PROGRAM BOOK

International Brain Initiative

Daegu Conference 2023

August 07(Mon.)-09(Wed.), 2023
KBRI, Daegu, Korea

Emotional Brain Mapping in Health & Disease

한국뇌연구원
Korea Brain Research Institute

August 7-9, 2023

IBI Daegu Conference 2023

Korea Brain Research Institute, Daegu, Korea

Welcome address

Dear Colleagues,

It is our great pleasure to welcome you to the 2nd IBI Daegu Conference 2023, scheduled for August 7-9, 2023 at the Korean Brain Research Institute (KBRI) in Daegu, South Korea. The primary goal of our conference is to advance neuroscience research through international collaboration and knowledge sharing, specifically focusing on circuitry and molecular multiscale brain mapping related to emotions. Furthermore, we are striving to develop comprehensive brain functional maps that specifically relate to emotions, providing valuable resources for future research and clinical applications.

To achieve these aims, we closely collaborate with accomplished neuroscientists worldwide, specializing in diverse fields such as neuro-engineering, neuroimaging, and related disciplines, in addition to basic neuroscience. We host the annual IBI Daegu Conference with the title 'Emotional Brain Mapping in Health and Disease' for fostering an open exchange of knowledge and insights within the neuroscientific community. By integrating expertise from these various fields, the project seeks to illuminate the neural mechanisms underlying emotions and their potential implications in mental health. This multidisciplinary approach enables us to investigate emotions and psychiatric disorders from multiple perspectives, delving deeply into the intricacies of brain function.

I look forward to seeing you all in Daegu and making this meeting a scientific summit and a memorable festivity with you.

Sincerely,

President, KBRI

Pann-Ghill Suh, D.V.M., Ph.D.

Organizing committee

Title		Name (Affiliation)
Executive Committee	President	Pann-Ghill Suh (KBRI, S.Korea)
	Chairperson	Ja Wook Koo (KBRI, S.Korea)
	Vice Chairperson	Jong-Cheol Rah (KBRI, S.Korea)
Steering Committee (IBI Emotional Brain Working Group)		Bernard Balleine (UNSW Sydney, Australia) Scott Russo (Mount Sinai, US) Matt Girgenti (Yale Univ., US) Vincent Vialou (Inserm, France) Weidong Li (Shanghai Jiao Tong Univ., China) Satoshi Kida (Tokyo Univ., Japan) Paul Frankland (Univ. of Toronto, Canada) Yong-Seok Lee (Seoul Nat'l Univ., S.Korea) Jong-Cheol Rah (KBRI, S.Korea) Ja Wook Koo (KBRI, S.Korea)
Working Committee		Dongha Lee (KBRI, S.Korea) Minyoung Jung (KBRI, S.Korea) Namsun Chou (KBRI, S.Korea) Ji Young Mun (KBRI, S.Korea) Gunsoo Kim (KBRI, S.Korea) Juhyun Kim (KBRI, S.Korea) Beomsue Kim (KBRI, S.Korea) Taekwan Lee (KBRI, S.Korea) Taekwon Son (KBRI, S.Korea) Jong-Cheol Rah (KBRI, S.Korea) Ja Wook Koo (KBRI, S.Korea)
Public Relations & Management	Public Relations	Sang Yeon Kim (KBRI, S.Korea) Ra Gyung Kim (KBRI, S.Korea) Ji Eun Cheon (KBRI, S.Korea)
	Management	Hyo-Yung Noh (KBRI, S.Korea) Hyejin Cho (KBRI, S.Korea) Sungsoo Lee (KBRI, S.Korea) Seung Kook Choi (KBRI, S.Korea) Sangu Byeon (KBRI, S.Korea)

Program at a glance

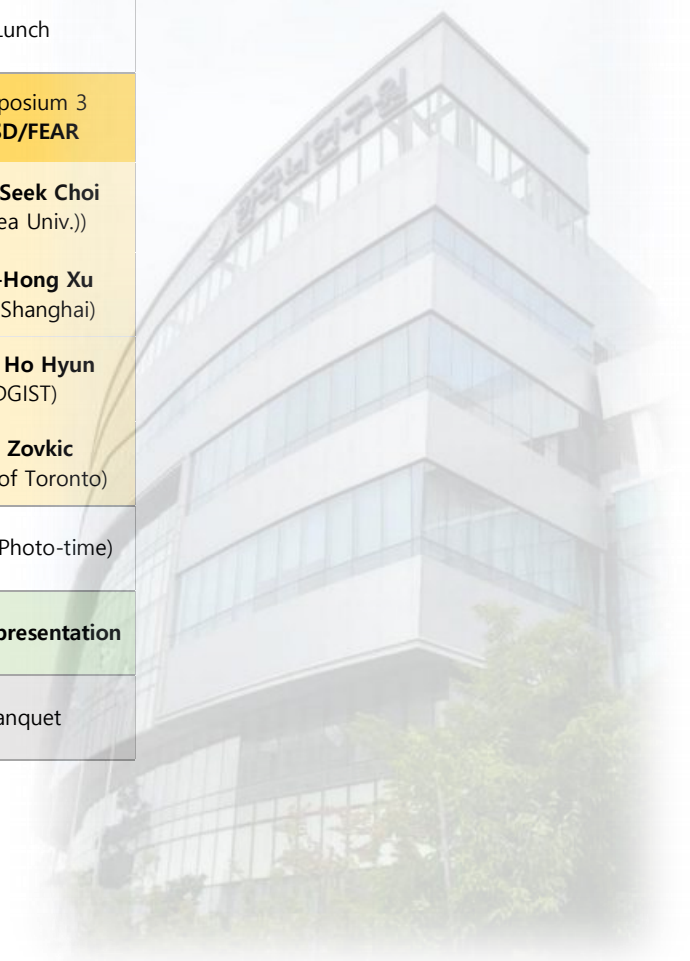
Schedule

Day 1 (Aug. 07, 2023)	
~ 14:00※	Registration
14:00 ~ 14:10	Welcome Address **Pann-Ghill Suh** (KBRI)
14:10 ~ 14:50	Opening Lecture **Bernard Balleine** (UNSW Sydney)
14:50 ~ 15:00	Break
15:00 ~ 17:00	Symposium 1 **Reward/Addiction**
15:00 ~	**Jessica Ables** (Mount Sinai)
15:30 ~	**Ja-Hyun Baik** (Korea Univ.)
16:00 ~	**Hyung Jin Choi** (Seoul Nat'l Univ.)
16:30 ~	**Sam Golden** (Univ. of Washington)

Day 2 (Aug. 08, 2023)	
09:30 ~ 10:20	Plenary Lecture **Eric Nestler** (Mount Sinai)
10:20 ~ 10:30	Break
10:30 ~ 12:30	Symposium 2 **Stress/Depression**
10:30 ~	**Scott Russo** (Mount Sinai)
11:00 ~	**Kenji Tanaka** (Keio Univ.)
11:30 ~	**Ming-Hu Han** (SIAT CAS)
12:00 ~	**Joung-Hun Kim** (POSTECH)
12:30 ~ 14:00	Lunch
14:00 ~ 16:00	Symposium 3 **PTSD/FEAR**
14:00 ~	**June-Seek Choi** (Korea Univ.))
14:30 ~	**Xiao-Hong Xu** (ION Shanghai)
15:00 ~	**Jung Ho Hyun** (DGIST)
15:30 ~	**Iva Zovkic** (Univ. of Toronto)
16:00 ~ 16:10	Break (Photo-time)
16:10 ~ 18:00	**Poster presentation**
18:30 ~ 20:00	Banquet

Day 3 (Aug. 09, 2023)	
09:30 ~ 11:30	Symposium 4 **Neurodevelopmental abnormalities**
09:30 ~	**Minyoung Jung** (KBRI)
10:00 ~	**Katrina Choe** (McMaster Univ.)
10:30 ~	**Hirotaka Kosaka** (Univ. of Fukui)
11:00 ~	**Weidong Li** (SJTU)
11:30 ~ 12:00	Closing Ceremony

※ Korean Standard Time (GMT+9)



Lectures

Amygdala-striatal control of predictive learning and its influence on decision-making

Bernard Balleine, PhD

Scientia Professor and NHMRC Senior Investigator
Head, Decision Neuroscience Lab, School of Psychology, University of New South Wales, Sydney, Australia

[Date] Aug 07 / [Time] 14:10-14:50

Abstract :

The amygdala has been found to play an essential role in striatal function both via its direct connections and indirectly through its contribution to various cortical and subcortical circuits that influence broad areas of dorsal and ventral striatum. In this talk I will present recent evidence that both the direct and indirect connections of the amygdala with the ventral striatum, most notably the accumbens shell, play an essential role in the encoding and retrieval processes necessary for predictive learning to influence decision-making. We have found the direct basolateral amygdala input to the accumbens shell plays an essential role in encoding predictive associations between stimuli and reward, inducing specific cellular changes that are not necessary for predictive learning per se but that are necessary for this learning to influence choice and decision-making. The retrieval of these amygdala-generated associations also involves the amygdala but indirectly via its activation of the infralimbic projection to accumbens shell, initiating activity in a cortical-basal ganglia feedback circuit that ultimately modifies action selection and so choice between distinct courses of action.

Keywords :

Instrumental conditioning, Pavlovian conditioning, Basolateral amygdala, Accumbens shell, Reward and decision-making

Education and Training :

1992	PhD, University of Cambridge, UK
1988	BA, University of Sydney, AUS

Professional Positions :

2020-present	Senior Investigator, National Health and Medical Research Council of Australia
2017-present	Appointed Scientia (Distinguished) Professor , University of New South Wales, Sydney, Australia
2016-present	Professor & Head, Decision Neuroscience Laboratory School of Psychology, University of New South Wales, Sydney, Australia
2015-2019	Senior Principal Research Fellow, National Health and Medical Research Council
2011-2013	Visiting Professor, Caltech
2009-2015	Professor, Brain and Mind Research Institute, University of Sydney, Australia Laureate Fellow, Australian Research Council
2005-2009	Director, Research Brain Research Institute, UCLA
2004-2009	Professor, University of California, Los Angeles, USA
2000-2004	Associate Professor, University of California, Los Angeles, USA
1996-2000	Assistant Professor, University of California, Los Angeles, USA
1989-1992	Commonwealth Scholar and Churchill College Scholar PhD candidate, University of Cambridge, UK

Lectures

Transcriptional and Epigenetic Mechanisms of Drug Addiction

Eric Nestler, MD, PhD

Nash Family Professor of Neuroscience
Director of the Friedman Brain Institute
Dean for Academic Affairs, Icahn School of Medicine at Mount Sinai, NY, USA

[Date] Aug 08 / [Time] 09:30-10:20

Abstract :

Drug addiction can be viewed as a stable form of drug-induced neural plasticity, whereby long-lasting changes in gene expression mediate some of the stable behavioral abnormalities that define an addicted state. Our laboratory has focused on transcriptional pathways in addiction, deduced from large RNA-sequencing datasets of RNAs that show altered expression in brain reward regions of mice as a consequence of drug self-administration, withdrawal, and relapse. Activation or induction of certain transcription factors represent homeostatic adaptations that oppose drug action and mediate aspects of drug tolerance and dependence. In contrast, induction of other transcription factors exerts the opposite effect and contributes to sensitized responses to drug exposure. We are also characterizing a range of chromatin mechanisms that act in concert with these transcription factors to control gene expression. These studies are identifying many of the molecular targets of drug self-administration in brain reward regions and the biochemical pathways most prominently affected. Parallel work has focused on homologous regions in the brains of addicted humans examined postmortem. These advances can now be mined to develop improved diagnostic tests and treatments for addictive disorders.

Keywords :

Cocaine, Opioids, Nucleus Accumbens, Chromatin, Gene expression

Education and Training :

1983	MD, Yale University, CT, USA
1982	PhD, Department of Pharmacology, Yale University, CT, USA
1976	BA and MS, Department of Molecular Biophysics and Biochemistry, Yale University, CT, USA

Professional Positions :

2016-present	Dean for Academic and Scientific Affairs, Mount Sinai School of Medicine, NY, USA
2008-present	Professor, Nash Family Department of Neuroscience, Mount Sinai School of Medicine, NY, USA Director, Friedman Brain Institute, Icahn School of Medicine at Mount Sinai, NY, USA Dean for Academic and Scientific Affairs, Mount Sinai School of Medicine, NY, USA Member, Medical Staff, The Mount Sinai Medical Center, NY, USA
2008-2016	Chair, Department of Neuroscience, Mount Sinai School of Medicine, NY, USA
2000-2008	Professor, Department of Lou and Ellen McGinley Distinguished of Psychiatry, Texas University of Sourthwestern Medical Center at Dallas, TX, USA
1987-2000	Assistant Professor, Department of Psychiatry and Pharmacology, Yale University School of Medicine, CT, USA Assistant Professor, Elizabeth Mears and House Jameson Associate Professor, Elizabeth Mears and House Jameson Director, Division of Molecular Psychiatry, Yale University School of Medicine, CT, USA

MEMO

Nos1 in the interpeduncular nucleus mediates oxycodone tolerance

Jessica Ables, MD, PhD

Assistant Professor, Department of Neuroscience & Pasychiatry, Icahn School of Medicine at Mount Sinai, NY, USA

[Date] Aug 07 / [Time] 15:00-15:30

Abstract :

Previously we found that nitric oxide synthase 1 (NOS1) is upregulated by chronic nicotine exposure in Chrna5+ cells in the interpeduncular nucleus (IPN) and we recently expanded these findings to include chronic oxycodone exposure. Systemic administration of a NOS1 inhibitor can prevent development of analgesic tolerance to opioids, reverse established tolerance, as well as prevent and reverse withdrawal to chronic opioids. Our current studies explore whether an increase in NOS1 in the IPN is necessary for development of tolerance to the rewarding and aversive effects of oxycodone by knocking down NOS1 expression in the IPN using a short hairpin RNA virus (n=17). Control animals received a scrambled shRNA virus (n=20). After allowing 2-3 weeks for the virus to express, mice were divided into oxycodone-drinking and water-drinking groups. After allowing mice to habituate to their drinking condition over 1 week, a biased CPP paradigm was run conditioning mice to their least preferred side with oxycodone. As expected, the scramble injection group with regular drinking water(n=12) demonstrated robust preference for the chamber paired with 5 mg/kg oxycodone, while the scramble injection group given oxycodone (n=8) in the drinking water showed significantly less preference after chronic oxycodone, which is suggestive of reward tolerance. However, mice with NOS1 knocked down in the IPN did not show a significant difference in preference between the water (n=7) and oxycodone-drinking groups (n=10) which suggests that NOS1 in the IPN is necessary for reward tolerance. Understanding the mechanisms of nitric oxide production in the IPN and the impact on drug tolerance behavior may lead to better treatment options for those struggling with opioid addiction and other substances impacted by nitric oxide and NOS1.

Keywords :

Opioids, Tolerance, Interpeduncular Nucleus, Reward

Education and Training :

2019	Psychiatry Residency, Icahn School of Medicine at Mount Sinai, NY, USA
2015	Postdoctoral, The Rockefeller University, NY, USA
2011	MD, Icahn School of Medicine at Mount Sinai, NY, USA
2009	PhD, Texas University of Sourthwestern Medical Center at Dallas, TX, USA
2003	BS, Southwestern University, Georgetown, TX, USA

Professional Positions :

2019-present	Assistant Professor, Investigator Track, ISMMS (Principal Investigator), NY, USA
2018-present	Staff Research Physician, Depression and Anxiety Center, ISMMS (Laboratory of James Murrough, MD), NY, USA
2015-2019	Psychiatry Resident, Physician Scientist Track, ISMMS (Laboratory of Paul Kenny, PhD), NY, USA
2011-2015	Postdoctoral Associate, The Rockefeller University (Laboratory of Ines IbañezTallon, PhD), NY, USA
2005-2009	MSTP Student, UTSW (Laboratory of Amelia Eisch, PhD), TX, USA
2004	Stanley Summer Scholar, UTSW (Laboratory of Amelia Eisch, PhD), TX, USA
2002	Welch Summer Scholar, Southwestern University (Laboratory of Kerry Bruns, PhD), TX, USA

MEMO

Dopaminergic control of compulsive eating : Role of dopamine D2 receptor

Ja-Hyun Baik, PhD

Full Professor, College of Life Sciences and Biotechnology, Department of Life Sciences, Korea University, Seoul, Republic of Korea

[Date] Aug 07 / [Time] 15:30-16:00

Abstract :

Dopamine regulates emotional and motivational behavior and the dopamine reward system would be the most prominent system in control of appetite and motivational feeding behavior. Motivation toward the palatable food involves reward learning and conditioning processes and pathological overeating is associated with dysregulation of reward-related behavioral components such as impulsivity and compulsivity. Dysfunctional dopaminergic neurotransmission, especially involving dopamine D2 receptor (D2R), has been proposed to be a mechanism underlying these maladaptive behaviors. We observed that D2R knockout mice consumed significant amounts of palatable food in the aversive context, displaying compulsive eating behavior. We demonstrated that D2R–expressing neurons from the central nucleus of the amygdala critically contribute to regulate impulsive and compulsive eating behavior. I will present recent findings obtained in our laboratory in the analysis of role of dopamine system in compulsive eating. These studies may provide a basis for the development of new approaches to the management of neuropsychiatric and metabolic disorders associated with maladaptive eating behaviors.

[Supported by Bio & Medical Tech. Dev. Program (2016M3A9D5A01952412) of the MSIP, South Korea]

Keywords :

Dopamine receptor, Food reward, Central amygdala, compulsive eating

Education and Training :

1992	PhD in Molecular and Cellular Pharmacology (Life Sciences), University Paris 6 (Pierre et Marie Curie), Paris, France
1987	MS in Biochemistry, University Paris 6, Paris, France
1985	BS in Biochemistry, Yonsei University, Seoul, Korea

Professional Positions :

2006-present	Full Professor, College of Life Sciences and Biotechnology, Dept. of Life Sciences, Korea University, Seoul, Korea
2003-2006	Associate Professor, College of Life Sciences and Biotechnology, Dept. of Life Sciences, Korea University, Seoul, Korea
1996-2003	Assistant/Associate Professor, Medical Research Center, College of Medicine, Yonsei University, Seoul, Korea
1992-1995	Post-Doctoral fellow, IGBMC (Institut de Genetique et de Biologie Moleculaire et Cellulaire, Director: Dr. Pierre Chambon), CNRS, Strasbourg, France

MEMO

Neuropeptide Y neurons in nucleus accumbens promote palatable food memory

Hyung Jin Choi, PhD

Associate Professor, Department of Biological Sciences & Anatomy, Neuroscience Research Institute, Wide River Institute of Immunology, Seoul National University College of Medicine, Seoul, Republic of Korea

[Date] Aug 07 / [Time] 16:00-16:30

Abstract :

The nucleus accumbens (NAc) has been recognized as a prime center for the reward. However, the mechanism by which neuron in NAc controls food-specific memory, especially for palatable food, remains unknown. Neuropeptide Y (NPY) has long been considered to have a profound orexigenic influence on the entire brain. Among the diverse molecular cell types in NAc, the role of NPY-expressing neurons is not yet fully understood. Here, we demonstrated that NPY neurons in NAc promote palatable food memory. Using calcium imaging, we showed that the NAcNPY neurons respond to eating behavior. This response depended on the palatability of the food. More interestingly, we further demonstrated that the neural activity of NAc NPY increased as the learned value of reward-associated cues increased. Using optogenetics, we discovered that the NAcNPY neuronal activation significantly increased palatable food (high-fat food) intake, not normal chow intake. Furthermore, optogenetic activation of NAcNPY neurons served as an unconditioned stimulus for the formation of palatable food memory. In contrast, optogenetic inhibition of NAcNPY neurons blocked the formation of palatable food memory. In conclusion, these experiments provide strong evidence that NAcNPY encodes positive memory for palatable food. Our findings could lead to the development of novel therapeutic strategies to prevent and treat obesity and food addiction.

Keywords :

Appetitive memory, Nucleus accumbens, Reward, Feeding, NPY

Education and Training :

2013	PhD in Medicine (Molecular & Genomics), Seoul National University, Seoul, Korea
2011	MS in Internal Medicine, Seoul National University, Seoul, Korea
2002	MD (Bachelor of Medicine, Bachelor of Surgery), Seoul National University, Seoul, Korea

Professional Positions :

2019-present	Associate Professor
2015-2019	Assistant Professor Functional Neuroanatomy of Metabolism Regulation Lab, Department of Biomedical Sciences Department of Anatomy and Cell Biology, Seoul National University College of Medicine, Korea
2012-2015	Clinical Assistant Professor, Chungbuk National University Hospital, Division of Endocrinology, Department of Internal Medicine, Korea
2010-2012	Clinical Fellow, Seoul National University Hospital, Korea
2009-2010	Researcher (Public Health Doctor), Korea National Institute of Health, Center for Genomic Science
2007-2009	Public Health Doctor, Mokpo National Hospital, Korea
2003-2007	Resident, Seoul National University Hospital, Department of Internal Medicine, Korea
2002-2003	Intern, Seoul National University Hospital, Korea

MEMO

Sensitization of a claustrum-amygdalar-accumbens neural system precedes incubation to palatable food craving

Sam Golden, PhD

Assistant Professor, Department of Biological Structure, University of Washington, Seattle, WA, USA
Faculty, Center for Excellence in the Neurobiology of Addiction, Pain and Emotion (NAPE), University of Washington, WA, USA

[Date] Aug 07 / [Time] 16:30-17:00

Abstract :

In rodent models, reward seeking progressively increases across abstinence in a phenomenon known as 'incubation of craving'. We recently established a mouse model of incubation of palatable food craving and applied unbiased single-cell activity mapping to demonstrate that incubation is associated with wide-spread neural activity beyond canonical reward centers (Madangopal, Szelenyi et al, 2022). From these data we hypothesize that select neural systems are sensitized as a function of abstinence duration that primes the brain towards incubation of craving and relapse. Here, we extend our analyses of a recently generated 'incubation of craving' whole-brain activity dataset and apply advanced image processing and statistical approaches to probe for sensitization of neural systems evoked by food craving. We found that early food craving induced a significant increase in activation across a temporally conserved neural system consisting of the ventral claustrum (vCl), basomedial amygdala (BMA), and the hedonic nucleus accumbens (hNAc). This effect was sensitized as a function of abstinence duration, recruiting proximal to adjacent regions. Expansion of the vCl-BMA-hNAc food craving system corresponded with increased functional connectivity defined by a recruitment of early abstinence modular connectivity hubs into a singular hub at late incubation. Thus, incubation of food craving is preceded by a systems-level sensitization process. Early abstinence from palatable food initialized and maintained activation of a vCl-BMA-hNAc neural system. vCl-BMA-hNAc undergoes a recruited sensitization of brain activation as a function of abstinence duration, leading to a complete functionally connected brain state and induction of incubation. These results provide critical insight into the neural mechanisms driving relapse to palatable food and offer novel therapeutic entry points into the dysregulation of reward seeking behavior.

Keywords :

Incubation, reward, whole brain activity, fos, light sheet fluorescent microscopy

Education and Training :

2015	PhD, Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, NY, USA
2006	BS, Department of Neuroscience, Honors, Bates College, Lewiston, ME, USA

Professional Positions :

2019-present	Assistant Professor, Department of Biological Structure, University of Washington, Seattle, WA, USA
2015-2018	Postdoctoral Fellow, National Institute on Drug Abuse, Baltimore MD, USA

MEMO

Neural circuitry controlling social behavior

Scott Russo, PhD

Professor, Nash Family Department of Neuroscience
Director, Brain Body Research Center, Icahn School of Medicine at Mount Sinai, New York, NY, USA

[Date] Aug. 08 / [Time] 10:30-11:00

Abstract :

Aggressive social interaction or "bullying" is a form of social stress in humans known to increase risk for the development of neuropsychiatric syndromes such as depression. Using preclinical social defeat models our group has characterized adaptations within the brain's reward circuitry in aggressive mice and socially defeated mice. In highly aggressive individuals, social subordination of another animal can activate primary reward centers thereby reinforcing aggressive acts. Conversely, in victims of the aggressive act, we've found evidence for increased activation of stress centers that occlude social reward and promote long lasting social avoidance behavior. In this talk, I will discuss both published and unpublished evidence that provides a circuit level framework to understand the causes and consequences of such aggressive social behavior.

Keywords :

aggression, stress, reward, lateral septum, lateral habenula

Education and Training :

2003	PhD, Department of Biological Psychology, The Graduate School and University Center of the City University of New York, USA
1999	BA, Department of Psychology, State University of New York at Buffalo, USA

Professional Positions :

2023	Leon Levy Director, Brain Body Research Center, Icahn School of Medicine at Mount Sinai (ISMMS), NY, USA
2021	Director, Brain Body Research Center ISMMS, NY, USA
2019	Endowed Professor of Affective Neuroscience, ISMMS, NY, USA
2017	Professor of Neuroscience and Psychiatry, ISMMS, NY, USA
2017-present	Director, Center for Affective Neuroscience, ISMMS, NY, USA
2016-2017	Associate Professor with tenure, Department of Neuroscience, ISMMS, NY, USA
2014-2015	Associate Professor, Department of Neuroscience, ISMMS, NY, USA
2008-2014	Assistant Professor, Department of Neuroscience, ISMMS, NY, USA
2008-2014	Assistant Instructor, Department of Psychiatry, UT Southwestern Medical Center (UTSW), TX, USA
2007-2008	Assistant Instructor, Department of Psychiatry, UTSW, TX, USA
2003-2007	Postdoctoral Fellow, Department of Psychiatry, UTSW, TX, USA

MEMO

Shared GABA transmission pathology in dopamine agonist- and antagonist-induced dyskinesia

Kenji Tanaka, MD, PhD

Professor, Division of Brain Sciences, Keio University School of Medicine, Tokyo, Japan

[Date] Aug. 08 / [Time] 11:00-11:30

Abstract :

Dyskinesia is involuntary movement caused by long-term medication with dopamine-related agents: the dopamine agonist, L-DOPA, to treat Parkinson's disease (L-DOPA-induced dyskinesia [LID]) or dopamine antagonists to treat schizophrenia (tardive dyskinesia [TD]). However, it remains unknown why distinct types of medications for distinct neuropsychiatric disorders induce similar involuntary movements. Here, we searched for a shared structural footprint using magnetic resonance imaging-based macroscopic screening and super-resolution microscopy-based microscopic identification. We identified the enlarged axon terminals of striatal medium spiny neurons in both LID and TD model mice. The striatal overexpression of vesicular gamma-aminobutyric acid transporter (VGAT) was necessary and sufficient for modeling these structural changes; VGAT levels gated the functional and behavioral alterations in dyskinesia models. Our findings indicate that lowered type 2 dopamine receptor signaling with repetitive dopamine fluctuations is a common cause of VGAT overexpression and late-onset dyskinesia formation, and that reducing dopamine fluctuation rescues dyskinesia pathology via VGAT downregulation.

Keywords :

L-DOPA-induced dyskinesia, tardive dyskinesia, brain volume, structural plasticity, GPe, SNr, VGAT, GABA, medium spiny neuron, dopamine fluctuation

Education and Training :

2003	PhD, Department of Neuropsychiatry, Keio University Graduate School of Medicine, Tokyo, Japan
1997	MD, Department of Medicine, Keio University School of Medicine, Tokyo, Japan

Professional Positions :

2021-present	Professor, Division of Brain Sciences, Advanced Medical Research Institute, Keio University School of Medicine, Tokyo, Japan
2016-2021	Associate Professor, Department of Neuropsychiatry, Keio University School of Medicine, Tokyo, Japan
2012-2016	Research Associate Professor, Department of Neuropsychiatry, School of Medicine, Keio University, Tokyo, Japan
2008-2012	Assistant Professor, Division of Neurobiology and Bioinformatics, National Institute for Physiological Sciences, Okazaki, Japan
2006-2008	Postdoctoral Research Scientist in Center for Neurobiology & Behavior, Columbia University, NY, USA
2004-2006	Assistant Professor, Division of Neurobiology and Bioinformatics, National Institute for Physiological Sciences, Okazaki, Japan
2003-2004	Postdoctoral fellow with Dr. Kazuhiro Ikenaka, Division of Neurobiology and Bioinformatics, National Institute for Physiological Sciences, Okazaki, Japan
1999-2003	PhD, with Dr. Haruo Kashima, Department of Neuropsychiatry, Keio University Graduate School of Medicine, Tokyo, Japan
1997-1999	Resident, Department of Psychiatry, Keio University Hospital, Tokyo, Japan

Symposium

BNST CRF Neurons Play a Key Role in the Establishment of Stress Resilience

Ming-Hu Han, PhD

Chair Professor, Investigator, Executive Chair Department of Mental Health and Public Health Faculty of Life and Health Sciences Shenzhen Institute of Advanced Technology Chinese Academy of Sciences
Adjunct Professor, Department of Pharmacological Sciences Friedman Brain Institute, ISMMS, NY, USA

[Date] Aug. 08 / [Time] 11:30-12:00

Abstract :

It is known that cumulative stress is a major risk factor for developing major depressive disorder (susceptibility), yet not everyone experiencing chronic stress develops depression (resilience). To understand when susceptible and resilient behavioral phenotypes are segregated during stress accumulation and what is the underlying neural mechanism, this study takes advantage of a 10-day chronic social defeat stress (CSDS) mouse model for depression. We identified that day 7-10 is a critical period for the segregation of behavioral phenotypes and that bed nucleus of stria terminalis (BNST) corticotrophin-releasing factor (CRF) neurons play an important role in the establishment of resilience. Our retrospective study shows that social interaction (SI) level is similar in susceptible and resilient mice on day 1, 4 and 7, but decreased in susceptible mice with a maintained level of SI level in the resilient group on day 10. The firing activity of BNST CRF neurons has a similar pattern with the individual behavioral alterations and is significantly correlated with SI measurement. We further demonstrate a causal link between the firing activity of these neurons and phenotypical behaviors. Our data provide new insight into the role of stress responsive BNST CRF neurons in the stress history-dependent establishment of resilience.

Keywords :

Stress, Depression, Susceptibility, Resilience, CRF

Education and Training :

1999	PhD, Neurobiology, Shanghai Institute of Physiology, Chinese Academy of Sciences, Shanghai, China
1993	MS, Image Processing and Pattern Recognition, South China University of Technology, Guangzhou, China
1983	BS, Computer Science, Shenyang Institute of Technology, Shenyang, China

Professional Positions :

2021-present	Investigator, Center for Brain Connectome and Behavior, The Brain Cognition and Brain Disease Institute, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, China Chair Professor, Executive Chair, Department of Mental Health and Public Health, Faculty of Life and Health Sciences, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, China Adjunct Professor, Department of Pharmacological Sciences and Friedman Brain Institute, Icahn School of Medicine at Mount Sinai (ISMMS), New York, USA
2020-2021	Professor, Department of Neuroscience and Friedman Brain Institute, ISMMS, New York, USA Professor, Department of Pharmacological Sciences and Institute for Systems Biomedicine, ISMMS, New York, USA
2017-2021	Deputy Director, Center for Affective Neuroscience, Department of Neuroscience and Friedman Brain Institute, ISMMS, New York, USA
2016-2021	Leader, Center of Excellence in Neuropharmacology, Department of Pharmacological Sciences, ISMMS, New York, USA
2015-2020	Associate Professor, Department of Neuroscience and Friedman Brain Institute, ISMMS, New York, USA Associate Professor, Department of Pharmacological Sciences and Institute for Systems Biomedicine, ISMMS, New York, USA

Symposium

Npas4-mediated dopaminergic regulation of safety memory consolidation

Joung-Hun Kim, PhD

Professor, Department of Life Sciences, POSTECH, Pohang, Republic of Korea

[Date] Aug. 08 / [Time] 12:00-12:30

Abstract :

Amygdala circuitry encodes associations between conditioned stimuli and aversive unconditioned stimuli, and also controls fear expression (Pape and Pare, 2010). However, whether and how non-threatening information for unpaired conditioned stimuli (CS-) is discretely processed remains unknown. Following administration of restraint stress, the fear expression toward CS- is abnormally elevated and thus the discriminability to ambient cues is drastically compromised. Interestingly, defensive behavior toward CS- is robust immediately after fear conditioning even without stress exposure, but then becomes negligible after memory consolidation. The synaptic plasticity of neural pathway from the lateral to the anterior basal amygdala gates the fear expression of CS-, depending upon Npas4-mediated Drd4 synthesis, which is precluded by stress exposure or corticosterone injection. In here, we show cellular and molecular mechanisms regulating the non-threatening (safety) memory consolidation which supports the fear discrimination.

Keywords :

Npas4, Drd4, Amygdala, Fear discrimination

Education and Training :

2000	PhD, Department of Neurobiology, Imperial College of Sciences, Technology & Medicine, UK
1996	MS, Department of Medicine, Seoul National University, Seoul, Korea
1992	BS, Department of Microbiology, Seoul National University, Seoul, Korea

Professional Positions :

2005-present	Assistant, Associate Professor & Professor, POSTECH, Pohang, Korea
2001-2005	Associate, HHMI, Columbia University, New York, NY, USA
2000-2005	Postdoctoral Research Scientist, Columbia University, NY, USA

Symposium

Neural representation of approach and avoidance during Naturalistic Foraging

June-Seek Choi, PhD

Professor, Department of Psychology, Korea University, Seoul, Republic of Korea

[Date] Aug. 08 / [Time] 14:00-14:30

Abstract :

Foraging in the wild requires coordinated switching of critical functions, including goal-oriented navigation and context-appropriate action selection. Nevertheless, few studies have examined how different functions are represented in the brain during naturalistic foraging. In the current study, we recorded multiple single-unit activities from rats as they sought sucrose rewards in the presence of a robotic predator, Lobsterbot, which posed periodic threats. We focused on the prelimbic (PL) and infralimbic (IL) areas of the medial prefrontal cortex (mPFC), known to process value and decision-making in both humans and animals. Simultaneously recorded ensemble activities from 10-24 neurons captured rat navigation from the nest towards a zone where a foraging or avoidance decision is made to avoid an unpredicted Lobsterbot's attack. Population analyses employing various machine learning algorithms, including a deep artificial neural network (dANN), revealed highly heterogeneous encoding by the region within the foraging arena. In particular, the accuracy of the dANN, which uses ensemble activity to estimate the distance from the Lobsterbot, exhibited the highest accuracy in the arena's center while its performance deteriorated at both extremities. Subsequent analyses revealed that the disruption of spatial encoding emerged prominently due to non-navigational behaviors such as grooming, rearing, and sniffing, along with the dynamic-decision-making between food procurement and evasion in front of the Lobsterbot. To account for the nature of this heterogenous encoding, we focused on the predictive encoding by the same population of neurons about the goal-related behaviors around the time of food consumption and avoidance. The Bayesian classifier was built and trained to predict the success and failure of avoidance using ensemble activity. The classifier could predict the avoidance outcome as much as 6 seconds before head withdrawal. These findings suggest that the mPFC neurons may adopt at least two modes of encoding depending on the spatial context and the imminent situational challenge that needs to be processed.

Keywords :

Fear, Foraging, Prefrontal Cortex, Avoidance, Ensemble recording

Education and Training :

1999	PhD, Department of Neuroscience and Behavior, University of Massachusetts Amherst, MA, USA
1991	MS, Department of Biological Psychology, Korea University, Seoul, Korea
1989	BS, Department of Biology, Sogang University, Seoul, Korea

Professional Positions :

2015-present	Vice Dean, Korea University International Summer Campus, Korea
2013-2014	Director, BK21 Plus Mind, Brain and Psychological Science Center, Korea
2012-present	Professor, Department of Psychology, Korea University, Seoul, Korea
2010-2011	Visiting scholar, Department of Psychology, University of Washington, WA, USA
2007- 2011	Associate Professor, Dept. of Psychology, Korea University, Seoul, Korea
2004-2006	Assistant Professor, Dept. of Psychology, Korea University, Seoul, Korea
2002-2004	Postdoctoral fellow, Center for Neural Science, New York University, NY, USA
1999-2002	Postdoctoral associate, Dept. of Psychology, Yale University, CT, USA

Symposium

A simple behavioral paradigm to explore individual differences in anxiety and curiosity

Xiao-Hong Xu, PhD

Principal Investigator, Institute of Neuroscience, Chinese Academy of Sciences, Shanghai, China

[Date] Aug. 08 / [Time] 14:30-15:00

Abstract :

Despite extensive research on the neural circuitry underlying anxiety behaviors, the specific neural mechanisms responsible for individual variations in anxiety traits and in the exploration of new objects remain poorly understood. In this study, we conducted a novel object exposure test and discovered consistent differences in exploration and avoidance behaviors among individuals, irrespective of the type of object presented. To gain further insights, we performed in vivo recordings in male mice, which revealed that the activity of AHN GABAergic (AHNVgat+) neurons increased consistently when animals approached unfamiliar objects in an open field (OF) or explored the open arm of an elevated plus-maze (EPM). Additionally, we observed that the activation of AHN neurons in response to objects overlapped with their response to predator cues, and these neuronal activities correlated with the degree of object and open-arm avoidance. Importantly, we demonstrated that optogenetic inhibition of AHNVgat+ neurons, triggered by exploration, led to a reduction in object and open-arm avoidance. Furthermore, through retrograde viral tracing, we identified the ventral subiculum (vSub) of the hippocampal formation as a significant input to AHNVgat+ neurons, playing a crucial role in driving avoidance behaviors in anxiety-inducing situations. Overall, our findings suggest that the convergent activation of AHNVgat+ neurons serves as a common mechanism linking anxiety and predator defense, facilitating behavioral avoidance, while the inhibition of these neurons promotes the exploration of novel objects.

Keywords :

Anxiety, Curiosity, Anterior hypothalamic nucleus, Hippocampus, Individual Differences

Education and Training :

2012	Post Doc, Department of Anatomy, University of California, San Francisco, CA, USA
2006	PhD, Department of Neurosciences, Case Western Reserve University, Cleveland, OH, USA
2000	BS, Department of Biotechnology, School of Life Sciences, Peking University, Beijing, China

Professional Positions :

2012-present	Principal Investigator, Institute of Neuroscience, Chinese Academy of Sciences, Shanghai, China

Symposium

Molecular tools for tagging neural ensembles to help treat brain illness

Jung Ho Hyun, PhD

Assistant Professor, Department of Brain Sciences, Daegu Gyeongbuk Institute of Science and Technology, Daegu, Korea

[Date] Aug. 08 / [Time] 15:00-15:30

Abstract :

Verifying causal effects of neural circuits is essential for proving direct a circuit-behavior relationship. However, techniques for tagging only active neurons with high spatiotemporal precision remain at the beginning stages. Here we developed the soma-targeted Cal-Light (ST-Cal-Light) which selectively converts somatic calcium rise triggered by action potentials into gene expression. Such modification simultaneously increases the signal-to-noise ratio (SNR) of reporter gene expression and reduces the light requirement for successful labeling. Because of the enhanced efficacy, the ST-Cal-Light enables the tagging of functionally engaged neurons in various forms of behaviors, including context-dependent fear conditioning, lever-pressing choice behavior, and social interaction behaviors. We also targeted kainic acid-sensitive neuronal populations in the hippocampus which subsequently suppressed seizure symptoms, suggesting ST-Cal-Light's applicability in controlling disease-related neurons. Thus, the versatile ST-Cal-Light system links somatic action potentials to behaviors with high temporal precision, and ultimately allows functional circuit dissection at a single cell resolution.

Keywords :

Cal-Light, Labeling, Active neurons, Seizure, Blue light

Education and Training :

2015	PhD, Department of Physiology, Seoul National University College of Medicine, Seoul, Korea
2010	MS, Department of Physiology, Seoul National University College of Medicine, Seoul, Korea
2007	BS, Department of Biology, Pusan National University, Pusan, Korea

Professional Positions :

2021-present	Assistant Professor, Daegu Gyeongbuk Institute of Science and Technology, Daegu, Korea
2019-2021	Research Fellow, Johns Hopkins University School of Medicine, Baltimore, MD, USA
2015-2019	Postdoctoral Scholar, Max Planck Florida Institute for Neuroscience (MPFI), FL, USA
2006-2007	Research Internship at Molecular Neurobiology lab, POSTECH, Pohang, Korea
2005-2006	Undergraduate Research Opportunity Program, University of California, Berkeley, CA, USA

Symposium

An emerging role of histone H2A variants in behavioural regulation and Alzheimer's disease

Iva Zovkic, PhD

Associate Professor, Department of Psychology
Adjunct Professor, Department of Cell and Systems Biology, University of Toronto, Mississauga, Canada

[Date] Aug. 08 / [Time] 15:30-16:00

Abstract :

Epigenetic modifications have an established role in learning and memory, but a role for histone variants in behavioral regulation was only recently uncovered. I will discuss evidence that the histone variant H2A.Z suppresses memory formation and that distinct histone variants contribute to memory in unique ways. Effects will be discussed in the context of transcriptional changes in the mouse hippocampus and related to sex differences in Alzheimer's disease and age-related memory decline. This work lays the foundation for uncovering the combinatorial roles of histones in precise regulation of complex behaviours, whereby incorporation of distinct histone subtypes into chromatin fine-tunes neuronal function by adjusting stimulus-induced transcription.

Keywords :

Histone variants, H2A.Z, chromatin, memory, Alzheimer's disease

Education and Training :

2011	PhD, Department of Psychology (Behavioural Neuroscience), Brock University (St. Catharines), Ontario, Canada
2005	BA, Department of Psychology, Brock University (St. Catharines), Ontario, Canada

Professional Positions :

2014-present	Associate Professor, Department of Psychology, University of Toronto Mississauga, Canada Adjunct Professor, Department of Cell and Systems Biology, University of Toronto, Canada
2011-2014	Postdoctoral Fellow, Department of Neurobiology, University of Alabama at Birmingham, AL, USA

Symposium

Imaging-genetics in neurodevelopmental disorder: Effects of genotype and methylation on the neural processing of sensory

Minyoung Jung, PhD

Senior Researcher, Cognitive Science Research Group, Korea Brain Research Institute, Daegu, Republic of Korea

[Date] Aug. 09 / [Time] 09:30-10:00

Abstract :

Neurodevelopmental disorders affect approximately 3% of the population and lead to difficulties in social behavior and sensory processing. Establishing imaging-genetic biomarkers of neurodevelopmental disorders using multimodal brain imaging is a key step for diagnosing and evaluating treatment effect. The imaging-genetic biomarkers will provide a more complete picture of the neuropathology of neurodevelopmental disorders, which will significantly enhance our understanding. Nevertheless, the mechanisms underlying the association among genes, brain, and behavior in neurodevelopmental disorders remains unclear. To study imaging-genetic mechanism of neurodevelopmental disorders, we applied imaging-genetic method using the MRI to explore brain and genetic changes in neurodevelopmental disorders, as well as the association between these changes and clinical outcomes. In this talk, I will present a recent imaging-genetics approach to understand neurobiological mechanisms on neurodevelopmental disorder.

Keywords :

Neurodevelopmental disorder, MRI, Sensory abnormality

Education and Training :

2015	PhD in Child Development, Osaka University, Osaka, Japan
2013	MS in Disability Science, University of Tsukuba, Ibaraki, Japan
2009	BS in Rehabilitation Psychology, Daegu University, Gyeongsan, Korea

Professional Positions:

2021-present	Senior Researcher, Cognitive Science Research Group, KBRI, Daegu, Korea
2019-2021	Senior Assistant Professor, Department of Neuropsychiatry, University of Fukui, Fukui, Japan
2017-2019	Assistant Professor, Research Center for Child mental Development, University of Fukui, Fukui, Japan
2015-2017	Postdoctoral Fellow, Department of Psychiatry, Harvard Medical School (MGH), MA, USA
2014-2015	Research Fellow, Japan Society for the Promotion of Science (JSPS), Osaka, Japan

Symposium

Investigating the link between ASD-risk genes, oxytocin, and social behaviour

Katrina Choe, PhD

Assistant Professor, Department of Psychology, Neuroscience & Behaviour, McMaster University, Hamilton, Ontario, Canada

[Date] Aug. 09 / [Time] 10:00-10:30

Abstract :

Difficulties with social interactions and communication are core symptoms of autism spectrum disorders (ASD). Although the neurobiological mechanisms of social difficulties in ASD remain poorly understood, recent evidence suggests that oxytocin, a neurohormone with an established role in social bonding and trust, could be involved. Using genetically-engineered mouse models and brain-mapping approaches, my laboratory's research aims to explore the possibility that several gene mutations implicated in ASD converge onto a common neurobiological mechanism that disrupts oxytocin signalling in the brain, lowering sociability. In this talk, I will discuss previous and current evidence that supports this hypothesis.

Keywords :

Oxytocin, autism spectrum disorders, social behavior, mouse model

Education and Training :

2013	PhD, Centre for Research in Neuroscience, Department of Neurology and Neurosurgery, Faculty of Medicine McGill University, Montreal, Quebec, Canada
2006	BS, Major in Zoology, Double Minor in Physiology and Psychology, University of Toronto, Toronto, Ontario, Canada

Professional Positions:

2020-present	Assistant Professor (Tenure-track) and Principal Investigator, Department of Psychology, Neuroscience & Behaviour, McMaster University, Hamilton, Ontario, Canada
2019-2020	Associate Project Scientist, Semel Institute for Neuroscience and Human Behavior, David Geffen School of Medicine University of California, Los Angeles, CA, USA
2019	Postdoctoral Fellow, Semel Institute for Neuroscience and Human Behavior, David Geffen School of Medicine University of California, Los Angeles, CA, USA
2015-2018	Postdoctoral Fellow Department of Neurobiology, David Geffen School of Medicine University of California, Los Angeles, CA, USA

Symposium

Brain MRI researches for social brain in youth with autism spectrum disorders (ASD)

Hirotaka Kosaka, MD, PhD

Professor, Department of Neuropsychiatry, University of Fukui, Fukui, Japan

[Date] Aug. 09 / [Time] 10:30-11:00

Abstract :

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in socialization, communication, and range of interests. Furthermore, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) added sensory abnormalities as a core symptom to the diagnostic criteria for ASD. The overall ASD prevalence is 2.76% (one in 36) (Maenner et al., MMWR Surveill Summ, 2023), and it is not an uncommon psychiatric disorder. It often causes functional impairments and social adjustment problems. However, the neurological basis is unknown. We have conducted neuroimaging researches with collaborators in adolescents/adults with high-functioning ASD, and I will introduce our social brain and sensory characteristics researches for ASD. Regarding the brain structure, we explored gray matter volume using voxel-based morphometry in young male adults with ASD compared to normal male control subjects. ASD group showed significantly less gray matter volume in the right inferior frontal gyrus and the right insula. We also researched social brain functions during emotional face recognition, self-face processing, self-relevant processing, eye-contact and joint attention, and resting state. These results suggest that it is not dysfunction of a specific region, but rather aberrant functions of some regions, as well as differences of the network between each region. Next, we investigated the association between brain morphological changes and sensory characteristics using FreeSurfer. There was a significant positive correlation between visual sensory sensitivity scores and the right lingual cortical thickness. These findings suggest that brain morphological changes may trigger sensory symptoms in adults with ASD. The findings of the present researches suggest abnormal brain structures and functions in various regions exist in individuals with ASD. Although both social impairment and sensory impairments are autistic core symptoms, they are completely different symptoms and seem unrelated, both symptoms are probably related via various brain networks.

Keywords :

Autism spectrum disorders (ASD), Functional magnetic resonance imaging (fMRI), Social brain, Sensory processing

Education and Training :

2004	PhD, Department of Neuropsychiatry, School of Medical Sciences, University of Fukui, Fukui, Japan
1998	MD, School of Medical Sciences, University of Fukui, Fukui, Fukui, Japan

Professional Positions:

2018-present	Professor, Department of Neuropsychiatry, School of Medical Sciences, University of Fukui, Fukui, Japan
2014-2018	Professor, Research Center for Child Mental Development, University of Fukui, Fukui, Japan
2012-2014	Associate Professor, Research Center for Child Mental Development, University of Fukui, Fukui, Japan
2005-2012	Assistant Professor, Department of Neuropsychiatry, School of Medical Sciences, University of Fukui, Fukui, Japan
2004-2005	Medical Staff in Department of Psychiatry, Fukui Prefectural Hospital, Fukui, Japan

Symposium

Depressive Impacts of restrain or isolation on mice and human

Weidong Li, MD, PhD

Tenured Full Professor, Executive Dean, Institute of Psychology and Behavioral Science, Vice Dean, Bio-X Institutes,
Director, Center for Brain Health and Brain Technology, Global Institute of Future Technology, Shanghai Jiao Tong University, Shanghai, China

[Date] Aug. 09 / [Time] 11:00-11:30

Abstract :

Among the various environmental factors, isolation or restrain stress has impacts on pathogenetic of depression. However, the complex mechanism needs multi-modeling investigation for further understanding the disorder. We developed a mouse model of 24-hour-restraint and found that the mice displayed depression-like phenotype 35 days after the acute restraint. Since SIRT1 activity is elevated in the model, we studied whether potential inhibitor Nicotinamide (NAM) was capable of attenuating depressive behaviors. Surprisingly, the application of NAM significantly rescued the depressive behaviors by regulating ATP independent of SIRT1 activity. We also found the neuronal demyelination in the mouse model, and Clemastine could promote myelin regeneration and reverse depressive behaviors. The findings suggest new possibilities for depression treatment. In the global efforts to combat Covid-19, researchers have increasingly recognized the profound mental impacts of society isolation. Especially, the most restrict lockdown in China give us the invaluable chance to investigate the outcome of the social lockdown. Here, we report the several striking results of human population in Shanghai during the lockdown.

Keywords :

Depression, Restrain stress, ATP, Social lockdown, Covid-19

Education and Training :

2001	MD& PhD, Department of Neuroplasticity, Shinshu University School of Medicine, Japan
1996	BM, Department of Medicine, China Medical University, China

Professional Positions :

2023-present	Director, Center for Brain Health and Brain Technology, Global Institute of Future Technology, SJTU
2021-present	Executive Dean, Institute of Psychology and Behavioral Science, SJTU
	Principal Investigator, WLA Laboratories, World Laureates Association, Shanghai
2020-present	Tenured Ful Professor of Shanghai Jiao Tong University
2018-2021	Scientific Program Committee Leader for World Laureates Forum, World Laureates Association
	Secretary-General of Young Scientists Forum of World Laureates Forum, WLA
2015-present	Deputy Director, Brian Science and Technology Research Center, SJTU
2016-2021	Deputy Dean, Research Management Division, SJTU
2009-present	Principal Investigator, Bio-X Institutes, SJTU
2007- 2010	Assistant Researcher, Department of Neurobiology, UCLA, USA
2002-2007	Postdoctoral Researcher, Department of Neurobiology and Psychology, UCLA, USA
2001-2002	Postdoc, Department of Neuroplasticity, Shinshu University School of Medicine, Japan

Posters

[A-01] DNA methylation of oxytocin receptor (OXTR) and arginine vasopressin receptor (AVPR) 1A/1B genes and the altered sensory brain in autism spectrum disorders

Yong Jeon Cheong[1], Jihyun Bae[1], Seonkyoung Lee[1], Hyo Eun Ko1[1], Hirotaka Kosaka[2], Minyoung Jung[1]

[1] Cognitive Science Research Group, Korea Brain Research Institute, Daegu, Republic of Korea
[2] Department of Neuropsychiatry, University of Fukui, Fukui, Japan.

As a behavioral endophenotype of autism spectrum disorder (ASD), atypical responses to the sensory-rich environment have recently drawn attention besides social deficits. Despite potential roles of oxytocin and vasopressin systems, little is known about the relationships between epigenetic modifications of oxytocin receptor (OXTR) and Arginine Vasopressin Receptor (AVPR) genes, brain, and sensory behavior in ASD. Using information of epigenetic changes in these genes, altered sensory behavior, and brain structure and function as features for XGboost modeling, this study investigates how ASD is predicted by DNA methylation (DNAm) levels of the two genes, behavioral indicators of sensory abnormality, volumes of cortical and subcortical regions, and values of resting-state functional connectivity (rs-FC). This study includes 34 individuals with ASD (M = 22, mean [SD] age = 26.0 [4.24] yrs old) and 72 typically developing individuals (M = 33, mean [SD] age = 32.0 [12.73]). Information of OXTR and AVPR gene DNAm was extracted from participants' salivary samples. Abnormality in sensory behavior was assessed by Adolescent/Adult Sensory profile. Structural and rs-functional MRI data were acquired using a 3-T MR scanner. We considered demographic information, DNAm values, AASP scores, volumes of brain regions, and thalamic rs-FC values as potential predictive features. Using Shapley additive explanation values, we ranked predictive importance of the features, and used the top 30 features for the final modeling. We achieved F-score 0.96, ROC-AUC 0.93, and PR-AUC 0.95. Exclusion of epigenetic predictors showed a great loss in predictive accuracy (F-score 0.93, ROC-AUC 0.85, and PR-AUC 0.90). ASD is known for its heterogenous etiology. This study suggests that generalizable prediction of ASD can be achieved when considering interaction of epigenetic modification, brain function and structure, and sensory behaviors.

Keywords : Adolescent/Adult Sensory profile, ASD, AVPR, DNA methylation, OXTR

[A-02] Depression and brain network connectivity in children; Resting state fMRI study

Jihyun Bae[1], Yongjeon Choeng[1], Seonkyoung Lee[1], Jihyeong Ro[1], Suin Choi[1], Yeseul Ryu[1], Jian Ha[1], Hyoeun Ko[1], Minyoung Jung[1]

[1] Cognitive Science Research Group, Korea Brain research Institute, Daegu, Republic of Korea

Depression as a main component of mental infringement is a risk factor of atypical cognitive and sociopathic development during childhood. Previously researchers have considered brain network connectivity (BNC) as reliable neuro-markers of depressed adolescents. Major depressive disorder is characterized by hyper- or hypoconnectivity within the default mode network (DMN) and the frontoparietal control network (Kaiser et al., 2015). However, little is known how BNC relates to depression in earlier stages of child development. The current study aims at investigating whether BNC is associated with depression in children. A total of 165 children (male = 94, mean age [SD] = 8.99 [1.65] years, range = 6-11) were recruited for this study. We assessed the level of depression using parent-report questionnaire Korean version of Children's Depression Inventory (K-CDI 2:P) that consists of two subscales, emotional and functional problems. Using a Siemens 3T MRI, we collected resting state functional MRI data that was pre-processed by SPM12. Functional connectivity (FC) values were extracted by CONN toolbox ROI-to-ROI correlation analysis. We concatenated 3-Dimension array with FCs of each ROI for all subjects and then calculated correlations between CDI scores with FCs. CDI emotional problem score showed a significantly positive association with increased FC between right lateral parietal cortex of DMN and right frontal eye field cortex in dorsal attention network (DAN) ($r=0.3066$, $p<0.0001$). The current study provides additional pieces of evidence for significant association between depression and the hyperconnectivity within the multiple BNCs in children's brain. As a potential neural signature of depression, the altered connectivity arisen by an interaction DMN and DAN suggests that children may reflect difficulties in social interaction and relationship by depression.

Keywords : Resting state functional MRI, Brain network connectivity (BNC), Functional connectivity (FC), Korean version of children's depression inventory (K-CDI 2:P)

Posters

[A-03] Children's depression and asymmetric volume changes in the thalamic subfield

Jian Ha[1], Yongjeon Choeng[1], Seonkyoung Lee[1], Jihyeong Ro[1], Suin Choi[1], Yeseul Ryu[1], Jihyun Bae[1], Minyoung Jung[1,*]

[1] Cognitive Science Research Group, Korea Brain research Institute, Daegu, Republic of Korea

Previous studies have shown not only that depression is associated with volumetric changes in subcortical structures but also that hemispheric asymmetry is suggested as an indicator of major depressive disorder (MDD). However, a majority of studies have investigated effects of depression on the human brain structure with individuals with MDD or dysthymia. It restricts our understanding of how development of depression in childhood affects changes in the brain structure over time. Using the Children's Depression Inventory - Self Report (CDI) and structural neuroimaging, the present study examines whether the CDI scores is related to hemispheric asymmetry in volumes of thalamic subfields. A total of 157 children (F = 73, mean [SD] age = 9.06 [1.72]) participated in this study. The 26 asymmetry index (AI = (L-R) / (L+R)) was computed with 52 thalamic subfield volumes that was extracted by FreeSurfer. Controlling for age, sex, handedness and intracranial volume, we found significant partial correlations between emotional problems, which is a subscale of CDI, and AIs of three subfields: (1) medial dorsal nucleus (MDm, r = 0.271, FDR q<0.05), (2) anterior pulvinar (PuA, r = 0.269, FDR q<0.05), and (3) whole thalamus (THA, r = 0.253, FDR q<0.05). Additionally, CDI total score positively correlates with AI in lateral geniculate nucleus (LGN, r = 0.249, FDR q<0.05). We divided into two groups (High vs. Low CDI score) to further examine whether level of depression affects changes in AI of these subfields. Individuals with high CDI scores showed the significantly enlarged left volumes in four subfields: MDm (t = 2.59, p<0.05), PuA (t = 2.54, p<0.05), LGN (t = 4.49, p<0.001), and THA (t = 2.79, p<0.01). Children's depression is related to asymmetry of thalamic structures among typically developing children. Relatively enlarged left or reduced right volume of MDm, PuA, LGN and THA found in highly depressed children suggests that AI of thalamic subfields can be used as a potential biomarker for behavioral signs of depression.

Keywords : Child depression, Brain asymmetry, Thalamic subfield, K-CDI

[A-04] The different effects between oxytocin receptor genes for sensory behaviors and cortical structures in the autism spectrum

Yeseul Ryu[1], Yongjeon Cheong[1], Seonkyoung Lee[1], Minyoung Jung[1,*]

[1] Cognitive Science Research Group, Korea Brain Research Institute, Daegu, Republic of Korea

Autism spectrum disorder (ASD) is characterized by atypical sensory behaviors and brain structures compared with typical development (TD). Recent studies of genetic risk factor in ASD have identified that A allele of two oxytocin receptor single nucleotide polymorphisms (OXTR SNPs), rs237887 and rs2254298, is considered as a genetic risk factor for ASD relative to GG genotype. To explore the connections between behavior, brain, and gene in ASD, we investigated associations among atypical sensory behaviors, brain structures, and risk alleles of OXTR SNPs. In this study, we recruited 79 adults with TD (39 males, mean age [SD] = 27.24[6.95] years old) and 35 adults with ASD (24 males, mean age [SD] =28.06 [5.77] years old). We measured level of atypical sensory behaviors from a self-report questionnaire adolescent-adults sensory profile (AASP). Using FreeSurfer, we derived thickness and volume information of brain structure data collected from 3T MRI scanner. Genotype data for the two OXTR SNPs (rs237887 and rs2254298) were extracted from participants' salivary samples. We split data based on diagnosis (TD/ASD) and OXTR SNPs (A carrier/GG) to perform two-way ANOVA and Bonferroni tests. We found a significant difference in touch only for ASD group in rs237887: A carriers had higher AASP touch score than GG homozygote (p=0.0003). There were significant differences in cortical features only for ASD group: (1) rs237887 A carriers had smaller right frontal pole (FP) volume than GG (p=0.002), and (2) rs2254298 A carrier had larger right transverse temporal cortical thickness than GG (p=0.0002). Differently, TD group had no difference of AASP scores and brain structure depending on types of SNPs. Supporting previous reports on an association between social touch and FP activities, the present study suggests a potential mediating role of OXTR SNPs, specifically rs237887, in atypical touch behavior and FP. The current findings imply that distinct OXTR SNPs differentially contribute to sensory system of ASD in a complex way.

Keywords : ASD, OXTR, rs237887, rs2254298, touch, frontal pole, transverse temporal

Posters

[A-05] Relationship among smart media addiction, depression and brain structural of children

Jihyeong Ro[1], Yongjeon Cheong[1], Seonkyoung Lee[1], Suin Choi[1], Yeseul Ryu[1], Jian Ha[1], Jihyun Bae[1], Hyoeun Go[1], Minyoung Jung[1,*]

[1] Cognitive Science Research Group, Korea Brain Research Institute, Daegu, Republic of Korea

The number of smart media users in children is growing. Excessive smart media usage leads to depression in social relationships. Addiction is known for its association with depression and structural changes in the human brain. The present study aims to examine how smart media addiction (SMA) and depression are associated with brain structure among typically developing children. The present study includes 80 children (F=36, mean age [SD]=10.83[0.81] years old). We assessed participant's SMA and depression levels using 4 self-report questionnaires: (1) Smartphone Addiction Scale (S-scale), (2) Smartphone-Overdependence Scale (SO-scale), (3) Smart Media Addictive Tendency Scale (SM-scale), and (4) Children's Depression Inventory (CDI). We extracted surface area and brain volume information of 68 brain regions using 3T MRI and FreeSurfer. We found significant correlations after adjusting age, sex, handedness, and intracranial volume: (1) SMA Scales had significant correlations with CDI total and all subscales, (2) left fusiform gyrus (FFG) area showed significant correlations with CDI total score (r=0.44) and two CDI subscales (Emotional Problems scale: r=0.48; Negative Mood/Physical Symptoms scale: r=0.47), (3) left FFG volume showed significant correlations with CDI total score (r=0.38) and two CDI subscales, (Emotional Problems: r=0.41; Negative Mood/Physical Symptoms: r=0.4), and (4) right pericalcarine cortex(PCAL) volume showed significant correlation with two CDI subscales (Emotional Problems, r=0.38; Negative Mood/Physical Symptoms: r=0.41). All p-values for significant correlations are corrected at FDR q=0.05. We found the best optimization model as followed: SMA→Emotional Problem→left FFG volume and right PCAL volume (TLI=0.991, RMSEA=0.043, SRMR=0.06, NFI=0.971). Our findings suggest that SMA directly involves dysregulation of emotional problem domain in depression. Furthermore, it seems that SMA indirectly contributes to alteration of depression-related brain structures.

Keywords : Smart media addiction(SMA), Depression, Fusiform gyrus, Pericalcarine cortex, Children

[A-06] Effects of parenting stress and depression on the brain of caregivers

Suin Choi[1], Seonkyoung Lee[1], Yongjeon Cheong[1], Jihyeong Ro[1], Yeseul Ryu[1], Jihyun Bae[1], Jian Ha[1], Minyoung Jung[1,*]

[1] Cognitive Science Research Group, Korea Brain Research Institute, Daegu, Republic of Korea

It is widely accepted that Parenting Stress (PS) closely correlates with depression, and depression is associated with changes in various brain regions. However, little is known about how the association between PS and depression affects the human brain. This study aims at investigating the causal effects of between PS and depression on the brain structure of primary caregivers. The present study includes 200 participants who take care of elementary school children (female = 189, mean age [SD] = 40.82 [3.11] years old). We assessed PS and depression with two self-report questionnaires: Parenting Stress Index (PSI) and Beck Depression Inventory (BDI). The PSI measures parental stress in child and parent domains, each with subscales. We collected structural magnetic resonance imaging data on which we calculated areas of 68 brain regions using 3T MRI and FreeSurfer. We performed partial correlation analysis, the statical threshold was set to p<0.01. We confirmed significant positive association between PS and depression. PS had a correlated with right fusiform gyrus area (FFG): parenting stress total score (r = -0.230), child domain (adaptability: r = -0.269; reinforces parent: r = -0.189; mood: r = -0.250; acceptability: r = -0.219; child domain: r = -0.264) and parent domain (competence: r = -0.185). Depression level showed correlation with left entorhinal cortex area (ERC, r = -0.198). We further conducted structural equation model analysis. We observed that depression increased PS, which led to a reduction in the right FFG area (NFI = 0.980, CFI = 0.996, RMSEA = 0.034). In the child and parent domains, PS increased depression level which subsequently reduction left ERC area (PSI child domain: NFI = 0.976, CFI = 0.999, RMSEA = 0.015; PSI parent domain: NFI = 0.959, CFI = 0.986, RMSEA = 0.049). The current study suggests that PS and depression exert a mutual negative influence on each other, both affect area reduction of brain involved in negative emotional memory (e.g., ERC and FFG).

Keywords : parenting stress, depression, brain, entorhinal cortex, fusiform gyrus

Posters

[A-07] A Role of Myelin Basic Protein (MBP) on Cocaine Seeking Behaviors in Mice

Sejin Jeong[1,4], Hyoungseok Jeon[2], Soo Min Lee[5], Jin Young Bae[3], Dae-Si Kang[1,6], Murim Choi[2], Yong Chul Bae[3], Ja Wook Koo[1,6,*]

[1] Emotion, Cognition and Behavior Research Group, Korea Brain Research Institute, Daegu, Republic of Korea
[2] Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Republic of Korea
[3] Department of Anatomy and Neurobiology, School of Dentistry, Kyungpook National University, Daegu, Republic of Korea
[4] Department of Life Sciences, Yeungnam University, Daegu, Republic of Korea
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Numerous studies have demonstrated various changes caused by chronic cocaine exposure in mice. While demyelination is known to be one of the consequences of cocaine use, the impact of cocaine on oligodendrocytes has yet to be determined. In the present study, we investigated neurobiological dynamics induced by chronic cocaine exposure, specifically focusing on 1) structural changes, 2) oligodendrocyte dysfunction, and 3) methods and effects of recovery. Initially, we observed that mice injected with cocaine for 5 days showed sensitization to cocaine after a 3-week withdrawal period. These mice demonstrated significant alterations in the thickness of myelin sheath and the expression levels of various oligodendrocyte-related genes, which are related to the oligodendrocyte maturation stage. To restore the myelin sheath, which is reduced by chronic cocaine exposure, we employed miconazole drug injection or viral injection of myelin basic protein (MBP) overexpression. Consequently, remyelination was able to restore mRNA levels of oligodendrocyte-related genes and inhibit cocaine-seeking behaviors. Collectively, our findings suggest that cocaine exposure induces functional impairment of oligodendrocytes, which could affect neuronal transmission. These results can provide a foundation for understanding the causal relationship between oligodendrocytes and neurons affected by cocaine, highlighting a potential target for ameliorating cocaine-induced deficits.

Keywords : Cocaine, Nucleus accumbens, Oligodendrocyte, Myelination, scRNA-seq

[A-08] Prediction of emotional dimensions using AlexNet

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Emotion recognition has an important role in social relations and human interactions. Emotion can be represented in two emotional dimensions: valance and arousal. In this study, we conducted a behavioral task in which participants classified each facial expression stimulus according to emotional dimensions, and built a behavioral representation dataset using the acquired behavioral data. However, little research has been conducted on behavioral recognition using deep neural network. Therefore, we aimed to see whether CNNs could predict the emotional dimension of behavioral representation and, if they could, to suggest which CNN best indicated the behavioral representations. We trained the behavioral RDM dataset on AlexNet, VGG16, VGG19, GoogLeNet, InceptionV3, ResNet18, and ResNet101 with 10-fold cross-validation. Our results show that the AlexNet, VGG19, GoogLeNet, and ResNet18 performed better emotional dimensions classification than other models with 96.21% accuracy. It is also unclear if a deep learning model trained from behavioral representations can predict the emotional dimensions of neural representations. To investigate this question, in the fMRI experiment, participants were presented with facial expression stimuli used in behavioral tasks, and neural RDMs were generated using the neural data expressed while detecting facial expression stimuli. We evaluated the performance of our behavioral prediction model using the neural representation dataset. The principal finding was that AlexNet predicts the emotional dimension of neural representation better than other models.

Keywords : Convolutional Neural Network, Behavioral representation prediction, Neural respresentation prediction, AlexNet, Emotional dimension classification

Posters

[A-09] Ventral tegmental area to nucleus accumbens dopaminergic circuit regulates motivated behaviors in an effort-based social decision-making task

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Motivation is essential in an animal's goal-directed behaviors, making animals withstand many hardships. For highly social animals like humans and some rodents, social interaction per se is a powerful driving force to endure effortful conditions. However, the underlying mechanism of motivation for social rewards has not yet been well studied. Effort-based social decision-making (ESDM) task was designed for this study and it was suitable for evaluating the social motivation levels. With this behavior paradigm, we analyzed the effort-based 'HARD' choice behaviors of male mice to meet female. When the interaction time with the female was given as a freely accessible social reward, the male mice chose to meet the female (EFB-). Interestingly, we observed that the male mice chose to meet female even if they had to climb the barrier (EFB+) more frequently than the EFB- group on the last day of the task. To explain these phenomena, we first investigated gene expression levels of dopamine receptor D1 (Drd1a) and D2 (Drd2) in the nucleus accumbens (NAc), the key brain region that mainly receives dopaminergic projections, by quantitative PCR. As a result, Drd1a gene expression, but not Drd2, was significantly higher in the EFB+ group than in other groups. To confirm the role of the D1 receptor in triggering social motivation, we infused D1R antagonist SCH-23390 directly into the NAc and found that 'HARD' choice level was decreased in the EFB+ group. Using in vivo fiber photometry, we measured spontaneous real-time dopamine signal activity in the NAc on the first day and the last day of the task. Consistent with our behavioral results, the doapmine signals during decision-making for 'HARD' choice were reinforced on the last day comapred to the first day. Since the ventral tegmental area (VTA) is the principal region for releasing dopamine, we manipulated the VTA-to-NAc circuit during the decision-making. Optogenetic inhibition reduced the 'HARD' choice level in the EFB+ group. Conversely, activation on the second training day increased the level. Taken together, these data suggest that NAc D1-cells receiving signals from VTA are possibly involved in effort-based decision-making for the social reward.

Keywords : Social behavior, Decision-making, Motivation, Nucleus accumbens, Dopamine

[A-10] Synaptotagmin-4 causes susceptibility to chronic stress through BDNF signaling in the medial prefrontal cortex

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Stressful circumstances are significant contributors to mental illnesses, such as major depressive disorder. Anhedonia, which is the loss of the ability to enjoy pleasure in pleasurable situations, including rewarding activities or social contexts, is considered a key symptom of depression. Although stress-induced depression is associated with anhedonia in humans and animals, the underlying molecular mechanisms of anhedonic responses remain poorly understood. In this study, we demonstrated that synaptotagmin-4 (SYT4), which participates in the release of neurotransmitters and neurotrophic factors, is implicated in chronic stress-induced anhedonia. Employing chronic unpredictable stress (CUS), we determined two subpopulations based on sucrose preference, which was highly correlated with social reward: susceptible (SUS, anhedonic) vs. resilient (RES, non-anhedonic) groups. The FosTRAP (targeted recombination in active populations) system and optogenetic approach revealed that the neural activity in the medial prefrontal cortex (mPFC) was substantially associated with the CUS-induced anhedonic behavioral phenotypes. We identified Syt4 as a hub gene in a gene network unique to anhedonia by conducting a weighted gene co-expression network analysis of the RNA sequencing data from the mPFC of SUS and RES mice. We also confirmed that Syt4 overexpression in the mPFC was pro-susceptible, while the Syt4 knockdown was pro-resilient; the pro-susceptible effects of SYT4 were mediated through reduction of brain-derived neurotrophic factor (BDNF)-tropomyosin receptor kinase B (TrkB) signaling in the mPFC. These findings suggested that SYT4-BDNF interactions in the mPFC could be a crucial regulatory mechanism of anhedonic susceptibility to chronic stress.

Keywords : Anhedonia, Chronic unpredictable stress, Prefrontal cortex, Synaptotagmin-4, Weighted gene correlation network analysis (WGCNA)

Posters

[A-11] Dyrk1A-Induced Epigenetic Alterations in the Prefrontal Cortex Contribute to Cognitive Impairment in Depression

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Dyrk1A (Dual-specificity tyrosine-(Y)-phosphorylation-regulated kinase 1A), crucially regulates gene expression by interacting with and phosphorylating the carboxy-terminal domain of RNA polymerase II (RNAP II), impacting its association with target promoters. Although Dyrk1A is associated with a variety of intellectual disabilities, epigenetic modification in Dyrk1A associated with cogtive impairment in depression is largely unknown. In this study, we investigated the epigenetic role of Dyrk1A in an animal model of chronic social defeat stress (CSDS). Using manganese-enhanced magnetic resonance imaging, we observed reduced prefrontal frontal cortex (PFC) activity in CSDS susceptible individuals, while pharmacological inhibition of Dyrk1A increased PFC activity to levels comparable to the control group. Also, viral-inhibition of Dyrk1A specifically in the PFC restored CSDS-induced depressive-like behavior, while Dyrk1A overexpression resulted in pronounced depressive symptoms even under subthreshold stress conditions. Moreover, episodic memory measurement via what-where-when task, revealing that increased Dyrk1A expression led to severe cognitive impairment and depressive-like behaviors, which were alleviated by Dyrk1A inhibition. Interestingly, in female mice, Dyrk1A overexpression induced depressive-like behavior but did not elicit cognitive impairment, suggesting a potential sex-specific role of Dyrk1A. Finally, we demonstrated that Dyrk1A facilitates the recruitment of RNAP II to the MAO-A promoter, promoting the transcription of MAO-A and subsequent serotonin degradation, resulting in depressive symptoms and cognitive impairment.

Keywords : Dyrk1A, Epigenetics, Chronic social defeat stress, Depression, Cognitive impairment, Prefrontal Cortex

[A-12] Neural circuit and molecular mechanisms of social dominance

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Social animals compete for limited resources, resulting in a social hierarchy. Although different neuronal subpopulations in the medial prefrontal cortex (mPFC), a hub brain region of social hierarchy, encode distinct social competition behaviors, their identities and associated molecular underpinnings have not yet been identified. In this study, we found that mPFC neurons projecting to the nucleus accumbens (mPFC-NAc) encode social winning behavior, whereas mPFC neurons projecting to the ventral tegmental area (mPFC-VTA) encode social losing behavior by monitoring and manipulating neural circuit activity. High-throughput single-cell transcriptomic analysis and projection-specific genetic manipulation revealed that the expression level of POU domain, class 3, transcription factor 1 (Pou3f1) in mPFC-VTA neurons controls social hierarchy. Optogenetic activation of mPFC-VTA neurons increases Pou3f1 expression and lowers social rank. Together, these data demonstrate that discrete activity and gene expression in separate mPFC projections oppositely orchestrate social competition and hierarchy.

Keywords : social hierarchy, social competition, medial prefrontal cortex, nucleus accumbens, ventral tegmental area, single cell RNA sequencing

Posters

[A-13] Inhibition of CDK4/6 regulates neuroinflammation and cognitive function through DYRK1A/STAT3 signaling

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Repurposing approved drugs is an emerging therapeutic development strategy for neuroinflammation-related diseases. The CDK4/6 inhibitor abemaciclib mesylate is an FDA-approved drug for breast cancer treatment. However, whether abemaciclib mesylate affects neuroinflammation, and Aβ/LPS-mediated cognitive impairment is unknown. In this study, we investigated the effects of abemaciclib mesylate on cognitive function and Aβ/tau pathology and found that abemaciclib mesylate improved spatial and recognition memory by regulating the dendritic spine number and neuroinflammatory responses in 5xFAD mice, an Aβ-overexpressing model of Alzheimer's disease (AD). Abemaciclib mesylate also inhibited Aβ accumulation by enhancing the activity and protein levels of the Aβ-degrading enzyme neprilysin and the α-secretase ADAM17 and decreasing the protein level of the γ-secretase PS-1 in young and aged 5xFAD mice. Importantly, abemaciclib mesylate suppressed tau phosphorylation in 5xFAD mice and tau-overexpressing PS19 mice by reducing DYRK1A and/or p-GSK3β levels. In wild-type (WT) mice injected with lipopolysaccharide (LPS), abemaciclib mesylate rescued spatial and recognition memory and restored dendritic spine number. In addition, abemaciclib mesylate downregulated LPS-induced microglial/astrocytic activation and proinflammatory cytokine levels in WT mice. In BV2 microglial cells and primary astrocytes, abemaciclib mesylate suppressed LPS-mediated proinflammatory cytokine levels by downregulating AKT/STAT3 signaling. Taken together, our results support repurposing the anticancer drug, CDK4/6 inhibitor abemaciclib mesylate as a multitarget therapeutic for neuroinflammation-related diseases including AD.

Keywords : Abemaciclib mesylate, cognitive function, neuroinflammation

[A-14] Unraveling metabolite dynamics underlying sex difference in depression within the Nucleus Accumbens

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The higher prevalence of depression in females is widely recognized, but the underlying neural circuitry and cellular mechanisms responsible for this sex difference remain largely unknown. Previously, we identified several key brain areas that respond differently to acute physical stress in a sex-dependent manner, with a particular focus on the nucleus accumbens (NAc). In our current investigation, we employed a modified sub-chronic variable stress (SCVS) model to induce depression selectively in female mice and conducted whole-cell patch clamp recordings from medium spiny neurons (MSNs) in the NAc. We also performed region-specific sampling to measure metabolic differences associated with the SCVS model. We found distinct passive and active neuronal properties of NAc MSNs between males and females, as well as differences between the NAc core and shell regions. However, we observed no significant differences between MSNs expressing different dopamine receptor types, except for spontaneous excitatory postsynaptic currents (sEPSCs) in the NAc core. Interestingly, we observed lower levels of arachidonic acid (AA) levels in the striatum of stressed female mice compared to female controls. Treatment with URB597, a regulator of AA levels, restored depressive behaviors in stressed females but had no effect in males. Therefore, we propose that this behavioral change may be attributed to alterations in sEPSCs in the NAc core and modulated by the levels of AA in the brain.

Keywords : Depression, sex difference, Nucleus Accumbens, electrophysiology, metabolite

Posters

[A-15] Validation of a modified sub-chronic variable stress animal model for studying sex differences in depression

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Sex influences the development of mood disorders; however, current animal models mostly focus on male rodents, neglecting sex differences. Sub-chronic variable stress (SCVS) is a depression model that has been reported to induce depressive symptoms only in female mice but occasionally in males in our laboratory. In this study, we modified the SCVS model by reducing stress intensity to validate behavioral changes by using various tests related to depression. We found that the modified SCVS induced depressive symptoms in female C57BL/6 mice, while both male and female mice displayed anxiety-like behavior in the noveltysuppressed feeding test. Further analysis of the tail suspension test (TST) using K-mean cluster analysis and receiver operating curve (ROC) analysis revealed increased mobility per bout, initial mobility, and overall immobility in females and brief but frequent struggles in males. We also examined the impact of the modified SCVS on the medial prefrontal cortex (mPFC) and found distinct changes depending on the subareas of mPFC. In the infralimbic cortex, SCVSexposed males showed a higher firing threshold, impaired firing activity on strong stimuli, reduced excitatory amplitude, and increased inhibitory frequency. Only females exhibited increased excitability and reduced inhibitory frequency in the prelimbic cortex. Our study highlights the potential of the modified SCVS model to explore sex differences in depression, as evidenced by various criteria in the TST and alterations in mPFC activity. By considering both sexes, this model provides a valuable tool for further research on mood disorders.

Keywords : Sub-chronic variable stress, depression, sex difference, animal model

[A-16] Deletion of Phospholipase C eta 1 in habenula astrocytes induces depressive behavior in mice

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Phospholipase C (PLC) enzymes play a crucial role in intracellular calcium-signaling transduction, mediating cellular activities in the brain. In astrocytes, PLC involves the release of gliotransmitters such as glutamate by increasing intracellular calcium, which contributes to neural activity. Recently PLCη subtype has been identified and is known to be enriched in astrocytes. However, its physiological function is not yet fully understood. This study aimed to investigate the role of the PLCη1 subtype in the lateral habenula (LHb) astrocytes and its potential impact on mood behavior. Here, we show that genetic deletion of PLCη1 in astrocyte reduces morphological complexity, as indicated by decreased total process length and the number of branches in Aldh1l1-CreERT2; Plch1f/f mice. We also found a reduced tonic AMPAR/NMDAR current, increased synaptic efficacy, and impairment of extrasynaptic long-term depression (LTD) in the LHb. Furthermore, silencing of astrocytic PLCη1 in LHb by injection of AAV-Gfap-Cre into LHb of Plch1f/f mice, showed depressive-like behaviors, including helplessness and anhedonia, without affecting anxiety, locomotion, or cognitive functions. Lastly, we found a decreased expression of Plch1 mRNA in mice after restraint stress, a well-known depression-like behavior model. Our findings reveal a previously unexplored role of PLCη1 in LHb astrocytes for shaping morphologies and neuronal activities associated with mood regulation.

Keywords : phospholipase C eta 1, astrocyte, depression, lateral habenula, tonic glutamate, extrasynaptic long-term depression

Posters

[A-17] Investigation of the role of LB1 using ADLD patient-derived iPSCs and mouse model

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Microenvironments surrounding cells, including physical properties, maintain and regulate cellular behaviors. Among them, mechanical stimuli, the stiffness of the niche, can directly regulate cell fates through mechanotransduction during the developmental stage. Lamins are not only key components of the nuclear lamina, but also act as mechano-sensor that senses forces from outside to respond to environmental changes. Unlike A-type lamins, B-type lamins are present in all cell types including stem cells and required for brain development when using mouse models. Interestingly, LaminB1 (LB1) overexpression in migrating neurons showed neuronal migration delay in developing mouse models, and stiffness was increased in those migrating neurons, suggesting that increased LB1 level may affect at the level of brain development. Predictably, not only developing mouse brains, but also human brains express LB1. Autosomal-dominant leukodystrophy (ADLD) is a progressive and rare genetic neurodegenerative disease resulted from overexpression of LB1 due to LMNB1 gene duplication or deletion of upstream of the gene. Demyelination is reported to be one of the most significant features of ADLD, however, cell type or cellular mechanisms, which are responsible for ADLD, are still ambiguous. To address this issue, we developed a model iPSC using ADLD patients and control human dermal fibroblast (HDF). Here we will present the recent data using ADLD patient-derived iPSCs and mouse models using in utero electroporation.

Keywords : Autosomal Dominant Leukodystrophy (ADLD), LaminB1, iPSC, organoid, in utero electroporation (IUE)

Posters

[B-01] Neural sound processing in noise in the mouse auditory midbrain

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The ability to perceive meaningful sounds in noisy environments is an essential ability for animals and humans. However, the underlying neural mechanisms remain poorly understood. Recent evidence suggests that while neural signatures of signal extraction are most prominent in the auditory cortex, substantial extraction already occurs in subcortical structures. Here, we investigated the processing of sound stimuli mixed with noise in the inferior colliculus (IC), a major midbrain auditory integration center. We recorded IC neural activity in anesthetized mice while presenting 1) dynamic random chords (DRCs) or 2) mouse vocalization stimuli, mixed with background noise at different signal-to-noise ratios (SNRs). To compare the effects of different types of background noise, mouse vocalization stimuli were presented with either a spectrum-matched broadband noise or a water stream sound. The degrees to which the "signal" is preserved in the IC population activity were quantified by reconstructing the signal at different SNRs. Our preliminary results show that the similarity between the clean and the reconstructed DRC stimuli decreased rapidly with decreasing SNRs ($r = 0.2$ at SNR of +5dB, $n = 6$ neurons). In contrast, the similarity between the clean and the reconstructed vocalization stimuli decreased more slowly with decreasing SNRs ($r = 0.7$ with the broadband noise and $r = 0.8$ with the water stream at SNR of +5dB, $n = 6$ neurons). In the case of vocalization stimuli, the decrease in reconstruction quality with decreasing SNRs was slower with the water stream than with the broadband noise. Our results show that IC neural population represents mouse vocalizations in a more background noise-resistant manner than DRCs, an artificial sound signal. The noise-resistant encoding by neural populations may facilitate the perception of behaviorally meaningful sounds in noisy environments.

Keywords : Sound processing, Auditory midbrain, Inferior colliculus, Stimulus reconstruction

[B-02] Role of arginine vasopressin receptor (AVPR) genotypes in modulating the association between cortical thickness and sensory processing

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Sensory processing is the process by which the central nervous system gathers, interprets, and regulates sensory stimuli in response to environmental cues. However, our understanding of the genetic factors and neuroanatomical correlations that influence sensory processing is limited. The arginine vasopressin system modulates sensory input responsiveness, making it a potential candidate for further investigation. Therefore, this study examined the relationship between functional polymorphisms in arginine vasopressin receptor (AVPR) genes, sensory profiles, and neuroanatomical correlations. We used structural magnetic resonance imaging (MRI) and the Adolescent/Adult Sensory Profile (AASP) questionnaire to assess sensory processing and identified seven single nucleotide polymorphisms (SNPs) in ninety-eight healthy adults (44 males, mean age [SD] = 26.8 [6.8] years old). We found that A-allele carriers of rs1042615 in AVPR had higher scores for 'sensory sensitivity' and 'sensation avoiding' compared to GG homozygous. Increased scores on the 3 AASP subscales (i.e., 'low registration', 'sensory sensitivity', and 'sensation avoiding') in A carriers were found to be associated decreased cortical thickness in various regions, including the right precentral, paracentral, and fusiform gyri, as well as bilateral inferior temporal gyri. This study sheds light on the potential role of the genetic variations in AVPR in modulating sensory processing and correlation with cortical thickness and has important implications for understanding sensory abnormalities in neurodevelopmental disorders.

Keywords : Sensory processing, Adolescent/adult sensory profile, Arginine vasopressin receptor, SNP, Cortical thickness

Posters

[B-03] The Correlation between corticospinal tract microstructure laterality and a SNP variation in the OXTR gene in youth with autism spectrum disorders.

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Background : Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social and communication impairments. Neuroimaging studies have indicated that lateral differences in the brain were different between ASD and typical development (TD), whereas genetic studies have indicated that ASD is related to the single nucleotide polymorphism (SNP) of oxytocin receptor (OXTR) in particular rs53576. Therefore, we evaluated the relation between laterality of the white matter microstructure, as measured by diffusion tensor imaging (DTI) and polymorphisms of rs53576.
Methods : We studied 40 youths with ASD (age: 27.8±5.7) and 83 youths with TD (age: 27.8±7.3). DTI analysis by tractography, which reconstructs white matter fiber bundles in three-dimensional space used FreeSurfer Software (version 6.0.0). Then, we calculated diffusion tensor index (fractional anisotropy: FA, axial diffusivity: AD) of each 12 brain white matter area. For evaluating laterality of FA and AD, we used the Laterality Index (LI = (Left-Right)/(Left+Right)). A two-way ANOVA was performed to analyze the effect of Group (TD, ASD) and Genotypes of rs53576 (GG, GA, AA) on LI for FA and AD values. Additionally, we performed linear regression analysis for the gene dosage effect of A allele of rs53576 on LI for FA and AD values in ASD.
Results : There were positive correlations between LI for FA and AD of the corticospinal tract (CST) and autism-spectrum quotient (AQ) score in the ASD group (CST-FA; $r=0.478$, $p=0.004$, CST-AD; $r=0.501$, $p=0.002$), and significant differences between the correlation of both groups (CST-FA; $p=0.001$, CST-AD; $p<0.001$). A two-way ANOVA revealed that there were significant interactions between of LI for CST-FA and CST-AD of Group and Genotypes (CST-FA; $F(2, 113)=7.83$, $p<0.001$, CST-AD; $F(2,113)=7.52$, $p<0.001$). Additionally, linear regression analysis revealed that A allele of rs53576 had significant gene dosage effects on LI for CST-FA ($\beta=0.390$, $p=0.001$) and CST-AD ($\beta=0.384$, $p=0.006$).
Conclusion : These findings indicated that the laterality of the white matter microstructure of the CST is related ASD trait, and the more A allele for rs53576 in ASD, the larger the laterality. We suggested that the OXTR SNP differentially may affect the neurobiological basis of ASD.

Keywords : Laterality, Diffusion tensor imaging (DTI), Corticospinal tract, Oxytocin receptor (OXTR) rs53576, Single nucleotide polymorphism (SNP)

Posters

[B-04] The way my brain sees my body: Associations between eating disorder examination-questionnaire scores and brain morphology in healthy adolescent females.

Kaie Habata[1], Kotaro Kowada[1], Daichi Shiotsu[1], Takuya Makino[1], Taku Kamiya[1], Riku Sanada[1], Hidehiko Okazawa[2,3,4], Yongjeon Cheong[5], Minyoung Jung[5], Hirotaka Kosaka[1,3,4,*]

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Background : It is a quite prevalent phenomenon for healthy adolescent females to have abnormal eating behaviors, excessive focus on body weight control, and preoccupation with body shape and weight, which is highly likely to lead to eating disorders like anorexia nervosa. Although these behaviors are life threatening, the neuroanatomical underpinnings of these psychological alterations remain underexplored.
Methods : The present study included 31 healthy adolescent female participants (mean age 16.6±2.6). Using structural magnetic resonance imaging we computed values of surface area for 168 distinctive regions via Freesurfer. In order to assess abnormality of participants' eating behavior, we used a self-report instrument, the Eating Disorder Examination-Questionnaire (EDE-Q). We performed a series of partial correlation analysis between the EDE-Q scores and surface area of each brain region while controlling age, weight, and intracranial volume.
Results : We found a significant positive correlation between the EDE-Q total score and the surface area of the right rectus gyrus (Spearman's rho=0.616, p=0.0004). There was no significant correlation between the EDE-Q scores and other brain regions.
Conclusion : Previous studies have reported an association between eating disorder and structural anomalies in specific brain regions, especially the prefrontal cortex. As an innermost and lower portion of the frontal lobe, the rectus gyrus, is also considered as a part of the orbitofrontal cortex (OFC). Given the OFC serves as a reward system, its abnormalities may contribute to shaping of distorted image of the body, which further lead to disordered eating behaviors and excessive weight control. This study suggests that the rectus gyrus plays a pivotal role in shaping eating behaviors via the misrepresentation of the body.

Keywords : Adolescent females, Eating behavior, Eating disorder examination-questionnaire (EDE-Q), surface area, the rectus gyrus

Posters

[B-05] Relationship between body image gap and brain surface area and brain gray matter volume in healthy adolescent females.

Kotaro Kowada[1], Kaie Habata[1], Daichi Shiotsu[1], Takuya Makino[1], Taku Kamiya[1], Riku Sanada[1], Hidehiko Okazawa[2,3,4], Minyoung Jung[5], Hirotaka Kosaka[1,3,4,*]

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Background : The prevalence of anorexia nervosa (AN) in Japan has seen rapidly increasing during the COVID-19 pandemic, affecting individuals at increasingly younger ages. Distorted body image is a key diagnostic criterion for AN, and AN has been shown to be associated to brain activity in the right sensorimotor region (insula, premotor area) (Friederich et al., 2010). This study aimed to investigate whether distorted body image is associated with brain volume and surface area alterations in specific brain regions among healthy adolescent Japanese females, with the goal of shedding light on the pathogenesis of AN.
Methods : Thirty-two adolescent healthy females (mean age 16.6±2.6) were included in this study. 3-Tesla MRI scans were performed, and the cortex was divided into 168 different regions using FreeSurfer software to calculate surface area and gray matter volume. Participants also provided subjective self-ratings of body image using the Basic Olomouc Body Rating (BOBR) scale (Šrámková et al., 2015), consisting of ten body image silhouettes representing different BMI (Body Mass Index) values. The degree of body image distortion was determined by calculating the difference between the participant's actual BMI and the BMI corresponding to their subjective self-selected body image silhouette. Partial correlation analysis, adjusting for BMI, weight, age, and Estimated Total Intracranial Volume (ETIV), was performed to examine the relationship between the degree of body image distortion and brain volume/surface area.
Results : Negative correlations with the degree of body image gap were shown for the surface area of the left upper insular sulcus ($r=-0.745$, $p<0.0001$, Pearson) and the gray matter volume of the left upper insular sulcus ($r=-0.668$, $p=0.0001$, Pearson).
Conclusion : Our finding reveal that greater body image distortion was associated with reduced surface area and gray matter volume of the left insular sulcus in healthy adolescent females. These results provide new insight into association between distorted body image and brain structure, and may allow for future study on the neurological pathophysiology of AN.

Keywords : Adolescent females, Eating disorder, Body image, Brain morphology, Insula

Posters

[B-06] Claustral neurons convey mPFC synaptic inputs to the sensory cortices.

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The claustrum is one of the most enigmatic structures in the brain mainly due to difficulties to identify its anatomical structures. Recent histological studies using viruses and retrograde tracers have revealed the connections between the claustrum and other brain structures and suggested the prefrontal cortex as the most intensively connected structure to the claustrum. However, the functional connectivity between medial prefrontal cortex (mPFC) and the claustrum has not been directly tested. Since anatomical axo-dendritic map is not always correlated to functional synaptic map, I investigated the direct synaptic connections between the claustrum and the medial prefrontal cortex. To label visual or barrel cortex-targeting claustral neurons, I injected retrograde tracers into those sensory cortices. To determine whether those sensory cortex-targeting claustral neurons receive synaptic inputs from the medial prefrontal cortex, I expressed Channelrhodopsin (ChR2) in the mPFC. The sensory cortex-targeting claustral neurons responded to the photostimulation of the mPFC ChR2 inputs. TTX perfusion completely shut down the synaptic responses but addition of 4AP revealed monosynaptic responses back. By measuring the synaptic response at both 0 mV and -70 mV holding potentials, I also found that sensory cortex-targeting claustral neurons receive both excitatory and inhibitory inputs from the mPFC. Considering the significant roles of the mPFC in modulating cognition and emotion and the wide connectivity of the claustrum throughout the brain, these results suggest that the claustrum plays a key top-down mediator in sensory information processing.

Keywords : Claustrum, Medial prefrontal cortex, Sensory cortex

[B-07] Chronic Ketamine Administration Impairs Short-Term Memory Performance and Reduces Glutamatergic Transmission

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Short-term memory (STM) refers to the ability to hold and process immediate information for a brief period. Although the precise neural circuitry underlying STM remains elusive, previous research has highlighted the crucial role of persistent neural activity in high-order cortical regions, particularly the prefrontal cortex. This persistent activity has been linked to the activation of muscarinic acetylcholine receptors (mAChRs) and concurrent depolarizing current influx in the medial prefrontal cortex (mPFC), which is believed to serve as a physiological substrate for STM. In the context of schizophrenia (SZ), the glutamate hypothesis proposes that antagonism of N-methyl-D-aspartate receptors (NMDARs) leads to various symptoms, including deficits in STM. In our recent study, we investigated the effects of chronic ketamine administration, a partial NMDAR antagonist, on STM performance. Our findings revealed a significant impairment in an STM-dependent behavioral task following long-term ketamine treatment. We also observed a reduced fraction of mPFC neurons exhibiting mAChR-dependent persistent activity, along with decreased frequency and duration of this activity. While intrinsic membrane properties and excitability of the neurons appeared unchanged, we concluded that chronic ketamine administration resulted in diminished glutamatergic synaptic transmission based on the following observations: a decrease in the frequencies of both spontaneous excitatory postsynaptic currents (sEPSCs) and miniature excitatory postsynaptic currents (mEPSCs), and a reduction in short-term depression elicited by consecutive 10 Hz stimulation. Furthermore, our study provided evidence for reduced glutamate release and vesicular refilling in a mouse model of SZ. Together, our results suggest that hypoglutamatergic state in the SZ brain may stem from weakened glutamate release and compromised vesicular refilling.

Keywords : Schizophrenia, short-term memory, medial prefrontal cortex, synaptic transmission

Posters

[B-08] Disrupted Encoding and Opposite Directional Activities in the Posterior Parietal Cortex during Erroneous Decision-Making

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Making accurate decisions in a complex and dynamic environment poses a formidable challenge for the brain, inevitably leading to occasional inaccuracies. Recent studies have implicated the posterior parietal cortex (PPC) in representing accumulated evidence during perceptual decision-making. In this study, we aimed to investigate whether erroneous decision-making in the PPC is associated with inaccurate representation of visual stimuli or the decay of correct representations. To test this hypothesis, we utilized in vivo two-photon Ca^{2+} imaging to measure neuronal activity in the PPC of head-restrained mice performing a delayed two-alternative decision-making task based on visual stimuli. Employing a novel method using the generalized linear model, we recorded activities from 2,867 neurons exhibiting epoch- or stimulus-specific activation. Among these neurons, approximately 36.4% demonstrated selective increases in firing frequency during specific epochs, 30.5% exhibited dependence on sensory stimuli, and 27.1% displayed choice-dependent firing patterns. Notably, we observed a significant fraction of neurons with activities associated with the opposite direction in error trials, including sensory-related (15.1%) and choice-related (13.6%) neurons within the PPC. Furthermore, we identified a pronounced disruption in encoding capability, particularly during the delay epoch of the decision-making trials. These findings shed light on the neural mechanisms underlying erroneous decision-making in the PPC and provide insights into the functional dynamics of encoding in the context of perceptual decision-making.

Keywords : Decision making, 2-photon calcium imaging, posterior parietal cortex, erroneous trials

[B-09] Investigation of the Role of Mechanotransduction-Related Gene Driven by Stiffness Stimulation in Neural Differentiation

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The mechanical properties of the extracellular microenvironment, including its stiffness, play a critical role in stem cell differentiation. Although previous studies have shown that the developing brain exhibits spatiotemporal diversity in stiffness (Iwashita et al., Development, 2014), it remains unclear how neural stem cells sense the stiffness of their microenvironment and change their fate toward specific neural lineages at molecular resolution in vivo. To address this question, we performed a reconstitution assay combined with RNA Sequencing using brain stiffness-mimicking gels established by our group from tilapia skin collagen (Iwashita et al., Scientific Reports, 2019). Neural stem cells derived from mouse embryonic brains were cultured on "soft" and "hard" gels, mimicking local tissue stiffness in the developing brain. Through bioinformatics analysis, we identified the ER stress pathway gene that was differentially expressed between "Soft" and "Hard" conditions in the differentiated neurons derived from neural stem cells. Interestingly, this gene driven by stiffness stimulation is a causative gene for microcephaly. To investigate its functions, we analyzed the expression pattern of the neural-specific markers Ctip2 (expressed in layer V) and Satb2 (expressed in layer II/III). Gain-of-function and loss-of-function analysis in vivo revealed a shift in the expression pattern of Ctip2 and Satb2 during neural differentiation. ER stress pathway inhibitor analysis in vitro induced the differences in the expression pattern of Ctip2 and Satb2 as similar to in vivo. Our results suggest that the ER stress pathway responds to brain stiffness during brain development.

Keywords : Mechanotransduction, Extracellular Microenvironment, Stiffness, ER stress pathway, Neural Differentiation

Posters

[B-10] Investigation of regulatory mechanism of neural and astrocyte differentiation from neural stem cells promoted by cyclin-dependent kinase inhibitors with stage dependent manner

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The aim of this study is to disclose the mechanism of specific neural and astrocyte differentiation from Neural Stem Cells (NSCs) correlated with Cyclin-Dependent Kinase Inhibitor (CDKI). By observing the expression patterns of astrocyte-specific marker, Aldh1l1, and endogenous CDKIs, p18 and p27, in various embryonic stages of Aldh1l1-EGFP reporter mouse, we found that EGFP in the ventricular zone was gradually increased from E15.5. Notably, expression level of CDKIs was accompanied in the same manner. Next, we introduced CDKIs to embryonic mouse brain by in utero electroporation, and recognized that the CDKIs can regulate the generation of astrocyte in both in vitro and in vivo. We also found stage-dependent difference of gene expressions by performing RNA sequencing after inducing p18-overexpression in mouse brain using conditional knock-in mouse model. Functional analysis of specifically upregulated genes via p18-overexpression suggests novel mechanisms of neural and astrocyte differentiation in the developing cortex. Taken together, we concluded that CDKIs are involved in neural and astrocyte differentiation pathway with stage dependent manner.

Keywords : Neural stem cells, CDKI, Differentiation, Neuron, Astrocyte

[B-11] Fabrication of an Amperometric Acetylcholine Biosensor for Alzheimer’s Disease Research

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Alzheimer's disease is a complex neurodegenerative disorder believed to be caused by multiple factors. One proposed factor is the choline hypothesis, which suggests that abnormal acetylcholine secretion or loss of function in neurons contributes to the disease's symptoms. Since acetylcholine activity is closely associated with memory and cognition, investigating and understanding its role in the brain is crucial for advancing research on Alzheimer's disease treatment.
In this study, we fabricated a sensor for detection of acetylcholine and conducted performance evaluations through an in-vitro test. The sensor was fabricated using chitosan, which formed a porous structure, and cross-linked with chitosan and enzyme using glutaraldehyde. The manufactured acetylcholine sensor will be applied in an in-vivo test.

Keywords : Acetylcholine sensor, Alzheimer’s disease, Chitosan, Porous structure

Posters

[B-12] A systemic integration for parallel recording of electrophysiological signals and fluorescence images

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Various kinds of multifunctional neural interfaces have been recently presented to understand the functional connectivity of neural circuits. However, the developed systems so far have an apparent limitation as it behaves in vivo imaging while the head is fixed, which restrains the animal's behavior. Here, we show the multimodal neural interface unified with an electrocorticography (ECoG) electrode array and commercial micro-endoscope for parallelly recording ECoG signals and fluorescent images. The ECoG electrode array is based on high flexibility and transparency substrate for incorporating complicated micro-endoscope and the simultaneous recording of fluorescence images and electrophysiological signals. A headstage was designed to tightly associate between ECoG array and micro-endoscope and miniaturized to minimize the behavioral restrictions of animals. The recording capability of the developed multifunctional neural interface has been validated to perform the parallel recording of ECoG signals and fluorescence images in freely moving mice.

Keywords : Multimodal neural interface, Microelectrodes, Electrophysiology, Micro-endoscope, Freely moving

[B-13] Shuttle-assisted Flexible Neural Probe for Neural Recording in Non-Human Primates

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Long-term neural monitoring plays a crucial role in the study of brain circuits and electroceuticals. The demand for long-term monitoring has prompted the development of flexible neural probes designed to match the mechanical properties of brain tissue. This engineering approach aims to minimized the risk of tissue damage and inflammation, enabling long-term implantation and reliable signal recording. Despite the considerable advantages offered by flexible neural probes, their utilization is hindered by the inherent challenge posed by their flexibility, which impedes precise insertion into brain tissue. This limitation has largely restricted the application of such probes to small animals like rodent where depth of insertion required is minimal. Larger animals, such as non-human primates, present a greater challenge due to the need for deeper probe placement. NHPs are crucial component of this type of research, given their complex brain connectivity and neuroanatomy that closely resembles that of humans. In this study, we develop a bioresorbable, shuttle-assisted flexible neural probe specifically designed for the deep brain regions of NHPs. The study employed a 32-electrode PI neural probe, designed narrowly in two layers to reduce brain invasion. The electrode, initially patterned with Au, were coated with Pt and IrOx. A disaccharide shuttle was attached to the probe to provide temporary mechanical stiffness during insertion. Upon insertion into the deep brain regions, the shuttle rapidly dissolves, exposing the electrodes to the brain tissue and facilitating signal recording. We recorded local field potentials (LFPs) in the NHP's lateral hypothalamic area (LHA) during phases with and without food for a month. The recorded LFPs were converted into image-like time-frequency representation, called sclaograms and uses as input for Convolutional Neural Network (CNN) to classify the eating phases. This CNN-based classifier was subjected to five-fold cross validation. This high accuracy suggests promising applications for brain circuit research and the development of electronic medicine.

Keywords : Neural probe, Deep Learning, Non-human primates

Posters

[B-14] Battery-Free Neural Recorder for studying eating behavior in Non-Human Primates

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Advancements in wireless brain neural recorders have substantially extended their utility in neuroscience research. Among these advancements, the integration of wireless power transfer technology has been a focal point in recent years since it obviates the demand for potentially damaging batteries and ensures long-term monitoring. However, most neural recorders have been limited to small-animal models such as rodents because of the limitation of the wireless power transfer range. Non-human primates, which can provide more clinical insights than rodents do, require more advanced wireless power transfer technology than rodents because they jump, stand, and move freely. Here, we introduce a wireless neural recorder for non-human primates with unique functional thin layers, which operates through power received wirelessly via a magnetically coupled double-coil-based wireless power transfer system. The system comprises a top module for wireless power harvesting and a bottom module for signal recording and wireless communication. The top module contains a coil for the harvesting of wireless power and a full wave rectifier circuit. By using an analytical circuit model in the top module and finite element simulations, the distance between the coils of the wireless power transmission system is precisely determined to maximize wireless power transfer efficiency. This design approach allows for a wireless power transfer range of up to 60 cm from the transmitter coil. The power harvested by the top module drives the active embedded circuit in the bottom layer, enabling local field potential recording and wireless communication. With the developed system, we recorded local field potentials during eating behaviors in freely moving NHPs over a period of one month. The result demonstrates that our system is capable of recoding real-time neural signal in an untethered monkey without the need for a harmful battery, a promising prospect for future pre-clinical experiments.

Keywords : Neural recorder, Wireless power transfer, Non-Human Primates

[B-15] Small molecule probe for fluorescent visualization of living choroid plexus

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The choroid plexus is responsible for producing and quality-controlling cerebrospinal fluid (CSF). Emerging evidence has been pointing to choroid plexus (ChR) as crucial for developing and maintaining the CNS, such as adult neurogenesis and the immune system of the CNS. Despite functional necessity, the ChR is one of the most unrevealed architectures of the human brain, regarding its development and regulation. Here, we developed a small molecule fluorescence probe, which can fluorescently label the live ChR in the cultured human neural organoids as well as mouse brain *in vivo*. The probe-positive ChR appeared after around 35 days of human neural organoids differentiation culture and their staining was superimposed with the ChR marker protein expression such as TTR and AQP1. In the three types of cell layers of the ChR, the probe selectively stains the ChR epithelial cells, which are developed from the roof plate of the neural tube and evolutionarily conserved in lower vertebrates to humans. Taken together, our new approach makes it possible to visualize the live ChR in both mice and humans, which can be applied to the study of the development, physiology, and pathophysiology of choroid plexus with enhancing temporal and spatial resolution.

Keywords : Choroid plexus, small molecule probe, human neural organoid

Posters

[B-16] Nano-scale imaging of neuronal cells by genetically encoded tag and volume electron microscopy

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Contacts between mitochondria and ER (MERC) are very dynamic and specialized protein-enriched region that determines their structure and functions. The contact site important play role in the essential biological regulation of the exchange of calcium and lipids, which involves autophagosome formation and mitochondrial fission. Recently, many researchers have shown that disturbances to mitochondria and ER contacts occur in neurodegenerative diseases like Alzheimer's disease, Parkinson's disease, and Amyotrophic Lateral Sclerosis.
Visualization of this network between mitochondria and ER has been attempted using super-resolution fluorescence imaging and light microscopy; however, the limited resolution is insufficient to observe the membranes between the mitochondria and ER in detail. Transmission electron microscopy provides good membrane contrast and nanometer-scale resolution for the observation of cellular organelles. However, it is very difficult to distinguish between fragmented ER and other membrane structures (e.g. Golgi structure or vesicles) in electron micrographs. In addition, these highly curved cellular organelles are present in a three-dimensional structure throughout the cell. Therefore, we observed the morphology of mitochondria and ER via correlative light-electron microscopy (CLEM) and volume electron microscopy techniques using enhanced ascorbate peroxidase 2 (APEX2) and horseradish peroxidase (HRP) staining. An en bloc staining method, ultrathin serial sectioning (array tomography), and volume electron microscopy were applied to observe the 3D structure.
In this study, we suggest a combination of CLEM and 3D electron microscopy to perform detailed structural studies of mitochondria and ER in neuronal cells.

Keywords : APEX2, array tomography, volume microscopy, MERC

[B-17] Chronic observations of hippocampal place cells using miniaturized fluorescent microscope

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The intricate neural network that underlies place cells has been extensively studied in neuroscience. However, most of studies have used electrophysiological methods which are not ideal for longitudinal analysis. Here, we investigate the properties of place cells in freely behaving mice using Ca^{2+} imaging in familiar environment and novel environment. We found that place cells in novel arenas show higher firing rates compared to the place cells in familiar arena. This finding confirms previous reports that disinhibition occurs in place cells when mice are exposed to a novel environment. Furthermore, we were able to observe consistent activity patterns when monitoring the place cells over a period of days. We will use this technique to study how place cells are modulated during spatial learning and memory in healthy and diseased brains.

Keywords : Place cell, In vivo calcium imaging, novel arena, familiar arena

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