

編號 No.	投稿學會 Society	研究領域 Topic	題目Title	投稿者 Name	作者 CO-Author	作者(Co-Author)	單位(Affiliation)	關鍵字(Keywords)	poster number
20200709000920	台灣基礎神經科學學會	工程	High-Speed Lightsheet for brain imaging	Prof. 朱麗安	朱麗安, 張煒賢, 田雪峻, 劉彥廷, 曹杰, 馮冠霖, 呂杰翰, 陳聖彰, 江安世	Li-An Chu1, 2, *, Wei-Kun Chang2, Xuejiao Tian2, Yen-Ting Liu3, Chien Tsao3, Kuan-Lin Feng2, 4, Chieh-Han Lu5, Bi-Chang Chen2, 3, *, Ann-Shyn Chiang2, 4, 6, 7, *	1 Department of Biomedical Engineering and Environmental Science, National Tsing Hua University, Hsinchu, Taiwan 2 Brain Research Center, National Tsing Hua University, Hsinchu, Taiwan 3 Research Center for Applied Sciences, Academia Sinica, Taipei, Taiwan 4 Institute of Systems Neuroscience, National Tsing Hua University, Hsinchu, Taiwan 5 Department of Genetics and Complex Diseases, Harvard T H Chan School of Public Health, Boston, MA, USA 6 Institute of Molecular and Genomic Medicine, National Health Research Institutes, Zhunan, Miaoli, Taiwan 7Department of Physics, National Sun Yat-sen University, Taiwan, ROC 2Department of Physics, National Tsing Hua University, Hsinchu, Taiwan	lightsheet microscopy, Drosophila, Mice, Bioimaging	1
20200810214023	台灣計算神經科學學會	基礎	Connectivity preference and varying degree of randomness within the olfactory network in the Drosophila mushroom body	Ms. Li-Shan Cheng	鄭力珊 1,2, 簡嘉萱 3, 強啟哲 3, 朱麗安 4,5, 羅中炎 3,4, 江安世 3,4,6,7,8 and 李定國 1,2,4,8*	Li-shan Cheng 1,2, Chia-Hsuan Chien 3, Ching-Che Chang 3, Li-An Chu 4,5, Chung-Chan Lo 3,4, Ann-Shyn Chiang 3,4,6,7,8 and Ting-Kuo Lee 1,2,4,8*	1Department of Physics, National Sun Yat-sen University, Taiwan, ROC 2Department of Physics, National Tsing Hua University, Hsinchu, Taiwan 3Institute of Systems Neuroscience, National Tsing Hua University, Hsinchu, Taiwan, ROC 4Brain Research Center, National Tsing Hua University, Hsinchu 30013, Taiwan, ROC 5Department of Biomedical Engineering and Environmental Sciences, National Tsing Hua University, Hsinchu, Taiwan, ROC 6Institute of Molecular and Genomic Medicine, National Health Research Institutes, Miaoli, Taiwan, ROC 7Kavli Institute for Brain and Mind, UCSD, California, USA	Olfactory sensation, Drosophila, Connectomics, Mushroom body	2
20200710123159	台灣基礎神經科學學會	基礎	Towards Deciphering interneurons in olfactory information coding	Prof. Ya-Hui Chou	蔡國鼎, 楊己任, 劉南甫, 張穎馨, 謝折潤, 沈軒維, 黃皓偉, Michael Panganiban, 周雅惠	Kuo-Ting Tsai, Chi-Jen Yang, Nan-Fu Liou, Hao-Hsin Chang, Hsin-Ti Hsieh, Hsuan-Wei Shen, Hao-Wei Huang, Michael Panganiban, Ya-Hui Chou*	Institute of Cellular and Organismic Biology, Academia Sinica	Olfaction, Interneuron, Behavior, Neural circuit, Drosophila	3
20200730113521	無	工程	Recurrent Mutual Inhibition Generates Flexible Operational Modes in Neural Circuits	Mr. Alexander James White	劉沛強, 羅中炎	Pei-Hsein Belle Liu, Dr. Chung Chuan Lo	National Tsing Hua University, Institute of Systems Neuroscience	Recurrent Networks, Inhibition, Computational Model, Flexibility	4
20200808135359	中華民國生物醫學工程學會	基礎	Define the sensitivity of mouse neuron and hippocampal tissue upon ultrasound stimulation	Ms. Hsiao-Hsin Tai	戴小芯 王兆麟	Hsiao-Hsin Tai and Jaw-Lin Wang	Department of Biomedical Engineering, National Taiwan University, Taipei, Taiwan	Ultrasound, Neuron sensitivity, p-ERK	5
20200809102732	台灣計算神經科學學會	工程	Covariance Representation Analysis (CRA): An Automatic Tool for Quality Assessment of Large-Scale EEG/MEG Data	Ms. Min-Jiun Tsai		Min-Jiun Tsai, Hsin-Yuan Chang, Ya-Lin Huang, Hsi-Yang Hung, Intan Low, Chun-Chih Huang, Chuan-Yu Yu, Tung-Ping Su, Jen-Chuen Hsieh, Li-Fen Chen, Chun-Shu Wei	Institute of Mathematical Modeling and Scientific Computing, National Chiao Tung University	Covariance, t-distributed stochastic neighbor representation, Machine Learning	6
20200802184516	台灣認知神經科學學會	認知	Neurophysiological Correlates of Semantic Anomalies Detection and Their Relationship with Statistical Learning in Foreign Language	Mr. Andhika Renaldi	林晏佑, 方云柔, 吳嫻	Zi-You Lin, Yun-Jou Fang, Denise Hsien Wu	Taiwan International Graduate Program in Interdisciplinary Neuroscience, National Central University and Academia Sinica, Taipei, Taiwan Institute of Cognitive Neuroscience, National Central University, Zhongli, Taiwan	semantic anomalies detection, statistical learning, foreign language learning, .	7
20200730172707	台灣認知神經科學學會	認知	Intersubject representational similarity analysis uncovers individual variations in experiencing effortful	Ms. Chih-Yin Esther Lu	呂至穎, 楊子柔, 陳品豪	Chih-Yin Esther Lu, Tzu-Jou Avery Yang, Pin-Hao Andy Chen	Department of Psychology, National Taiwan University	fMRI, Self-control, Ego-depletion, IS-RSA, Decoding experience	8
20200730151830	台灣基礎神經科學學會	認知	Age-related differences in young and older adult neural engagement during belief updating	Mr. Yu-Shiang Su	蘇煜翔, 吳恩賜	Yu-Shiang Su, Joshua Goh	National Taiwan University	Cognitive neuroscience, fMRI, aging, decision-making, belief updating	9
20200810233703	台灣認知神經科學學會	認知	Profiling the Sequence Learning in Speech and Manual Responses via Distributional Analyses	Prof. Erik Chihhung Chang	張智宏	Erik Chang	Institute of Cognitive Neuroscience, National Central University, Taiwan	sequence learning, reaction time, statistical learning, distribution fitting	10
20200731122213	台灣基礎神經科學學會	基礎	Disorders of Consciousness: Towards A Methodology for Integrative Diagnosis	Dr. Paola Di Maio		Paola Di Maio	Center for Systems, Knowledge Representation and Neuroscience, Taiwan	disorder of consciousness, biomarkers, methodology, neuroscience, integrated	11
20200728172737	台灣基礎神經科學學會	基礎	Identifying hypothalamic SF-1 neurons as a functional neural component mediating exploratory	Mr. 林士哲	林士哲, 陳一誠, 楊世斌	Shih-Che Lin, Yi-Chen Cheng, Shi-Bing Yang	Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan Department of Life science, College of Life science, National Taiwan University, Taipei, Taiwan	Exploratory behaviors, Steroidogenic factor 1, Fiber photometry, Circuits mapping, In vivo Calcium imaging	12
20200810151109	台灣基礎神經科學學會	基礎	Functional mapping of the VMH SF1 neurons in adult mice	Mr. 陳一誠	陳一誠1, 林士哲2, 楊世斌1	Yi-Cheng Chen1, Shih-Che Lin2, and Shih-Bin Yang1	1. Institute of Biomedical Sciences, Academia Sinica 2. Department of Life Science, National Taiwan University, Taipei, Taiwan	Steroidogenic factor 1, Ventromedial hypothalamus, Fiber photometry, Retrograde tracing, olfactory sensory	13
20200730105756	台灣基礎神經科學學會	基礎	In vivo longitudinal recording of cerebellar calcium imaging signals on awake-behaving mice	Dr. Jye-Chang Lee	李志昌, 盧亮昕, 陳衣凡, 潘明楷	Jye-Chang Lee*, Liang-Yin Lu, Yi-Fan Chen, Ming-Kai Pan	Department and Graduate Institute of Pharmacology, National Taiwan University, Taipei, Taiwan	Calcium imaging, movement coordination, Cerebellum, Purkinje neuron, microdomains	14
20200810235928	台灣基礎神經科學學會	基礎	A pathway from the parabrachial nucleus to the VTA negatively regulates feeding	Ms. Chia-Ying Chiang		Chia-Ying Chiang1, Jen-Hui Tso3, Shih-Ying Ni2, and Hau-Jie Yau1	1 Taiwan Graduate Institute of Brain and Mind Sciences (GIBMS), National Taiwan University, Taipei, Taiwan. 2 National Taiwan University School of Medicine, Taipei, Taiwan. 3 Synaptic Plasticity Section, Intramural Research Program, National Institute on Drug Abuse (NIDA), National Institutes of Health (NIH), Baltimore, MD, USA.	feeding, negative emotions, optogenetics, ventral tegmental area, parabrachial nucleus	15
20200731130451	無	基礎	Develop a novel strategy for optogenetic control of synaptic transmission	Ms. Yung-Wen Chen	陳永文, 林宛蓁	Yung-Wen Chen and Wan-Chen Lin	Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan	optogenetics, neurotransmission, synapse,	16
20200730125937	台灣基礎神經科學學會	基礎	Investigating the effect of a specific GSK3 inhibitor during neonatal period on the amelioration of schizophrenia-related deficits in Akt1	Prof. 賴文崧	萬詩君, 劉迪笙, 賴文崧	Shih-Chun Wan, Dee-Hseng Liu, Wen-Sung Lai	Department of Psychology, National Taiwan University	schizophrenia, Akt1 mice, GSK3 inhibitor, neonatal period, behavior	17

20200727202452	台灣生物精神醫學暨神經精神藥理學會	臨床	The association between oxidative stress and dopamine transporter activity in patients with bipolar disorders	Dr. Cheng-Chen Chang		Cheng-Chen Chang1,2, Ta-Tsung Lin3, Chin-San Liu3,4, Yi-Ting Hsieh5, Hui Hua Chang6,7,8,9, Po See Chen5,10	1 Department of Psychiatry, Changhua Christian Hospital, Changhua, Taiwan 2 School of Medicine, Chung Shan Medical University, Taichung, Taiwan, 3 Vascular and Genomic Research Center, Changhua Christian Hospital, Changhua, Taiwan, 4 Graduate Institute of Integrated Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan 5 Department of Psychiatry, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan 6 Institute of Clinical Pharmacy and Pharmaceutical Sciences, National Cheng Kung University, Tainan, Taiwan 7 School of Pharmacy, College of Medicine, National Cheng Kung University, Tainan, Taiwan 8 Department of Pharmacy, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan 9 Department of Pharmacy, National Cheng Kung University Hospital, Dou-Liou Branch, Yunlin, Taiwan Taiwan International Graduate Program in Interdisciplinary Neuroscience, National Yang-Ming University and Academia Sinica, Taipei, Taiwan	bipolar disorders,oxidative stress,dopamine transporter	18
20200715121544	台灣基礎神經科學學會	其他	Dietary curcumin ameliorates neural connectivity and neuropsychiatric behaviors in Tsc2+/- mouse model via alterations of gut microbiota diversity	Ms. Christine Chin-Jung Hsieh	謝昀容 羅仔君 李宜到 陳儀莊 陳右穎	Christine Chin-jung Hsieh Yu-Chun Lo Yi-Chao Lee Yijuang Chen You-Yin Chen	Taiwan International Graduate Program in Interdisciplinary Neuroscience, National Yang-Ming University and Academia Sinica, Taipei, Taiwan Department of Biomedical Engineering, National Yang-Ming University, Taipei, Taiwan PhD Program for Neural Regenerative Medicine, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan	Diffusion tensor imaging,Neuropsychiatric disorders,Tuberous sclerosis complex,Gut microbiota	19
20200730135158	台灣生物精神醫學暨神經精神藥理學會	臨床	The association of executive function, prefrontal excitatory and inhibitory balance and social cognitive function in euthymic bipolar	Dr. Huai-Hsuan Tseng	曾懷萱, 李佳寧, 魏士郁, 張惠華, 陳柏熹	Huai-Hsuan Tseng, Chia Ning Lee, Shyh-Yuh Wei, Hui Hua Chang, Po See Chen	Department of Psychiatry, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan Institute of Behavioral Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan Institute of Clinical Pharmacy and Pharmaceutical Sciences, National Cheng Kung University, Tainan, Taiwan	Bipolar disorder,Magnetic resonance spectroscopy,Social cognition,Neurocognition,Excitatory/Inhibitory balance	20
20200810231427	無	基礎	Using deep learning techniques to classify major depressive disorder and bipolar disorder based on MEG	Mr. Chun-Chih Huang		Chun-Chih Huang 1, Chun-Yu Yu1, Intan Low2,3, Tung-Ping Su4, Jen-Chuen Hsieh2,3,5, Li-Fen Chen2,3,5	Faculty of Medicine, National Yang-Ming University	Major depressive disorder,Bipolar disorder,classification,deep learning	21
20200810154329	台灣認知神經科學學會	認知	Comparisons of Brain Activity in Processing Different Emotions of Facial Expressions in Sequential Discrimination Task	Prof. Shih-Tseng T. Huang	黃世瑋	Shih-tseng Tina Huang, Sing-Rong Sie, Yen-Ju Lu	Department of Psychology, National Chung-Cheng University Center for research in Cognitive Science, National Chung-Cheng University, Taiwan	Emotion, Facial expression, Discrimination, Brain activity, congruency	22
20200728113632	台灣基礎神經科學學會	基礎	A novel non-invasive technique to detect the acute phase of inflammation and pain in the complete Freund's adjuvant-induced rheumatoid arthritis mouse model	Mr. 羅正威	羅正威, 陳安璇, 楊竣傑, 陳志成, 孫維欣	Cheng-Wei Lo (1,2), Tzu-Hsuan Chen (1), Chun-Chieh Yang (1), Chih-Cheng Chen (2,3), Wei-Hsin Sun (1)	1.Department of Life Sciences & Institute of Genome Sciences, National Yang-Ming University, Taipei, Taiwan 2.Taiwan Mouse Clinic, National Comprehensive Mouse Phenotyping and Drug Testing Center, Academia Sinica, Taipei, Taiwan 3.Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan	novel, non-invasive, acute, inflammation, rheumatoid arthritis	23
20200615231921	台灣生物精神醫學暨神經精神藥理學會	臨床	Will melatonin be beneficial to prevent episodic migraine? From the view of network meta-analysis	Ping-Tao Tseng	曾秉濤, 楊鈞百, 蘇冠賢, 陳彥文, 薛佑玲	Ping-Tao Tseng, Chun-Pai Yang, Kuan-Pin Su, Yen-Wen Chen, Yow-Ling Shiue	Prospect Clinic for Otorhinolaryngology & Neurology, Kaohsiung, Taiwan	melatonin, network meta-analysis, episodic migraine, neuropsychiatry, evidence-based medicine	24
20200706134454	台灣基礎神經科學學會	基礎	Neurological basis of statin induced sngception	Mr. Md Tauhid Siddiki Tomal		Md Tauhid Siddiki Tomal, Chih Cheng Chen	Interdisciplinary Neuroscience Program in Taiwan International Graduate Program, Academia Sinica, Taipei, Taiwan Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan Life Science School, National Yang-Ming University, Taipei, Taiwan Mouse Clinic – National Comprehensive Phenotyping and Drug Testing Center, Academia Sinica, Taipei, Taiwan	Sngception, Hyper-mechanosensitivity, Statin, Ion-Channel, Circuitry	25
20200729111313	台灣基礎神經科學學會	基礎	ASIC3 regulates nerve degeneration and contributes to chronic pain induced by nerve injury	Prof. 許佳雲	許佳雲, 秦茵, 鄧志宇, 陳宥任, 孫維欣	Jia-Yun Hsu, Yin Chin, Chih-Yu Teng, You-Ren Chen, Wei-Hsin Sun	Department of Life Sciences and Institute of Genome Sciences, National Yang-Ming University	ASIC3, Wallerian degeneration, Neuropathic pain	26
20200729105133	台灣基礎神經科學學會	基礎	Effects of α6-containing GABAAR-selective positive allosteric modulators in the trigeminal ganglia: An electrophysiological study	Mr. Chen-Jiun Yeh		Chen-Jiun Yeh1, Werner Sieghart2, Margot Ernst2, Daniel E. Knutson3, James Cook3, Chih-Cheng Chen4,5 and Lih-Chu Chiou1,6	1 Graduate Institute of Pharmacology, College of Medicine, National Taiwan University, Taipei, Taiwan. 2 Department of Molecular Neurosciences, Center for Brain Research, Medical University of Vienna, Vienna, Austria 3 Department of Chemistry and Biochemistry, Milwaukee Institute for Drug Discovery, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin, United States 4 Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan 5 Taiwan Mouse Clinic – National Comprehensive Phenotyping and Drug Testing Center, Academia Sinica, Taipei, Taiwan	α6-containing GABAA receptor, trigeminal ganglia, whole cell patch-clamp, dissociated primary culture	27
20200810145703	無	基礎	Plastic change in the function of synapse at Nav1.8 nociceptive fiber onto spinothalamic tract neuron in mice with neurogenic pain	Mr. Wei-Chen Hung	洪瑋辰, 嚴震東, 閔明源	Wei-Chen Hung, Chen-Tung Yen, Ming-Yuan Min	National Taiwan University, Department of Life Science	spinothalamic tract, neuropathic pain, Nav1.8	28
20200810175954	無	基礎	The Profile of Neuron activation in Trigeminal Sensory Nuclei in Mice Receiving Acidic Buffer injection into the Masseter Muscle	Ms. Hsing-Chun Tsai		Cheng-Han Lee(2), Ming-Yuan Min(1), Chih-Cheng Chen(2)	(1)Department of Life Science, National Taiwan University, Taipei, Taiwan (2)Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan	Pain, Trigeminal nucleus, von Frey	29
20200810182241	台灣疼痛醫學會	基礎	Functional connectivity of the PVA neurons in nociceptive circuit in mice	Dr. Wei-Hsin Chen		Wei-Hsin Chen1, Selomon Assefa Mundaye1,2, Mohamed Abbas1,2, Chien-Chang Chen 1	1 Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan 2 Taiwan International Graduate Program, Interdisciplinary neuroscience, Academia Sinica, Taipei, Taiwan	nociceptive circuit, paraventricular thalamus, in vivo calcium imaging	30
20200730114642	台灣基礎神經科學學會	認知	Emotions bias pain modulation associated with positive but not negative pain expectancy	Ms. 蔡昕芸	蔡昕芸 曾明宗	Hsin-Yun Tsai Ming-Tsung Tseng	Taiwan International Graduate Program in Interdisciplinary Neuroscience, National Taiwan University and Academia Sinica, Taipei, Taiwan. Graduate Institute of Brain and Mind Sciences, National Taiwan University College of Medicine, Taipei, Taiwan	pain, pain expectation, emotion, cognitive modulation on pain, fMRI	31
20200808214833	台灣生物精神醫學暨神經精神藥理學會	臨床	The correlation between functional connectivity and the heart rate variabilities after aromatherapy intervention	Dr. Wei Hung Chang	張維毓1,3, 李佳寧1, 郭哲好1, 蕭郁芸4, 陳柏熹1,2, 楊廷光1,2	Wei Hung Chang1,3*, Chia Ning Lee1, Che Yu Kuo1, Yu-Yun Hsiao4, Po See Chen1,2, Yen Kuang Yang1,2	1.Department of Psychiatry, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan 2.Institute of Behavioral Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan 3.Department of Psychiatry, National Cheng Kung University Hospital, Dou-Liou Branch, Yunlin, Taiwan 4.Institute of Tropical Plant Sciences and Microbiology Orchard Research and Development Center Department of Life Sciences	Aromatherapy, Heart rate variabilities, functional MRI	32
20200730173953	台灣認知神經科學學會	認知	From brain to trait: Establishing a brain white matter model to predict restraint trait	Ms. Yun-Jie Christina Wu	吳筠潔, 陳品柔	Yun-Jie Christina Wu, Pin-Hao Andy Chen	Department of Psychology, National Taiwan University	Diffusion tensor imaging, Personality Neuroscience, Machine-learning	33

20200728154027	台灣認知神經科學學會	認知	Gamma oscillations demonstrate the mechanism of TMS treatment in Treatment-Resistant Depressed patients	Ms. Yi-Chun Tsai	蔡怡君、蔡忠志、張偉光、黃鈞、李正達、阮啟弘	Yi-Chun Tsai1, Chong-Chih Tsai1, Wei-Kuang Liang1,2, Norden E. Huang3, Cheng-Ta Li1,4-6, Chi-Hung Juan1,2*	1 Institute of Cognitive Neuroscience, National Central University, Jhongli, Taiwan 2 Cognitive Intelligence and Precision Healthcare Center, National Central University, Taiwan 3 Key Laboratory of Data Analysis and Applications, First Institute of Oceanography, SOA, Qingdao, China 4 Department of Psychiatry, Taipei Veterans General Hospital, Taipei, Taiwan 5 Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan 6 Division of Psychiatry, Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan	repetitive TMS (rTMS),intermittent TBS (iTBS),brain oscillations,Treatment-Resistant Depressed patients (TRD),Holo-Hilbert spectral analysis (HHS)	34
20200805005249	台灣認知神經科學學會	臨床	A holo-spectral EEG analysis provides early detection of cognitive decline and predicting progression to Alzheimer's Disease	Dr. 朱國大	朱國大、梁謙益、吳明修、傅中玲、王翠君、黃鈞、張偉光、阮啟弘	Kwo-Ta Chu1,2, Weng-Chi Lei2,3, Ming-Hsiu Wu4, Jong-Ling Fu5, Shuu-Jiun Wang5, Norden E. Huang3,6, Wei-Kuang Liang2,3, and Chi-Hung Juan2,3,7	2 Institute of Cognitive Neuroscience, National Central University, Taoyuan City, Taiwan 3 Cognitive Intelligence and Precision Healthcare Center, National Central University, Taiwan ; 4 Department of Neurology, Chi Mei Medical Centre, Tainan City, Taiwan 5 Neurological Institute, Taipei Veterans General Hospital and National Yang-Ming University Schools of Medicine, Taipei, Taiwan, 6 Key Laboratory of Data Analysis and Applications, First Institute of Oceanography, SOA, Qingdao, China. 7 Department of Psychology, Kaohsiung Medical University, Kaohsiung City, Taiwan	Holo-Hilbert Spectral Analysis (HHS),Mini-Mental Status Examination (MMSE),Clinical Dementia Rating (CDR),Mild Cognitive Impairment (MCI),Alzheimer's disease (AD)	35
20200731102247	台灣基礎神經科學學會	基礎	Therapeutic Effects of Cortical Electrical Stimulation on Parkinsonian Rats	Dr. Chi Wei Kuo	郭紀偉1、曾惠群1、任祖儀2、潘建源1、謝宗勳3	CHI-WEI KUO1, HUI-CHIU TSENG1, TSU-YI JEN 2, CHIEN-YUAN PAN1, TSUNG-HSUN HSIEH3	1 Department of Psychology, Kaohsiung Medical University, Kaohsiung City, Taiwan 2 Department of Psychology, National Taiwan University, Taipei, Taiwan 3 School of Physical Therapy and Graduate Institute of Rehabilitation Science, Chang Gung University, Taoyuan, Taiwan	Parkinson's disease,cortical electrical stimulation,6-hydroxydopamine,motor function,gait	36
20200709105113	台灣基礎神經科學學會	基礎	Mitochondrial transplantation via nose-to-brain delivery for treatment of Parkinson's diseases in rats	Prof. 張瑞芝	張瑞芝、趙翔淳、鄭文玲、林達聰、劉青山	Jui-Chih Chang, Yi-Chun Chao, Wen-Ling Cheng, Ta-Tsung Lin, Chin-San Liu	Vascular and Genomic Center, Changhua Christian Hospital	Parkinson's diseases,Intranasal infusion,Mitochondrial transplantation,Mitochondrial function,Dopaminergic neurons	37
20200728101246	無	工程	Intelligent machine learning system of EEG features prescreening ADHD symptoms with Kiddie Continuous Performance Test in preschool-age children	Mr. Chih-Hao Chang	張智豪、柯立偉、陳怡君	Chih-Hao Chang, Li-Wei Ko, I-Chun Chen	National Chiao Tung University	ADHD,machine learning,KCPT,EEG	38
20200625000528	台灣復健醫學會	臨床	The efficacy and safety of transcranial direct current stimulation for cerebellar ataxia: a systematic review and meta-analysis	Mr. Chen-Ya Yang		Chen-Ya Yang, Tiffany X. Chen, Gloria Wilson, Chih-Chun Lin, Sheng-Han Kuo	1 Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, NY, USA. 2 Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, NY, USA 3 Department of Physical Medicine and Rehabilitation, Taichung Veterans General Chiayi and Wanqiao Branch, Chiayi, Taiwan 4 Department of Biomedical Engineering, Whiting School of Engineering, Johns Hopkins University, Baltimore, MD, USA.	brain stimulation,ataxia,cerebellum	39
20200716105159	台灣疼痛醫學會	臨床	Application of stem cell exosomes in neuropathic pain model	Dr. Raju Poongodi		Raju Poongodi,1 Pavani Pannuru,1 Yi-Wei Hung,1 Tsuei-Yu Chu,1 Kuender D. Yang,2,3 Hsin-Yi Lin,4,5 Jen-Kun Cheng 1,6,7,*	1 Department of Medical Research, Mackay Memorial Hospital, Taipei, Taiwan. 2 Institute of Biomedical Science, Mackay Medical College, New Taipei City, Taiwan. 3 Department of Paediatrics', Mackay Memorial Hospital, Taipei, Taiwan. 4 Department of Chemical Engineering and Biotechnology, National Taipei University of Technology, Taipei, Taiwan. 5 Graduate Institute of Biochemical and Biomedical Engineering, National Taipei University of Technology, Taipei, Taiwan. 6 Department of Medicine, Mackay Medical College, New Taipei City, Taiwan. 7 Department of Anaesthesiology, Mackay Memorial Hospital, Taipei, Taiwan.	Exosome,Intrathecal,Mesenchymal stem cell,Scaffold,Neuropathic pain	40
20200810172613	台灣基礎神經科學學會	基礎	Effect of arecaine-derived dipeptides on cognition and memory	Prof. 黃翊恭	吳皖瑛、陳映潔、洪浩淵、黃翊恭	Wan-Chuan Wu, Ying-Jie Chen, Hao-Yuan Hung, Eagle Yi-Kung Huang	Dept. of Pharmacology, National Defense Medical Center, Taiwan	Arecaine,dipeptide,memory,Alzheimer's disease	41
20200721130108	台灣基礎神經科學學會	基礎	A novel inhibitor of the equilibrative nucleoside transporter 1 (J4) prevents Tau-mediated neurodegeneration and neuroinflammation	Dr. Ching-Pang Chang		Ching-Pang Chang1, Ya-Gin Chang1, Pei-Yun Chuang1, Thi Ngoc Anh Nguyen1, Fang-Yi Chou2, Shin-Jhong Cheng1,3, Hui-Mei Chen1, Lee-Way Jim4, Luc Bue6,6, David Blum5,6, Yung-Feng Liao7, Chun-Lung Lin2, YiJiang Chern1.*	1. Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan; 2. School of Pharmacy, National Taiwan University, Taipei, Taiwan; 3. Neuroscience Program of Academia Sinica, Academia Sinica, Taipei, Taiwan; 4. Department of Pathology and Laboratory Medicine, University of California Davis, Sacramento, CA, USA; 5. Univ. Lille, Inserm, CHU Lille. U1172 - LiNCog - Lille Neuroscience & Cognition, F-59000 Lille, France; 6. Alzheimer & Tauopathies, LabEx DISTALZ, LiCEND, F-59000 Lille, France; 7. Institute of Cellular and Organismic Biology, Academia Sinica, Taipei, Taiwan	Alzheimer's disease,Tauopathy,Adenosine,AMPK,ENT1	42
20200803113109	台灣基礎神經科學學會	基礎	Formulated Chinese medicine Shaoyao Gancuo Tang reduces NLRP1 and NLRP3 in Alzheimer's disease cell and mouse models for neuroprotection and cognitive	Dr. Ya-Jen Chiu	邱雅貞、張國軒、李桂楨	Ya-Jen Chiu, Kuo-Hsuan Chang, Guey-Jen Lee-Chen	Department of Life Science, National Taiwan Normal University	Alzheimer's disease,Aβ,Anti-inflammation,Neuroprotection,Therapeutics	43
20200722184448	台灣基礎神經科學學會	基礎	Roles of ventral tegmental area, nucleus accumbens, and caudate-putamen in different types of environmental enrichment reducing methamphetamine-induced behavioral sensitization	Mr. Cai-N Cheng		Cai-N Cheng, Andrew Chih Wei Huang, and Shaw-Jye Wu	National Central University, Fo Guang University	environmental enrichment,behavioral sensitization,methamphetamine,ventral tegmental area,nucleus accumbens	44
20200726122324	台灣基礎神經科學學會	基礎	Optogenetics photostimulations in the cingulate cortex, prelimbic cortex, or infralimbic cortex affect morphine-induced conditioned taste aversion in conditioning and extinction	Mr. 余英豪	余英豪、歐貞吟、黃智偉	Ying Hao Yu1,2, Chen Yin Ou1, and Andrew Chih Wei Huang1	1 Department of Psychology, Fo Guang University, Yilan County, Taiwan 2 Department of Biotechnology and Animal Science, National Ilan University, Yilan County, Taiwan	morphine,conditioned taste aversion,prelimbic cortex,infralimbic cortex,optogenetics	45
20200726161553	台灣基礎神經科學學會	基礎	Does footshock - induced stress disrupt place conditioning learning induced by morphine in the animal	Mr. 盧裕壬	盧裕壬、黃智偉	Yu Ren Lu and Andrew Chih Wei Huang	Department of Psychology, Fo Guang University, Yilan County, Taiwan	morphine,stress,conditioned place preference /aversion,drug addiction	46
20200725161308	台灣基礎神經科學學會	基礎	Withdrawal effects of methamphetamine's reward and aversion: Tests of the paradoxical effects hypothesis of abused drugs	Mr. 吳承恩	吳承恩、黃智偉	Cheng En Wu and Andrew Chih Wei Huang	Department of Psychology, Fo Guang University, Yi-Lan, Taiwan	the paradoxical effect of abused drugs,conditioned taste aversion,conditioned place preference,the withdrawal phase,amphetamine	47
20200720165305	台灣基礎神經科學學會	基礎	Interactions between prelimbic cortex and basolateral amygdala contribute to morphine-induced conditioned taste aversion in conditioning and	Prof. 黃智偉		ing Hao Yu, Chen Yin Ou, Alan Bo Han He, and Andrew Chih Wei Huang*	Department of Psychology, Fo Guang University	morphine,infralimbic cortex,conditioned taste aversion,cingulate cortex,prelimbic cortex	48

20200731210322	台灣基礎神經科學 會	基礎	Does footshock - induced stress change morphine ' s reward in conditioned place preference and aversion in conditioned taste aversion: Reexamination of the paradoxical effect hypothesis of	Mr. Yi Chun Yu		Yi Chun Yu, Yung Chen Hsu, and Andrew Chih Wei Huang	Department of Psychology, Fo Guang Universit	Morphine, Footshock, conditioned taste aversio	49
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High-Speed Lightsheet for brain imaging

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Chieh-Han Lu⁵, Bi-Chang Chen^{2,3,*}, Ann-Shyn Chiang^{2,4,6,7,*}

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Abstract

Brain is an organ that controls animal behavior and form memories. To better understanding the brain function, scientists have been using different ways to investigate the brain function, and imaging is one of the most direct way to visualizing brain structural and functional changes.

Modern lightsheet microscopy provides high-speed, high axial resolution feature, which provides numerous opportunities for scientists to visualize living process of whole animal brain in 3 dimensions in high-resolution, and to image large sample such as whole mouse brain in cellular resolution or super-resolution within few hours. Here we demonstrate using high-speed lightsheet microscopy to visualize synaptic protein distribution in whole fly brain in 20 nm resolution, whole mouse brain dopamine distributions in cellular resolution, even the brain tumor metastasis. We also demonstrated that with the volumetric live imaging, we can visualize calcium responses in entire mushroom body across different odorants, and further investigate odor coding changes after olfactory memory formation.

Connectivity preference and varying degree of randomness within the olfactory network in the *Drosophila* mushroom body

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Abstract

The mushroom body (MB) is one of the olfactory information processing centers of *Drosophila melanogaster*. Several types of Kenyon cells (KCs), the intrinsic neurons of MB, receive upstream information from projection neurons and further translate the olfactory relative stimulus into higher-order cognitive responses, such as learning and memory formation. Previous studies suggest the network structure of KCs is highly random. Yet, only accessing a limited size of KC-to-PN connections inevitably introduces certain stochastic factors in observed data. Thus, the statistical analysis used to distinguish randomness from stereotyping may not preach a reliable conclusion. Based on the recently released FlyEM dataset which has identified about 70~80 percent of PN-to-KC connections, we separately examine the randomness of each type of KC connectome by several theoretical analyses.

Here we show that different subtypes of KC configurations not only demonstrate various degrees of randomness but also preferentially innervate with specific glomeruli. Specifically, we found that γ connectome, the learning-associative KC-lobe, is highly random, while other subtypes of KC, which are both memory-associative, only have moderate randomness. In general, recognizable stereotyping can only be detected if more than 50% of connections are successfully discerned. Furthermore, we observe each subtype tends to form connections with particular types of PNs, and the connectivity preference strongly correlates with the developmental order of KCs. The biological significance of having a varying degree of randomness will be discussed.

Keywords

Olfactory sensation, *Drosophila*, Connectomics, Mushroom body

Towards Deciphering interneurons in olfactory information coding

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Abstract

Drosophila olfactory local interneurons (LNs) in the antennal lobe are highly diverse and variable. How and when distinct types of LNs emerge, differentiate and integrate into the olfactory circuit is unknown. It also remains elusive how distinct types of LNs function to compute and integrate olfactory information. We built a set of LN drivers to label distinct types of LNs and found that LNs are sequentially recruited to the adult olfactory circuit in three groups. These findings provide a road map to understand how LNs develop and contribute to constructing the olfactory circuit. We then overcame the hurdle of frame-to-signal translation and developed a treadmill system with camera-based detection. By extracting and quantifying certain features of walking dynamics with high temporal resolution, we found that depending on their internal state, flies employ different walking strategies to approach environmental cues. We are currently combing the LN drivers, the treadmill system and mathematic modeling to explore how distinct types of LNs differentially involved in olfactory information coding and decoding.

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Recurrent Mutual Inhibition Generates Diverse Flexible Operational Modes in Neural Circuits

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Abstract

Recurrent mutual excitation, and feedback inhibition have been well studied, yet the role of mutual inhibition is not well explored theoretically. Here using a spiking neuron model, we show how networks with recurrent inhibition are key in expanding the functionality of the circuit, far beyond what feedback inhibition alone can accomplish. By adding mutual inhibition to small neural motifs, decision-like functionality is off loaded into the inhibitory subnetwork. This frees up recurrent excitation for working memory, and feedback inhibition to oscillate allowing a plethora of central pattern generators to coexist with decision networks. All of these functionalities can be flexibly switched using changes in each neuron's bias current. This allows for quick, robust and flexible external control, without changing any synaptic weights. Taking advantage of dynamical systems theory and bifurcation analysis we show mutual inhibition doubles the number of cusp bifurcations in the system. This multi-functionality allows robust control of the underlying bifurcation structure by using bias current to push the system through lower codimension bifurcations. Thus changes in bias current can quickly switch between different unique functionalities. Impressively, we were able to identify 8 different logical operations with 3 different classes of inputs, distinguishing between differences in magnitude, timing, and phase. Furthermore we uncovered several types of central pattern generation, working memory, and chaos. Finally we show that this principle continues to operate for larger neural networks.

Define the sensitivity of mouse neuron and hippocampal tissue upon ultrasound stimulation

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Abstract

Background

Applications of ultrasound are hopeful to provide a non-invasive therapeutic intervention in addition to pharmaceutical remedy. However, the molecular basis of the ultrasound to the brain is not clear. Here we use an in vitro stimulation system to investigate the ultrasonic induced cellular responses. We aim to set up a platform for cell signaling study. The phosphorylation of extracellular-signal-regulated kinase (ERK) is known to indicate cellular responses such as cell migration, cell proliferation, and differentiation. Thus, phosphorylated ERK (p-ERK) as a neuronal response was assayed upon ultrasound stimulation. We discover that acid-sensing ion channel 1a (ASIC1a) channel play a role in mechanosensitive responses of neuron.

Methods

Ultrasound stimulation (US) was applied to cell culture in a custom designed chamber (Figure 1a) at 1 MHz. The 900mVpp (duty factor 1%) input voltage results in an I SPTA of 1 mW/cm² whereas the 100mVpp (duty factor 0.1% and 1%) input voltage results in an I SPTA of 2x10⁻⁴ mW/cm² and 0.02mW/cm² respectively. No significant temperature change was detected during ultrasound exposure. Western blots analysis probing p-ERK (Cell Signaling Technology, USA) and ERK (Abcam, USA) were performed using neonatal mouse hippocampal tissues either left untreated, or US stimulated, or stimulated in combination with chemical treatments. To test whether the response was due to neuron or astroglial lineages, cortical primary culture was subjected to immunofluorescent staining of p-ERK (Cell Signaling Technology, USA) and neuronal marker MAP2 (Sigma-Aldrich, USA) in similar design of experimental groups. Nuclear p-ERK immunofluorescence intensities (gray levels) of neuron cells were quantified. To test whether mechanosensitive channels play a role in ultrasound signaling, EGTA (5mM), Gadolinium (10nM), or PcTx1 (50nM) (Abcam, USA) were applied to the experiments of p-ERK Western blotting.

Results

In mouse hippocampus, p-ERK levels increased during US exposure at 1% duty factor in Western blot (Figure 1b). Specifically in neurons, the p-ERK intensity was significantly increased when the cells were stimulated by US in immunofluorescence. Nuclear p-ERK translocation percentage upon US was higher than control. Also, p-ERK level correlated positively to US exposure time in Western blot. When the hippocampal tissues were treated with PcTx1, p-ERK increase upon US was abolished (Figure 1c), indicating the role of ASIC1a in ultrasonic mechanotransduction.

Covariance Representation Analysis (CRA): An Automatic Tool for Quality Assessment of Large-Scale EEG/MEG Data

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Abstract

Recently, the accumulation of neuroscience data has accelerated the exploration in brain research. Massive collection of EEG/MEG data plays a critical role in the discovery of mental illness as well as the development of clinical tools based on deep learning. While deep-learning-based modeling often requires a significant amount of high-quality data, there is a lack of standardization of quality assessment for EEG/MEG data. Conventional procedures rely on well-trained, experienced technicians to examine the EEG/MEG signal quality, making the quality assessment of large-scale EEG/MEG data extremely time-consuming and laborious. This work aims to develop a novel tool, covariance representation analysis (CRA) for automatic assessment of the quality of large-scale EEG/MEG data in an intuitive and instantaneous fashion. First, a sliding time window segments EEG/MEG data into short sections, and the covariance matrix of each section evaluates the characteristics of EEG/MEG data in a recording session. Then, the covariance matrices of EEG/MEG data across time and across subjects are mapped and visualized in a low-dimensional domain using the t-distributed stochastic neighbor representation (t-SNE). The clustering of EEG/MEG covariance representations provides an in-depth assessment of data quality based on the inter-/intra-subject variability. We validate the efficacy of CRA using real MEG data collected from more than a hundred subjects including psychiatric patients and normal controls. Our demonstration suggests the usefulness of CRA in facilitating automatic quality assessment of large-scale EEG/MEG data.

Neurophysiological correlates of semantic anomalies detection and their relationship with statistical learning in foreign language learners

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Abstract

Every language has well established semantic and syntactic rules, which are important for language learners to master. Previous studies had found that sentences with semantic and syntactic anomalies elicited specific neurophysiological components across native speakers in different languages, reflecting respective semantic and syntactic proficiencies that are supported by different cortical processes. However, whether learners of a foreign language would rely on comparable components to detect semantic and syntactic anomalies is still an open question. In addition, whether statistical learning (SL), the ability to extract regularities in the environment and is associated with learning to read, would correlate with foreign-language learners' sensitivity to semantic and syntactic anomalies is still unknown. To address these questions, college students who are native Mandarin speakers read normal and abnormal English sentences when their brain activities were recorded by EEG. The event-related potentials (ERPs) elicited by semantic and syntactic anomalies were analyzed and correlated with individual participants' performance in the tests of visual and auditory SL, as well as with that in conventional tests of implicit motor learning, working memory, and IQ. Foreign-language learners' behavioral and ERP results showed distinct responses to semantic and syntactic anomalies. Consistent with the findings from native speakers, detection of semantic anomalies evoked strong effects in the P200 and N400 components in the central and the centro-parietal regions of the brain, respectively, in these foreign-language learners. Furthermore, the magnitude of the N400 effect correlated with participants' auditory SL accuracy, suggesting the contribution from SL to detecting semantic anomalies. On the other hand, sensitivity to syntactic anomalies did not correlate with any specific ERP components or performance in the SL tests, but only behavior accuracy in syntactic acceptability judgment correlated with working memory and IQ. The results suggested that these foreign-language learners did not engage comparable syntactic processing mechanisms to comprehend English sentences as in native speakers, but they rely on general cognitive abilities to perform the task. In summary, the present findings indicated that SL might be a critical ability to support acquisition of semantics but not syntax of a foreign language in late learners.

Intersubject representational similarity analysis uncovers individual variations in experiencing effortful self-control

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Abstract

What is the experience when someone is engaging in effortful self-control? A common term used to describe this experience is called ego-depletion. A classical view of ego-depletion is based on the assumption that a limited pool of self-control resources would be depleted after exertion of self-control.

However, some evidence suggests that feeling about being depleted is not caused by a limited resource,

but by individuals' beliefs in the availability of willpower. Thus, in the current study, we were interested in whether individual variability in the beliefs of willpower might be associated with individual variability in their experiences while engaging in an effortful self-control task. We used intersubject representational similarity analysis (IS-RSA) to identify brain regions in which similarity in participants' self-reported preferences for beliefs of willpower were associated with similarity in temporal brain dynamics. Thirty-six subjects were recruited in the effortful control group, and eighteen subjects were recruited in the effortless control group. While both groups were asked to watch the same 7-min long bighorn documentary movie with interleaved words shown on the screen, the mere difference between two groups was that those in the effortful control group were asked to restrain themselves from reading those words, while those in the effortless control group had no such restraint. Our results showed that, in the effortful control group, similarity in beliefs of willpower was associated with similarity in brain dynamics in the fronto-parietal executive control network, whereas no such association was shown in the effortless control group. Lastly, we adopted meta-analytic decoding to explore which psychological processes might be most likely engaged in effortful self-control experience. We found that effortful self-control experiences revealed stronger associations with executive control, conflict, and cognitive control than effortless self-control experiences did. Our findings demonstrated that IS-RSA can reveal new insights into experiences of ego-depletion in a naturalistic neuroimaging paradigm.

Age-related differences in young and older adult neural engagement during belief updating

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Abstract

Updating posterior beliefs to match the truth requires accurate integration of past experience with new evidence. In this present study, we postulated that age alters the neural circuits recruited for belief updating in young and older adults that reflects different ability to integrate past and new experiences. In a functional magnetic resonance imaging (fMRI) experiment, participants first learned about different proportions of red, blue, or green balls contained within different boxes. At test, participants were told that sets of three balls would be drawn from one of the boxes and they had to guess the majority color of the balls drawn with the source box identity hidden from participants. Outcomes of the drawn ball colors were then provided with correct guesses rewarded. Thus, participants had to update their posterior beliefs about which was the source box by integrating prior beliefs about the box and the likelihood of the drawn colors. Critically, source boxes were intermittently switched so that participants had to notice the outcome changes and transition to new beliefs. This pilot study recruited 6 younger (age: 23.81 ± 4.42 ; 5 female) and 5 older (age: 70.30 ± 2.38 ; 4 female) adults. Older adults required more trials to reach young-levels of accuracy. Older adults had more responses than younger adults indicating a belief that the source box was the previous source box ($t(7.30) = -3.74$, $p = 0.007$) and fewer responses indicating belief about the correct source box ($t(8.58) = +3.51$, $p = 0.007$). Both age groups showed similar proportions of responses reflecting a belief about irrelevant boxes ($t(8.95) = -0.91$, $p = 0.39$). Younger adults engaged lateral orbitofrontal cortex (LOFC) activity during updating under incongruent outcomes whereas older adults recruited more medial prefrontal cortex (MPFC) activity. These findings are consistent with stronger evidence integration to update posterior beliefs in younger adults in contrast to stronger maintenance of self-referential prior beliefs in older adults.

Profiling the Sequence Learning in Speech and Manual Responses via Distributional Analyses

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Abstract

Implicit acquisition of sequential motor skill poses an illuminating counterpart of perceptually or conceptually driven statistical learning processes. Sequential motor learning has been examined extensively with the Serial Reaction Time Task (SRTT). Extant studies on SRTT have focused exclusively on the evolution of the central tendency of RT throughout learning blocks, which largely ignored the progression of essential characteristics of RT distribution in learning. The current study carried out distributional analysis on the performance of manual and speech SRTT by fitting the shifted-Wald distribution on blocked RTs, and compared the trends of learning as revealed in parameters capturing the onset, variation around mode, and right-tail mass of distribution. The results indicate that all shift-Wald parameters of the RT distribution decrease as the task proceeds, reflecting the general trend of learning. Interestingly, speech appears to contain stronger variation than manual response throughout different phase of learning. The learning index of these various measures were found to be comparable between response modalities. As such, our study demonstrated a richer and fruitful approach of re-examine implicit learning in SRTT via distributional analysis.

Disorders of Consciousness: Towards A Methodology for Integrative Diagnosis

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Abstract

Damage resulting from stress and trauma has been difficult to localize, identify and assess clinically, and generally relies on self reported behavioural and cognitive symptoms. In recent years Posttraumatic Stress Disorder (PTSD) has become better understood and has been diagnosed in individuals exposed to various categories of traumas, from the experiences in war and conflicts, serious accidents and persistent exposure to abuse. New research identifies a wide range of biomarker variables correlating stress and cognitive and behavioural symptoms[1] In addition evidence has emerged that PTSD may impact not only mental and cognitive functions such as attention and coherent speech, but also contribute to physiological dysfunctions, and that can be detected in a wide range of biomarkers[2]. Similar symptoms are present in patients afflicted by different kinds of Disorders of Consciousness. Thanks to the availability of brain imaging techniques and more accessible research equipment and data, it is possible to visualize and compare the brain scans of different categories of patients afflicted by a range of cognitive and behavioural disorders.

Preliminary results of a meta analysis of literature points to a similarity of biomarker data, and comparative cognitive and behavioural symptoms observed in individuals afflicted by PTSD as well as in individuals suffering from emotional stress disorders . Among common characteristics there are changes to certain brain areas implicated in the stress response include amygdala, hippocampus, and prefrontal cortex [3] . As the newest insights point to the need for the use of advanced computational and statistical methods that can co evaluate wide arrays of potential biomarkers, disorder indicators and clinical manifestations in PTSD, that leverage machine learning methods capable to address such computational challenges and account for the intricate interrelation of many relevant factors [4] an integrated methodological approach is proposed that evaluates PTSD disorders in relation to other

Identifying hypothalamic SF-1 neurons as a functional neural component mediating exploratory social behaviors

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Abstract

Steroidogenic factor 1 (SF-1) expressing neurons in the ventromedial nucleus of the hypothalamus (VMH) are previously known for their essential roles in maintaining energy homeostasis and initiating innate behaviors that are essential for the individual survival. Prior studies that applied artificial stimulation on the VMH SF1-expressing neurons elicit defensive behaviors and trigger various anxious-like response against predator-associated cues; nevertheless, the involvement of SF1 neurons in conspecific interaction and the underlying neural mechanisms remain elusive. In this study, we aimed to construct the output neural circuits of the hypothalamic SF-1 neurons and to establish the relationship between the SF-1 neurons' activities and the exploratory social behaviors. To determine the targeting regions of the hypothalamic SF1-neurons, we conducted Cre-dependent axonal-fiber-based anterograde viral tracing in the SF1-cre mice. We found that the SF1-neurons projected to multiple social-interaction-associated brain regions, including the periaqueductal gray, bed nucleus of stria terminalis and paraventricular nucleus etc. Such results indicated that the SF-1 neurons might engage in initiating or modulating innate behaviors that are associated with social interactions. Next, we performed in vivo calcium imaging to monitor the SF-1 neuronal activities under various social and non-social cues exposure in free-roaming mice. We found that, while the conspecific exposure robustly activated SF1 neurons, other non-conspecific stimulations, including predator-associated cues and unsociable objects, only modestly evoked SF-1 neuronal activities. Our detailed behavioral analysis further suggested that, among all the behavior subtypes, the SF-1 neural activity strongly correlated with exploratory behaviors. In conclusion, the VMH SF-1 neurons might be a potential neural component in initiating exploratory social behaviors.

Functional mapping of the VMH SF1 neurons in adult mice

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Abstract

The ventromedial nucleus of the hypothalamus (VMH) plays a crucial role in initiating and sustaining vital physiological activities, such as energy metabolism and sexually dimorphic social behaviors, including conspecific aggression in males and lordosis in females. Steroidogenic factor 1 (SF1) is a transcription factor that is essential for gonadogenesis and VMH development, as gonads and the VMH fail to develop in animals lacking functional SF1. Our GCamp6-based fiber-photometric calcium imaging showed that the VMH-SF1 neurons were rapidly excited by assorted novel objects, and the pharmacological ablation of olfaction suppressed these novel-object induced neuronal activities in SF1 neurons. As hypothalamus does not receive direct inputs from the peripheral sensory system, how do the olfactory cues manipulate the VMH-SF1 neurons is largely unknown. In this study, we aimed to apply viral vector based tracing methods to identify the input and output neural circuits of the VMH SF1 neurons. Our AAV-based cell-type specific anterograde tracing results showed that in adult mice, the VMH-SF1 neurons projected widely into several subcortical areas, including ANH, BNST, Mtu and PAG. Next, our pseudotyped rabies viral vector based retrograde tracing showed that the VMH SF1 neurons received inputs from various subcortical areas, including LS, BNST, MPOs, PVA, PVN, SO, AHN, ARC, MM and MTu. Nevertheless, we did not find any rabies vector labeled neurons in the olfactory circuit. In summary, our data demonstrated that adult VMH-SF1 neurons have distinct input and output projection patterns, and the input olfactory cues may manipulate the VMH-SF1 neuronal activities via intercepting the neurons that innervate the VMH. In the future, we will manipulate the VMH-SF1 projecting neurons by chemo-activated Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) and photo-activated channelrhodopsins (ChR2) to identify the upstream targets of the VMH SF1 neurons.

In vivo longitudinal recording of cerebellar calcium imaging signals on awake-behaving mice

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Abstract

The highly repetitive 3-layer structure of the cerebellum is composed of micro-domains that provide the essential neuronal substrates for movement coordination. To reveal the dynamic activations of cerebellar micro-domains, we recorded the calcium imaging signals by using a two-photon imaging system and a synchronized movement tracing system at a head-fixed setup. The Pcp2-GCaMP6f mice express signals in molecular and Purkinje layers which located at the depth around 70 to 200 microns beneath the surface of lobule 4, 5, and 6. We successfully recorded the same cerebellar location multiple times on awake-behaving mice over one month. The distribution of the Purkinje neuron micro-domains was various among different mice. In some mice, we observed the patch-form micro-domains and each patch contained only 10-20 Purkinje neurons. While in one mouse we observed a continuous region with over 200 Purkinje neurons within a field of 1700 x 1000 micron. Note that when we observed from top-view, the flat dendritic arbors forming parallel lines distributed 40-80 microns exactly above the Purkinje neuron. The raw calcium imaging data were processed through an analysis pipeline: building image stack, stabilization, setting ROI, extracting intensity, and correlation analysis. The identification of the micro-domain was based on the synchronization of the calcium activation profile. We found more activating Purkinje neurons were recruited during the voluntary or forced movement episode. Multiple micro-domains appeared within the same observation region in an intermingled manner. The firing pattern of micro-domains revealed the movement coordination was synergistically operated by multiple micro-domains. This study is supported by MOST 108-2321-B-002 -059 -MY2.

A pathway from the parabrachial nucleus to the VTA negatively regulates feedingChia-Ying Chiang ¹, Jen-Hui Tsou ³, Shih-Ying Ni ², and Hau-Jie Yau ¹

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Abstract

Although the parabrachial nucleus (PBN) has been shown to relay signals associated with aversion, such as visceral malaise, pain, itch, and cues associated with potential threats, the function of its efferent projection to the ventral tegmental area (VTA) remains elusive.

To address this question, I first employed retrograde targeting approach to selectively target VTA-projecting PBN neurons. I found VTA-projecting PBN neurons are distinct from the renowned CGRP PBN neurons. By combining activity-dependent c-Fos staining with different behavioral paradigms, I found that subpopulations of VTA-projecting PBN neurons were functionally involved in stress and fear, but not thermal pain, malaise and feeding. These results suggest that the PBN-to-VTA inputs may relay aversive emotions such as stress and fear. Consistent with the functional mapping results, by combining optogenetic manipulation with a food self-administration paradigm, I found VTA-projecting PBN neurons were not required in food seeking behavior. Instead, activating PBN-to-VTA inputs is sufficient to dampen the food self-administration behavior.

To specify the downstream mediator of the PBN-to-VTA inputs, I employed the activity-dependent targeting approach (Targeted Recombination in Active Populations, TRAP) to selectively target VTA neurons activated by PBN input. I found that VTA neurons activated by the PBN input were mostly non-dopaminergic cells. Moreover, these neurons sent projections to several downstream brain regions, including posterior lateral hypothalamus (PLH) and lateral habenula (LHb). Considered together, these results suggest the PBN may relay negative emotion information to the VTA to inhibit food seeking behaviors.

Develop a novel strategy for optogenetic control of synaptic transmission

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Abstract

To decode function and circuitry in the central nervous system (CNS), tools and methods that enable precise manipulation of neuronal signaling are always in high demand. Conventional pharmacological or genetic manipulations often suffer from: (a) off-target drug effects; (b) insufficient spatial and/or temporal precision of the manipulation; and (c) compensatory effects caused by genetic modifications of the endogenous proteins. These limitations impede further deciphering of the delicate interplay of neural cells. We aim to develop new optogenetic/chemogenetic techniques to overcome these obstacles. Here we focus on developing strategies to specifically control inhibitory synaptic transmission in the CNS. We seek to manipulate the activity of endogenous GABA_A receptors, the major mediators of synaptic inhibition, in a cell-type selective manner. Our approach employs an artificial loading dock (LD) protein that recruits chemical modulators to target synaptic GABA_A receptors. The LD comprises a self-labeling tag (e.g., HaloTag) for drug tethering, a transmembrane domain for membrane anchoring, and an intracellular motif for subcellular targeting. Through the interaction between the intracellular motif and a postsynaptic scaffold protein, the LD is expected to be enriched at the inhibitory synapses. We have designed a series of LD candidates and examined their synaptic targeting in cultured hippocampal neurons by fluorescent microscopy. To optogenetically manipulate synaptic inhibition, we will optimize surface expression and targeting specificity of the LD, and then tether it with a photoswitchable modulator for GABA_A receptors. Furthermore, the same strategy can be applied to engineer LDs that target other subcellular domains, enabling functional dissection of GABAergic transmission within neurons. The successful development of next-generation optogenetics will advance the decryption of brain activity and circuitry to the next milestone, offering high-resolution mechanistic insights into CNS function and disorders.

Investigating the effect of a specific GSK3 inhibitor during neonatal period on the amelioration of schizophrenia-related deficits in Akt1 mutant mice

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Abstract

Schizophrenia is considered as a neurodevelopmental disorder that leads to behavioral, neuronal, and biochemical abnormalities throughout adulthood. Accumulating evidence suggests that AKT1 (protein kinase B α) contributes to susceptibility to schizophrenia and the AKT-GSK3 signaling pathway is involved in the pathogenesis of schizophrenia. GSK3, a key kinase modulating the development of the nervous system, is largely regulated by one of its upstream targets – AKT1. Convergent evidence indicates a decrease in AKT1 protein levels and levels of phosphorylation of GSK3 β in the peripheral lymphocytes and brains of individuals with schizophrenia. Furthermore, it has been reported that direct inhibition of active GSK3 by GSK3 inhibitors alleviated the schizophrenia-like behaviors in adult Akt1^{-/-} mutant mice. Given the involvement of AKT-GSK3 signaling pathway in the pathogenesis of schizophrenia, in this study, we aim to investigate whether direct inhibition of GSK3 during early developmental period could rescue schizophrenia-related deficits in adulthood using Akt1^{+/-} mutant mice as a model. SB216763 (a GSK3 inhibitor) was selected and administered intraperitoneally to both male and female Akt1^{+/-} mutant mice and their wild-type littermates every other day from postnatal day (PND) 7 to 27. The protein expression of Akt1 and GSK3 α/β in the hippocampus were measured after last injection at PND 27. At 3 months of age, the puzzle box task (for problem solving ability) and fear conditioning task (for associative learning and memory) were performed to evaluate hippocampus-related behavioral deficits in these mice. Furthermore, neuromorphological alterations in the hippocampus were further examined in these mice crossed with a reporter strain, Thy1-GFP-labeled mice. Compared to vehicle controls, the administration of SB216763 during neonatal period resulted in a significant increase in phosphorylated GSK3 α and GSK3 β in the hippocampus of male and female Akt1^{+/-} mice at PND 27. At 3 months of age, sex-specific behavioral deficits were observed in Akt1^{+/-} mice. In the puzzle box task, Akt1^{+/-} female mice displayed impaired long-term memory and problem solving activity, which were rescued by the neonatal GSK3 inhibition. In the fear conditioning task, Akt1^{+/-} male mice had deficits in contextual fear memory, which was ameliorated by the neonatal GSK3 inhibition. Neuromorphological analysis of hippocampal CA1 pyramidal neurons in GFP-labeled Akt1^{+/-} mice further revealed that the administration of SB216763 during neonatal period rescued the complexity of basal dendrites in female mice. Collectively, our current findings indicated that long-term administration of SB216763, a GSK3 inhibitor, during neonatal period efficiently inhibited active GSK3 and alleviated observed hippocampal-related behavioral deficits and neuromorphological alterations in Akt1 mutant mouse model of schizophrenia.

The association between oxidative stress and dopamine transporter activity in patients with bipolar disorders

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Abstract

Compelling evidences have shown that mitochondrial dysfunction and increased oxidative stress are common features in bipolar disorder (BD). Abnormal striatal activation has also been observed in patients with BD. However, the association between striatal activity and mitochondrial DNA copy number (MCN) or oxidative stress remains elusive in patients with BD. We aim to explore the association between striatal dopamine transporter activity and oxidative stress in clinically stable patients with BD. 108 Patients diagnosed with BD according to the DSM 5 criteria and 66 healthy controls (HC) were enrolled in this study. The patient's psychopathology was evaluated using the 17-item Hamilton Depression Rating Scale (HDRS) and the 11-item Young Mania Rating Scale (YMRS). Striatal dopamine transporter (DAT) availability was assessed using [99m Tc] TRODAT-1 single-photon emission computed tomography (SPECT). Leukocyte MCN and oxidative stress (delta CT) were assessed using a LightCycler Instrument. All patients will provide written informed consent for participation in the trial which is reviewed and approved by the Institutional Review Board at National Cheng Kung University Hospital. The mean age and gender distribution were not statistically different between the BD and HC groups. The HADS and YMRS were 3.82 ± 5.11 and 1.85 ± 3.41 in the BD patients. Leukocyte MCN, delta CT and the striatal DAT availability was not significantly different between the two groups. In the BD patients, MCN was negatively correlated with metabolic syndrome and BMI. Delta CT was negatively correlated with cholesterol and LDL-C. MCN and delta CT level were not correlated with striatal DAT activity after adjustment. Our results showed MCN and oxidative stress were not significantly different between the BD and HC groups. The may be due to drug treatment or disease severity. Complex I (NADH dehydrogenase) and complex IV (cytochrome-c-oxidase) of the mitochondrial electron transport chain have been implicated in the pathophysiology of major psychiatric disorders, such as BD. In a meta-analysis by Holper et al., Alzheimer's disease and Parkinson's disease showed the strongest effect sizes for shared deficits in complex I and IV instead of MDD or BD which is in line with our findings. Dopamine can be an important link for the mitochondrial dysfunction seen in BD, lithium and valproate exert protective effects against mitochondrial dysfunction, this may partially explain why striatal DAT activity was not correlated with MCN or delta CT level.

Dietary curcumin ameliorates neural connectivity and neuropsychiatric behaviors in *Tsc2*^{+/-} mouse model via alterations of gut microbiota diversity

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Abstract

Tuberous sclerosis complex (TSC) is genetic disease that causes the growth of benign tumors in multiple organs, including the brain, due to the overactivation of the mammalian target of rapamycin (mTOR). In addition to the brain lesions, TSC patients also exhibit neuropsychiatric disorders include cognitive dysfunction, social behavioral deficits, and anxiety. Based on the overactivation of mTOR in TSC, we have used curcumin, a diet-derived natural mTOR inhibitor, to treat the behavioral deficits of *Tsc2*^{+/-} mice. Imaging research on neuropsychiatric symptoms has suggested that a decreased neural connectivity is an important factor contributing to the deficits. Diffusion tensor imaging (DTI) is a type of magnetic resonance imaging modality that has been used to characterize the microstructural properties in the brain, that contribute to the connectivity between the nodes. In this study, we aim to test whether the treatment of curcumin can improve the altered brain connectivity, as well as the neurocognitive deficiencies, in TSC. In addition, since curcumin is administered orally with the chow, we are interested in the underlying mechanisms by assessing the gut microbiota compositional changes in pre- and post-treatment groups. We deployed DTI to determine fractional anisotropy (FA), mean, axial, and radial diffusivity (MD, AD, RD) of the fiber tracts in between the brain nodes associated with cognitive and social behavior deficits in *Tsc2*^{+/-} mice. Next, we assessed the changes in behavioral performance and DTI metrics after curcumin therapy. Finally, we analyzed the gut microbiota flora alterations after treatment and further confirmed the gut-brain axis communication in TSC. Our results showed that the microstructural alterations in various brain regions of *Tsc2*^{+/-} mice, as suggested by the increased FA and decreased MD values in the anterior cingulate cortex (ACC) and the field CA1 of the hippocampus. Opposed to the gray matter regions, we found a decreased FA, an increased RD in the white matter of TSC. Second, curcumin-treated *Tsc2*^{+/-} mice showed enhancement in their learning and recognition memory and social behavior in a dose-dependent manner. These changes correlated with the improvements in the neuroimaging data. Furthermore, the gut microbiota species greatly differed in the three groups of mice, suggesting gut environment changed after treatment. Finally, we found that the complexity of myelinated axons is decreased in the ACC and the expression level of glial fibrillary acidic protein (GFAP) is increased. These molecular changes corresponded to the FA and MD values

The association of executive function, prefrontal excitatory and inhibitory balance and social cognitive function in euthymic bipolar disorder patients

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Abstract

Social cognitive deficits are observed across mood episodes and euthymic phase in patients with bipolar disorder (BD). Cognitive impairment also exists in euthymic phase of BD and contribute to social cognitive deficits. The imbalance of prefrontal excitatory glutamatergic and inhibitory GABAergic system is one of the hypothetical neural underpinning of social cognitive deficits in BD. The current study aims to evaluate the relationship between social cognitive function, neurocognitive function, and excitatory/inhibitory balance in euthymic phase of BD.

To date, we recruited 29 euthymic BD patients and 38 healthy controls (HCs). The glutamatergic (Glx) and GABAergic (GABA) metabolites in the medial prefrontal cortex (mPFC) were measured by proton magnetic spectroscopy (¹H-MRS). The ratio of glutamate to GABA metabolites (Glx/GABA) was calculated as the index of excitatory and inhibitory balance (E/I ratio). Social cognitive function was measured using Diagnostic Analyses of Nonverbal Accuracy, Taiwanese Version (DANVA-2-TW). Neurocognitive function was measured using Wisconsin card sorting test (WCST) and continuous performance test (CPT).

The BD group performed significantly worse in both social cognitive ($p < 0.001$) and neurocognitive measurements ($p < 0.001$). A significantly higher level of mPFC Glx was observed in BD patients. The E/I ratio was similar between groups. Social cognitive ability and neurocognitive ability were positively correlated across groups, while a negative association was observed between social cognition and E/I ratio mainly in BD group ($r = -0.58$, $p = 0.011$). WCST categories completed and E/I ratio predicted social cognitive ability across groups. In HC group, E/I ratio negatively predicted social cognitive ability, but in BD group the association was not observed.

The worse social cognitive and neurocognitive functions were associated with their glutamatergic/GABAergic balance status in prefrontal cortex. In HC, better executive function and better medial prefrontal inhibitory function (lower E/I ratio) contributed to better social cognition. The modulatory role of E/I balance was disrupted in euthymic BD. Additional modulatory factors that may contribute to social cognitive function in BD, such as dopaminergic function, need further investigation.

Using deep learning techniques to classify major depressive disorder and bipolar disorder based on MEG signals

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Abstract

Major depressive disorder (MDD) and bipolar disorder (BD) are increasingly common mental illnesses with different etiologies and treatments but are clinically challenging to distinguish. Brain waves-based automatic classification and diagnosis using deep learning techniques could be a promising solution. For classification, convolutional neural network (CNN) is a powerful method to extract spatial features while recurrent neural network (RNN) works excellent on extracting features on time series. In this study, 55 MDD patients, 61 BD patients, and 74 normal controls (NC) were recruited. For each participant, 3-minute eyes-open and eyes-closed resting-state magnetoencephalography (MEG) data were recorded using a whole-head 306-channel MEG system (Vectorview, Elekta Neuromag) with a sampling rate of 1001.6 Hz. Sensor-level MEG signals were preprocessed and bandpass-filtered into seven frequency bands (delta, theta, alpha, low beta, mid-beta, high beta, gamma) based on literature. Brain features, including mean absolute band power and asymmetry ratio, were subsequently calculated and extracted from 4-sec Fourier-transformed filtered signals. Therefore, two classes of training inputs were used: filtered signals without feature extraction and the abovementioned extracted brain features. Deep learning models, including CNN, recurrent CNN (R-CNN), and recurrent neural network (RNN), were applied. As a result, CNN and R-CNN models trained using filtered signals (without feature extraction) of either all channels or channels of interest failed to classify different groups. In contrast, by using asymmetry ratio, RNN achieved an accuracy of 88.5% in classifying MDD, BD, and NC from each other. Furthermore, representative features were majorly from high beta frequency band. These results showed that a priori feature extraction based on expert knowledge is still critical to machine learning and deep learning applications.

Comparisons of Brain Activity in Processing Different Emotions of Facial Expressions in Sequential Discrimination Task

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Abstract

The study attempted to investigate the brain activity in processing different categories of emotion in a sequential discrimination task with the judgment of whether the emotion of the target stimuli was congruent with the previously presented stimuli. In the experiment, 22 college students (aged 20-25) participated and their functional magnetic resonance imaging data were collected during the experimental procedure when they viewed the previous and target stimuli and pressed the bottom to determine that the stimuli were having a congruent or incongruent emotion. Three emotional categories were used including angry, fear and happy as well as neutral facial expressions. For each participant, the experiment procedure involved eight of runs with ninety-six of trials in each. The major analysis conducted by a 2 (condition: prime/target) x 2 (congruency: congruent/incongruent) x 4 (emotion type: angry, fear, happy, and neutral). The results suggested main effects of consistency and emotion type as well as an interaction between them. It was found differences in between the congruent and incongruent conditions at right precentral gyrus (rPG) with congruent higher than incongruent. In terms of the main effect of emotion, the activity involved were at rPG, right lentiform nucleus (rLN), right middle occipital gyrus (rMOG) and left superior frontal gyrus (LSFG) with the neutral faces greater at LSFG and right inferior occipital gyrus than angry expressions. The fear expressions were greater at rLN than the neutral, and higher in happy than neutral at rPG. The neutral were found greater activity at MOG and LSFG than fear expressions, at rMOG and LSFG than happy expressions. The fear expressions were greater at rLN and rSFG than angry and at rLN than the happy expressions. The happy expressions were greater at rPG and right middle frontal gyrus than angry, and higher at rPG than fear expressions. For the interaction, the congruent was found greater activity at lentiform nucleus than the incongruent of fearful, and at LN of happy expressions. In congruent condition, fearful was found greater at LN than angry, happy and neutral stimuli, and happy was found greater at PG than angry expressions.

A novel non-invasive technique to detect the acute phase of inflammation and pain in the complete Freund's adjuvant-induced rheumatoid arthritis mouse model

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Abstract

Rheumatoid arthritis (RA) is a chronic autoimmune disorder and its' incidence is 1% worldwide. RA is characterized with chronic joint inflammation and pain. The acute phase of pain seems to associate with joint inflammation in early RA, but chronic phase of pain turns independent, essentially becoming its own disease. It remains unclear how the acute phase of RA is transitioned to chronic phase and how the transition is detected. We have established RA mouse model that has long-lasting inflammation and chronic pain and also showed clinical RA characteristics: lower pH in the joints, higher pannus, lasting bone erosion and cartilage damage. A transition from acute phase to chronic phase in RA mice seems to occur between 4-12 weeks which is characterized with high interleukin 17 level. In this study, a non-invasive technique was developed to detect the acute phase of RA. Complete Freund's adjuvant (CFA) was injected into the right ankle of the mouse once a week for four consecutive weeks to induce the inflammation and pain. The infrared detector was used to detect surface temperature of paws and ankles. Temperature change in RA or control mice were correlated with the arthritis scores, pain, and cytokine levels. After CFA injection, paw temperature was increased with time, peaked at week 4 (30°C) and then declined to the baseline (25°C). Similar results were found in ankle temperature and temperature was changed from 29°C to 31°C. Paw temperature showed a good correlation with arthritis scores (inflammation) and mechanical allodynia (pain) at week 4, but not at week 8 and 12. As a result, paw temperature change can be an indicator of the acute phase of RA using the non-invasive infrared detector.

Will melatonin be beneficial to prevent episodic migraine? From the view of network meta-analysis

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Abstract

From the latest network meta-analysis (NMA) published in *J Pineal Res.* 2020 Sep;69(2): e12663, our team tried to throw around a new issue about the potential benefit by melatonin to the episodic migraine (EM) prophylaxis. In one important randomized controlled trial (RCT) published in *JAMA Neurology* (*JAMA Neurol.* 2017 Jun 1;74(6):744-745), the role of melatonin in patients with EM had been demonstrated to be effective in EM prophylaxis. This beneficial effect had been proven to be similar with that of amitriptyline in another one RCT (*J Neurol Neurosurg Psychiatry.* 2016 Oct;87(10):1127-32). However, there was lack of sufficient RCTs to prove the direct comparability of efficacy between melatonin and the other FDA approval medication for EM prophylaxis. Therefore, this NMA aimed to provide the comparative evidence of the efficacy between melatonin and the other FDA approval medication for EM prophylaxis through the NMA. In this published NMA, we did not merge the treatments of different dosage of melatonin supplement into one treatment arm because there had been different physiologic effect by the different dosage of melatonin supplement based on the result of our previous NMA (*Sleep Med Rev.* 2020 Apr;50:101235). Therefore, based on the results of NMA of 25 RCTs and 4499 participants, it demonstrated that oral melatonin 3 mg/day at bedtime was associated with the greatest improvement in migraine frequency [mean difference = -1.71 days, 95% confidence interval (CI): -3.27 to -0.14 days compared to placebo] and the second highest response rate (odds ratio = 4.19, 95% CI = 1.46 to 12.00 compared to placebo). In addition, to provide additional clinical information to the clinicians, we calculated the value of overall preference through the surface under the cumulative ranking curve (SUCRA) value of (1) improvements in migraine frequency, (2) response rate, (3) drop-out rate, and (4) rates of any adverse events. According to the calculated value of overall preference, the oral melatonin 3 mg at bedtime was the most preferred treatment. This pilot NMA threw around a potential issue developing future RCT investigating the potential benefit of EM prophylaxis by melatonin.

Neurological basis of statin induced sngception

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Abstract

Sng (pronounced as 'sŋng') is a Taiwanese word that solely describes soreness, where in English, usage of soreness and pain is dubious. Somatosensory sensation of sng, sngception is induced by various stimulation such as tissue acidosis and response could be evoked by mechanical stimulation. As a perception, sng is different from long-established pain, even though they overlap sometimes. It can be described as a type of hyper-mechanosensitivity that includes a tenderness or stiffness of muscle. Unfortunately, the neurological mechanisms involved in sngception, remain largely unknown. Previous studies have associated sngception with acid sensitivity of deep tissue, specifically involving the Acid Sensing Ion Channels (ASICs). Perhaps, this connection has only widened the gap in our understanding of ASIC's role in nociception and anti-nociception as well as involvement of sngception in it. Additionally, there is no suitable and established animal model for the study of sngception. However, statin class drug induced sng is proved to be promising. Clinical studies have already shown that statin class drugs induce soreness in human subjects. Preliminary experiments show that systemic administration of statin can induce similar sng-like hyper-mechanosensitivity of muscles in mice. Therefore, investigation of statin sensitive ion channels and neuronal ensembles involved in statin induced hyper-mechanosensitivity in the murine nervous system holds a demand to be investigated. Neurophysiological and histological techniques could elucidate the effect of statin-induced sng on neuronal circuitry in the peripheral and central nervous system, as well as its physiological importance.

ASIC3 regulates nerve degeneration and contributes to chronic pain induced by nerve injury

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Abstract

Neuropathic pain is triggered by lesions to the peripheral nervous system (PNS) or the central nervous system (CNS) that induces spontaneous pain and abnormal painful sensation. Injury of peripheral nerves causes demyelination of Schwann cells and axonal degeneration, called Wallerian degeneration. Blocking nerve degeneration delays the onset of hypersensitivity induced by the nerve injury. The nerve injury and degeneration/regeneration marker, activating transcription factor 3 (ATF3), is induced under acidosis condition. Therefore, nerve injury could cause local acidosis that regulates nerve degeneration and pain. Acid-sensing ion channel 3 (ASIC3), a proton sensor, is involved in acid-induced and inflammatory pain. However, the roles of ASIC3 in nerve degeneration and neuropathic pain remains unclear. To address this question, we used chronic constriction injury of the sciatic nerve (CCI) as a neuropathic pain model to examine the influence of ASIC3 gene deletion on nerve degeneration and CCI-induced pain. We have demonstrated that CCI surgery caused long-lasting mechanical allodynia (at least 14 weeks), reduced number of sensory neurons, Schwann cell demyelination, and increased ATF3 expression and calcium signals in soma of sensory neurons. Interestingly, ASIC3 gene deletion reversed mechanical allodynia after week 8. The number of small-diameter dorsal root ganglion (DRG) sensory neurons are also recovered at week 8, which is related to more small neurons expressed ATF3 gene. Accordingly, ASIC3 gene deletion increased ATF3 expression at week 8 in small neurons to promote small neuron regeneration, which contributes partially to shortening of mechanical allodynia.

Effects of $\alpha 6$ -containing GABA_A R-selective positive allosteric modulators in the trigeminal ganglia : An electrophysiological study

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Abstract

The $\alpha 6$ subunit-containing GABA_A receptor ($\alpha 6$ GABA_AR) is an under-studied GABA_AR subtype because of the unavailability of subtype-selective ligands. In 2013, our collaborating group identified a series of pyrazoloquinolinones to be $\alpha 6$ GABA_AR-highly selective positive allosteric modulators PAMs.¹ Previously, we have showed that $\alpha 6$ GABA_ARs are highly expressed in trigeminal ganglia (TG), a hub involved in the pathogenesis of migraine and oral facial pain and pyrazoloquinolinone Compound 6 was effective in a rat migraine model,² suggesting the therapeutic potential of $\alpha 6$ GABA_AR PAMs for trigeminal-related pain, including migraine. However, how $\alpha 6$ GABA_AR PAM affects GABAergic transmission in TG at cellular levels remains unclear.

Here we employed the whole cell patch-clamp recording techniques in dissociated TG neurons isolated from 6-8 week-old adult male ICR mice to investigate how Compound 6 affects GABA-elicited currents (I_{GABA}). Interestingly, GABA induced an inward current in adult TG neurons as in dorsal root ganglia, instead of the general outward current observed in adult GABAergic synapses in the brain. The I-V relationship demonstrated the I_{GABA} was mediated by chloride channels, the reversal potential was 7.9 ± 1.8 mV close to the equilibrium potential (0 mV) of Cl⁻ ions ($Cl^-_o/Cl^-_i = 141/140$ mM). The EC₅₀ of GABA was 58.5 ± 2.7 μ M, which was parallelly right-shifted by bicuculline (1 μ M), a selective GABA_AR antagonist, to 134.4 ± 3.1 μ M. To quantify the positive modulatory effect of Compound 6 on I_{GABA} , we acquired the I_{GABA} , EC₅₀ in each individual neuron. Compound 6 (1 μ M) increased I_{GABA} , EC₅₀ to 131.5 ± 6.4 % of control, and this potentiating effect of Compound 6 (1 μ M) was reduced to 97.7 ± 5.9 % (n=11) in the presence of furosemide (100 μ M), a selective $\alpha 6$ GABA_ARs antagonist. Furosemide *per se* slightly decreased the I_{GABA} , EC₅₀ (87.6 ± 5.2 % of control), and further application of Compound 6 failed to increase I_{GABA} (80.4 ± 4.6 % of control) (n=12). These results suggest that $\alpha 6$ GABA_ARs in TG neurons are functional and are positively modulated by Compound 6. Thus, $\alpha 6$ GABA_AR PAMs likely enhance depolarization block effect of GABA in TG neurons, which may contribute to their anti-migraine or anti-oral facial pain effect *in vivo*.

¹Varagic et al. Br J Pharmacol. 2013 May;169(2):384-99.

²Fan et al. Neuropharmacology. 2018 Sep 15;140:1-13.

Plastic change in the function of synapse at Nav1.8 nociceptive fiber onto spinothalamic tract neuron in mice with neuropathic pain

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Abstract

Peripheral nerve injury could result in mechanical hypersensitivity; it's believed that changes in the function of neuronal circuit at spinal cord level are important to its development. The spinothalamic tract (STT) neurons convey nociceptive signals from the nociceptive dorsal root ganglion (DRG) neurons to the thalamus. In this study, we address whether the development of neuropathic pain was associated with a change in the synaptic function of the nociceptive fibers expressing voltage-gated sodium channel 1.8 (Nav1.8) onto STT neurons in mice with the spared nerve injury (SNI). The L3-L5 spinal cord slices were prepared from transgenic mice that expressed channelrhodopsin2 (ChR2) under Nav1.8 promotor for optogenetic activation of the Nav1.8 nociceptive fibers; the mice were also infused with a retrograde tracer, cholera toxin subunit b, into their ventrobasal thalamus to label STT neurons for whole-cell recording. We found a significant decrease in the paired-pulse ratio of Nav1.8-STT EPSCs and an increase in the frequency of spontaneous EPSCs in the SNI mice than in the sham mice at 4 days after the surgery. Interestingly, there was no significant difference in the ratio of AMPA receptor-mediated signal to that of NMDA receptor between the SNI and shame groups. However, change in the firing pattern of the STT neurons was observed. Our results show a presynaptic change in the nociceptive synaptic transmissions from DRG to STT neurons during the early state of neuropathic pain. Furthermore, there is also a change in the firing properties of STT neurons.

The Profile of Neuron activation in Trigeminal Sensory Nuclei in Mice Receiving Acidic Buffer injection into the Masseter Muscle

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Abstract

The pain model induced by injection of acidic buffer into gastrocnemius muscle has been widely used as a fibromyalgia-like pain model and the model is dependent on activation of acid-sensing ion channel 3 as reported by previous studies. Recently, it has been suggested that the dis-comfort sensation caused by acidic buffer injection could be a distinct sensory modality that is different from pain-sensation and is expressed as “Sng” in the Chinese cultured societies. In this study, we wish to test whether Sng and pain are actually different sensory modalities by examining whether the Sng pathway could be discriminated from the nociceptive pathway. We take anatomical advantage of the trigeminal system over the spinal system to address this question, as the nociceptive and proprioceptive pathways are anatomically separated in the brainstem in the trigeminal system. Acid buffer (pH 4.0) was administered into the masseter muscle, which resulted in similar profile of behavior hypersensitivity compared to the results of the acidic buffer administration to the gastrocnemius muscle. In addition, the results of immunohistochemistry study using anti-c fos antibodies revealed an increase in the number of c fos positive neurons in the principle trigeminal nucleus (Pr5) and spinal trigeminal nucleus (sp5) but not in the mesencephalic trigeminal nucleus (Me5) in mice receiving acidic buffer injection to the masseter muscle (n=3), compared to the results from mice receiving pH 7.4 buffer (n=3). Since, a previous study reported that inflammatory pain induced by injection of Mustard oil into masseter muscle increased neuronal activity in sp5 pars caudalis but not in Pr5. The aforementioned preliminary data support that Sng is conveyed to brain via a pathway that could be discriminated from nociception.

Functional connectivity of the PVA neurons in nociceptive circuit in mice

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Abstract

Pain-related diseases are the top leading causes of years living in disability globally and in Taiwan. Therefore, identifying brain regions and neuronal circuitry involved in persistent neuronal changes will provide new insights for developing efficient chronic pain treatment. Previously, we found anterior nucleus of paraventricular thalamus (PVA) plays an essential role in the development of mechanical hyperalgesia in acid-induced chronic muscle pain, neuropathic pain and inflammatory pain in mice. Inhibition of the neuronal activity of PVA could reverse the pain behavior. Therefore, PVA is an important brain locus for the pain modulation. Recently, we found that the *vgltu2+* neurons in PVA are involved in inflammatory pain model. Pharmacological and optogenetic data also indicated that the innervation of the PVA to bed nucleus of the stria terminalis (BNST) is an important nociceptive circuit. Using *in vivo* calcium imaging in freely moving mice, we found a specific population of PVA neurons were activated in response to mechanical stimulation. We continuously observe the PVA neurons activity using *in vivo* calcium imaging at different time points in formalin model. We found that group of PVA neurons activity increased and those neurons which response to mechanical stimulation change dynamically. The findings from this study are expected to provide an important insight into the mechanism of chronic pain and also provide a target brain area for a therapeutic approach to reduce the suffering of patients with chronic pain.

Emotions bias pain modulation associated with positive but not negative pain expectancy

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Abstract

Expectations about upcoming painful events substantially shape the experience of pain in humans. Positive expectations (i.e., expecting decreased pain) and negative expectations (i.e., expecting increased pain) toward pain respectively lead to the alleviation and exacerbation of pain. However, psychological modulators involved in pain modulations by expectations remain unclear. In this study, we aim to delineate whether and how emotions modulate effects of expectation on pain. We induced pleasant, neutral, and unpleasant emotions of participants with pictures selected from the International Affective Picture System when participants positively or negatively anticipated painful stimulations. Meanwhile, we applied fMRI technology to investigate neural correlates of emotional modulations in pain expectancy effects. Behaviorally, we observed ubiquitous effects of positive and negative expectations on pain perception across different emotional states. More importantly, unpleasant emotions significantly suppressed the modulation of positive expectations on pain perceptions, whereas no emotional effect was found on negative expectations. At the neural level, brain activation patterns associated with pain modulation by positive expectations differed among different emotional conditions, with the unpleasant condition associated with increased activations in prefrontal regions, compared with the neutral or pleasant condition. Negative emotions diminish pain modulation by positive expectations of decreased intensity, which is mirrored by changes in activations within pain- and emotion processing-related cerebral circuitries. However, the effect of negative expectations on pain may be independent of emotional modulations. The current research enhances our knowledge on how expectations interact with emotions to shape human responses to pain.

The correlation between functional connectivity and the heart rate variabilities after aromatherapy intervention

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Abstract

Aromatherapy is well known as complementary therapy for anxiety symptoms, The exact neurological mechanism is still unknown. We used purified and quantified oil extracted from orchid and lavender. Resting state functional MRI was performed before and after aromatherapy intervention.

Heart rate variations (HRV) represented as autonomic system functioning was also measured before and after the intervention. Sixty normal healthy subjects were recruited, and the subjects were randomized categorized into orchid, lavender and control groups. The results showed all the aromatherapy group has decreased functional connectivity in right thalamic-inferior temporal gyrus circuits after the aromatherapy intervention. Furthermore, the positive correlation exists between decreased functional connectivity and changes in high frequency, total power and negative correlations in low frequency, only in lavender group. Our study highlights the possible functional connectivity changes by aromatherapy intervention and the possible correlations between autonomic system influence.

**From brain to trait:
Establishing a brain white matter model to predict restraint trait**

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Abstract

Long-term weight control is extremely difficult for most of the population, but for successful chronic dieters, it is not a difficult job. What makes these dieters succeed in achieving long-term self-control goals? Some evidence suggests that individual differences in traits, especially concern-for-dieting (CD), are the most determinant factor. Although there have been some attempts to relate personality traits to white matter integrity of the brain, few studies have tried to establish the link between individual differences in CD and their differences in white matter integrity. In this study, we were interested to examine whether we could use machine-learning methods to establish a white matter integrity model to predict CD in a training dataset and then make an out-of-sample prediction in an independent testing dataset. The present study recruited 112 female subjects and their diffusion tensor imaging (DTI) data as well as self-reported CD scores were collected. We used their fractional anisotropy (FA) images, a general measure of white matter integrity in DTI data to establish the predictive model. The whole FA dataset was divided into two independent datasets, one as the training dataset and the other as the testing dataset. Our results showed that we achieved a moderate cross-validated correlation, $r = 0.43$, by using leave-one-subject-out cross-validation method. We then used the predictive brain model established in the training dataset to make an out-of-sample prediction in the testing dataset. A high correlation between predicted CD values and subjects' actual CD scores, $r = 0.57$, $p < 0.001$, was found in the testing dataset. Findings from our study demonstrated that personality traits related to long-term success in self-control might be reflected in anatomical brain structure, especially in white matter integrity. Machine-learning methods could be useful to train predictive brain models to examine the link between personality traits and brain structure.

Gamma oscillations demonstrate the mechanism of TMS treatment in Treatment-Resistant Depressed patients

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Abstract

Recently, FDA in the U.S. have approved that repetitive TMS (rTMS) and intermittent TBS (iTBS) as an effective management in treatment-resistant depressed (TRD) patients. Nevertheless, the mechanisms of variant outcome of TMS treatment revealed by the brain oscillation were not fully understood. The present study aimed to investigate the variety of the brain oscillations during resting state which influenced by TMS treatment in TRD patients. Total 51 TRD patients were recruited and were randomly distributed to iTBS (N=17), 10 Hz rTMS, or sham TMS (N=17) group with a double blind design. Each participant was involved in ten sessions treatment phase and the resting state electroencephalography (EEG) with all eye-closed was recorded before and after the treatment phase. The efficacy of TMS was mainly evaluated by the 17-item Hamilton depression rating scales (HDRS-17) before the beginning of the TMS treatment (W0), and after the end of the treatment (W2). The non-linear analytical method, namely Holo-Hilbert spectral analysis (HHSA; Huang et al., 2016), was applied to the resting-state EEG data. This analytical method provides not only the carrier frequency information but also the amplitude modulation which can fully represent the complex nonlinear information in the EEG. Approximately one third of TRD respond to TMS treatment. The EEG results have shown the positive correlation between resting EEG of all participants and the scores of HDRS-17 involving W0 and W2 in gamma frequency band across whole brain. This may indicate that the more serious of the depression, the higher gamma power would show. Furthermore, the TMS effect was shown in precluding the increment of gamma frequency band compared to sham group. In addition, the increasing of theta modulation was shown in iTBS effect while the increasing of alpha and beta bands was shown in rTMS effect which indicated the different mechanisms of rTMS and iTBS on TRD. Given these patterns of results, gamma, alpha, theta oscillations could be the EEG predictors for determining the optimal TMS treatment in TRD.

A holo-spectral EEG analysis provides early detection of cognitive decline and predicting progression to Alzheimer's Disease

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Abstract

Aims: Using resting-state EEG (rsEEG), Holo-Hilbert Spectral Analysis (HHSA) and machine learning algorithms to differentiate patients with mild cognitive impairment (MCI) and Alzheimer's disease (AD) from cognitively normal individuals, and to predict the progression of MCI to AD within a 3-year longitudinal follow-up.

Methods: We recruited 205 participants from three hospitals, which include cognitive normal (n=51, MMSE>26), MCI (n=42, CDR=0.5, MMSE≥25), AD1 (n=61, CDR=1, MMSE<25), AD2 (n=35, CDR=2, MMSE<16), and AD3 (n=16, CDR=3, MMSE<16) and rsEEG were recorded. Seventy-two patients with MCI (CDR=0.5) longitudinally followed with two rsEEG recordings within three years, which subdivided into two groups, one is MCI-stable group (n=36), the other is MCI-converted group (n=36). We used HHSA-based feature engineering in conjunction with machine learning algorithms to analyze the rsEEG.

Results: (a). At the group level analysis, the contrasted HHSA between MCI and different stages of AD show prominent increasing power of lower frequency (e.g., delta and theta bands) oscillations while decreasing power of higher frequency (e.g., beta and gamma bands) oscillations. The alpha frequency oscillation shows slightly increasing power across MCI to the AD2 stage but a reverse trend at the AD3 stage. (b) At the individual level analysis, implementing machine learning algorithms can discriminate between cognitive normal (CN) individuals vs. MCI, CN vs. AD1, CN vs. AD2, and CN vs. AD3 with sensitivity and specificity of 0.88 and 0.95, 0.94 and 0.85, 0.79, and 0.95, 0.75 and 1, respectively. (c) In the longitudinal follow-up MCI groups, the initial contrasted HHSA between MCI-converted and MCI-stable shows significant decreasing power of alpha and beta bands oscillations. (d) At the individual level analysis of the longitudinal MCI groups, deploying machine learning algorithms with eight features give rise to the best sensitivity of 0.8 by the k-nearest neighbor classifier, whereas with thirteen features give rise to the best specificity of 0.9 by the ensemble bagging classifier.

Conclusions: Integrating HHSA of EEG signals and machine learning algorithms can not only be a clinical tool to differentiate between normal cognitive individuals and cognitive decline patients but also predict progression at the MCI stage.

Therapeutic Effects of Cortical Electrical Stimulation on Parkinsonian RatsCHI-WEI KUO¹, HUI-CHIUN TSENG¹, TSU-YI JEN², CHIEN-YUAN PAN¹, TSUNG-HSUN HSIEH³¹Department of Life Science, National Taiwan University, Taipei 112, Taiwan² Department of Psychology, National Taiwan University, Taipei 112, Taiwan³ School of Physical Therapy and Graduate Institute of Rehabilitation Science, Chang Gung University, Taoyuan 333, Taiwan**Abstract**

Background: Parkinson's disease (PD) is one of the prevalent neurodegenerative disorder. The pathologic hallmark of the disease results from degeneration of the dopaminergic neurons (DA) in the substantia nigra (SN), several motor disturbances. Cortical electrical stimulation (CES) has been developed for modulating cortical excitability via plasticity-like mechanism and is considered having therapeutic potentials in PD. However, the therapeutic value of such approach for PD is still unclear. Accordingly, we adopted the PD rat model for elucidating the possible therapeutic effects of CES.

Methods: A hemiparkinsonian rat model, induced by unilateral injection of 6-hydroxydopamine (6-OHDA) into the medial forebrain bundle (MFB), was applied to investigate the therapeutic roles of CES in motor functions following long-term CES treatment for 4 weeks. After CES intervention, the detailed functional behavioral tests including gait, bar test, open field, and apomorphine-induced rotational analysis as well as DA degeneration level were assessed up to 4 weeks.

Results: After CES treatment, we found that 4 weeks of CES intervention ameliorates the motor deficits in gait pattern, akinesia, locomotor activity, and apomorphine-induced rotation.

Immunohistochemistry, tyrosine hydroxylase (TH) staining analysis demonstrated that the dopamine neurons were significantly preserved. Similar results were obtained in Western blot.

Conclusions: This study documents the efficacy of CES in preventing motor and dopaminergic system abnormalities in rat model of PD. This long-term CES treatment model may serve as a bridge between animal and PD human studies. Future preclinical studies are still needed to further identify the underlying mechanisms, leading to improve CES protocols and therapies in human.

Mitochondrial transplantation via nose-to-brain delivery for treatment of Parkinson's diseases in rats

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Abstract

Since intranasal administration regulates brain cell function through the Olfactory bulb pathway, this study evaluated the feasibility of mitochondrial delivery for treatment of unilateral 6-OHDA-induced rat model of Parkinson's disease (PD) and related machinery. It expects to simplify the procedure of mitochondrial transplantation and avoid the occurrence of side effects caused by surgery. The experiment used the allogeneic mitochondria labeled with BrdU before isolated from livers. A nasal infusion with 200 µg of mitochondria with (P-Mito) or without Pep-1 conjugation (Mito) was executed once a week at the ipsilateral side of lesioned brain. After three months of treatments, a significant improvement of apomorphine-induced rotational behavior and locomotor behavior in PD rats was found in both of mitochondria-treating groups in contrast to Sham group and Pep-1 group, and P-Mito has a slightly higher expression level than Mito. The survival of dopaminergic (DA) neurons in substantia nigra (SN) and striatum (ST) of lesioned sides revealed by staining of Nissl and tyrosine hydroxylase furtherly showed the treatment effect of Mito and P-Mito with more than 50% recovery compared to the intact sides. The mechanism was associated with the restoration of mitochondrial function in depleted DA neurons of SN. Besides, Pep-1 conjugation attenuated the plasma level of inflammatory cytokines induced by infused mitochondria. The presence of foreign mitochondria, indicated by BrdU signal, in rostral migratory stream (RMS) connected the infused-side olfactory bulb to the periventricular regions, and in both sides of ST DA neurons reflected an effective nose-to-brain delivery of mitochondria. However, the expression was absent in SN whether in the lesioned side or intact contralaterally side. The doublecortin (Dcx) staining in anterior commissure confirmed the mitochondrial internalization and sending in the axon of olfactory neurons to express in two cerebral hemispheres. This study demonstrated an effective route of intranasal infusion for mitochondrial transplantation therapy of PD rats.

Intelligent machine learning system of EEG features prescreening ADHD symptoms with Kiddie Continuous Performance Test in preschool-age children

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Abstract

Attention deficit hyperactivity disorder (ADHD) is the most prevalent neurodevelopmental disorder affecting children. Regarding preschool ADHD, the prevalence ranges from 2.1% to 5.7%, which is lower than or comparable to that in school-age children and adolescents. Furthermore, heterogeneous neurobehavioral deficits and phenotypes have been reported in ADHD such as inattentiveness, impulsivity, emotional dysregulation, and difficulties in maintain vigilance or sustained attention, or combined with these symptoms. Fully characterizing children at risk for ADHD at preschool age and providing individual early intervention are imperative. The aim of this study, which recruited 28 ADHD preschoolers and 30 aged-matched children with typical development (TD), not only differentiate ADHD group with TD peers, but also prescreen varied aspects of ADHD symptoms using machine learning technique with EEG spectral powers and KCPT (Kiddie Continuous Performance Test) scores. In the first step of the study, different classifiers including SVM, Random Forest, Gaussian Classifier and KNN were used to validate our data and compare with different sets of EEG features according to previous literatures. In different classifiers, the accuracies of our model were observed to be 98% in SVM, 97.53% in Random Forest (RF), 81.64% in Gaussian classifier and 98.5% in KNN by using ten-fold cross validation; which we used theta and beta power in Fp1, Fp2 and Fz obtained from Sequential Feature Selection(SFS). Moreover, we conducted regression technique to distinguish different aspects of ADHD symptoms such as inattentive, sustain attention and vigilance by using EEG band powers and KCPT scores; which accuracies can reach to around 90%. The results manifest that EEG band powers can be used as features to identify different aspects of ADHD symptoms, also we can use and may provide specialists information for planning early intervention and educational strategies.

The efficacy and safety of transcranial direct current stimulation for cerebellar ataxia: a systematic review and meta-analysis

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Abstract

Background: A promising new approach, transcranial direct current stimulation (tDCS) has recently been used as a therapeutic modality for cerebellar ataxia. However, in the current literature, the strength of the conclusions drawn from individual studies may be constrained by the small sample size of each trial.

Methods: Following a systematic literature retrieval of studies, meta-analyses were conducted by pooling the standardized mean differences (SMDs) using random-effects models to assess the efficacy of tDCS on cerebellar ataxia, determined by standard clinical rating scales. Domain-specific effects of tDCS on either gait ataxia or hand function were further assessed by measuring with 8-meter walk and 9-hole peg test times, respectively. To evaluate the safety of tDCS, the incidences of adverse effects were analyzed using risk differences.

Results: Out of the 293 citations, 5 randomized controlled trials involving a total of 72 participants with cerebellar ataxia were included. Meta-analysis indicated a 26.1% ($p = 0.003$) improvement in ataxia immediately after tDCS with sustained efficacy over months (28.2% improvement after 3 months, $p = 0.04$) when compared to sham stimulation. tDCS for cerebellar ataxia is also domain-specific as it enhances gait (16.3% improvement, $p = 0.04$) but not hand function ($p = 0.10$) with respect to sham stimulation. The incidence of adverse events in tDCS and sham groups was similar.

Conclusion: tDCS is an effective intervention for mitigating ataxia symptoms with lasting results that can be sustained for months. This treatment has preferential effects on gait ataxia and is relatively safe.

Application of stem cell exosomes in neuropathic pain model

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Abstract

Nerve injury-induced neuropathic pain can be difficult to treat. In this regard, we have previously demonstrated the effectiveness of intrathecal gabapentin, minocycline, cannabinoid receptor agonists and Cav3.2 blockers in the L5/6 spinal nerve ligation (SNL) neuropathic pain rat model. With that experience, we now examined the effects of exosomes derived from human umbilical cord mesenchymal stem cell (UCMSC) and the corresponding results are reported here. In the SNL model, the single intrathecal injection of exosomes reversed SNL-induced mechanical and thermal hypersensitivities at early and well-developed pain stages. Moreover, continuous intrathecal infusion of exosomes achieved excellent preventive and reversal effects for SNL-induced pain. In immunofluorescent study, Exo-green labelled exosomes could be found majorly in the ipsilateral L5 spinal dorsal horn, dorsal root ganglion (DRG) and peripheral axons, suggesting the homing ability of exosomes. They also appeared in the central terminals and cell bodies of IB4⁺, CGRP⁺ and NF200⁺ sensory neurons. In addition, exosome treatment suppressed SNL-induced upregulation of c-Fos, CNPase, GFAP, and Iba1. All these data suggested that the analgesic effects of exosomes may involve their actions on neuron and glial cells. Exosomes also inhibited the level of TNF- α and IL-1 β , while enhanced the level of IL-10, brain-derived neurotrophic factor (BDNF), and glial cell line-derived neurotrophic factor (GDNF) in the ipsilateral L5/6 DRG of SNL rats, indicating anti-inflammatory and proneurotrophic abilities. Protein analysis revealed the content of vascular endothelial growth factor C (VEGF-C), angiopoietin-2 (Ang2), and fibroblast growth factor-2 (FGF2) in the exosomes. In cell culture assay, the exosomes induce neurite outgrowth of PC12 cells and protect PC12 and HEK293 cells against formaldehyde acid treatment. When applied with alginate scaffold around the ligated L5/6 spinal nerves, the exosome-scaffold (EX-SC) also possesses analgesic effect. After implantation for 21 days, the EX-SC enhanced the expression of myelin basic protein (MBP) and IL-10 in injured L5/6 axons. Overall, our results demonstrated that the UCMSC exosomes applied intrathecally or peripherally gives an excellent preventive and reversal effects on SNL-induced pain model.

Effect of arecaidine-derived dipeptides on cognition and memoryWan-Chuan Wu, Ying-Jie Chen, Hao-Yuan Hung, *Eagle Yi-Kung Huang*¹ Dept. of Pharmacology, National Defense Medical Center, Taipei, Taiwan, R.O.C.**Abstract**

In our previous study using the on-bead (Tenta Gel, Germany) combinatorial dipeptide library, we have identified two arecaidine-derived dipeptides (ADDP) showing high binding affinities to cholinergic muscarinic receptors after screening. Being a bio-active ingredient of areca nuts, arecaidine was known to act on muscarinic receptors as a partial agonist. It has been tested for its possible effects on anti-dementia clinically. Although it can enhance certain types of cognition and memory in patients of Alzheimer's disease (AD), there are several drawbacks for the application of arecaidine, including possible carcinogenicity, M1 vs. M2 selectivity, and pharmacokinetics. For its application, the main goals are to mask and reduce the nitrosylation (known to induce carcinogenicity), to increase M1 selectivity and ability to ameliorate dementia, and to be absorbed and cross blood-brain barrier quickly and stably. Currently, the Taiwanese group is trying to synthesize these two identified ADDPs in a large quantity both on both solid phase and liquid phase. As shown in the preliminary results of hippocampal LTP and LTD, arecaidine was found to inhibit both LTP and LTD. This could be connected with its effects on memory. Thus, the ADDPs will be examined for their effects on hippocampal LTP and LTD, too. The ability of ADDPs to cross blood-brain barrier will be also examined. These peptides will be also delivered to Czech and tested by the Czech group (using water maze, T-maze, fear conditioning) to examine whether they can reverse amnesic effect of scopolamine in rats. The identified two ADDPs have shown higher binding affinities than that of arecaidine itself. We speculate that they could be the best compounds with least unwanted effects. Furthermore, we will proceed to evaluate its effects on transgenic rat model of AD established by the Czech group, using the same repertoire of behavioral paradigms.

A novel inhibitor of the equilibrative nucleoside transporter 1 (J4) prevents Tau-mediated neurodegeneration and neuroinflammation

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Abstract

Tauopathy and dysfunction of adenosine homeostasis in the brain are common neuropathological features among various neurodegenerative diseases, including Alzheimer's disease (AD). Both Tau protein and adenosine have been implicated in a wide variety of fundamental physiological functions. Disruption of adenosine homeostasis has been observed in the frontal cortex of human AD brains. Moreover, elevated adenosine tone in the brain has been found to provide beneficial effects on several neurological and neurodegenerative diseases, including AD. The intracellular and extracellular adenosine level is tightly controlled by adenosine metabolic enzymes and adenosine transporters (e.g. equilibrative nucleoside transporter 1, ENT1) in the brain. Here, we developed an orally active-, BBB permeable- inhibitor of the ENT1 (designed as J4). In the present study, we reported that chronic treatment of J4 in a mouse model of tauopathy, Thy-Tau22 (Tau22) provided significant beneficial effects. Briefly, J4 treatment ameliorated spatial memory deficiency, synaptic plasticity impairment, and gliosis in Tau22 mice. Moreover, J4 reduces abnormally hyperphosphorylated Tau and restores disturbed energy balance (e.g. AMPK overactivation and mitochondria dysfunction) in the hippocampus of Tau22 mice. The bulk RNA-seq analysis showed that immune response associated genes in Tau22 mice could be restored by chronic J4 treatment. Furthermore, J4 significantly reduced gliosis, reactive microglia-expressed C1q and TNF- α , reactive astrocyte-expressed cytotoxic A1 astrocyte genes. Collectively, our findings suggested that the blockage of ENT1 by J4 normalizes energy and neuro-immune dysfunctions in the hippocampus of Tau22 mice, which provides a new therapeutic strategy for tauopathy, and may contribute to the development of treatment for AD.

Formulated Chinese medicine Shaoyao Ganciao Tang reduces NLRP1 and NLRP3 in Alzheimer's disease cell and mouse models for neuroprotection and cognitive improvement

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Abstract

Amyloid β (A β) plays a major role in the pathogenesis of Alzheimer's disease (AD). The accumulation of misfolded A β causes oxidative and inflammatory damages that lead to apoptotic cell death. Traditional Chinese herbal medicine (CHM) has been widely used in treating neurodegenerative diseases by reducing oxidative stress and neuroinflammation. We examined the neuroprotective effect of formulated CHM Shaoyao Ganciao Tang (SG-Tang) in AD cell and mouse models. Conditioned medium with pro-inflammatory factors was prepared from interferon (IFN)- γ -activated HMC3 microglia to provide inflammatory damage. Neuronal phenotypes in inflammation-primed A β -GFP SH-SY5Y cells, and cognitive behaviors in streptozocin-induced hyperglycemic APP/PS1/Tau triple transgenic (3 \times Tg-AD) mice were evaluated to assess the anti-inflammatory and neuroprotective potentials of SG-Tang. Levels of nitric oxide (NO), tumor necrosis factor (TNF)- α , interleukin (IL)-1 β , and IL-6 were increased upon stimulation of HMC3 microglia with IFN- γ . In A β -GFP-expressing 293 and SH-SY5Y cells, SG-Tang reduced A β aggregation and reactive oxygen species (ROS) production, as well as improved neurite outgrowth. In A β -GFP SH-SY5Y cells primed with conditioned medium of IFN- γ -activated HMC3, SG-Tang suppressed expressions of inducible nitric oxide synthase (iNOS), NLR family pyrin domain containing 1 (NLRP1) and 3 (NLRP3), TNF- α , IL-1 β and IL-6, attenuated caspase 1 activity and ROS production, and promoted neurite outgrowth. In streptozocin-induced hyperglycemic 3 \times Tg-AD mice, SG-Tang also reduced expressions of NLRP1, NLRP3, A β and Tau in hippocampus and cortex, as well as improved working and spatial memories in Y maze and Morris water maze. Collectively, our results demonstrate the potential of SG-Tang in treating AD by moderating neuroinflammation.

Roles of ventral tegmental area, nucleus accumbens, and caudate-putamen in different types of environmental enrichment reducing methamphetamine-induced behavioral sensitization

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Abstract

Whether the ventral tegmental area (VTA), nucleus accumbens (NAc), and caudate-putamen (CPu) were involved in different environmental enrichment (EE) for the reduced effect of amphetamine-induced behavioral sensitization remains unclear. All mice were randomly assigned in the No EE/Saline, No EE/MAMPH, standard EE/MAMPH (STEE/MAMPH), physical EE/MAMPH (PEE/MAMPH), cognitive EE/MAMPH (CEE/MAMPH), and social EE/MAMPH (SEE/MAMPH) groups. The present results showed that MAMPH induced higher distance travelled and speed. Only, the STEE/MAMPH revealed a lower total distance travelled and speed compared to the No EE/MAMPH group. However, the other EE groups did not show the reduced effect for MAMPH-induced behavioral sensitization. The standard EE is the best one to reduce MAMPH-induced behavioral sensitization.

The spent time in center of the STEE/MAMPH group was not significant differences with that of the No EE/MAMPH group; the spent time in center of the PEE/MAMPH, CEE/MAMPH, and SEE/MAMPH groups were significantly lower than that of the No EE/MAMPH group, indicating that the PEE/MAMPH, CEE/MAMPH, and SEE/MAMPH groups showed anxiety behavior.

The c-Fos data showed that the STEE/MAMPH, PEE/MAMPH, and CEE/MAMPH groups were hypoactive in c-Fos expressions in the NAc, VTA, and CPu. However, the SEE/MAMPH did not show the reduced effect in c-Fos expression in any neural substrates. Interestingly, the STEE/MAMPH group was seemingly to be the lowest c-Fos expressions in the NAc, VTA, and CPu. The VTA, NAc, and CPu were involved in the reduced effect of behavioral sensitization. The findings will provide some insights for amphetamine addiction in clinical aspects.

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Keywords: environmental enrichment, behavioral sensitization, methamphetamine, ventral tegmental area, nucleus accumbens, caudate-putamen, mice.

Optogenetics photostimulations in the cingulate cortex, prelimbic cortex, or infralimbic cortex affect morphine-induced conditioned taste aversion in conditioning and extinction

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Abstract

Using optogenetic photostimulations excites the cingulate cortex area 1 (Cg1), the prelimbic cortex (PrL) or the infralimbic cortex (IL) to affect morphine-induced conditioned taste aversion (CTA) in conditioning and extinction remain unclear; moreover, following behavioral tests, the c-Fos expressions in the subareas of the medial prefrontal cortex (i.e., PrL, infralimbic cortex [IL], cingulate cortex 1 [Cg1]), basolateral amygdala (BLA), central amygdala (CeA), hippocampus (i.e., dentate gyrus [DG]), nucleus accumbens core (NAc core), nucleus accumbens shell (NAc shell), ventral tegmental area (VTA), and piriform cortex (Pir). During conditioning, excitation of the Cg1 glutamate neurons via optogenetic ChR2 excitatory photostimulations facilitated morphine-induced CTA during light on; the PrL optogenetic ChR2 excitatory photostimulations did not affect morphine-induced CTA; the IL optogenetic ChR2 excitatory photostimulations also facilitated morphine-induced CTA during light off. During extinction, only the PrL optogenetic ChR2 excitatory photostimulations disrupted morphine-induced CTA but the Cg1 and IL did not affect morphine-induced CTA. In the conditioning phase, when the Cg1 was excitation, the expression of c-Fos was hypoactive in the PrL, IL, NAc shell, CeA, but hyperactive in the BLA. When the IL was photostimulations, the Cg1, PrL, NAc core, NAc shell, BLA, and VTA were hypoactive in c-Fos expressions. In extinction, when the PrL glutamatergic neurons was hyperactive via optogenetic ChR2 photostimulations, the expression of c-Fos was hypoactive in the IL but hyperactive in the NAc core. The findings provide some implications for morphine addiction and dependence.

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Keywords: morphine, conditioned taste aversion, prelimbic cortex, infralimbic cortex, cingulate cortex, optogenetics

Does footshock-induced stress disrupt place conditioning learning induced by morphine in the animal model?

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Abstract

Stress might sensitize the brain dopamine reward system and facilitate abused drugs-induced conditioned place preference. In the clinical aspect, patients with drug addiction always suffer from stress in daily life and thereby induce a stronger reward resulting in a severe symptom of abused drugs. This present study focused on this issue that how footshock-induced stress affected conditioned place preference induced by morphine in animal model. During the beginning phase, rats were respectively assigned into no footshock and footshock treatments. The footshock treatment was given 3 mA for 10 seconds in the footshock box once a trial. Then, rats were given the treatment of conditioning for CPP with morphine injections to pair with a specific compartment of the CPP box for 30 min. The unpaired treatment with normal saline was with another compartment of the CPP box for 30 min. The paired-unpaired regimen was for 10 trials. Finally, the CPP test was performed for 10 min. The present results indicated that (a). morphine induced conditioned place aversion but not preference. (b). footshock decreased morphine-induced conditioned place aversion. Therefore, footshock-induced stress could reduce morphine-induced conditioned place aversion. The findings might offer some implications in drug addiction for clinical studies.

Keywords: morphine, stress, footshock, conditioned place preference/aversion, drug addiction

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Withdrawal effects of methamphetamine's reward and aversion: Tests of the paradoxical effects hypothesis of abused drugs

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Abstract

A growing body of data has shown that abused drugs such as amphetamine, morphine, and alcohol can simultaneously induce the paradoxical- reward and aversion. However, during the withdrawal phase, whether the paradoxical effect of abused drugs was changed or not remains unclear. The present study concerned this issue and tested it. In the beginning of experiments, all rats were assigned into the control and experiment groups. Rats in the experiment group were given a 0.1 % saccharin solution (conditioned stimulus, CS1) for 15 min and were then injected methamphetamine (1 mg/kg, served as US) to be conditioned taste aversion (CTA). Later, rats received another conditioned stimulus to expose the compartment (conditioned stimulus 2, CS2) of conditioned place preference (CPP) for 30 min to produce a CPP effect. After that, all rats were given no methamphetamine for seven days in the no drug phase. The withdrawal procedure was conducted later. The control and experimental rats were given CS1-saline injection-CS2 procedure. The results will be anticipated to show that the aversive effect of CTA was to drink a lot, but the rewarding effect of CPP was to decrease in the withdrawal phase. The data can provide some implications for drug addiction, particularly to the paradoxical effect of methamphetamine.

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Keywords: the paradoxical effect of abused drugs, conditioned taste aversion, conditioned place preference, the withdrawal phase, amphetamine, rats

Interactions between prelimbic cortex and basolateral amygdala contribute to morphine-induced conditioned taste aversion in conditioning and extinction

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Abstract

The consequences of exciting or destroying the prelimbic cortex (PrL) or the basolateral amygdala (BLA) remain unclear, including the effects on morphine-induced conditioned taste aversion (CTA) in the conditioning and extinction phases, plasma corticosterone (CORT) levels, and c-Fos/p-ERK expressions in the subareas of the medial prefrontal cortex (i.e., PrL, infralimbic cortex [IL], cingulate cortex 1 [Cg1]), basolateral amygdala (BLA), central amygdala (CeA), hippocampus (i.e., CA1, CA2, CA3, and dentate gyrus [DG]), nucleus accumbens (NAc), lateral hypothalamus (LH), and piriform cortex (PC). During conditioning, excitation of the PrL glutamate neurons via NMDA injections disrupted morphine-induced CTA and decreased plasma CORT levels; moreover, c-Fos and p-ERK expression was hyperactive in the PrL and IL but hypoactive in the Cg1 and BLA. In conditioning, excitation of the BLA glutamate neurons via NMDA injections facilitated morphine-induced CTA and increased plasma CORT levels. The expression of c-Fos and p-ERK was hypoactive in the PrL and IL but hyperactive in the BLA. During extinction, lesion of the PrL glutamate neurons via NMDA injections impaired morphine-induced CTA extinction and enhanced plasma CORT levels. The expression of c-Fos and p-ERK was hypoactive in the PrL and IL but hyperactive in the BLA. In extinction, excitation of the PrL glutamatergic neurons via NMDA injections facilitated morphine-induced CTA extinction and did not affect plasma CORT levels; moreover, the expression of c-Fos and p-ERK was hypoactive in the Cg1, PrL, and IL but hyperactive in the BLA. Altogether, the interaction between the PrL and BLA plays a balancing role in morphine-induced CTA conditioning and extinction. During conditioning, the activity of the PrL correlated negatively with plasma CORT secretions, whereas the activity of the BLA correlated positively with the plasma CORT levels. During extinction, the activity of the PrL correlated negatively with plasma CORT secretions; however, the activity of the BLA may be negatively associated with the plasma CORT levels. The data presented here provide some implications for morphine addiction and dependence.

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Keywords: morphine, conditioned taste aversion, prelimbic cortex, infralimbic cortex, cingulate cortex, basolateral amygdala

Does footshock-induced stress change morphine's reward in conditioned place preference and aversion in conditioned taste aversion: Reexamination of the paradoxical effect hypothesis of abused drugs?

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Abstract

The abused drugs can simultaneously induce the paradoxical effect-reward and aversion is an interesting issue in drug addiction. This study manipulated footshock-induced a severe stress like as post-traumatic stress disorder and then tested how the severe stress change morphine's aversion in conditioned taste aversion and reward in conditioned place preference. In the initial phase, all rats were placed in the home cage to habituate the environment of the home cage for at least 7 days. Later, rats were subjected to a footshock (3 mA, 10s) and they stayed the footshock box for 2 minutes. After three days, rats received a procedure of situational reminder without any footshock for 2 min in the footshock box. Only the last day of the situational reminder, the freezing behavior was measured for 2 minutes. After that, all rats were given the experimental procedure of conditioned taste aversion and then conditioned place preference for 10 days (including intermittent 5 day-paired and 5 day-unpaired days). Finally, rats were tested for 15 min on conditioned taste aversion and 15 min on conditioned place preference. The results showed that footshock stress was a significant effect and it was shown in freezing behavior in the situational reminder phase. The results showed that footshock disrupted morphine-induced conditioned taste aversion; meanwhile, it might facilitate conditioned place preference. The discrepancy of the present data was shown in reward and aversion induced by morphine. The findings should be discussed for the paradoxical effect hypothesis of abused drugs. These present evidence may provide some insights for morphine addiction.

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Keywords: Morphine, footshock, conditioned taste aversion, conditioned place preference, stress, the paradoxical effect hypothesis of abused drugs.