	順序編號	英文姓名	中文姓名	Title
03-1	3	Hsiao-Chen Liu	劉曉甄	Transient activation of Npas1 neurons recreates ensemble bursting in the basal forebrain
03-2	3	Szwen Liu		Decoding the focus of cross-modal selective attention in single trials via neuronal activity in the basal forebrain
03-3	3	Hsin-Pei Lee	李欣蓓	Inhibitory Control of the Thalamic Reticular Nucleus by the Basal Forebrain
03-4	3	Yi-Chieh Huang		The subthreshold basis of spike synchrony between hippocampal parvalbumin interneurons
03-5	3	Yu-Cheng Liu	劉又誠	γ-TuRC regulates neuronal migration during embryonic cortical
03-6	3	Guan Yu Wu	吳觀宇	The Role of ASIC Channels in The Response of N2a Cells to The Micropipette Guided Ultrasound Stimulation
03-7	3	Nguyen Phan Nguyen Nhi	阮潘妮	Genetically encoded tools applying in iPSC derived neurons and astrocytes for phenotypic/functional screening
03-8	3	是瑋 陳		The efficient induction of human retinal ganglion-like cells provides a platform for studying optic neuropathies
03-9	3	Cheng-En Shen		Toward a novel strategy for optogenetic control of synaptic transmission
03-10	3	Chun-Shu Wei	魏群樹	ExBrainable: An Open-Source GUI for EEG Decoding and Model Interpretation Based on Explainable Neural Networks
03-11	3	Ching Tsuey Chen	陳景萃	Nonlinear Dendritic Activity Drives Hippocampal Place-Field Forming Plasticity as A Function of Synaptic Input Dynamics And State
03-12	3	Srimayee Bhattacharjee		Investigation of the heterogeneity of calcium activity in the motor cortical and the striatal astrocytes
03-13	3	Pin Ju Chou		Common Topological Properties and Self-similarity Shared by Neurons with Diverse Morphology in Drosophila melanogaster

O3-14	3	Cheng-Yu Chen	陳政佑	Construction of forebrain projectome in adult zebrafish
P3-15	3	Yi-Hsuan Liao	廖奕瑄	HIGH-RESOLUTION FUNCTIONAL MAPPING OF FOREBRAIN ACTIVITY IN BEHAVING ZEBRAFISH.
P3-16	3	Kai Hsin HSU	徐楷昕	Large-scale and automated construction of multi-compartmental models for neurons in the FlyCircuit database
P3-17	1	Li-shan Cheng		Hybrid network architecture of memory center in the Drosophila brain
P3-18	3	Ning Chang		Inhibition and stability in head-direction neural circuits
P3-19	3	Ming Ju Hsieh	謝明儒	The Dynamical System and Application of Recurrent Neural Network
P3-20	3	Guan-Ren Huang	黃冠仁	Decision Making : Dynamical phase transition of meta-neurons
P3-21	3	Wei-Chao Huang	黃威超	Proteomic and Transcriptomic Analysis of Gria3 Mutant Mice Suggests Dysregulation of Neuronal Pentraxins in Schizophrenia
P3-22	3	Hsu-Wen CHAO CHAO	趙需文	CPEB3-downregulated Nr3c1 mRNA translation confers resilience to developing PTSD-like behavior in fear-conditioned mice
P3-23	3	Peeraporn Varinthra	王燕潼	Peroxiredoxin 6 Knockout Mice Demonstrate Anxiety Behavior and Attenuated Contextual Fear Memory after Receiving Acute Immobilization Stress
P3-24	3	Pavithra Suresh		Attenuation of HECT-E3 ligase expression rescued memory deficits in 3xTg-AD mice
P3-25	3	Tanita Pairojana		Standardized Extract of IM01 Prevents Cued Fear Memory Deficit and Reduction of Hippocampal Long-Term Potentiation in 3xTg-AD Mice
P3-26	3	Chen-Jiun Yeh	葉宸濬	α6GABAAR-Selective Positive Allosteric Modulators Relieved Dental Pulp Injury-Induced Facial Allodynia in Mice via Enhancing GABA Currents in Trigeminal Ganglia
P3-27	3	Yin Chin	秦茵	The proton-sensing receptors, TDAG8 and OGR1 involved in CCI-induced neuropathic pain by modulating different neuron populations

P3-28	3	Sitt Wai Fong	馮旭輝	Acid sensing TDAG8 and ASIC1a are molecular determinants of acid-induced antinociceptive sngception in a mouse model of fibromyalgia.
P3-29	3	Yi-Ching Chen	陳怡情	Investigating the role of Advillin in regulating neurite outgrowth on PDMS substrates of different stiffness levels
P3-30	3	Chien-Hsin Chu	朱建勳	Translocation of Paxillin to the Nucleus Supports Early Postnatal Neuron Maturation
P3-31	3	Fang-Yu Hsu	許芳瑜	Systematic Characterization of A Putative Novel Long Noncoding RNA in the Spinal Cord
P3-32	3	Ya-Ping Yen	顏雅萍	m6A epitranscriptome: The role of RNA modification during motor neuron development and degeneration
P3-33	3	Chi Wen Liong	梁啟雯	Retinal Innervation Pattern in Central Clock, Suprachiasmatic Nucleus of Mice
P3-34	3	Ern-Pei Chua		Light-induced spatiotemporal circuit from ipRGCs to the suprachiasmatic nucleus
P3-35	3	PingYen Wu		Correlating locomotion behaviours with three-dimensional spatiotemporal dynamics of astrocytic Ca2+ signalling in the Motor Cortex in vivo
P3-36	3	YiKo Chen		Interactive dynamics of the somatosensory and motor cortices during forelimb movement in mice
P3-37	3	HAO-TUNG YANG	楊浩東	Neuronal responses under ultrahigh frequency stimulation
P3-38	3	Yen-Yuan Chen	陳妍媛	Advancing fabrication of implantable multichannel-electrode arrays (MEAs) for in vivo chronic large-scale electrophysiology
P3-39	3	Yu-Jui Li		Circuit mechanisms underlying CB1R mediated suppression of dentate granule cell recruitment by cortical input
P3-40	3	Jei-Wei Wu	吳哲瑋	Regulation of Hippocampal Dynamics by Hilar Mossy Cells
P3-41	3	Syun-Ruei Lee	李珣睿	Mapping the inputs and outputs of the paraventricular nucleus of the thalamus

P3-42	3	Ping-Chen Ho	何秉臻	Functional characterization of afferent inputs from the ventral midbrain to the zona incerta
P3-43	3	Hsiang-Wei Hsing	邢翔威	Activity-dependent feedback regulation of thalamocortical axon development by Lhx2 in cortical layer 4 neurons
P3-44	3	WEI-NI LIN	林薇妮	Mechanoresponsive phosphorylation and subcellular redistribution of septin-2 upon low-intensity pulsed ultrasound (LIPUS) stimulation
P3-45	3	YUCHEN LU	盧鈺臻	Mechanoresponsive of NMDAR2B and CamKIIa phosphorylation in mouse hippocampus stimulated by ultrasound
P3-46	3	Pei-chun Hsu	徐霈君	Developmental abnormalities of the nigrostriatal pathway in mice with dopamine synthetic defect
P3-47	3	Wen-Wei Lin	林文蔚	Interaction between reward learning and punishment learning
P3-48	3	Tsai-Chun Hung	洪采君	Haptic perception and motor function ability with or without musician
P3-49	3	Chia-Shu Lin	林嘉澍	Meta-analytic Neuroimaging Evidence of the Association between Orofacial Pain and Mastication
P3-50	3	Peter Kuan-Hao Cheng		Evaluation of age-related development of executive function by using the Conners K-CPT 2 and event-related potential component in a three-stimulus auditory oddball task
P3-51	3	Wan-Yu Shih		The human orbitofrontal cortex represents the subjective value of the present, and the past food rewards
P3-52	3	Lin-Yuan Tseng	曾令元	Attention related changes in aperiodic neural activity with time-on-task
P3-53	3	Evgeny Parfenov		Stability of the heartbeat counting task for measuting interoception
P3-54	3	Chien Ming Lo	駱建銘	Relating interneuron populations to spontaneous neural activity properties across the human cortex
P3-55	3	I-Hui Hsieh	謝宜蕙	Musical Training Shapes the Processing of Degraded Speech in Noisy Environment

投稿學會：台灣基礎神經科學學會 | 編號: P3-15

HIGH-RESOLUTION FUNCTIONAL MAPPING OF FOREBRAIN ACTIVITY IN BEHAVING ZEBRAFISH

Yi-Hsuan Liao & Kuo-Hua Huang

Institute of Molecular Biology, Academia Sinica, Taipei, Taiwan

Abstract

The forebrain controls cognitive functions, emotions, hormone release, biological cycles and voluntary body movements. In the past, investigation of forebrain functions have been hampered by the difficulties to monitor a large portion of neurons in the brain at high resolution during behavior. In recent years, the zebrafish has become a popular animal model to study behavior and brain functions due to its small brain for optical recording of activities and dense reconstruction of neuronal circuits. Unlike the larval zebrafish, the adult zebrafish exhibit diverse social behaviors, including aggression, mating, shoaling and schooling. However, high-resolution activity measurements and functional mapping of the forebrain are still lacking in adult zebrafish. Here, we recorded movements of the tail, eyes and gills of a head-restrained adult zebrafish using a custom-built behavioral recording system and analysis pipeline. Simultaneously, the forebrain activity was non-invasively measured using two-photon calcium imaging in animals expressing GCaMP6f pan-neuronally. Currently, we are able to record ~200 neurons across 30% of forebrain in depth (200 μm) at a volume rate of 5Hz by using a resonant scanner and a piezo-controlled objective lens. First, we found that the movements of the eyes and the tail are highly correlated. Neurons in the forebrain region Dc (potential homologs of the isocortex) often exhibit positive or negative correlations to the eye and tail movements. On the other hand, a subset of neurons in Dl (potential homolog of hippocampus) exhibit activities that specifically correlate to the eye movements. In addition, neurons in the forebrain region Dm (homologous to the basolateral amygdala) tend to become active while the animal stopped moving. We are currently classifying and mapping these behavior-related neurons and other types of neurons across dorsal forebrain regions. This investigation of neuronal population activity could be combined with neuronal projectome data to establish the foundation for studying forebrain functions in a small vertebrate model.

投稿學會：台灣計算神經科學學會 | 編號: P3-16

Large-scale and automated construction of multi-compartmental models for neurons in the FlyCircuit database

Kai-Hsin Hsu , Chi-Tin Shih ,Chung-Chuan Lo

National Tsing Hua University institute of Systems Neuroscience

Abstract

Understanding the functions of neural circuits is one of the most important topics in systems neuroscience. To study the detailed neural network functions at the whole-brain level, we propose to construct detailed computational models for each neuron in the FlyCircuit database, one of the largest neuronal imaging databases for Drosophila melanogaster. The proposed project can be divided into four phases. We first collaborate with the Brain Research Center at National Tsing Hua University and obtain detailed electrophysiological and neuronal structure information for several sample neurons. Second, we create multi-compartmental models for these neurons using the open-source NEURON simulator and use the SSO (simplified swarm optimization) algorithm for parameter search in order to find parameters that accurately reproduce the passive (subthreshold) properties of the neurons. We also add active zones (action-potential initiation sites) on the axon initial segments based on observations made in the Brain Research Center. Third, we will derive a set of algorithms that can translate the morphology of neurons into model parameters based on what we learned from modeling the sample neurons. Finally, we will create multi-compartment models for each neuron in the database using the algorithms and release the models in the FlyCircuit database. In this presentation we will describe our progress on the first two phases of the project.

投稿學會：台灣計算神經科學學會	編號: P3-17

Hybrid network architecture of memory center in the Drosophila brain

Li-shan Cheng 1, Ching-Che Charng 2,3, Ruei-Huang Chen 2,3, Kuan-Lin Feng 2,3, Chung-Chan Lo 2, Ann-Shyn Chiang 2,3,4, and Ting-Kuo Lee 1

1 Department of Physics, National Tsing Hua University, Hsinchu 30013, Taiwan 2 Institute of Systems Neuroscience, National Tsing Hua University, Hsinchu 30013, Taiwan, ROC 3 Brain Research Center, National Tsing Hua University, Hsinchu 30013, Taiwan, ROC 4 Department of Biomedical Engineering and Environmental Sciences, National Tsing Hua University, Hsinchu 30013, Taiwan, ROC 5 Institute of Molecular and Genomic Medicine, National Health Research Institutes, Miaoli 35053, Taiwan, ROC

Abstract

Bio-signal encoding mechanisms are heavily determined by the architecture of underlying neural circuits. Mushroom body (MB) is the olfaction memory center of Drosophila. Previous studies support opposite perspectives to the upstream organization of MB, that is, completely random or stereotypic, based on experimental evidence of the connectivity at the mesoscopic level. Here we identify the hybrid network structure of Drosophila calyx that three Kenyon cell (KC) classes leverage different levels of input expansion by maintaining the spatial map across the olfactory system. We construct a simulation model of the MB tuning profile by integrating the response pattern of the receptor neurons with the connectome of olfactory system The model successfully predicts the odor-evoked activity of MB in the lobe region. The hybrid structure differentiates the chemical sensitivity of KCs and likely determines the innate tuning features of MB output neurons. Our results provide insights into the computational benefit of a calyceal hybrid network for translating molecular signals into higher-order perception.

投稿學會：台灣計算神經科學學會 | 編號: P3-18

Inhibition and stability in head-direction neural circuits

Ning Chang, Hsuan-Pei Huang, Chung-Chuan Lo

Institute of Systems Neuroscience, National Tsing Hua University.

Abstract

Navigation of insects is supported by the central complex which consists of extremely complex neural circuits. Previous studies of Drosophila central complex reported that the head-direction, essential information for navigation, is encoded by localized activity (termed activity bump) in two subregions, the ellipsoid body (EB) and the protocerebral bridge (PB). Moreover, detailed connectomic analysis of EB and PB revealed that they form attractor circuits, a network architecture that can support activity bumps based on theories of neural networks. These theories further suggest that feedback inhibition is crucial for the stability of activity bumps. However, several different sets of inhibitory neurons innervate the EB-PB circuits, their roles and relative contributions to the bump stabilization is still not fully understood. To address this issue, we constructed and systematically investigated several variants of biologically realistic neural circuit models based on the recently published EM (electronic microscopy) connectomic data. The circuit models share the basic EB-PB recurrent circuits, which maintain and update the active bump. The differences are the inhibitory mechanism, which is either by ring neurons (ER1) or by delta 7 neurons, and the connectomic databases the models based on. We further analyzed the differences in ring neuron and delta 7 neuron in different conditions. First, we tested the robustness of each model by scanning the available parameter in a large range. Second, we tested the maximum rotational speed that can be supported by the models. Last, we tested how multiple visual stimuli affect bump formation. Our study showed that the models using ring neurons as the inhibitory mechanism provides the best stability and robustness over other variants of models.

投稿學會：台灣計算神經科學學會	編號: P3-19

The Dynamical System and Application of Recurrent Neural Network

Ming-Ju Hsieh Alexander White Belle Liu Chung-Chuan Lo

Department of Physics, Nation Tsing Hua University, Taiwan Institute of System Neuron Science, Nation Tsing Hua University, Taiwan
Department of Applied Mathematics, University of Washington, Seattle WA Institute of System Neuron Science, Nation Tsing Hua University, Taiwan

Abstract

Recent development in connectomic research has enabled us to study complex neural circuit structures at the single-neuron levels. One of the most common features founds in almost all species under investigation is the motifs of recurrent connections at the micro-circuit levels. We hypothesize that these types of motifs may hold the key to the flexibility and multi-functionality of neural networks. To demonstrate how recurrent circuits work, we propose the Coupled Recurrent Inhibitatory and Recurrent Excitatory Loops (CRIRELs), which preserve the key features of the commonly observed neural motifs. CRIRELs contain two excitatory neurons and two inhibitory neurons. We found that by changing the biases of neurons, CRIRELs can perform different logic-gate-like functions. In the present study, we further explore the dynamics of CRIRELs. To analyze it mathematically, we replace the leaky integrate-and-fire model with the firing-rate model. Next, we use semi-analytical methods to study the detailed dynamics and bifurcation structure of CRIRELs. This analysis allows us to explain how we can rapidly switch CRIRELs between different functions simply by changing bias inputs. Finally, we found that such an “on-line” function switch has enormous applications in neuromorphic engineering. We demonstrate it by creating an “adder” using CRIRELs. Instead of using four logic gates as in the classical 1-bit full adder, using CRIRELs, we need only two gates. One gate acts as the carry-out and toggle between AND and OR gates, while the other gate acts as summation and toggle between XOR and XNOR gates. Add an excitatory neuron to the CRIRELs so that the loops can switch between the two logic-like functions in the same connection weight. Therefore, the new network can perform a full adder. This 1-bit full adder can be scaled up by connecting multiple adders in series to form a ripple-carry adder. By studying the dynamics of CRIRELs, we gain more insights into the multifunctionality of neural circuits. Moreover, our results show that CRIRELs have great potential in neuromorphic engineering as they can be used to create the lightweight and multifunctional artificial neural networks.

投稿學會：台灣計算神經科學學會	編號: P3-20

Decision Making : Dynamical phase transition of meta-neurons

Guan-Ren Huang Hsiu-Hau Lin

Department of Physics National Tsing Hua University

Abstract

Meta-neurons are neuronal populations with internal synaptic connections, yet still can be captured by appropriate effective neuron models. Here we show that a meta-neuron undergoes a dynamical phase transition as internal synaptic connections strengthen. Similar to the magnetic phase transition for the spin systems, the synaptic strength connecting neurons plays the role as the exchange coupling between spins, while the external current stimulus mimics the magnetic field. It is rather remarkable the phase boundary of the transitions can be derived from the Legendre transform of the gain function relating the neuronal activity and the external stimulus. Despite its apparent similarity to the thermal phase transition, the dynamical phase transition includes competitions between all local minima and exhibits rich temporal evolutions, vital for information processing between neurons.

投稿學會：台灣基礎神經科學學會 | 編號: P3-21

Proteomic and Transcriptomic Analysis of Gria3 Mutant Mice Suggests Dysregulation of Neuronal Pentraxins in Schizophrenia

Wei-Chao Huang1, Ryan Kast1,2,3, Borislav Dejanovic1, Hasmik Keshishian4, Kevin Bonanno4, Gouping Feng1,2,3, Morgan Sheng1,2

1. Stanley Center for Psychiatric Research, Broad Institute of Harvard University and MIT, Cambridge, MA, USA 2. Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA 3. McGovern Institute for Brain Research, Massachusetts Institute of Technology, Cambridge, MA 4. Proteomics Platform, Broad Institute of Harvard University and MIT, Cambridge, MA, USA

Abstract

The exact causes of schizophrenia, a chronic mental disorder mainly characterized by psychotic symptoms, are still unclear. Gria3 encodes AMPA glutamate receptor subunit 3 and has been found to be associated with schizophrenia. The mechanisms underlying Gria3 mutation contributes to schizophrenia progression remain little known. Here, we examined synaptosome proteomics of the cortex of the mice with a Gria3 mutation identified by the SCHEMA (SCHizophrenia Exome Meta-Analysis) project. We found downregulation of neuronal pentraxin (Nptx) 1 and 2 in the 1-month-old mutant mice. Transcriptome analysis on the somatosensory cortex also showed significantly decreased expression of Nptx2. Similarly, 3-month-old mutant mice have reduced expression of Nptx1 and 2. Our proteomic and transcriptomic analyses indicate Nptxs dysregulation in the brain of Gria3 mutant mice. Recent studies found that NPTXs were reduced in cerebrospinal fluid of individuals with schizophrenia and could activate the classical complement cascade. Our synaptosome proteomics showed significant downregulation of C1qa, b, and c levels in the 3-month-old mice, suggesting that Gria3 mutation might affect complement pathways in the brain. Overall, our study highlights a role of Nptx-complement signaling in the pathology of schizophrenia.

投稿學會：台灣基礎神經科學學會 | 編號: P3-22

CPEB3-downregulated Nr3c1 mRNA translation confers resilience to developing PTSD-like behavior in fear-conditioned mice

Hsu-Wen Chao, Wen-Hsin Lu, Pei-Yi Lin, Yi-Shuian Huang

1. Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan 2. Department of Physiology, College of Medicine, Taipei Medical University, Taipei, Taiwan.

Abstract

Posttraumatic stress disorder (PTSD) is a trauma-induced psychiatric disorder, which depends on not only the intensity of trauma but also genetic risk factors; the latter may result in enhanced fear memory formation and/or impaired fear extinction after exposure to trauma reminders. Susceptibility or resilience to PTSD depends on one's ability to appropriately adjust synaptic plasticity for coping with the traumatic experience. Activity-regulated mRNA translation synthesizes plasticity-related proteins to support long-term synaptic changes and memory. Hence, cytoplasmic polyadenylation element-binding protein 3-knockout (CPEB3-KO) mice, showing dysregulated translation-associated synaptic rigidity, may be susceptible to PTSD-like behavior. Here, using a context-dependent auditory fear conditioning and extinction paradigm, we found that CPEB3-KO mice exhibited traumatic intensity-dependent PTSD-like fear memory. A genome-wide screen of CPEB3-bound transcripts revealed that Nr3c1, encoding glucocorticoid receptor (GR), was translationally suppressed by CPEB3. Thus, CPEB3-KO neurons with elevated GR expression exhibited increased corticosterone-induced calcium influx and decreased mRNA and protein levels of brain-derived neurotrophic factor (Bdnf). Moreover, analysis of two GEO datasets revealed decreased transcriptomic expression of CPEB3 but not NR3C1 in peripheral blood mononuclear cells of humans with PTSD. Collectively, this study reveals that CPEB3, as a potential PTSD-risk gene, downregulates Nr3c1 translation to maintain proper GR-BDNF signaling for fear extinction.

投稿學會：台灣基礎神經科學學會 | 編號: P3-23

Peroxiredoxin 6 Knockout Mice Demonstrate Anxiety Behavior and Attenuated Contextual Fear Memory after Receiving Acute Immobilization Stress

Sarayut Phasuk 1,2, Peeraporn Varinthra 1, Andaman Nitjapol 3, Korakod Bandasak 3, and Ingrid Y. Liu 1*

1 Institute of Medical Sciences, Tzu Chi University, Hualien 970, Taiwan 2 Department of Physiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand 3 Faculty of Medical Science, Naresuan University, Phitsanulok 65000, Thailand

Abstract

Stress can elicit glucocorticoid release to promote coping mechanisms and influence learning and memory performance. Individual memory performance varies in response to stress, and the underlying mechanism is not clear yet. Peroxiredoxin 6 (PRDX6) is a multifunctional enzyme participating in both physiological and pathological conditions. Several studies have demonstrated the correlation between PRDX6 expression levels and stress-related disorders. Our recent finding indicates that lack of the Prdx6 gene leads to enhanced fear memory. However, it is unknown whether PRDX6 is involved in changes in anxiety response and memory performance upon stress. The present study reveals that hippocampal PRDX6 level is downregulated 30 min after acute immobilization stress (AIS) and trace fear conditioning (TFC). In human retinal pigment epithelium (ARPE-19) cells, the PRDX6 expression level decreases after being treated with the stress hormone corticosterone. Lack of PRDX6 caused elevated basal H_2O_2 levels in the hippocampus, basolateral amygdala, and medial prefrontal cortex, brain regions involved in anxiety response and fear memory formation. Additionally, this H_2O_2 level was still high in the medial prefrontal cortex of the knockout mice under AIS. Anxiety behavior of Prdx6−/− mice was enhanced after immobilization for 30 min. After exposure to AIS before a contextual test, Prdx6−/− mice displayed a contextual fear memory deficit. Our results showed that the memory performance of Prdx6−/− mice were impaired when responding to AIS, accompanied by dysregulated H_2O_2 levels. The present study helps better understand the function of PRDX6 in memory performance after acute stress.

投稿學會：台灣基礎神經科學學會 | 編號: P3-24

Attenuation of HECT-E3 ligase expression rescued memory deficits in 3xTg-AD mice

Pavithra Suresh1 , Sureka Jasmin2 , Yun Yen3,4,5,6,7, Hao Jen Hsu8, Peeraporn Varinthra1, Tanita Pairojana1, Chien-Chang Chen9, Ingrid Y. Liu1*

1 Institute of Medical Sciences, Tzu Chi University, Hualien, Taiwan 2 Department of Molecular Biology and Human Genetics, Tzu Chi University, Hualien, Taiwan 3 Ph.D. Program for Cancer Molecular Biology and Drug Discovery, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan. 4 Graduate Institute of Cancer Biology and Drug Discovery, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan. 5 TMU Research Center of Cancer Translational Medicine, Taipei Medical University, Taipei, Taiwan. 6 Cancer Center, Taipei Municipal WanFang Hospital 7 Center for Cancer Translational Research, Tzu Chi University 8 Department of Life Science, Tzu Chi University, Hualien, Taiwan 9 Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan

Abstract

Alzheimer's disease (AD) is one of the most common progressive neurodegenerative disorders that cause deterioration of cognitive functions. Recent studies suggested that the accumulation of inflammatory molecules and impaired protein degradation mechanisms might both play a critical role in the progression of AD. Autophagy is a major protein degradation pathway that can be controlled by several HECT-E3 ligases, which then regulates the expression of inflammatory molecules. E3 ubiquitin ligases are known to be upregulated in several neurodegenerative diseases. Here, we studied the expressional change of HECT-E3 ligase using M01 on autophagy and inflammasome pathways in the context of AD pathogenesis. Our results demonstrated that the M01 treatment reversed the working memory deficits in 3xTg-AD mice when examined with the T-maze and reversal learning with the Morris water maze. Additionally, the electrophysiology recordings indicated that M01 treatment enhanced the long-term potentiation in the hippocampus of 3xTg-AD mice. Together with the improved memory performance, the expression levels of the NLRP3 inflammasome protein were decreased. On the other hand, autophagy-related molecules were increased in the hippocampus of 3xTg-AD mice. Furthermore, the protein docking analysis indicated that the binding affinity of M01 to the WWP1 and NEDD4 E3 ligases was the highest among the HECT family members. The western blot analysis also confirmed the decreased expression level of NEDD4 protein in the M01-treated 3xTg-AD mice. Overall, our results demonstrate that the modulation of HECT-E3 ligase expression level can be used as a strategy to treat early memory deficits in AD by decreasing NLRP3 inflammasome molecules and increasing the autophagy pathway.

投稿學會：台灣基礎神經科學學會 | 編號: P3-25

Standardized Extract of IM01 Prevents Cued Fear Memory Deficit and Reduction of Hippocampal Long-Term Potentiation in 3xTg-AD Mice

Tanita Pairojana 1, Sarayut Phasuk 1, Mayuree H. Tantisira 2, Kai-Chi Liang 1, Sittiruk Roytrakul 3, Narawut Pakaprot 4, Supin Chompoopong 5, Sutisa Nudmamud-Thanoi 6, Yang Ming 1, and Ingrid Y Liu 1*

1 Institute of Medical Sciences, Tzu Chi University, Taiwan, 2 Faculty of Pharmaceutical Sciences, Burapha University, Thailand, 3 National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Thailand, 4 Department of Physiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand, 5Department of Anatomy, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand, and 6Department of Anatomy, Faculty of Medical Science, Naresuan University, Thailand

Abstract

Alzheimer's disease (AD) is the most common form of dementia with a progressive memory decline and synaptic dysfunction. Finding the drug that can prevent the development of such pathologies received more attentions in the field. A standardized extract IM01 isolated from the widely used Asian herb was recently reported to enhance memory and hippocampal long-term potentiation (LTP) in rats. Thus, it suggests the potential use of IM01 to prevent or attenuate the pathogenesis of AD. Our previous study reported that the triple transgenic AD (3xTg-AD) mice, an AD mouse model having both amyloid plaques and neurofibrillary tangles started to demonstrate impaired fear memory and synaptic dysfunction at the age of 6 months old. Administration of IM01 (doses; 10, 30 and 100 mg/kg) into 3xTg-AD mice from 5 months old for 30 consecutive days rescued impaired fear memory and enhanced hippocampal LTP in 3xTg- AD mice. Subsequent proteomic and western blot analyses showed that the major molecules in LTP induction and maintenance including brain-derived neurotrophic factor (BDNF), tyrosine receptor kinase B (TrkB) and its network proteins, extracellular signal-regulated kinase 1 and 2 (ERK1 and 2), were upregulated in the hippocampus and amygdala of 3xTg-AD mice after treatment of IM01. Our results indicate that IM01 is promising drug to help prevent cognitive decline and synaptic dysfunction in AD.

投稿學會：台灣基礎神經科學學會 | 編號: P3-26

α 6GABAAR-Selective Positive Allosteric Modulators Relieved Dental Pulp Injury-Induced Facial Allodynia in Mice via Enhancing GABA Currents in Trigeminal Ganglia

Chen-Jiun Yeh,1 Ming-Tatt Lee,1 Chih-Cheng Chen,3 Werner Sieghart,4 Daniel E. Knutson,5 James Cook,5 and Lih-Chu Chiou1, 2 *

1Graduate Institute of Pharmacology, 2Graduate Institute of Brain and Mind Sciences, College of Medicine, National Taiwan University, Taipei, 10051 Taiwan. 3Institute of Biomedical Sciences, Academia Sinica, Taipei 11529, Taiwan. 4Department of Molecular Neurosciences, Center for Brain Research, Medical University of Vienna, Spitalgasse 4, A-1090 Vienna, Austria.5Department of Chemistry and Biochemistry, Milwaukee Institute for Drug Discovery, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin 53211, USA.

Abstract

The α6 subunit-containing GABAA receptors (α6GABAARs) are highly expressed in trigeminal ganglia (TG), the hub of the trigeminal sensory system involved in the pathogenesis of migraine or orofacial pain. Previously, we have identified a series of pyrazoloquinolinones (PQ) to be α6GABAAR-selective positive allosteric modulators (PAMs), and substantiated that the Compound 6 and its deuterated derivative, DK-I-56-1, were effective in two rodent models of migraine. TG also play an important role in orofacial pain. Using dental pulp injury (DPI)-induced facial allodynia, we elucidated how PQ compounds exert TG inhibition to achieve their possible therapeutic effects on TG-related orofacial pain. Compound 6 (1, 3, 10 mg/kg, i.p.) significantly attenuated DPI-induced facial allodynia on post-surgical day1. The anti-allodynic effect of Compound 6 was significantly prevented by furosemide, a brain-impermeable α6GABAAR antagonist, given by either systemic administration (20 mg/kg, i.p.) or intra-TG microinjection (10 nmol/0.5 µl, i.tg.), suggesting the site of action of Compound 6 is the α6GABAARs in TG. DK-I-56-1, compared with Compound 6, displayed a similar efficacy but a longer action time (1.5hr vs. >3hrs). We further investigated the cellular mechanism of Compound 6 on isolated TG neurons by whole-cell and perforated patch clamp. The GABA currents (IGABA) induced by focal application of various concentrations of GABA obtained in whole-cell configuration showed an EC50 of GABA at 13.5±3.3 µM. Next, we assessed the potentiating effect of Compound 6 on GABA currents induced by EC50 of GABA (IGABA, EC50) in each neuron. On average, Compound 6 at 1 µM increased (IGABA, EC50) by 29.2±7.4 %. Importantly, this potentiating effect of Compound 6 was prevented by furosemide (100 µM). We further used perforated configuration to maintain the chloride gradient of TG neurons. Results showed that GABA induced membrane depolarization in TG neurons concentration dependently. Importantly, the anti-allodynic effect of Compound 6 can be mimicked by intra-TG injection of KCl, which can depolarize TG neurons. These results suggest that α6GABAAR-selective PAMs can potentiate the chloride conductance mediated by α6GABAARs in TG, which may induce depolarization block of the trigeminal sensory transmission, ultimately leading to the suppression of mechanical allodynia in mice with DPI.

投稿學會：台灣基礎神經科學學會 | 編號: P3-27

The proton-sensing receptors, TDAG8 and OGR1 involved in CCI-induced neuropathic pain by modulating different neuron populations

SYin Chin, hih-Ping Dai, Chun Chieh Yang, Wei-Hsin Sun*

Department of Life Sciences and Institute of Genome Sciences, National Yang-Ming University

Abstract

Neuropathic pain caused by a lesion or disease of the somatosensory nervous system is usually accompanied by nerve degeneration, neuroinflammation, focal ischemia and acidosis of the injury site. However, it remains unclear when acute pain becomes chronic pain and which receptors are responsible for this transition. Given that proton-sensing G-protein coupled receptors (GPCRs) including GPR4, TDAG8, OGR1 and G2A, are fully activated in the range of pH6.4-6.8, these receptors could be involved in the early stage of neuropathic pain to initiate persistent pain. In this study, we used chronic constriction injury of sciatic nerve (CCI) as a model of neuropathic pain and found that CCI surgery in mice induces persistent pain (>14 weeks). Acid-induced calcium signals in dorsal root ganglia (DRG) neuron culture were observed at different time points after CCI surgery. In DRG neurons ranged <35 μm in diameter, calcium signals were increased after surgery and peaked at week 2; in DRG neurons >35μm in diameter calcium signals were peaked at week 8. We then injected shRNA plasmids intraplantarly to inhibit gene expression of proton-sensing GPCRs in peripheral afferents. After knockdown of TDAG8 and OGR1 genes, the mechanical allodynia was alleviated post CCI 1-4 weeks and 4-14 weeks, respectively. Calcium signals were also inhibited by TDAG8 knockout at week 2 in DRG neurons <20μm; calcium signals were inhibited by OGR1 knockdown at week 4 on DRG neurons ranged 20-35 μm and at week 8 on DRG neurons >35μm. The acute phase of mechanical allodynia from 1 to 4 weeks is mainly regulated by TDAG8 in DRG neurons <20μm, while the chronic phase from 4 to 14 weeks is modulated by OGR1 in DRG neurons of 20-35 μm at 4-8 weeks and in DRG neurons >35μm at 8-14 weeks. Accordingly, mechanical allodynia is mediated by more than one receptor and by distinct neuron populations.

投稿學會：台灣基礎神經科學學會	編號: P3-28

Acid sensing TDAG8 and ASIC1a are molecular determinants of acid-induced antinociceptive sngception in a mouse model of fibromyalgia.

Sitt Wai Fong, Cheng-Han Lee, Wei-Hsin Sun, Chih-Cheng Chen

Academia Sinica.

Abstract

For years, in human study, acid has been widely considered as the key for triggering chronic muscle pain and the cause of this involves two principal types of proton-sensing ion channels, namely, ASIC3 and TRPV1. In our previous study, we demonstrated for the first time acid not only respond to ASIC3 and TRPV1, but also trigger acid-induced antinociceptive effect via a non-ASIC3, non-TRPV1 neuron population. TDAG8 is a member of ORG family and it is a proton sensitive GPCR which exclusively found in small-diameter DRG neurons that are responsible for nociception. In the present study, two acid injection on TDAG8 KO prolonged chronic mechanical hyperalgesia for more than 10 wks, suggesting TDAG8 may play a role in modulating pain. BTB09089, a TDAG8 agonist, reversed acid-induced hyperalgesia in WT mice, but not in TDAG8 KO. SM-SP inverted the pain in both WT and TDAG8 KO. In TDAG8 KO, acid-induced pERK activity was dramatic increased and APETx2, a selective blocker of ASIC3, co-injected with CZP, a selective TRPV1 antagonist, reduced the acid-induced pERK induction. Collectively, these results strongly indicate TDAG8 modulates pain nociception probably via TDAG8-induced SP antinociception in non-ASIC3, non-TRPV1 signaling. ASIC1a, another specific type of proton-sensitive channels, has been shown recently to induce antinociceptive effect on dextrose-mediated antinociception in mouse model of fibromyalgia. In this present study, PcTx1, a selective ASIC1a antagonist, blocked the antinociceptive effect in non-ASIC3, non-TRPV1 pathway with a delay of transient effect development on second acid-injection. In contrast, in the absence of TDAG8, PcTx1 reversed the acid-induced antinociception with an early appearance of transient hyperalgesia. ASIC1a KO prolonged chronic muscle pain with only a single acid insult, suggesting ASIC1a, like TDAG8, may play a vital role in acid-induced antinociception. In situ hybridization revealed SP co-expressed with TDAG8 and ASIC1a in DRG neurons, indicating a possible role for antinociceptive pain modulation. Taken together, although acid-induced muscle chronic pain is not a new idea, the present study here show acid can also play a major role in antinociception via TDAG8/ASIC1a signaling in non-ASIC3, non-TRPV1 positive neuron. More importantly, this dual action induced by acid, is vital for pain nociceptive regulation in sensory ganglia and thus preventing further neuronal sensitization. In other words, this crucial action is to make sure and keep the pain threshold at bay without causing further increased sensitivity or damage to the acid-induced chronic muscle pain.

投稿學會：台灣基礎神經科學學會 | 編號: P3-29

Investigating the role of Advillin in regulating neurite outgrowth on PDMS substrates of different stiffness levels

Yi-Ching Chen, Yu-Chia Chuang, Chih-Cheng Chen

Academia Sinica

Abstract

Advillin is an actin-binding protein strongly expressed in somatosensory neurons. It has been implicated in neurite growth, neuronal development, and cytoskeletal organization. Advillin is a key protein involved in neurite outgrowth, and colocalizes with the focal adhesion kinase, pFAK, at the tips of filopodia. Substrate stiffness has been previously shown to affect neurite outgrowth. However, the participation of Advillin in stiffness-dependent differential neurite growth is still unknown. Here, we aim to investigate whether Advillin has a role in coupling neurite outgrowth and cytoskeletal protein regulation to substrate stiffness of Neuro-2a (N2a) cells cultured on polydimethylsiloxane (PDMS) at three stiffness levels. Overexpressing advillin showed no phenotype in neurite length when compared to N2a with endogenous expression of Advillin in all stiffness levels. Overexpressing Advillin resulted in twice the linear density of filopodia along a neurite compared to control cells cultured on the 100 KPa and 1000 KPa PDMS substrates, demonstrating its role in regulating filopodia outgrowth on stiffer environments. Interestingly, when overexpressed, immunostaining suggests that Advillin accumulated at the filopodia roots 1000 times more than at the tips in all three substrates, despite different tip-to-root ratios in control expression levels.

投稿學會：台灣基礎神經科學學會	編號: P3-30

Translocation of Paxillin to the Nucleus Supports Early Postnatal Neuron Maturation

Chien-Hsin Chu, Chen Chen, Pei-Lin Cheng

Institute of Molecular Biology, Academia Sinica

Abstract

Neuron maturation is a multiple-step process in which each step involves switches on/off sets of protein isoform, structure, and function. Whether and how neurotrophin factor instructs the timely maturation transitions reminds illusive. In this study, we will share our recent findings on a novel function of nuclear paxillin, which harbors a neuron-specific phosphorylation modification at Ser119 (p-paxillinS119) mediated by BDNF signaling or cdk5 activation and dephosphorylated by PP2A. The Ser119-phosphorylation of nuclear paxillin peaks on the seventh day in vitro (DIV) and forms nuclear sparkles with phosphorylated SR proteins till 10 DIV, covering a developmental transition when numerous maturation-promoting factors are undergoing isoforms switch. Blockade of the Ser119-phosphorylation or mutations in the PY-type NLS of paxillin significantly causes a reduction in the paxillin nuclear translocation and alters AIS location. Mass spectrometry-based proteomics of DIV4 neurons reveals that multiple splicing regulators associate with neuronal paxillin upon BDNF stimuli. By deploying a minigene splicing assay to assess exon skipping efficiency, we found that paxillinS119 phosphorylation modulates the neuronal, stage-specific splicing events. To gain more insight into the detailed mechanism underlying the timed, paxillin-regulated splicing program, we will analyze mRNA/protein isoform expression profiles of Ser119-phosphorylation-deficient neurons.

投稿學會：	編號: P3-31

Systematic Characterization of A Putative Novel Long Noncoding RNA in the Spinal Cord

Fang-Yu Hsu and Jun-An Chen

Institute of Molecular Biology, Academia Sinica Genome and Systems Biology Degree Program, Academia Sinica and National Taiwan University

Abstract

Long non-coding RNAs (lncRNAs) are comprised of >200 nucleotides that are not translated into proteins. Accumulating evidence reveals that lncRNAs display more propensity in cell- or tissue-type specificity, thereby being regarded to contribute to specific cell-context dependent regulatory function. Although lncRNAs are traditionally considered to have no or little protein-coding potential, some recent reports indicated that lncRNAs could generate proteins. Here, we used spinal motor neurons (MNs) as a paradigm to investigate the functional role of a novel highly conserved MN-enriched lncRNA A730046J19Rik during MN development. To explore the role of A730046J19Rik during MN development, we utilized the mouse embryonic stem cell (ESC)-derived MN differentiation approach and established the A730046J19Rik knockout model to uncover several vital insights of this novel lncRNA. Interestingly, A730046J19Rik seems to only produce a protein at the postnatal stage albeit with already strong RNA expression in embryos. We are in the process to dissect the possible divergent role of A730046J19Rik RNA and protein at prenatal and postnatal stages respectively. We aimed to use A730046J19Rik as a proof of principle to shed light on the dual function of lncRNA during development, and this might open a new avenue of regulatory functional mode of lncRNA.

投稿學會：	編號: P3-32

m6A epitranscriptome: The role of RNA modification during motor neuron development and degeneration

Ya-Ping Yen and Jun-An Chen

Institute of Molecular Biology

Abstract

Emerging studies have shown that N6-methyladenosine (m6A), the most prevalent and abundant RNA modification that occurs in the mRNA of most eukaryotes plays a critical role in various developmental processes. This modification is installed by the m6A methylation “writers” (Mettl3/Mettl14 methyltransferase complex) and can be reversed by demethylases “erasers” (Fto and Alkbh5). Depletion of m6A methylation writer Mettl14 via Mettl14 knockout in mouse embryonic nervous systems prolongs cell cycle progression of radial glia and extends cortical neurogenesis into postnatal stages. Although m6A mRNA methylation has long been recognized as a posttranscriptional modification in mammalian cells, the roles of this posttranscriptional process and the biological significance of m6A modification in mammalian neuronal development and disease, particularly motor neuron (MN) development and degeneration, are completely unknown. To decipher the role of the m6A modification during MN development and neurological disorders, we conditionally inactivating an essential m6A writer component Mettl14 specifically in the cells using a Mettl14 conditional (floxed) mouse line in combination with oligodendrocyte Cre driver lines (Olig2-Cre). We observed that Olig2-Cre-mediated knockout of Mettl14 induces significant reduction of MN numbers suggesting that m6A might serve as important roles during MN development. In the future, we will conduct m6A-sequencing (m6A-seq) of embryonic stem cell (ESC)-differentiated motor neurons (MNs) to assess the m6A distribution. Then we will be able to determine the biological significance of m6A RNA modification during mammalian MN development. Overall, this study will result in the first blueprint of epitranscriptional profiling of mammalian MNs and provide a new avenue for the MNs development.

投稿學會：台灣基礎神經科學學會 | 編號: P3-33

Retinal Innervation Pattern in Central Clock, Suprachiasmatic Nucleus of Mice

Chi Wen Liong 1, Shih-Kuo Chen 2

National Taiwan University, Life Science Department, Taipei

Abstract

Circadian rhythms modulate our daily activity patterns and other body mechanisms, such as metabolic and neuroendocrine rhythms. In mammals, circadian rhythms are controlled by the central clock, suprachiasmatic nuclei (SCN). The external light signal could entrain SCN through intrinsically photosensitive retinal ganglion cells (ipRGCs). SCN contains different neurons, while AVP and VIP neurons are critical for the networking of circadian rhythm. AVP neurons are mainly expressed in shell region of SCN, while VIP neurons are expressed in core region. In a previous study, VIP neurons are suggested as light signal receiving neurons, and AVP neurons are the primary output neurons for the SCN. However, in single ipRGC tracing study suggested that ipRGCs innervation does not limit to VIP neurons specifically but throughout the whole SCN. In addition, the mechanisms of how SCN neurons communicate with each other's remain unknown. To explore the route of SCN neurons, we will use expansion microscopy to observe the connection and retinal innervation of SCN neurons. Revealing the circuit within SCN will advance our understanding of circadian rhythms, thus finding new treatments for circadian arrhythmic diseases.

投稿學會：台灣基礎神經科學學會 | 編號: P3-34

Light-induced spatiotemporal circuit from ipRGCs to the suprachiasmatic nucleus

Chua Ern Pei, Hsiao I Ling, Chang Yi Ting, Chen Shih Kuo.

Department of Life Science, National Taiwan University.

Abstract

The endogenous circadian clock exists in the organism. In the mammalian brain, the suprachiasmatic nucleus (SCN) is thought of as the central circadian clock, which can control the peripheral circadian rhythm of organs in the whole body. In the SCN, neurons are spatially divided into dorsal-medial (shell) and ventral-lateral (core) regions, which are enriched with arginine vasopressin (AVP) and vasoactive intestinal peptide (VIP) neurons respectively. According to previous studies in 2016, our group found that a single M1 ipRGC projects to either dorsal, medial, or ventral region in the SCN (Fernandez et al., 2016). Additionally, in hamsters, light-stimulating at different timing induced Fos expression in different regions of the SCN (Schöttner K, 2015; Samer Hattar, 2020). Therefore, the light-induced neural circuit in the SCN seems to contain both spatial and temporal cues. To test whether SCN could encode spatial or temporal information with distinct activation pattern, we used TRAP 2 mice and cFos immunostaining to identify the activated SCN neurons after different pattern of light exposure. Here we found that light source from above the animal and light source below the animal may activate different group of neurons in the SCN. Therefore, SCN may receive and compute spatial information in additional to brightness to control circadian photoentrainment.

投稿學會：台灣基礎神經科學學會 | 編號: P3-35

Correlating locomotion behaviours with three-dimensional spatiotemporal dynamics of astrocytic Ca2+ signalling in the Motor Cortex in vivo

Ping-Yen Wu1,2, Yu-Wei Wu 1, 2

1 Institute of Molecular Biology, Academia Sinica, Taipei 115, Taiwan 2 Neuroscience Program of Academia Sinica (NPAS), Academia Sinica, Taipei 115, Taiwan

Abstract

Astrocytes in the central nervous system define the brain environments and govern energy and metabolic support through neuron-astrocyte-blood vessel complex. Recent studies also found astrocytes regulate synaptogenesis, synaptic maintenance, and homeostasis of transmitters in neural circuits. Activation in astrocytic Ca2+ signalling is considered as the integrator linking neurovascular units and neuronal information to higher order physiological responses. Therefore, decoding astrocytic Ca2+ signalling is essential for the understandings of brain functions. Conventional method of studying calcium signals is based on only two-dimensional (2D) region-of-interest (ROI) analysis. However, highly divergent morphology of astrocytes and complex astrocytic Ca2+ dynamics make such conventional analysis a source of inconsistent results . Here we establish in vivo two-photon (2P) volumetric imaging on sparsely-labelled astrocytes using Aldh1l1-CreERT2::lck-GCaMP6f and Aldh1l1-CreERT2::Salsa6f transgenic mice. We monitor subcellular astrocytic Ca2+ dynamics in individual astrocytes in the primary motor cortex of awake mice. We developed a three-dimension (3D) analysis and tracking method to identify splitting and merging of Ca2+ events in the astrocytic territory. The event properties such as duration and maximum propagation detected in 3D are higher than that in 2D, which is consistent with our expectation that 3D analysis can reveal more insights. Furthermore, along with 2P Ca2+ imaging, we also recorded the animal locomotion behaviours simultaneously for animal pose estimations by DeepLabCut. By using these experimental methods and analysis pipeline, we aimed to decode the intricate astrocytic Ca2+ signals integrate from small subcellular microdomains to global compartments that affecting cortical mantle and coupling to behaviours .

投稿學會：台灣基礎神經科學學會 | 編號: P3-36

Interactive dynamics of the somatosensory and motor cortices during forelimb movement in mice

Yiko Chen(1, 3), Hao-Tong Yang(1, 2), Poulomi Adhikari(1, 3, 4), Abdulmalik Obaid(5), Shih-Hung Yang(6), Yu-Wei Wu(1, 3, 4, 7)

1 Institute of Molecular Biology, Academia Sinica, Taipei, Taiwan 2 Department of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University, Taipei, Taiwan 3 Neuroscience Program in Academia Sinica (NPAS), Academia Sinica, Taipei, Taiwan 4 Molecular and Cell Biology Program, Taiwan International Graduate Program (TIGP), Academia Sinica 5 Department of Materials Science and Engineering, Stanford University, Stanford, CA 94304, USA 6 Department of Mechanical Engineering, National Cheng Kung University, Tainan, Taiwan 7 Department of Life Science, College of Life Science, National Taiwan University, Taipei, Taiwan

Abstract

How neural signals in various brain regions coordinate to generate behavioral movement is an important question in understanding the brain function. It's been shown that the neural activities from primary motor cortex (M1), the final station before sending signals to spinal cord, is highly influenced by signals from other brain areas such as the somatosensory cortex (S1) and the pre-motor cortex (M2). However, how these cross-cortical activities interact with each other to initiate and control movement is not fully understood. We established a CMOS-multielectrode array (CMOS-MEA) to simultaneously record M1, M2, and S1 spike activities on mice during a forelimb food-pallet reaching task. After spike sorting, signals from more than a thousand of single- or multi-unit clusters are successfully obtained. Latent Factor Analysis via Dynamical Systems (LFADS) is applied to extract the denoised spike rates from single trials and to map neural signals to a low dimensional latent factor space. We showed the mice paw position can be successfully decoded with high precision ($R2 > 0.95$). Moreover, 38 low dimensional latent factors could also result in similar high performance of decoding ($R2 > 0.89$). It's also found that the dynamics of some latent factors corresponds to different functional roles of brain areas, such as preparational signals before motion in M2. In addition, comparing with the case of dropping S1 signals, the decoding performance decreases substantially (6%). This indicated that the interactive dynamics between motor cortices and S1 might be crucial in generating movement. These results demonstrated the different roles of different brain areas and their contribution in motion generation.

投稿學會：台灣基礎神經科學學會 | 編號: P3-37

Neuronal responses under ultrahigh frequency stimulation

Hao-Tung Yang Yu-Tsao John Hsing Hsin Chen Yu-Wei Wu

Department of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University, Taipei, Taiwan Institute of Molecular Biology, Academia Sinica, Taipei, Taiwan Institute of Electronics Engineering, National Tsing Hua University, Hsinchu, Taiwan Neuroscience Program in Academia Sinica (NPAS), Academia Sinica, Taipei, Taiwan Department of Life Science, College of Life Science, National Taiwan University, Taipei, Taiwan

Abstract

投稿學會：台灣基礎神經科學學會	編號: P3-38

Advancing fabrication of implantable multichannel-electrode arrays (MEAs) for in vivo chronic large-scale electrophysiology

Yen-Yuan Chen1,2,3, Iryna Bilous1,2,4, Jung-Chien (Rajer) Hsieh1,2, Yu-Tsao John Hsin1,2, Abdulmalik Obaid5, Yu-Wei Wu1,2,3,4*

1Institute of Molecular Biology, Academia Sinica, Taipei 115, Taiwan 2Neuroscience Program in Academia Sinica (NPAS), Academia Sinica, Taipei 115, Taiwan 3Genome and Systems Biology Degree Program, Academia Sinica and National Taiwan University, Taipei 106, Taiwan 4Taiwan International Graduate Program in Molecular Cell Biology, National Defense Medical Centre and Academia Sinica, Taipei 112, Taiwan 5Department of Materials Science and Engineering, Stanford University, Stanford, CA 94304, USA

Abstract

Deciphering neural information with single-neuron resolution requires implantable electrodes to record their action potentials. Bundled parallel microelectrode arrays have been demonstrated for in vivo large-scale cortical recording of spiking activity (Obaid et al., 2020). We further verified that spike recoding with microwire bundle implanted into cerebral cortex is chronically stable and caused minor tissue damage with wire diameter is smaller than 20 µm (Obaid & Wu et al., 2020). However, the fabrication of the microwire bundle is still not optimized. Arranging the microscopic and fragile wires into bundle format with an ideal pitch or a specific pattern is still challenging. Here, we developed scalable fabrication procedures for bundled microwire arrays. Platinum Iridium (PtIr) microwires with a diameter of 13 µm are coated with high dielectric constant material Parylene C (PaC) to create a sacrificial layer to reach a diameter of 100 to 150 µm for maintaining the straightness of the wires and defining the pitch between wires. A Perfluoroalkoxy alkane (PFA) heat-shrink tube is used to bundle the PaC-coated microwires in a hexagonal-close-packed manner. We further designed a patternable alignment system utilizing metal-guide plates and a semi-automatic wire-loading design. This fabrication procedure enables the arrangement of individual wires to a specific location and forms the desired patterns, i.e., an 8-by-8 square array or multiple square arrays. The bundled microwires can target neuronal populations of different cortical layers by shaping the wires into different lengths with an angled-polishing procedure to yield 3-dimensional microwire bundles. Finally, our in vivo implant demonstrated that the chronic stability of spike recording could reach more than six months, suggesting our microwire bundles are ideal neural interfacing for chronic recording in 3-dimensional brain tissue.

投稿學會：	編號: P3-39

Circuit mechanisms underlying CB1R mediated suppression of dentate granule cell recruitment by cortical input

Yu-Jui Li1, Chia-Wei Yeh1, and Cheng-Chang Lien1,2,*

1Institute of Neuroscience, 2Brain Research Center, National Yang Ming Chiao Tung University, Taipei, 112, Taiwan

Abstract

The neuromodulatory system plays an important role in regulating synaptic plasticity, signaling environmental cues and modulating cognitive functions. The cannabinoid type 1 receptors (CB1Rs) in the dentate gyrus (DG) have been implicated in cognition and emotion, and are highly expressed in GABAergic cholecystokinin-expressing interneurons (CCK-INs) and glutamatergic hilar mossy cells. Endocannabinoids released from the post-synaptic dendrites retrogradely target the pre-synaptic CB1Rs in an activity-dependent manner, and thereby lead to a reduction of neurotransmitter release. The DG, the first station of the hippocampus, receives multimodal inputs from the cortex and processes the information to downstream hippocampal CA regions. However, how the endocannabinoid system (ECS) modulates the DG input-output transformation remains unclear. Using ex vivo electrophysiological recording and pharmacological approaches, we found that activating endocannabinoid signaling by the CB1R agonist WIN 55,212-2 (5 μM) attenuated the perforant path (PP)-mediated granule cell population spikes (GC pSpikes) without affecting synaptic transmission of the PP. Moreover, CCK-INs appear to be essential for CB1R-induced suppression of GC activity because either blockade of GABAAR or chemogenetic inactivation of CCK-INs abolished the reduction of GC pSpikes after CB1R activation. The neural mechanism by which CB1R activation at CCK-INs contributes to suppression of GC responses to the cortical inputs remains unclear and awaits to be explored in the near future.

投稿學會：台灣基礎神經科學學會 | 編號: P3-40

Regulation of Hippocampal Dynamics by Hilar Mossy Cells

Jei-Wei Wu 1 and Cheng-Chang Lien 1,2

1Institute of Neuroscience, National Yang Ming Chiao Tung University, Taipei 11221, Taiwan 2Brain Research Center, National Yang Ming Chiao Tung University, Taipei 11221, Taiwan

Abstract

The hippocampus is one of the critical brain regions for learning and memory. The dentate gyrus (DG), the first relay station of the hippocampus, receives multimodal sensory inputs from cortical areas and participates in pattern separation and contextual fear memory. The DG is composed of two types of glutamatergic neurons, the granule cells (GCs) and the hilar mossy cells (MCs), as well as several types of GABAergic interneurons (INs). The axons of MCs project to both local and distal lamellae of the DG, and differentially modulate GC and IN activity in the local and distal DG. Activation of ventral MCs primarily excites GCs in the dorsal DG via longitudinal axonal projections whereas excitation of MC commissural projections (COM) preferentially recruits INs, thereby suppressing GC activity via feedforward inhibition. Long-term potential (LTP) is a synaptic substrate underlying learning and memory. Repetitive stimulation of MC axons induces LTP at MC-to-GC synapse via increasing excitation/inhibition balance in GCs, thereby enhancing GC output. Preliminary data from our lab showed that activation of MC COM projections enhances the performance of contextual fear memory.

投稿學會：台灣基礎神經科學學會	編號: P3-41

Mapping the inputs and outputs of the paraventricular nucleus of the thalamus

Syun-Ruei Lee and Hau-Jie Yau

Graduate Institute of Brain and Mind Sciences, National Taiwan University College of Medicine

Abstract

The paraventricular nucleus of the thalamus (PVT) is known to encode salience of reinforcing stimuli and regulate associative learning. How the PVT neurons acquire and relay valence to initiate proper responding remains elusive. To address this question, we first employed retrograde viral tracing in anterior and posterior parts of the PVT respectively to map their afferent inputs. We found that, comparing to anterior part of the PVT (aPVT), posterior part of the PVT (pPVT) received stronger innervations from cortical regions, such as medial prefrontal cortex (mPFC), insular cortex, anterior cingulate cortex (ACC), somatosensory cortex and entorhinal cortex. On the contrary, aPVT received stronger innervations from the subcortical regions, such as parabrachial nucleus and retromammiliary nucleus. Interestingly, we found that it was aPVT, but not pPVT, that received dense afferent input selectively from the ventral rather than dorsal CA1 (vCA1). We then focused on vCA1-to-aPVT input and employed anterograde viral tracing to examine its downstream projections. We detected axonal projections of vCA1-innervated aPVT cells across the brain, such as mPFC, ACC, nucleus accumbens, bed nucleus of the stria terminalis, amygdala and hypothalamus. Given that vCA1 is involved in social memory and regulates affection, we are currently employing optogenetic approaches to investigate the behavioral functions of vCA1-to-aPVT connection.

投稿學會：台灣基礎神經科學學會	編號: P3-42

Functional characterization of afferent inputs from the ventral midbrain to the zona incerta

Ping-Chen Ho and Hau-Jie Yau

Graduate Institute of Brain and Mind Sciences, National Taiwan University

Abstract

In nature, when animals perceive reward-related or danger stimuli, they show corresponding responses to retrieve the reward or avoid the threat. Recent studies have shown that the ventral tegmental area (VTA) and substantia nigra (SN) in the ventral midbrain can regulate defensive behaviors. Although both regions send projections to the ZI, which is shown to regulate defensive behaviors, the functional roles of midbrain-to-ZI connections remain elusive. As the first step to investigate the circuit function, we combined dual viral retrograde targeting approach with in situ hybridization (RNAscope) technique to study the neurochemical phenotypes of midbrain cells projecting to the ZI. We found that ZI-projecting VTA neurons consisted mostly of glutamatergic and a small population of GABAergic neurons, whereas ZI-projecting SN neurons consisted mostly of GABAergic and some dopaminergic neurons. We further characterized the behavioral involvement of ZI-projecting midbrain neurons in a mouse model of stress and performed neural activity-dependent c-Fos immunostaining assay. We found that ZI-projecting midbrain neurons were significantly involved in restraint stress. Moreover, we found that ZI-projecting SN neurons were significantly activated by TMT presentation, which mimics nature threat. We further employed excitatory optogenetic approach to causally examine behavior functions of this connection. We found that activation of SN-to-ZI input resulted in aversion in real time conditioned place preference assay. We then further developed a defensive behavioral paradigm and found that activation of the SN-to-ZI input significantly increased defensive behavior induced by TMT presentation. To sum up, our research has demonstrated a novel function of the SN-to-ZI input in regulating defensive behavior.

投稿學會：台灣基礎神經科學學會	編號: P3-43

MActivity-dependent feedback regulation of thalamocortical axon development by Lhx2 in cortical layer 4 neurons

Chia-Fang Wang, Jenq-Wei Yang , Zi-Hui Zhuang , Hsiang-Wei Hsing , Shu-Meng Hsu, Heiko J Luhmann , Shen-Ju Chou1

Institute of Cellular and Organismic Biology, Academia Sinica

Abstract

The development of neuronal circuits requires interactions between the pre- and postsynaptic neurons. To illuminate the mechanisms under circuit formation, we study the development of rodent barrel cortex, the largest component in the primary somatosensory cortex (S1). The development of barrel cortex is instructed by presynaptic thalamocortical axons (TCAs). In the first postnatal weeks, TCA terminals arborize in layer (L) 4 to fill in the barrel center, but it is unclear how TCA development is regulated. We previously demonstrated that the deletion of Lhx2 in the postmitotic cortical neurons in the Lhx2 conditional knockout (cKO) leads to TCA arborization defects, which is accompanied with deficits in sensory-evoked and spontaneous cortical activities and impaired lesion-induced plasticity following early whisker follicle ablation. Reintroducing Lhx2 back in L4 neurons in cKO ameliorated TCA arborization and plasticity defects. By manipulating L4 neuronal activity, we further demonstrated that Lhx2 induces TCA arborization via an activity-dependent mechanism. Additionally, we identified the extracellular signaling protein Sema7a as an activity-dependent downstream target of Lhx2 in regulating TCA branching. Thus, we discovered a bottom-up feedback mechanism for the L4 neurons to regulate TCA development and this process is important for the barrel cortex plasticity.

投稿學會：國立台灣大學醫療器材研發中心	編號: P3-44

Mechanoresponsive phosphorylation and subcellular redistribution of septin-2 upon low-intensity pulsed ultrasound (LIPUS) stimulation

Wei-Ni Lin1, Jormay Lim1, Ya-Cherng Chu1, Ya-Chih Chien2, Yeh-Shiu Chu3, Chih-Cheng Chen2, Jaw-Lin Wang1

1. Department of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University, Taipei, Taiwan. 2. Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan. 3. Brain Research Center, National Yang-Ming University, Taipei, Taiwan

Abstract

Septins are newly categorized as the fourth component of the cytoskeleton, which conventionally comprises microtubule, microfilament, and intermediate filament. Recent studies have suggested that septins interact with phosphoinositides(PIPs) to initiate exocytosis (Collins et al., 2020), guide microtubules (Short, 2011), and are often found close to mechanosensitive compartments, such as primary cilia and plasma membranes (Lam & Calvo, 2019). Although septins are correlated to mechanosensitive behaviors, for instance, the formation of membrane protrusions in cell migration and angiogenic invasion of endothelial cells, septins are mechanoresponsive has not been demonstrated. We aim to test the protein phosphorylation and subcellular re-distributions of septin-2 upon mechano-stimulation by application of ultrasound. To reveal the network among these diverse features of septins, we utilized LIPUS as non-invasive, mechanical stress to induce the phosphorylation of septin-2 and to further observe the corresponding subcellular localization in cells. By immunoblot analysis of the septin-2 phosphorylation in ultrasound-stimulated (600mVpp, 1MHz, 5min) chinese hamster ovary (CHO) cells, we discover that septin-2 phosphorylation increased dose-dependently as ultrasound's duty factor was elevated from 1% to 3%. Furthermore, such stimulation also induces clustering of septin-2 at the cortical actin-enriched sites of the cell periphery while the resting cells predominantly exhibit a microtubule pattern of septin-2. Since ultrasound has been a promising technology for neuronal modulations in the brain for therapeutic purposes, our findings provide a molecular basis for the considerations of how ultrasound should be administered. In short, our study provides a deeper understanding of septin dynamics in response to mechano-stimulation.

投稿學會：國立台灣大學醫療器材研發中心	編號: P3-45

Mechanoresponsive of NMDAR2B and CamKIIa phosphorylation in mouse hippocampus stimulated by ultrasound

Yu-Chen LU1, Jormay Lim1, Ya-Cherng Chu1, 1, Yu-Ju Chen2,3,Yu-Hen Hsieh2, Jaw-Lin Wang1

1.Department of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University, Taipei, Taiwan.
2.Department of Chemistry , College of Engineering, National Taiwan University, Taipei, Taiwan. 3.Institute of Chemistry, Academia Sinica,Taipei, Taiwan.

Abstract

Ultrasound stimulation is a promising approach to modulate neuronal activities for therapeutic purposes.Our lab previously identified Acid-Sensing Ion Channel 1a (ASIC1a) as a mechanoreceptor of ultrasound in the mouse brain (Lim et al., 2021). We also found that phosphorylated Extracellular signal-Regulated Kinase (p-ERK) responses to ultrasound in a dose dependent manner in isolated hippocampal tissues of mice (Lim et al., 2022). Therefore, we are interested in investigating the overall phosphorylation signals in mouse hippocampus. Using the Mass spectrometry method, we have performed an analysis of phospho-proteomics of mouse hippocampus stimulated by ultrasound. In this poster, we report the characterization of ultrasound induced phosphorylation of Ca2 +/calmodulin-dependent protein kinase II(CamKIIa) and N-methyl-D-aspartate receptor(NMDAR2B). CamKIIa is a kinase that can phosphorylate NMDAR2B ,which plays important roles in learning,memory, and depression. CamKIIa has been reported to phosphorylate S1303 of NMDAR2B (Tullis et al., 2021). The phosphorylation of S1303 alters the long term depression but not the long term potentiation of hippocampus (Tullis et al., 2021). On the other hand, NMDAR2B Y1070 phosphorylation inhibition has been associated with the resilience of mice suffering from the forced swimming test that causes depression (shi et al.,2021). In this study, 1Mhz ultrasound with input voltage of 900mVpp and duty factor of 5% is applied to the hippocampus dissected from postnatal day 7 ICR pups. Hippocampi are then homogenized and lysed in RIPA buffer and subsequently subjected to Western Blot Analysis to evaluate whether NMDAR2B (Grin2b, GluN2B) and CamKIIa are phosphorylated upon ultrasound. We discover that NMDAR2B is phosphorylated at both S1303 and Y1070 sites upon ultrasound stimulations. The phosphorylation is dose-dependently enhanced by increasing ultrasound input voltage. In addition, the phosphorylation is temporally regulated by ultrasound stimulation. Moreover, the dynamics of NMDAR2B phosphorylation are different from the phosphorylation of CamKIIa. We will further study whether these phosphorylation can be detected in ultrasound transcranial stimulation of the mouse brain. Our findings should alert a cautiousness of transcranial ultrasound for therapeutic applications.

投稿學會：	編號: P3-46

Developmental abnormalities of the nigrostriatal pathway in mice with dopamine synthetic defect

Pei-Chun Hsu, Tzu-I Chen, Ni-Chung Lee,Yu-Han Liu, Hao-Chun Wang, Yen-Hsu Lu, Yin-Hsiu Chien, Wuh-Liang Hwu

Department of Pediatrics and Medical Genetics

Abstract

The development of dopaminergic neurons is a complex process, and abnormalities in dopaminergic neuron development may be involved in diseases of dopamine deficiency. In the current study, single-nucleus RNA sequencing was employed to analyze midbrain cells of DdcKI mice, a disease model of dopamine synthetic defect, at postnatal day 0, 7, and 14. Two-dimensional t-distributed stochastic neighbor embedding of merged data from the wild-type and DdcKI mice identified cell clusters containing dopaminergic neurons (Th+) or DA neural precursors (Th-, Lmx1a+). Gene ontology analysis of differentially expressed genes revealed a delay in dopaminergic neuron axonogenesis and synapse formation in the DdcKI mice. Pseudotime analyses demonstrated an activation of dopaminergic neural precursors at postnatal day 7 in the DdcKI mice, with an increased expression of dopaminergic neuron development-related genes Otx2 and Pax5. Immunohistochemical staining of brain sections and cleared whole brain in the DdcKI mice further revealed dispersed dopaminergic nerve bundles and decreased dopaminergic innervation in the putamen. Therefore, dopamine deficiency may cause structural abnormalities in dopaminergic neuron exon extension and innervation, which could limit the treatment efficacy of those diseases.

投稿學會：台灣基礎神經科學學會 | 編號: P3-47

Interaction between reward learning and punishment learning

Wen-Wei Lin Ming-Tsung Tseng Pei-Yu Lee

Graduate Institute of Brain and Mind Sciences, NTU

Abstract

Reward and punishment often act as important factors that modulate human behavior through learning to maximize the former, and minimizing the latter. Although much is known about how reward and punishment contribute to guiding our behavior independently, how these two types of learning interact with each other remains largely unclear. Here, we used a probabilistic instrumental learning task with binary choice options in combination with functional magnetic resonance imaging to address this issue. Healthy participants were required to try their best to earn money and to avoid losing money or avoid painful stimulation throughout the learning task. Preliminary behavioral results from the first experiment suggest that when an option was simultaneously associated with rewarding and punishing outcomes, representing the interaction between the two types of learning, only the performance of reward learning was interfered by punishment learning, but not vice versa. Our second experiment was conducted to clarify the mechanism of the interference effect of punishment learning on reward learning. Results from the two experiments together provided better knowledge for understanding the asymmetry between reward learning and punishment learning with an interaction relationship and also the underlying mechanism of this behavior phenomenon.

投稿學會：	編號: P3-48

Haptic perception and motor function ability with or without musician

Tsai-Chun Hung, Yu-Ting Tseng

Department of Kinesiology, National Tsing Hua University

Abstract

Musicians have been found to show increased fine motor skills through extensive piano practice. Numerous studies have reported that proprioception is increased in musicians who regularly play musical instruments. However, little is known about haptic function, the combination of proprioception and touch perception, is improved in musicians. The purpose of this study was to systematically investigate haptic function and how it is linked to different domains of motor skills in musicians. Twenty-two musicians (age 21.91±3.05 years) and 22 controls without previous experience of music (age 21.77±3.09 years) participated. All participants performed two haptic tasks: 1) a haptic detection task and 2) a haptic discrimination task. The haptic block system consists of 18 plastic blocks with different curvatures on the top of block surfaces. During the detection task, participants touched a single haptic block with their dominant index fingers and were asked to judge whether the block was curved or not. In contrast, during the haptic discrimination task, participants explored two haptic blocks and identified which of the two blocks was more curved. The haptic sensitivity (measured by haptic detection thresholds) and haptic acuity (measured by discrimination thresholds) were obtained to measure haptic function. Bruininks-Oseretsky Test of Motor Proficiency, Second Edition, Long Form (BOT-2-LF) was used to assess different domains of motor functions. The independent t-test revealed that the musician group demonstrated a higher haptic sensitivity (decreased haptic detection thresholds) when compared to their controls ($p = .049$). However, haptic acuity was not significantly different between the two groups ($p = .108$). The Pearson product-moment correlation coefficient showed that the haptic detection thresholds significantly correlated with manual coordination measured by BOT-2-LF ($r = -.582$, $p < .01$). This study documented that musicians have higher haptic sensitivity, which is linked to their greater manual coordination.

投稿學會：台灣認知神經科學學會	編號: P3-49

Meta-analytic Neuroimaging Evidence of the Association between Orofacial Pain and Mastication

Chia-Shu Lin (1,2,3) and Ta-Chung Chen (4)

1 Department of Dentistry, National Yang Ming Chiao Tung University 2 Institute of Brain Science, National Yang Ming Chiao Tung University 3 Brain Research Center, National Yang Ming Chiao Tung University 4 Department of Stomatology, Taipei Veterans General Hospital

Abstract

Temporomandibular disorders, characterized by pain and impaired masticatory functions, are common chronic orofacial pain in adults. The Integrated Pain Adaptation Model (IPAM) predicts that the reduction in jaw movement is associated with increased pain and such an association varies between patients because of the inter-individual differences in pain. Critically, evidence from clinical, animal, and neuroimaging research has convergently revealed the brain mechanisms in both mastication and pain processing. The IPAM predicts the sensorimotor network of the brain may contribute to the pain-mastication association, a hypothesis not been fully investigated. We here provide meta-analytic evidence of potential brain mechanisms of the association between mastication and orofacial pain. An imaging meta-analysis was conducted for neuroimaging studies on the following three topics: Group A-chewing movement of healthy adults (13 studies), Group B-orofacial pain in patients with temporomandibular disorders (4 studies), and Group C-muscle pain in healthy subjects (3 studies). Consistent loci of brain activation were synthesized using Activation Likelihood Estimation (ALE) for the chewing studies (i.e., Group A, 111 foci from 13 studies, 160 subjects) and orofacial pain-related studies (i.e., Group B+C, 84 foci from 7 studies, 100 subjects). All the ALE results were thresholded by intensity ($p<0.05$, uncorrected) and cluster size ($p<0.05$, familywise error-corrected). The chewing studies consistently revealed consistent activation at the primary somatosensory cortex, the primary and secondary motor cortices, and the insula (predominantly the mid-posterior insula), as shown in our previous study (Lin, 2018). In contrast, the pain-related studies revealed consistent activation at the anterior cingulate cortex and the anterior insula. Notably, a conjunctional analysis of chewing and pain-related studies showed consistent activation at the bilateral anterior insula. The meta-analytical evidence suggests that the anterior insula, which has been widely conceived as a key region in pain, interoception, and salience processing, may contribute to the pain-mastication association. The findings provide an additional neural basis to the IPAM and suggest a focus on the insula in future research in mastication and orofacial pain.

投稿學會：台灣認知神經科學學會 | 編號: P3-50

Evaluation of age-related development of executive function by using the Conners K–CPT 2 and event-related potential component in a three-stimulus auditory oddball task

Peter Kuan-Hao Cheng1.2, Tzu-Ling Lin1.3, Wei-Jun Liao4, Pin-Han Wang5, Chia-Hui Chiu6, Fu-Yuan Chiu1.7, Yen-Ting Lai.8, Tzu-Hua Wang1.7*

1 Research Center for Education and Mind Sciences, National Tsing Hua University, 2 PhD Program in Cognitive Sciences, National Chung Cheng University, 3 Institute of Behavioral Medicine, National Cheng Kung University 4 Interdisciplinary Program of Education, National Tsing Hua University 5 Department of Early Childhood Education, National Tsing Hua University 6 Department of Early Childhood Education, University of Taipei 7 Department of Education and Learning Technology, National Tsing Hua University 8 Department of Physical Medicine and Rehabilitation, National Taiwan University Hospital Hsin-ChuBranch * Corresponding author.

Abstract

Objective: Human frontal lobe development is strongly linked to the development of executive functions, which are among the last mental processes to mature. In comparison to young adults, children have lower levels of executive function due to their unfully-developed frontal lobes. The P300 ERPs are regarded as an effective method of identifying changes in the frontal-parietal connection that are associated with executive dysfunction. On the other hand, the continuous performance tests measure impulsivity associated with inhibitory control, a key component of executive function. The purpose of this study is to evaluate the children's executive functions by using auditory oddball event-related potentials and the K-CPT2 test. Methods: The three-stimulus auditory oddball task is comprised of 240 frequent non-target tones (1 KHz, P=0.80), 30 rare target tones (2 KHz, P=0.10), and 30 rare novel non-target tones (0.5 KHz, P=0.10) given randomly one at a time with inter-trial intervals of 1500ms. An auditory oddball task was recorded from the midline sites (Fz, Cz, and Pz) of 18 aged 48 months to 97 months (M=69.33, SD=12.64) children. Participants were instructed to respond quickly to each target tone while inhibiting their responses to novel and non-target tones. After getting ERP data, K-CPT2 software was used to run a computerized continuous performance test. Results: Behavioral data showed that oddball hit rates increase with age. Further investigation of K-CPT 2 performance revealed that both the error rates of omission and hit response time were correlated with oddball task performance negatively. In terms of ERP analysis, for the target tones, the mean corrected amplitude of late positive components (adjusted by subtracting the ERP wave of the frequent tones) was increased linearly with age in Cz and Pz, but not in Fz channels. The mean corrected N2 amplitude in the Fz and CZ channels, which were triggered by rare novel tones, went down in a straight line with the number of commission errors made on the KCPT-2 task. Conclusion: The results suggest that combining the Conners K-CPT 2 and the three-stimulus auditory oddball task may be a feasible index for neuropsychological examinations of preschool children's executive function development.

投稿學會：台灣認知神經科學學會 | 編號: P3-51

The human orbitofrontal cortex represents the subjective value of the present, and the past food rewards

Wan-Yu Shih 1, Paul W. Glimcher 2, Hsiang-Yu Yu 3,4, Cheng-Chia Lee 4,5, Chien-Chen Chou 3,4, Chien Chen 3, Shih-Wei Wu 1,4

1 Institute of Neuroscience, National Yang Ming Chiao Tung University, Taipei, Taiwan 2 Neuroscience Institute, NYU Grossman School of Medicine, New York, NY, USA 3 Department of Neurology, Taipei Veterans General Hospital, Taipei, Taiwan 4 Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan 5 Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan

Abstract

Electrophysiological studies in monkeys and functional imaging in humans have shown that activity in the orbitofrontal cortex (OFC) encodes the subjective value (SV) of an option while making economic choices. Mounting evidences have suggested that OFC dynamically compute current value based on the recent experience of decision makers. However, these findings were mainly based on single-unit electrophysiology in non-human primates and have not been widely reported in humans. In this study, subjects indicated their subjective value for a variety of snack foods in a Becker-DeGroot-Marschack (BDM) auction task during stereo-electroencephalography (sEEG) recording. The event-related spectral perturbation for different frequency bands were extracted and regressed against the SV in the current trial and the SV in the previous trial. We found that the high frequency power (gamma and high-gamma, 30-150 Hz) in the OFC positively correlated with the current SV and negatively correlated with the previous SV. The low frequency power (theta and alpha, 4-12 Hz) also represented SV, but in opposite encoding directions. Furthermore, the significant results primarily came from electrodes in the central and medial OFC, but not lateral OFC.

投稿學會：	編號: P3-52

Attention related changes in aperiodic neural activity with time-on-task

Lin-Yuan Tseng, Niall Duncan

Graduate Institute of Mind, Brain and Consciousness Taipei Medical University

Abstract

Attentional state fluctuates from moment to moment, with sustained attention requiring dynamic patterns of brain network activity that are formed and dissolved to support this function. These patterns can be measured through electroencephalography (EEG). Such electrophysiological signals exhibit periodic, oscillatory, characteristics that are thought to exist in tandem with aperiodic fluctuations. This aperiodic activity has a 1/f-like distribution, the parameters of which appear to be influenced by age, task demands and cognitive state (He, 2014; Voytek et al., 2015). The steepness of this 1/f distribution has been suggested to represent the balance between excitatory and inhibitory neural activity (E:I balance; Gao et al., 2017). Previous studies have demonstrated the effect of attentional control on the oscillatory component of EEG signals with time-on-task (Shalev et al., 2019; Reteig et al. 2019). However, less is known about how attention affects their aperiodic component. As such, the aim of the current study was to investigate attention effects on the aperiodic component and how it is changed with time-on-task. The current study found that changes in aperiodic activity, as well as its behavioural relevance, may be linked to changes in the E:I balance and mean neural population spiking within underlying neural populations. The findings provide new insights into neural correlates of sustained attention in humans and point to the potential importance of changes in local excitation and inhibition balances to this process.

投稿學會：	編號: P3-53

TStability of the heartbeat counting task for measuting interoception

Evgeny A. Parfenov, Niall W. Duncan

Graduate Institute of Mind, Brain and Consciousness, Taipei Medical University, Taipei, Taiwan Brain and Consciousness Research Centre, TMU-Shuang Ho Hospital, New Taipei City, Taiwan

Abstract

Objective. Interoceptive awareness (IA) is the ability to perceive signals from the visceral organs of our body. One common task for evaluating IA is the heartbeat counting task (HCT) during which participants need to count their heartbeats over a period of time. It has been argued recently, however, that this task may not measure stable trait features and that it may involve non-interoceptive processes. This study therefore aimed to: 1) observe the HCT performance changes across multiple repetitions of the task; and 2) compare performance in the HCT with a visual counting task (VCT) to investigate generalized propensities of underreporting ambiguous stimuli. Methods. The study sampled 46 healthy subjects (25 females, mean age = 27.5 ± 4.2) with no history of neurological, psychiatric, or cardiac disorders; with normal or corrected-to-normal vision; and with a BMI < 30. Participants performed multiple repetitions of the HCT and the VCT designed to mirror the HCT. During the VCT participants were asked to count Gabors presented beneath variable noise. The frequency of the VCT stimulus presentation was matched to the individual's heart rate. Results. A one-way repeated measures ANOVA showed that IA did not change over the seven blocks of the HCT ($F = 1.3$, $p = 0.256$). In contrast, changes in visual accuracy derived from the VCT did differ across blocks ($F = 15.27$, $p < 0.001$), with performance degrading over time. No correlation was observed between participant's performance in the HCT and the VCT ($r = 0.28$, $p = 0.056$). Conclusion. Performance of the HCT is stable across repetitions of the task. This suggests an absence of a training effect or changing performance with increasing task's familiarity. The lack of correlation between the HCT and the VCT may point to different mechanisms underlying in exteroceptive and interoceptive processes or may reflect an inherent difference in their difficulty.

投稿學會：	編號: P3-54

Relating interneuron populations to spontaneous neural activity properties across the human cortex

Chien-Ming Lo, Niall Duncan.

Graduate Institute of Mind, Brain, and Consciousness

Abstract

The brain is built from complex networks of different neuron subtypes. The specific mix of types varies systematically across the brain according to regional function. This is particularly true of inhibitory interneurons, where there is significantly greater morphological variation than is seen for excitatory cells. Exactly how this microstructural variation is related to differences in overall network activity has not, however, been studied in humans. To begin outlining this microstructure-function relationship we used a combination of gene expression data and MEG recordings from across the cortical sheet. A manifold representing variation in inhibitory interneuron subtype marker genes was first calculated (the “gradient”), giving summary information at each vertex on what mix of cell types are present. The spatial arrangement of these cell markers was then related to the spatial layout of different features of resting-state MEG recordings from 100 healthy participants. This showed that the intrinsic timescale of this activity was correlated with the interneuron gradient. In addition, the functional inhibition/excitation balance of gamma band activity specifically was also correlated with this gradient. Finally, looking at local activity contributions to global avalanches, we found a dissociation with the interneuron gradient. A vertex’s contribution to global avalanches was instead determined by its anterior-posterior location. These results help advance our understanding of the structure-function relationship in the human brain. They show how local neural network properties are connected to the mass activity features revealed through neuroimaging techniques, linking these to specific biological substrates.

投稿學會：台灣認知神經科學學會	編號: P3-55

Musical Training Shapes the Processing of Degraded Speech in Noisy Environment

Yu-Jyun Guo and I-Hui Hsieh

Institute of Cognitive Neuroscience, National Central University

Abstract

Many neurophysiological and behavioral studies show that musical training benefits the encoding of speech in noisy environment. One putative explanation is that musicians can track the fundamental frequency (F0) information in speech better than non-musicians. Recent studies reported that flattening the F0 contours of Mandarin speech reduced speech intelligibility in noise for normal listeners. However, it is presently unknown whether musician advantage for speech-in-noise persists under conditions of degraded F0 speech contours. The current study investigates the effects of different levels of degraded F0 contour (i.e., conveying lexical tone or intonation information) on speech-in-noise performance in musicians. A cohort of twenty non-musicians and sixteen trained musicians were tested on the intelligibility of Mandarin Chinese sentences with natural, flattened-tone, flattened-intonation and flattened-all F0 contours (created via speech synthesizer) embedded in background noise masker under four signal-to-noise ratios (silence, 0, -5 and -9 dB). F0 pitch discrimination threshold was examined using an adaptive tracking procedure. Results showed that musicians outperformed non-musicians at encoding all types of flattened-F0 speech in noise. Speech intelligibility score declined with increasing signal-to-noise level, with the musicians more resilient to the detrimental effects of noise particularly for identifying flat-intonation and flat-F0 sentences. Compared to non-musicians, musicians relied more on tone-level than intonation-level F0 contour information at comprehending speech under difficult listening conditions. Smaller F0 pitch discrimination limen was found in musicians and correlated with higher intelligibility for understanding speech with degraded F0 information. Collectively, these results suggest that an advantage in tracking tone-level F0 pitch contour in musicians contributes to comprehending speech in noisy backgrounds. Our findings implicate that the potential use of music training to improve speech perception in complex listening environment may be contingent on an enhanced sensitivity to F0 pitch contours.