전윤하		www.ecsci.co.kr	Laboratory Instrument, Consumable Products, Reagents, Kits
매직트리	MAGICTREE	김식	02-355-5963	http://www.magictree.kr	LightSheet, Multi-Photon etc
(주) 뉴로링스	NeuroLynx	조한상	031-299-4792	www.neuro-lynx.com	비임상 약물평가 서비스
(주)텍스코코리아	Tecsco Korea Co.,LTD.	한찬구,이흥국	02-6239-3660	http://www.tecscokorea.com/	초고해상도 공초점 레이저 주사 현미경(STED), 라만 현미경, 원자간력 현미경 공급 및 서비스
Cyagen	Cyagen			https://www.cyagen.kr/	Humanized mouse model, CRO services
MDxK	MDxK	심성보		https://mdxk.co.kr/	Genomics / Multiomics Research Products
Packgene Biotech	Packgene Biotech			www.packgene.com	Cro&CDMO
Signal Transduction and Targeted Therapy	Signal Transduction and Targeted Therapy			https://www.nature.com/sigtrans/#about-the-journal	Signal Transduction and Targeted Therapy is an international, peer-reviewed, open-access journal
SpikeGadgets	SpikeGadgets			spikegadgets.com	In vivo elecrophysiology in animals
고마바이오텍(주)	KOMABIOTECH	문상훈	02-579-8787	komabiotech.co.kr	시약공급 및 서비스, 생명과학실험기기
라온바이오 주식회사	RAONBIO	나종성	031-283-4197	https://raonbio.co.kr/	동물 실험 장비, 실험동물 등
비보솔루션즈	VIVO Solutions	박미경		www.vivosolutions.co.kr	Imaging & Analysis, In vivo E.Physiology, Histology equipment
비투바이오 주식회사	B2BIO,Inc.	문경배	02-6409-9338	www.b2bio.co.kr	단백질정제시스템
아주대학교의료원	Ajou University Medical Center	한상욱	031-219-7887	https://www.ajoumc.or.kr/	인체자원 분양(인체유래물, 임상/역학정보, 뇌영상 등)
에비던트코리아 주식회사	EVIDENT KOREA CO.,LTD	YOSHIMOTO HIROYUKI	02-1800-9180	https://evidentscientific.com/ko/	광학현미경, 컨포컬현미경, 광학분석솔루션
엠디피아이 코리아	MDPI Korea	서운열	02-466-9708	www.mdpi.com	Academic Open Access Publishing (오픈 액세스 학술 출판)
주식회사 뉴머스	Neumous Inc.	박주영	070-7789-2558	http://neumous.com	뇌혈관장벽 개방을 위한 초음파 기기
한국생명공학연구원 국가영장류센터	KRIBB NPRC	이영전		https://portal.kribb.re.kr/primate	정부출연연구소 - 영장류 뇌과학 인프라 구축
바이오클론(주)	Bioclone Corp.	임재근	02-2690-0058	www.bioclone.co.kr	antibody, ELISA, chemical reagents 등 시약 공급
옵틱솔루션	Optic Solution	김태훈	031-968-7330	www.opticsolution.co.kr	광학 현미경
글로벌금융판매	KB FINANCIAL GROUP	김종선	010-6321-7170	https://www.kbfg.com/kor/index.jsp	금융서비스
대구경북첨단의료산업진흥재단	Daegu-Gyeongbuk Medical Innovation Foundation	박구선	053-790-5114	https://www.kmedihub.re.kr	의료기기 개발, 전임상 연구, 신약 개발, 임상 의약품 제조, 의약생산지원
주식회사 바이어스	VIUS Inc	장상원	010-9102-2547		AAV 제작 서비스
한화생명금융서비스	Hanwha Life Financial Services	이경근	02-2182-3135	https://www.hanwhalifefs.com/	보험대리점
(주)다온비에스	DAON BioSciences	김수진	010-6243-4188	www.daonbs.com	생명과학 연구용 기기 및 관련 시약 판매
(주)미래에스티씨	MIRAE STC	김정호	042-822-9801	http://www.miraestc.co.kr/	비임상 동물 실험 장비
(주)이지다이아텍	Ezdiatech Inc.	정용균	031-385-5455	www.ezdiatech.com	혈액기반 뇌질환 검사 장비 및 시약
(주)이츠바이오	ITSBIO	임병춘	02-3462-8658	http://itsbio.co.kr/	소동물용 실험장비 및 연구용 시약 및 소모품 생산 및 공급 업체
(주)필코리아테크놀로지	1st PhileKorea	박민봉	02-2105-7020	www.philekorea.kr	염기서열분석기,공간전사체분석기,분자생물학시약
Cell Signaling Technology	Cell Signaling Technology	Michael J. Comb		Www.cellsignal.com	Antibodies
MedChemExpress	MedChemExpress			www.medchemexpress.com	bioactive compounds
Takara Korea Biomedical Inc.	Takara Korea Biomedical Inc.	미야무라츠요시, 이동근, 이노우에코이치		takara.co.kr	Molecular Biology Reagents and Instruments
나노글리아	nanoglia	김동운	042-713-9079	https://www.nanoglia.com/	연구재료 및 시약 (표적치료용 주문제작형 나노입자 생산서비스)
노보 노디스크	Novonordisk	POULSEN KASPER ROSEEUW	02-2188-8900	https://www.novonordisk.co.kr/	당뇨병, 비만
뉴잉글랜드바이오랩스코리아	New England Biolabs Korea	Sue Yap	070-738-1128	www.neb.com	분자생물학용 효소 및 시약 개발·제조, 유전자 클로닝 및 PCR 관련 시약 공급, 생명과학 연구용 시약 서비스
다윈바이오	DAWINBIO	유선하	1588-9741	https://dawinbio.com/	생명과학 연구용 시약 및 장비 공급
동아에스티	DONG-A ST	정재훈	02-920-8796	www.donga-st.com	제약
바이오이미징데이터품질선도센터 (한국기초과학지원연구원)	Bio-imaging Data Curation Center (Korea Basic Science Institute)	권희석 책임연구원	042-865-3500	www.kbsi.re.kr	연구 및 개발
바이오테크니 코리아	Bio-Techne Korea	세인빅터보넌	010-8757-3021	https://www.bio-techne.com/	면역검정법장비, 시약 공급 및 서비스
영인과학(주)	YoungIn Scientific	김현철, 이순길, 이지민	02-519-7300	www.youngin.com	광학현미경, 크로마토그래피
주식회사 엘앤피솔루션	LNP solution Inc.	이다빈		https://www.lnpsolution.com/ko/	CRO 및 시뮬레이션 소프트웨어
토모큐브	Tomocube	박용근	042-863-1100	www.tomocube.com	Holotomography, 홀로토모그래피 현미경
서울대학교병원 치매 뇌은행	Seoul National University Hospital Brain Bank	박성혜	02-2072-7158	https://brainbank.snuh.org/	사후 뇌조직 바이오뱅크
진성인스트루먼트	JINSUNG INSTRUMENTS, INC.	이하원	042-823-5300	www.jinsunginst.com	레이저 시스템 및 측정기, 광학 부품류

기업명(국문)	기업명(영문)	대표자 성명	대표전화	기업 홈페이지 주소	기업 분야
(주)라이프텍	Lifetech Inc.	이한진	02-456-8566	www.lifetechinc.co.kr	생리측정 장치, NIRS system, Laser Doppler
바이오메디북	BIOMEDBOOK	주필체	010-3750-5497	WWW.BIOMEDBOOK.CO.KR	서적
상정상사(주)	Sang Chung Commercial Co., Ltd.	김재남	02-564-8766	http://www.sang-chung.co.kr/	동물 실험 장비 및 소모품
EN	Experimental Neurobiology				
(주)이우과학교역	IWOO SCIENTIFIC CORPORATION	강현철	02-3473-2332	https://www.iwoo.co.kr/	동물 실험 장비
라이노바이오(주)	Rhino Bio, Inc.	고태호	042-933-1620	www.rhinobio.co.kr	과학실험기기 및 전용 소모품
기초과학연구원	Institute for Basic Science			ibs.re.kr	Research
(재)한국과학기술젠더혁신센터	GISTeR	이혜숙	02-6205-9101	www.gister.re.kr	젠더혁신 교육, 인식개선, 글로벌협력 등
한국뇌연구원	Korea Brain Research Institute	서판길	053-980-8231	https://www.kbri.re.kr/	뇌 연구 공공기관
식품의약품안전처 식품의약품안전평가원	NIFDS	강석연	043-719-5206	https://www.nifds.go.kr/index.do	식품 및 의약품 규제
(주) 큐어버스	Cureverse	조성진	02-966-0203	https://cureverse.co.kr/	저분자화합물 기반 신약개발
뇌 체성 돌연변이 연구단	Center for Brain Somatic Mutations	이정호	042-350-0421	tnl.kaist.ac.kr	
뇌질환융합연구센터	Center for Convergence Research of Neurological Disorders	박상면	031-219-5060	https://www.ajoumc.or.kr/medicine/univ/profList.do?deptTp=004002000	연구센터
뉴로바이오젠(주)	NeuroBiogen Co., Ltd.	김상욱	010-7324-3161	https://www.neurobiogen.com	신약 개발
치매극복연구개발사업단	KOREA DEMENTIA RESEARCH CENTER	묵인희	02-3668-7399	www.kdrc.re.kr	치매연구개발지원
다물사이언스	DA MOOL SCIENCE	김윤숙	010-2403-4248	없음	실험동물(국내, 수입) 사료, 깔집, 기자재 등
기초과학연구원	Institute for Basic Science	노도영	042-878-8185	www.ibs.re.kr/ccs	기초과학
시냅스뇌질환연구단 (IBS로고)	Institute for Basic Science				
IBRO	IBRO				
ICONEUS	ICONEUS				
일리미스테라퓨틱스	ILLIMIS THERAPEUTICS, INC.	박상훈	02-445-6877	www.illimistx.com	퇴행성뇌질환 신약연구개발기업
블루셀	bluecell	이승희		www.bluecell.co.kr	Imaging Devices
마시모 코리아	Masimo Korea	김아경, 엘렌생텔미셸델레게엡찬스마이스터	010-5456-9111	https://www.masimo.kr/	의료기기
싸토리우스코리아(유)	Sartorius Korea LLC	김덕상	031-622-5700	www.sartorius.co.kr	생명과학 연구 및 제약•바이오 산업
에이비엘바이오(주)	ABL Bio, Inc.	이상훈	02-3456-7365	http://www.ablbio.com	의약품(신약) 개발
후각융합연구센터	Convergence Research Advanced Centre for Olfaction	문제일 센터장 (기관 대표: 이건우 총장)	053-785-7440	https://olfaction.dgist.ac.kr	연구개발
키스트 바이러스 퍼실러티	KIST VIRUS FACILITY	이승은	010-3572-3343		바이러스 벡터 개발 및 제작
한국한의학연구원	Korea Institute of Oriental Medicine	이진용	010-9207-7060	kiom.re.kr	한의학 연구
뉴로그린	Neurogrin	김선광, 정지훈	02-6953-6591	https://neurogrin.co.kr/	AI 기술 기반 뇌신경질환 진단 치료기업
Bruker Fluorescence Microscopy	Bruker Fluorescence Microscopy			www.bruker.com/fluorescence-microscopy	Imaging Devices
아이빔테크놀로지	IVIM Technology, Inc.	김필한	042-825-7450	www.ivimtech.com	생체현미경, 생체영상화서비스, 시약
한국오츠카제약	Korea Otsuka Pharmaceutical	문성호	02-3287-9000	https://www.otsuka.co.kr/	제약
한독	Handok	김영진	02-527-5114	https://www.handok.co.kr/	제약
Johnson&Johnson	Johnson&Johnson			www.jnjinnovation.com	Medicine
자이스 코리아	ZEISS	정현석	1661-3140	www.zeiss.co.kr/microscopy	광학 및 전자현미경
(주)비엠에스	Bio-Medical Science Co., Ltd.	김선기	02-3471-6500	www.bms.kr	기초장비, STEMCELL, 세포배양/분석, Genomics, 실험동물 등
자연과학(주)	CHAYON Loaboratories Inc.	김선기	02-3471-4100	www.chayon.co.kr	Drug Discovery, Spectrophotometer, 기초실험 장비, 시약 공급 및 서비스 등
브루커코리아(주)	Bruker Korea Co.,Ltd	조문주	02-403-9934	https://www.bruker.com/ko.html	질량분석기
GemPharmatech	GemPharmatech			www.gempharmatech.com	Mouse Models and Preclinical service
(주)싸이텍코리아	Scitech Korea Inc.	박찬승	02-986-4413	https://scitechkorea.com/	전기생리측정장비, 동물 실험 장비, 이미징 장비, 뇌신경과학 관련 장비 전반
기초과학연구원 LSI클러스터	IBS(Institute for Basic Science) LSI	노도영	042-878-8114	https://www.ibs.re.kr/lsi/	
주식회사 플래시오믹스	Flashomics Corp.	장재범	02-443-0717	flashomics.com	Imaging service
니콘인스트루먼트코리아	Nikon Instruments Korea	KIRIBUCHI KOJI, 마키 요시히로		https://www.microscope.healthcare.nikon.com/ko_KR/	Imaging Devices
라이브셀인스트루먼트	Live Cell Instrument Co. Ltd.	이용진	02-3391-0596	http://www.lcibio.com	광학현미경, 현미경 주변기기
주식회사 셀루션	Cellution Inc.	김용언	042-361-3990	https://cellution.co.kr	IMARIS, Confocal System, 광학현미경
(주)바이오엔진	BIOENGINE Inc.	이병하	031-564-0345	www.bioengine.co.kr	전기생리측정장비, 동물실험장비, 광학현미경, 실험장비 제작 등
(주)킴앤프렌즈	Kim & Friends	김광용	02-2647-6611	https://www.kimnfriends.co.kr/	동물 실험 장비, 조직슬라이드스캐너
써모피셔사이언티픽	Thermo Fisher Scientific	석수진	010-8736-9053	thermofisher.com	광학, 형광현미경, 공간생물학이미징 장비, 시약 등
주식회사 싸이큐브	SCIcube Co., LTD. (Leica Microsyctems)	박정인	043-214-4125	www.scicube.co.kr	광학현미경,
한미약품	Hanmi Pharmaceutical	박재현		www.hanmi.co.kr	R&D, 개량복합신약 중심의 제약회사
주식회사 지브레인	Gbrain Inc.	김병관, 양성구	070-5618-8193	https://www.gbrainlife.com	신경생리 기반 진단/치료 기기, 뇌 이식형 의료기기
RWD Life Science Co., Ltd.	RWD Life Science Co., Ltd.			www.rwdstco.com	Medical Devices, Imaging Devices, Lab Animal Care devices
주식회사 아임시스템	IMsystem Co., Ltd.	김진영	070-4905-1177	https://imsystem.kr	다중전극어레이(MEA) / 혈관 시뮬레이터
인천시					
인천관광공사					
지엔티파마	GNTPharma				
아주대학교	Ajou University				