編號 No.	投稿學會 Society	研究領域 Topic	題目Title	投稿者 Name	作者 C0-Author	作者(Co-Author)	單位(Affliation)	關鍵字(Keywords)	poster number
20200727145917	無	基礎	A virtual reality system to analyze neural activity and behavior in adult zebrafish	Prof. 黃國華	黃國華	Kuo-Hua Huang1,2, Peter Rupprecht1, Thomas Frank1, Koichi Kawakami3, Tewis Bouwmeester4 and Rainer W. Friedrich1	1.Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland. 2.Institute of Molecular Biology, Academia Sinica, Taipei, Taiwan. 3.Laboratory of Molecular and Developmental Biology, National Institute of Genetics, and Department of Genetics, SOKENDAI, Mishima, Shizuoka, Japan. 4.Chemical Biology & Therapeutics, Novartis Institutes for Biomedical Research,Basel, Switzerland.	In vivo imaging,zebrafish,virtual reality,social behavior,	1
20200621035957	台灣基礎神經科學學會	基礎	Long-range GABAergic connections between the bilateral dentate gyrus support contextual memory	Prof. Cheng-Chang Lien	顏廷耘, Hannah Monyer, 連正章	Ting-Yun Yen, Hannah Monyer, Cheng-Chang Lien	Institute of Neuroscience, National Yang-Ming University	hippocampus,memory,inhibition,optogenetics,	2
20200720102022	台灣基礎神經科學學會	基礎	Hippocampal Mossy Cell Circuitry Mediates Anxiolytic Effects	Ms.Kai-Yi Wang	王凱誼、吳哲瑋、連正章	Kai-Yi Wang, Jei-Wei Wu and Cheng-Chang Lien	Institute of Neuroscience, National Yang-Ming University, Taipei, Taiwan	GABA,Dentate gyrus,Mossy cell,Anxiety,Chemogenetics	3
20200624124416	台灣基礎神經科學學會	基礎	Neuropeptide F suppresses memory decay for long-term memory formation in Drosophila	Mr. 馮冠霖	馮冠霖，翁儒韻，陳俊朝，林瑩文，艾柏木，連正章，江安世	Kuan-Lin Feng, Ju-Yun Weng, Chun-Chao Chen, Hsuan-Wen Lin, Mohammed Bin Abu Baker, Cheng-Chang Lien and Ann-Shyn Chiang	1 Institute of Biotechnology, National Tsing Hua University, Hsinchu, Taiwan 2 Brain Research Center, National Tsing Hua University, Hsinchu, Taiwan 3 Institute of Neuroscience, National Yang-Ming University, Taipei, Taiwan.	Drosophila,memory,neuropeptide,forgetting,	4
20200729213929	台灣基礎神經科學學會	基礎	The influence of living partners on the stress resistance and lifespan in Drosophila melanogaster	Ms. Shivangi Malviya	郭崇涵	Tsung Han Kuo		Behavior,Lifespan,Cohousing	5
20200727110756	台灣基礎神經科學學會	基礎	Examining the motor, emotional and cognitive abilities in the natural aging mice	Dr. Ying-Ling Shen	沈映伶、陳志成	Ying-Ling Shen, Chih-Cheng Chen	Taiwan Mouse Clinic, Biomedical Translational Research Center, Academia Sinica, Taipei, Taiwan. Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan.	Natural aging,motor,emotion,cognitive,mice	6
20200727191704	台灣基礎神經科學學會	基礎	Central agonism of short-chain fatty acids modulates social memory formation and social novelty seeking	Mr. Chia-Wei Liou	劉嘉瑋，吳偉立	Chia-Wei Liou1, Wei-Li Wu1,2,3*,	1Institute of Basic Medical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan 2Department of Physiology, College of Medicine, National Cheng Kung University, Tainan, Taiwan 3Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA, USA	social memory,gut-brain axis,short-chain fatty acids (SCFA),gut metabolites,Bed nucleus of stria terminalis (BNST)	7
20200727145257	台灣生物精神醫學暨神經精神藥理學會	臨床	Dysregulation of leptin and decision consistency in the corticostriatal circuitry in bipolar II disorder	Dr. 魏士郁		Shyh-Yuh Wei, Huai-Hsuan Tseng, Hui Hua Chang, Yen Kuang Yang, Po See Chen	Department of Psychiatry, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan	caudate,functional connectivity,Iowa gambling task,ventrolateral prefrontal cortex,	8
20200807123752	台灣生物精神醫學暨神經精神藥理學會	臨床	Neurofilament light chain as novel blood biomarker of disturbed neuroaxonal integrity in patients with ketamine dependence	Dr. 黃名琪	劉玉麗	Yu-Li Liu	Society:Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology	Ketamine,Addiction,Axons,Neurofilaments,Depression	9
20200623151243	台灣營養精神醫學研究學會	基礎	Investigation of Gastrodia elata Blume Water Extracts in Unpredictable Chronic Mild Stress (UCMS) induced Depression-Like Behavior and Cognition Impairment ApoE-/- Mice Model	Ms. Huai Syuan Huang	黃懷萱1，林毓恩1，裴尤德1，沈立言1,2,3	Huai Syuan Huang1, Yu En Lin1, Suraphan Panyod1, Lee Yan Sheen1,2,3*	1 Institute of Food Science and Technology, National Taiwan University, Taipei, Taiwan 2 Center for Food and Biomolecules, National Taiwan University, Taipei, Taiwan 3 National Center for Food Safety Education and Research, National Taiwan	depression,cognitive impairment,Gastrodia elata Blume water extract,unpredictable chronic mild stress,β-amyloid 42	10
20200729111249	台灣基礎神經科學學會	基礎	Treatment with an ENT1 inhibitor ameliorates neurodegeneration in two mouse models of Alzheimer's disease with distinct pathogenesis	Dr. Chien-Yu Lin	林建宇, 張敬邦, 陳惠美, 陳儀莊	Chien-Yu Lin, Ching-Pang Chang, Hui-Mei Chen, Yijuang Chern	Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan	Alzheimer's disease,neurodegeneration,adenosine,amyloid-β plaques,tau tangles	11

20200810155556	台灣基礎神經科學學會	基礎	Altered Nociception in Alzheimer's Disease is Associated with STEP Signaling	Mr. 李倧輔	李倧輔、陳世彬、鄭菡若	Zhung-Fu Lee1,2,3, Shih-Pin Chen2,3,4,5,6,*, Irene Hanjuo Cheng1,5,6,*	1 Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan 2 Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan. 3 Division of Translational Research, Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan. 4 Institute of Clinical Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan. 5 Brain Research Center, National Yang-Ming University, Taipei, Taiwan. 6 These authors contributed equally. * Corresponding author	Alzheimer's disease,pain,striatal-enriched protein tyrosine phosphatase,APP transgenic mouse	12
20200804190932	台灣基礎神經科學學會	基礎	Phosphatidylinositol-4-Phosphate 5-Kinase Type 1α Attenuates Aβ Production by Promoting Non-amyloidogenic Processing of Amyloid Precursor Protein	Mr. Po-Fan Wu		Po-Fan Wu, Noopur Bhore, Yen-Lurk Lee, Yun-Wen Chen, Pei-Yi Wu, Yi-Shuian Huang, Pei-Jung Lu, and Yung-Feng Liao	Institute of Cellular and Organismic Biology, Academia Sinica, Taipei, Taiwan	Alzheimer's disease,amyloid-β,PIP5K type Iα	13
20200730145918	無	基礎	Role of NADPH oxidase 2 in the BDNF dysregulation and memory deficits after systemic inflammation	Prof. Ya-Ping Chen	陳雅萍、林博淨、林聖光、劉科宏、陳亭羽、吳鴻明	Ya-Ping Chen, Po-Te Lin, Shankung Lin, Ko-Hung Liu, Ting-Yu Chen, Hung-Ming Wu	Laboratory Animal Center, Changhua Christian Hospital, Changhua, Taiwan	sepsis,neuroinflammation,lipopolysaccharide,cognition,brain-derived neurotrophic factor	14
20200809233439	台灣基礎神經科學學會	基礎	FKBP51 regulates anxiety susceptibility involving regulation of hippocampal neuroinflammation and GABA synthesis after transient peripheral inflammation	Ms. 甘育菱	甘育菱1, 王震宇1, 何榕恒1, 許珮蒨1,2, 宋品樺1, 葉信顥2,3, 鄭瓊娟2,4, 黃名琪5,6,7*, 李怡萱1,2*	Yu-Ling Gan1, Chen-Yu Wang1, Rong-Heng He1, Pei-Chien Hsu1,2, Ping-Hua Sung1, Skye Hsin-Hsien Yeh2,3, Chung-Jiuan Jeng2,4, Ming-Chyi Huang5,6,7*, Yi-Hsuan Lee1,2*	1Department and Institute of Physiology, National Yang-Ming University, Taipei, Taiwan 2Brain Research Center, National Yang-Ming University, Taipei, Taiwan 3Biophotonic and Molecular Imaging Research Center, National Yang Ming University, Taipei, Taiwan 4Department and Institute of Anatomy and Cell Biology, National Yang-Ming University, Taipei, Taiwan 5Department of Psychiatry, Taipei City Psychiatric Center, Taipei City Hospital, Taipei, Taiwan 6Deparmtent of Psychiatry, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan 7Psychiatric Research Center,Taipei Medical University Hospital	Neuroinflammation,Anxiety,GABA	15
20200810170335	台灣基礎神經科學學會	基礎	Efficient Generation of Functional Microglia-like Cells from Human Induced Pluripotent Stem Cells by Defined Transcription Factors	Mr. 是瑋 陳	陳是瑋、范明基、翁雨蕙	Shih-Wei Chen, Ming-Ji Fann, Yu-Hui Wong	Brain Research Center, National Yang-Ming University, Taipei, Taiwan Department of Life Sciences and Institute of Genome Sciences, National Yang-Ming University, Taipei, Taiwan	iPSC,microglia,reprogramming,disease modeling	16
20200810233145	台灣神經罕見疾病學會	基礎	Impairment of Proteasome and Autophagy Leads to Ubiquitin and P62 Aggregates Underlying the Pathogenesis of Globoid Cell Leukodystrophy	Dr. Dar-Shong Lin	1: 林達雄 2: 何啟生 3: 蔣明富	Dar-Shong Lin, Che-Sheng Ho, Ming-Fu Chiang	1Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan 2 Department of Medicine and Institute of Biomedical Sciences, Mackay Medical College, New Taipei, Taiwan 3 Department of Pediatric Neurology, Mackay Memorial Hospital, Taipei, Taiwan 4 Department of Neurosurgery, Mackay Memorial Hospital, Taipei, Taiwan	AUtophagy,Proteasome,Ubiquitin,SQTM1/p62,Leukodystrophy	17
20200702135419	台灣基礎神經科學學會	基礎	Epigenetic regulation of WNT3A enhancer during regeneration of injured cortical neurons	Mr. Min-Zong Liang		Min-Zong Liang, Chu-Yuan Chang, Jui-Hung Hung, Ching-Chih Wu, Pei-Yuan Huang, Liang-Wei Huang, Linyi Chen	Institute of Molecular Medicine, National Tsing Hua University	Neuronal regeneraion,Traumatic brain injury,Enhancer regulation,WNT3A,	18
20200730204751	無	工程	Synthesis of Positron Emission Tomography Images through Deep Learning	Mr. 高家祥	高家祥、李瑋淇、陳麗芬	Chia-Hsiang Kao, Wei-Chi Li, Li-Fen Chen	National Yang-Ming University	Deep learning,Image synthesis,Synthesis of Positron Emission Tomography Images	19

20200806164942	中華民國生物醫學工程學會	工程	Development of High-resolution Multiple-contrast MRI for Imaging Postmortem Fetal Brain at 3T	Dr. Sheng-Min Huang		Sheng-Min Huang, Kuan-Hung Cho, Koping Chang, Pei-Hsin Huang, and Li-Wei Kuo	Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes Department of Pathology, National Taiwan University Hospital Graduate Institute of Pathology, National Taiwan University College of Medicine	ex-vivo fetal brain MRI,high resolution,multiple contrast	20
20200810174611	台灣認知神經科學學會	認知	Intrinsic cross frequencies coupling oscillation revealed with Holo-Hilbert spectral analysis in human	Mr. 陳彥勳	陳彥勳, 梁偉光, 阮啟弘	Yen-Hsun Chen, Wei-Kuang Liang, Chi-Hung Juan	1 Institute of Cognitive Neuroscience, National Central University, Jhongli, Taiwan 2 Cognitive Intelligence and Precision Healthcare Center, National Central University, Taiwan 3 Department of Psychology, Kaohsiung Medical University, Taiwan	individual intrinsic frequency,cross frequencies coupling,resting state electroencephalography (EEG),Holo-Hilbert spectral analysis,	21
20200810094604	台灣認知神經科學學會	認知	Motor inhibitory control as a function of grip force and its electrophysiological dynamics were revealed with Holo-Hilbert Spectrum Analysis	Mr. Trung Van Nguyen		Trung Van Nguyen1, Che-Yi Hsu1, Satish Jaiswal1, Neil G. Muggleton1-4, Norden E. Huang2,5, Wei-Kuang Liang1,2, Chi-Hung Juan1,2,6*	1Institute of Cognitive Neuroscience, National Central University, Taiwan; 2 Cognitive Intelligence and Precision Healthcare Center, National Central University, Taiwan; 3 Institute of Cognitive Neuroscience, University College London, London, UK; 4 Department of Psychology, Goldsmiths, University of London, London, UK; 5 Key Laboratory of Data Analysis and Applications, First Institute of Oceanography, SOA, 266061 Qingdao, China. 6 Department of Psychology, Kaohsiung Medical University, Taiwan;	selective stop signal task,ERM,force,inhibitory control,Holo-Hilbert Spectrum Analysis	22
20200809192713	台灣認知神經科學學會	認知	Musicians and non-musicians' dissonance/consonance perception: separate and joint analyses of event-related potential (ERP) and functional Magnetic Resonance Imaging (fMRI) experiments of the same design	Mr. Han Jo		HanShin Jo, Tsung-Hao Hsieh, Wei-Che Chien, Fu-Zen Shaw, Chun-Chia Kung, Sheng-Fu Liang	National Cheng Kung University (NCKU), Tainan, Taiwan	ERPs,fMRI,Consonance/Dissonance,Roughness,Musician	23
20200808224635	台灣認知神經科學學會	認知	Over- and underreaction in detecting regime shifts and the neurocomputational substrates for estimating probability of change	Ms. Muchen Wang		Mu-Chen Wang1, George Wu,2 Shih-Wei Wu1,3	[1] Institute of Neuroscience, National Yang-Ming University, Taiwan [2] University of Chicago Booth School of Business, USA [3] Brain Research Center, National Yang-Ming University, Taiwan	probability estimation,regime shift,judgment and decision making,,parietal cortex,ventromedial prefrontal cortex	24
20200810145850	台灣認知神經科學學會	認知	Interactive effects of timescale and formant frequency on frequency-sweep elicited mismatch negativity: an electroencephalography study	Prof. I-Hui Hsieh	葉菀婷、謝宜蕙	Wan-Ting Yeh and I-Hui Hsieh	Institute of Cognitive Neuroscience, National Central University	frequency sweep,mismatch negativity,timescale,speech encoding	25
20200805141238	台灣認知神經科學學會	認知	Collaboration and deception in strategic interaction: an fMRI hypercanning study	Ms. 沈珊筏		Siao-Shan Shen, Yi-Ren Hsu, Jen-Tang Cheng, Yi-Cing Chang, Ming-Hung Weng, Der-Yow Chen, Chun-Chia Kung	Department of Psychology, National Cheng Kung Univeersity	fMRI,social interaction,decision making,deception,Psychophysiological Interaction	26
20200810214609	台灣認知神經科學學會	認知	Past and current subjective-value signals in the human orbitofrontal cortex (OFC): A stereo-electroencephalography (sEEG) study	Ms. Wan-Yu Shih		Wan-Yu Shih, Shih-Wei Wu	Institute of Neuroscience, National Yang-Ming University, Taipei, Taiwan	decision-making,value representation,orbitofrontal cortex (OFC),stereo-electroencephalography (sEEG)	27
20200729125631	台灣認知神經科學學會	認知	The role of information lifespan and rate of information flow on decision making	Ms. 劉宜儒	劉宜儒 吳仕煒	Yi-Ju Liu Shih-Wei Wu	[1] Institute of Neuroscience, National Yang-Ming University, Taipei, Taiwan [2] Brain Research Center, National Yang-Ming University, Taiwan	decision making,opportunity cost,reaction time,cost-benefit tradeoff,leaky integration	28
20200728092736	台灣認知神經科學學會	認知	High gamma activity in the human prefrontal and insular cortices represent monetary gains and losses during decision making	Ms. Siao-Jhen Wu	吳孝真，吳仕煒	Siao-Jhen Wu, Shih-Wei Wu	Institute of Neuroscience, National Yang-Ming University	Decision making,Frontal cortex,Intracranial recordings,,	29

20200730094101	台灣認知神經科學學會	認知	Individual difference in social interaction pattern modulated brain activities in STS, insula, and cingulate cortex during coordination task	Ms. 張宜晴		Yi-Cing Chang, Chien-Hsin Cheng, Yi-Ren Hsu, Jen-Tang Cheng, Ming-Hung Weng, Chun-Chia Kung, Der-Yow Chen*	Department of Psychology, National Cheng Kung University	fMRI,Social interaction,coordination task,communication,decision making	30
20200810161245	台灣認知神經科學學會	認知	Brain Activity in Processing Static and Dynamic Facial Expressions	Ms. Sin-Rong Sie	謝幸融，黃世琤	Sing-Rong Sie, Shih-tseng Tina Huang	Department of Psychology, National Chung-Cheng University Center for research in Cognitive Science, National Chung-Cheng University, Taiwan	Facial Expression,Dynamic,Emotion	31
20200730211829	台灣認知神經科學學會	認知	Self-awareness impacts individual variations in perceiving appetitive cues	Ms. Tzu-Jou Avery Yang	楊子柔, 呂至穎, 陳品豪	Tzu-Jou Avery Yang, Chih-Yin Esther Lu, Pin-Hao Andy Chen	Department of Psychology, National Taiwan University	fMRI,Self-control,Food cue reactivity,Self awareness,IS-RSA	32
20200727100339	台灣生物精神醫學暨神經精神藥理學會	臨床	Combined Plasma CCL11 and Cotinine Levels to Predict Alcohol Dependence	Prof. Yu-Li Liu	劉玉麗*1, 黃名琪 2,3, 鍾仁華 4, 鄒小蕙 4,5, 劉膣夏 1, 陳雅筠 1, 郭湘維 1, 劉淑芝 1	Yu-Li Liu*1, Ming-Chyi Huang 2,3, Ren-Hua Chung 4, Hsiao-Hui Tsou 4,5, Tung-Hsia Liu 1, Ya-Yun Chen 1, Hsiang-Wei Kuo 1, Shu Chih Liu 1	1 Center for Neuropsychiatric Research, National Health Research Institutes, Zhunan, Miaoli County, Taiwan 2 Department of Psychiatry, Taipei City Psychiatric Center, Taipei City Hospital, Taipei, Taiwan 3 Department of Psychiatry, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan 4 Division of Biostatistics and Bioinformatics, Institute of Population Health Sciences, National Health Research Institutes, Miaoli County, Taiwan 5 Graduate Institute of Biostatistics, China Medical University, Taichung, Taiwan	Alcohol dependent,CCL11,Eotaxin-1,Beck Anxiety Inventory (BAI),Severity of Alcohol Dependence Questionnaire (SADQ)	33
20200809081100	台灣基礎神經科學學會	臨床	The gain-loss frequency and long-term outcome reassessed in the Soochow gambling task: Evidence from an internet addiction cases/internet gaming disorder cases study	Dr. Chao-Chih Wang		Chao-Chih Wang1,2, Ching-Jen Lin3, Chih-Hung Ko4,5, Yao-Chu Chiu6*, Ching-Hung Lin7,8*	1School of Education Science, Huizhou University, China 2Research Center for Education and Mind Sciences, National Tsing Hua University, Taiwan 3Department of Psychology, Kaohsiung Medical University, Kaohsiung, Taiwan 4Department of Psychiatry, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan 5Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan 6Department of Psychology, Soochow University, Taipei, Taiwan 7Department of Psychology, Kaohsiung Medical University, Kaohsiung, Taiwan 8Research Center for Nonlinear Analysis and Optimization, Kaohsiung Medical University, Kaohsiung, Taiwan	internet addiction,internet gaming disorder,expected value,gain–loss frequency,decision-making	34
20200728114540	台灣神經罕見疾病學會	基礎	Characterization of Dlgap2 mutant, a mouse model of autism spectrum disorder	Prof. Li-Jen Lee		Ming-Yen Hsieh, Ho-Ching Chang, Susan Shur-Fen Gau, Li-Jen Lee	Graduate Institute of Anatomy and Cell Biology, National Taiwan University, Taipei, Taiwan. Department of Psychiatry, National Taiwan University Hospital, Taipei, Taiwan. Institute of Brain and Mind Sciences, National Taiwan University, Taipei, Taiwan. Neurobiology and Cognitive Science Center, National Taiwan University, Taipei, Taiwan	autism,gene knockout,hippocampus,memory	35

20200718085115	台灣神經罕見疾病學會	基礎	Vacuolar ATPase Subunit Gene ATP6V1B2 Variation Causes Complex Brain Malformation and Hearing Impairment.	Dr. 蔡孟翰	蔡孟翰, 郭廷翰, 高毓佳, 張瑛昭, 黃兆祺	Meng-Han Tsai1,2*, Kuo Ting-Han3,Yu-Chia Kao4, Ying-Chao Chang5, Eric Hwang3,6,7*	1 Department of Neurology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan 2 School of Medicine, Chang Gung University, Taoyuan, Taiwan 3 Department of Biological Science and Technology, National Chiao Tung University, Hsinchu, Taiwan 4 Department of Pediatrics, E-Da Hospital, Kaohsiung, Taiwan 5 Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan 6 Institute of Molecular Medicine and Bioengineering, National Chiao Tung University, Hsinchu, Taiwan 7 Institute of Bioinformatics and Systems Biology, National Chiao Tung University, Hsinchu, Taiwan	ATP6V1B2,Brain Malformation,Vacuolar ATPase,Hearing Impairment,Intellectual Disability	36
20200729112932	台灣神經罕見疾病學會	基礎	Astrocytic Epm2a / laforin deficiency disrupts perineuronal astrocyte processes and synaptic integrity in Lafora disease animal and cell models	Dr. Chia-Chi Hung	1.洪家琪 2.李怡萱	1.Chia-Chi Hung 2.Yi-Hsuan Lee	1. Department and Institute of Physiology, National Yang-Ming University, Taipei, Taiwan 2. Brain Research Center, National Yang-Ming University, Taipei, Taiwan	Lafora disease (LD),Epm2a,Laforin,Glia-neuron mix culture,Glutamate homeostasis	37
20200728165717	台灣神經罕見疾病學會	基礎	Study on the function of phosphorylated paxillin at serine 119 in the developing brain	Ms. Chen Chen	陳蓁, 朱葭, 梁書暘, 鄭珮琳	Chen Chen, Ying Chu, Shu-Yang Liang, and Pei-Lin Cheng	Institute of Molecular Biology, Academia Sinica, Taiwan Institute of Neuroscience, National Yang-Ming University, Taiwan	paxillin,nucleus,genetic regulation,brain development	38
20200809145449	台灣神經罕見疾病學會	基礎	Efficient in Utero Gene Transfer to the Mammalian Inner Ears by the Synthetic Adeno-Associated Viral Vector Anc80L65	Ms. Yi-Hsiu Tsai		Yi-Hsiu Tsai1, Chin-Ju Hu2, Ying-Chang Lu2,3, Haw-Yuan Cheng3, Hiroki Takeda4, Chun-Ying Huang2, Ru Xiao5, Chuan-Jen Hsu8, Jin-Wu Tsai1,9, Luk H. Vandenberghe5,6, Chen-Chi Wu1,7, and Yen-Fu Cheng2,3,10,11	1 Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan 2 Department of Otolaryngology, National Taiwan University Hospital, Taipei, Taiwan 3 Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan 4Department of Otolaryngology-Head and Neck Surgery, Kumamoto University Graduate School of Medicine, Kumamoto City, Japan 5Grousbeck Gene Therapy Center, Schepens Eye Research Institute and Massachusetts Eye and Ear, Boston, MA, USA 6Department of Ophthalmology, Harvard Medical School, Boston, MA, USA 7Department of Medical Research, National Taiwan University Hospital Biomedical Park Hospital, Hsinchu, Taiwan 8Department of Otolaryngology, Taichung Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Taichung, Taiwan 9Brain Research Center, National Yang-	in utero microinjection,AAV2/Anc80L65,inner ears,gene therapy,hereditary deafness	39

20200727154122	台灣神經罕見疾病學會	基礎	Growth hormone rescue cerebellar degeneration in SCA3 transgenic mice	Mrs. Wen-Ling Cheng		Wen-Ling Cheng1, Shey-Lin Wu2, Ko-Hung Liu2, Shih-Li Su4,5, Yong-Shiou Lin2, Ta-Tsung Lin2, Yu-Shan Cheng2, Jui-Chih Chang2, Yu-Ling Wu2, Chin-San Liu1,2,3*	1 Vascular and Genomic Center, Changhua Christian Hospital, Changhua, Taiwan 2 Department of Neurology, Changhua Christian Hospital, Changhua, Taiwan 3Graduate Institute of Integrated Medicine College of Chinese Medicine, China Medical University, Taichung, Taiwan 4Division of Endocrinology and Metabolism, Department of Internal Medicine, Diabetes Education Center, Changhua Christian Hospital, Changhua, Taiwan 5Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan	Spinocerebellar ataxia type 3,Growth hormone,locomotor functions,Purkinje cells,DNA oxidative	40
20200729080019	台灣神經罕見疾病學會	基礎	Curcumin Analog JM17 Enhance the Degradation of Poly-Q Aggregation in cell Models of Spinocerebellar Ataxia-3	Dr. Yu-Ling Wu		Yu-Ling Wu1, Jui-Chih Chang1, Hardy Chan3, Chin-San Liu2	1 Vascular and Genomic Research Center, Changhua Christian Hospital, Changhua, Taiwan 2 Department of Neurology and Vascular and Genomic Research Center, Changhua Christian Hospital, Changhua, Taiwan 3 Allianz Pharmascience Limited, Taipei, Taiwan	Oxidative stress,mutant ataxin-3,mitochondrial respiratory function,JM17,Nrf2	41
20200810220301	台灣神經罕見疾病學會	基礎	From peptide probes to therapeutic peptides for neurodegenerative diseases	Dr. Jen-Tse Huang		Jen-Tse Huang	Institute of Chemistry, Academia Sinica, Taiwan	peptide drug,Huntington's disease,neuron degeneration,Amyotrophic Lateral Sclerosis	42
20200810154323	台灣神經罕見疾病學會	基礎	Development of small molecule agonists targeting TRKB for Alzheimer's disease treatment: virtual screening, molecular modeling and Tau/A cellular models	Ms. Te Hsien Lin		Te-Hsien Lin, Ya-Jen Chiu, Ying-Chieh Sun, Guey-Jen Lee-Chen	National Taiwan Normal University	Alzheimer's disease,TRKB,tau,molecular modeling,SPR	43
20200730092947	台灣神經罕見疾病學會	臨床	Functional Characterization of PIAS1 Gene Variants in Huntington's Disease	Ms. Yan-Hua Lee	李晏嫻, 蔡毓舜, 張哲菖, 何俊成, 陳惠美, 賴幸琳, 李宜中, 楊永正, 宋秉文, 鄭子豪, 陳儀莊	Yan-Hua Lee, Yu-Shuen Tsai, Che-Chang Chang, Chun-Chen Ho, Hui-Mei Chen, Hsing-Lin Lai, Yi-Chung Lee, Ueng-Cheng Yang, Bing-Wen Soong, Tzu-Hao Cheng, Yijuang Chern	Institute of Biomedical Sciences, Academia Sinica	Huntington's Disease,PIAS1,SUMOylation	44
20200730153054	台灣神經罕見疾病學會	基礎	The Protective Role of the Translin Associated Factor X (TRAX) in Huntington's Disease (HD)	Ms. Yu-Ting Weng	翁于婷, 陳惠美, 簡莛和陳儀莊	Yu-Ting Weng, Hui-Mei Chen, Ting Chien and Yijuang Chern	1Program in Molecular Medicine, National Yang-Ming University and Academia Sinica, Taipei, Taiwan. 2 Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan,	Translin Associated Factor X (TRAX),Huntington's Disease (HD),Gene regulation	45
20200730141637	台灣神經罕見疾病學會	基礎	Treadmill training increases the motor activity and neuron survival of the cerebellum in a mouse model of spinocerebellar ataxia type 1	Mr. Yi Chun Chao		Yi-Chun Chao1, Chieh-Sen Chuang1,2, Jui-Chih Chang1, Chin-San Liu1,2	1 Vascular and Genomic Center, Changhua Christian Hospital, Changhua, Taiwan 2 Department of Neurology, Changhua Christian Hospital, Changhua, Taiwan	neuronal Per Arnt Sim domain protein 4,Purkinje neurons,ribosomal protein S6,Spinocerebellar ataxia type 1,treadmill training	46
20200727150604	台灣神經罕見疾病學會	基礎	Insulin-like growth factor-1 (IGF-1) as a potential therapy for the spinal cerebellar ataxia type III	Ms. Yong-Shiou Lin		Yong-Shiou Lin Wen-Ling Cheng Chin-San Liu	Vascular and Genomic Research Center, Changhua Christian Hospital, Changhua, Taiwan	Insulin-like growth factor-1,spinal cerebellar ataxia type III,locomotor function,mitochondria	47
20200731114404	台灣神經罕見疾病學會	基礎	ERK activation precedes Purkinje cell loss in mice with Spinocerebellar ataxia type 17	Dr. Chia Wei Lin	林佳薇, 鍾妤涵, 范家豪, 張雅津, 謝秀梅	Chia-Wei Lin, Yu-Han Chung, Chia-Hao Fan, Ya-Chin Chang, Hsiu Mei Hsieh-Li	Department of Life Science, National Taiwan Normal University Department of Pharmacy, Taiwan Adventist Hospital	Spinocerebellar ataxia,ERK,gliosis,neurodegeneration,apoptosis	48
20200730145033	台灣神經罕見疾病學會	基礎	AMPK activation disrupts the nuclear import pathway in motor neurons and contributes to amyotrophic lateral sclerosis	Mr. Liu Yuju		Yu-Ju Liu, Hung-Chih Kuo, and Yijuang Chern	Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan	ALS,motor neuron,nuclear	49
20200804100748	無	臨床	Association of visual motor coordination and social cognition in schizophrenia	Dr. Pin-Yen Lu		Pin-Yen Lu, Yu-Lien Huang, Pai-Chuan Huang, Yi-Chia Liu, Shyh-Yuh Wei, Wei-Yun Hsu, Kao Chin Chen, Po See Chen, Huai-Hsuan Tseng	Jianan Psychiatric Center, Ministry of Health and Welfare, Tainan, Taiwan	schizophrenia,nonverbal emotion recognition,visual motor coordination,mentalization,social cognition	50

投稿學會：無	編號:1

A virtual reality system to analyze neural activity and behavior in adult zebrafish

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Abstract

Virtual realities are powerful tools to analyze and manipulate interactions between animals and their environment and to enable measurements of neuronal activity during behavior. In many species, however, optical access to the brain and/or the behavioral repertoire are limited. We developed a high-resolution virtual reality for head-restrained adult zebrafish, which exhibit cognitive behaviors not shown by larvae. We noninvasively measured activity throughout the dorsal telencephalon by multiphoton calcium imaging. Fish in the virtual reality showed regular swimming patterns and were attracted to animations of conspecifics. Manipulations of visuo-motor feedback revealed neurons that responded selectively to the mismatch between the expected and the actual visual consequences of motor output. Such error signals were prominent in multiple telencephalic areas, consistent with models of predictive processing. A virtual reality system for adult zebrafish therefore provides opportunities to analyze neuronal processing mechanisms underlying higher brain functions including decision making, associative learning, and social interactions.

投稿學會：台灣基礎神經科學學會 | 編號:2

Long-range GABAergic connections between the bilateral dentate gyrus support contextual memory

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Abstract

Contextual memory storage and recall are closely related to the activities of neuronal memory ensembles within the dentate gyrus (DG) of the hippocampus. Cortical glutamatergic input drives the formation of neuronal memory ensembles, whereas local GABAergic inhibitory interneurons (INs) constrain their size. A subset of GABAergic cells mediates long-distance inhibition between the DG. However, their function at the cellular and behavioral levels has remained enigmatic. Using a combination of electrophysiological and optogenetic approaches, we show that somatostatin-expressing contralateral-DG-projecting (SOM^+ cDG) neurons preferentially engage dendrite-targeting INs over principal cells. Single-unit recording from freely moving mice reveals that optogenetic stimulation of SOM^+ cDG-projections modulates the activities of GABAergic INs and principal cells over multiple timescales. Importantly, we demonstrate that optogenetic silencing of SOM^+ cDG-projections during contextual fear conditioning results in compromised DG-dependent memory tasks. Moreover, optogenetic stimulation of SOM^+ cDG-projections after encoding is sufficient to disrupt contextual memory recall. Collectively, our finding reveals that long-range-projecting GABAergic neurons mediate inhibition in the DG and are essential for learning and memory.

投稿學會：台灣基礎神經科學學會 | 編號:3

Hippocampal Mossy Cell Circuitry Mediates Anxiolytic Effects

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Abstract

Anxiety disorders have been associated with reduced γ-aminobutyric acid (GABA)-mediated inhibition and altered neuronal activity in hippocampal circuits. Glutamatergic mossy cells (MCs) of the dentate gyrus (DG) are known to recruit inhibitory GABAergic neurons. Loss of MCs causes DG granule cell (GC) hyperexcitability and increased anxiety-like behavior. However, the causal link between MC activity and the anxious state has not yet been addressed. Here, using calcium imaging in freely moving mice, we found that MC activity increased while mice explored anxiogenic environments. Consistently, selective chemogenetic enhancement of MC activity reduced a variety of avoidance behaviors. *In vivo* juxtacellular recordings showed that MC spiking preferentially recruited local-circuit GABAergic neurons and thereby suppressed GCs and hippocampal CA1 pyramidal neurons. Finally, we showed that enhancing MC activity reduced comorbid anxiety-like behaviors in chronic pain. Our results indicate an active role of MCs in suppressing anxiety, and suggest that targeting MCs may be a novel therapeutic strategy for anxiety disorders.

Keywords: GABA, dentate gyrus, mossy cell, anxiety, avoidance, chemogenetics

投稿學會：台灣基礎神經科學學會 | 編號:4

Neuropeptide F suppresses memory decay for long-term memory formation in *Drosophila*

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Abstract

After acquiring new information as memory, it starts undergo a decaying process. Attenuating the memory decay during consolidation phase could be one of essential mechanisms for long-term memory (LTM) formation. Whether and how memory decay process is regulated as to form LTM remains largely unknown. Here, we found that a subset of memory decay-promoting dopaminergic neurons (DANs) in the PPL1 regions are suppressed by neuropeptide F after 10x spaced training which forms LTM. And the inhibitory NPF signals to PPL1-DANs during consolidation phase is essential for LTM formation. We further show that the NPF is released from DAL2, a pair of newly characterized peptitergic neurons which suppresses the activities of PPL1-DANs after photo-activation. Remarkably, overexpressing NPF or enhancing excitability in DAL2 neurons was sufficient to form LTM after one single training session which normally could not. Therefore, NPF from DAL2 neurons acts to suppress memory decay during consolidation and thus allows LTM formation.

投稿學會：台灣基礎神經科學學會 | 編號:5

The influence of living partners on the stress resistance and lifespan in *Drosophila melanogaster*

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Abstract

Aging society and elderly population are growing rapidly worldwide. How to increase lifespan or the quality of long lifespan have become an important question in life science field in recent years. With different types of factors evolving its way into the daily life, studies have confirmed that multiple factors like mating, diet, stress, genetic distance and others could affect our health and lifespan. Research has applied different model organisms (fruit fly, mice, and nematodes) to explore the mechanism behind aging and the ways to extend lifespan. Fruit fly, *Drosophila melanogaster,* has many unique characteristics, including short life cycle and powerful genetic tools, which make it an ideal organism for the study of aging mechanisms. Research explores the influence of social partners on aging process. Whether exposure to different strains or different species could change lifespan of fly? What are the common characteristics existing among the affected strains or species, and what mechanisms are behind the modulation? Answering these questions may help in elucidating the primary physiological systems involved in aging and lifespan determination.

投稿學會：台灣基礎神經科學學會 | 編號:6

Examining the motor, emotional and cognitive abilities in the natural aging mice

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Abstract

Mice are widely used to model the aging and aged-related disorders in humans due to their similarities of humans. For example, the transgenic Tg4510 mice were used to model the Taupathy of the Alzheimer's disease and these animals showed the motor disabilities and cognitive dysfunctions ranging from 2.5 to 6 months of age. However, the physiological and neural changes along the natural aging are still lacking. Mice are defined as natural aging when they reach 18 months and are used in the present study to examine their motor, emotional, and cognitive changes in the open field test and Morris Water Maze. The aged group traveled less than their control company in the open field test, and the motor decline was also seen in the later Morris Water Maze. The aged group demonstrated more anxious behavioral expression that they avoid entering the central area, while they spent similar time in the outer area as the control group in the open field test. For the spatial learning in the Morris Water Maze, the aged group needed more time to find the target platform during the 4-day acquisition phase, but their memory performance was not different from the control group in probe test and two weekly retrieval tests. In the subsequent reversal learning, the control and aged groups performed similarly in the acquisition and memory test. Together, the natural aging mice showed the motor decline and more anxious emotions when they reached 18-month. However, they may slow the spatial learning, but their memory performance, retrieval, and strategy shift were not affected at this age. These evidences implied that the motor and emotional changes may occur before the cognitive dysfunctions along the process of natural aging.

投稿學會：台灣基礎神經科學學會 | 編號:7

Central agonism of short-chain fatty acids modulates social memory formation and social novelty seeking

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Abstract

Memorizing the conspecifics' features is a fundamental neural function crucial for gregarious animals to recognize and differentiate diverse individuals while living as a group. Clinical studies showed that altered gut microbiota compositions in people with autism spectrum disorder (ASD) and Alzheimer's disease (AD) which are convergently characterized by social memory impairment. The gut-brain axis is a bidirectional connection between brain and gastrointestinal (GI) tract that allows the gut microbiota-mediated signals could be delivered through various pathways to modulate brain functions, e.g., immune system, neuronal transmission, hormones and metabolites secretions. Short-chain fatty acids (SCFA) are the metabolites from bacteria-mediated dietary fibre fermentation and the major components are acetate, butyrate and propionate. Animal studies demonstrated that administration of butyrate rescued memory loss in AD model. On the other hand, intracerebroventricular (ICV) injection of propionate caused social deficit in rats. Thus, the role of SCFA on social memory and social recognition remain elusive. Herein, we injected SCFA cocktail to lateral ventricle during social memory test in the acquisition phase in microbiota-depleted mice. We found that infusion of SCFA reinforced social memory by decrease the exploration time on the stimulus mouse when presented the same stimulus mouse compared to mice infused with vehicle. Interestingly, mice injected with vehicle displayed a robust novelty exploration when presented a stranger stimulus mouse while this social novelty seeking behavior is disrupted in mice injected with SCFA. Our findings suggest that SCFA in the brain could reinforce social memory formation and disrupt social novelty seeking. These data suggest that SCFA might have multifaceted effects in the modulation of mouse behavior through different neural circuits.

投稿學會：臺灣生物精神醫學暨神經精神藥理學學會 | 編號:8

Dysregulation of leptin and decision consistency in the corticostriatal circuitry in bipolar II disorder

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Abstract

Leptin suppresses the dopaminergic neurons and rewarding efffects in animal studies, and may have a potential inflammatory role in bipolar disorder (BD). Furthermore, emotional regulation may modulate dietary decision-making via the corticostriatal circuitry; however, how leptin involves in these systems remains unclear. Our recent study found that BD II patients, in comparison to healthy controls, exhibited significantly lower functional connectivity (FC) between the dorsal caudate (DC) and the executive control network as well as the emotion regulation circuitry. Here we aimed to investigate whether such altered corticostriatal connectivity was associated with the leptin and decision-making in BD II.

Twenty-five BD II patients, as defined by the DSM-V, and 29 were enrolled in this study. The blood sample was taken for the measurement of leptin. The Iowa gambling task was conducted with four decks of different reward schedules, while the score of decision consistency was defined by the Explore-Exploit model. Brain network FC was measured during the resting-state using functional magnetic resonance imaging, and the DC was selected as the seed region. Only observed in healthy controls, the DC-ventrolateral prefrontal cortex FC was negatively correlated with the leptin level and decision consistency.

Our findings suggested that the modulation of leptin and decision consistency were perturbed in BD II, and such dysregulation may be resulted from the hypo-FC in emotion regulation circuitry. These results implied a maladaptive neuroplasticity in BD II and supported a potential role of leptin in inflammatory and metabolic disease in BD II.

投稿學會：臺灣生物精神醫學暨神經精神藥理學學會 | 編號:9

Neurofilament light chain as novel blood biomarker of disturbed neuroaxonal integrity in patients with ketamine dependence

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Abstract

Background: Chronic and heavy ketamine use has been associated with persistent neurocognitive impairment and structural brain abnormalities. However, the potential neurotoxicity of non-medical ketamine use remains poorly understood. Neurofilaments, cytoskeletal proteins exclusively expressed in neurons, are released into the extracellular space upon several forms of brain injury. Accordingly, neurofilament light chain (NFL) concentration in the blood was recently proposed as a measure of axonal integrity in several neuropsychiatric disorders. Aim of the study, was therefore, the assessment of blood NFL-levels in ketamine-dependent patients and healthy controls in order to characterize the axonal neurotoxicity of chronic ketamine use and its relationship to relevant clinical outcomes.

Methods: We enrolled 65 treatment-seeking ketamine-dependent patients (55 males and 10 females) and 60 healthy controls (51 males and 9 females). Blood NFL levels assessed by single molecule array (SiMoA) immunoassay. The NFL levels were compared between groups and regression analyses was used to identify clinical variables related to NFL levels.

Results: Ketamine-dependent patients had significantly higher NFL levels compared to controls ($p<.001$). A multivariate regression showed that age ($p<.05$) and lifetime history of major depressive disorder (MDD) ($p<.01$) predicted high NFL blood levels in patients. Subsequent group comparisons showed that specifically ketamine-dependent patients with a lifetime history of MDD had significantly increased NFL levels than those without ($p<.05$).

Conclusion: These results suggest substantial neuroaxonal alterations following chronic and heavy ketamine use. The pronounced increase of NFL levels in the MDD subgroup warrants further investigation of a potential neuroaxonal vulnerability of depressed patients to ketamine.

投稿學會：台灣營養精神醫學研究學會 | 編號:10

Investigation of *Gastrodia elata* Blume Water Extracts on Brain-Gut Axis in Unpredictable Chronic Mild Stress (UCMS) induced Depression-like Behavior and Cognition Impairment ApoE$^{-/-}$ Mice Model

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Abstract

The brain is the most important and complicated organ. Brain diseases include physiological and psychological problems. According to the World Health Organization report, depression will be the number one of the overall global burden diseases in 2030. Besides, depression is also a risk factor for other brain diseases, such as cognitive impairment. Under the stress condition, the hypothalamus-pituitary-adrenal (HPA) axis regulates stress hormone secretion affecting the immune system. Therefore, resolving immune response, stress hormones, and inflammation could prevent a negative effect on emotion and cognitive impairment. ApoE$^{-/-}$ mouse model is a desirable model for inducing depression disease and cognitive impairment due to the depletion of apolipoprotein E resulting in abnormal brain neurotransmitters, neurogenesis, and amyloid clearance rate. *Gastrodia elata* Blume (GE) is a traditional Chinese herbal medicine, and it has been reported its benefit for improving brain function. However, the study on its anti-depressive effects and cognitive improvement of GE in ApoE$^{-/-}$ mice model is not still examined yet. Therefore, this study aims to investigate the anti-depressive effect and cognitive improvement of GE in ApoE$^{-/-}$ mice induced by unpredictable chronic mild stress (UCMS). The ApoE$^{-/-}$ mice were orally administrated with water extract of GE (WGE) (5, 10, and 20 μL/g bw/day) for four weeks during UCMS experiment. The results demonstrated WGE prevented depression-like behavior by increasing the sucrose preference ($p<0.05$), and improved the cognition by increasing the discrimination ratio in novel objective recognition test as well as the concentration of serum β-amyloid 42 ($p<0.05$). Besides, WGE ameliorated the turnover rate of serotonin in the prefrontal cortex ($p<0.05$). Collectively, WGE potentially ameliorated depression-like behavior and cognitive impairment in UCMS induced ApoE$^{-/-}$ mice model. Thus, WGE could be used as preventative herbal medicine against depression and cognitive impairment.

投稿學會：台灣基礎神經科學學會 | 編號:11

Treatment with an ENT1 inhibitor ameliorates neurodegeneration in two mouse models of Alzheimer's disease with distinct pathogenesis

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Abstract

Alzheimer's disease (AD) is the world's most common cause of dementia. AD is a chronic neurodegenerative disease characterized by memory loss and cognitive dysfunction. The hallmarks of AD are the accumulation of extracellular amyloid-β fibers/plaques in the brain and the formation of microtubule-associated protein tau fibers/neurofibrillary tangles (NFTs) inside neurons. Until now, no drug was available to delay the disease progression of AD. The equilibrative nucleoside transporter 1 (ENT1) is a major adenosine transporter that recycles adenosine across the plasma membrane. We report here that treatment with an orally active adenosine analogue (designated J4), which inhibited ENT1, reversed the impairment of spatial learning memory in APP/PS1 and Thy-Tau22 mice after the onset of memory impairment. J4 treatment also lowered the level of hyperphosphorylated Tau in the hippocampus of Thy-Tau22 mice and reduced Aβ deposition in the cortex of APP/PS1 mice. Furthermore, J4 decreased the expression of a glial classical complement (C1q) expression in both mouse models. Our findings suggest that modulation of adenosine homeostasis by J4 provided beneficial effects on the memory impairment of two AD models with distinct pathogenesis. The underlying mechanism that mediates the beneficial effects of J4 is currently under investigation by RNAseq analysis and biochemical characterization. Collectively, our results suggested that J4 is a new drug candidate for AD, and that adenosine augmentation by the inhibition of ENT1 is a novel therapeutic strategy for AD.

投稿學會：台灣基礎神經科學學會 | 編號:12

Altered Nociception in Alzheimer's Disease is Associated with STEP Signaling

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[6] These authors contributed equally.
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Abstract

Alzheimer's disease (AD) is the most common form of dementia, accounting for approximately 60% of cases. In addition to memory loss, changes in pain sensitivity are found in a substantial proportion of AD patients. However, the mechanism of pain sensation deficits in AD is still unclear. Here, we hypothesize that the pain sensation abnormality in AD is due to the abnormal activation of striatal-enriched protein tyrosine phosphatase (STEP) signaling, which modulates proteins related to nociception transduction. Our results indicated that the trangenic mice carrying human *amyloid precursor protein* (*APP*) gene had lower sensitivity to mechanical and thermal stimulation than the WT group at the ages of 6, 9, and 12 months. These APP mice exhibited elevated STEP activity and decreased phosphorylation of proteins involved in nociception transduction in hippocampi. The pharmacological inhibition of STEP activity using TC-2153 further reversed nociception and cognitive deficits in the AD mice. Moreover, the phosphorylation of nociception-related proteins in the AD mouse model was also rescued after STEP inhibitor treatment, indicating the key role of STEP in nociception alteration. In summary, this study identifies a mechanism for the reduced pain sensitivity in an AD mouse model that could serve as a therapeutic target to improve the quality of life for AD patients.

投稿學會：台灣基礎神經科學學會 | 編號:13

Phosphatidylinositol-4-Phosphate 5-Kinase Type 1α Attenuates Aβ Production by Promoting Non-amyloidogenic Processing of Amyloid Precursor Protein

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Abstract

Alzheimer's disease (AD) is characterized by a chronic decline in cognitive function and is pathologically typified by cerebral deposition of amyloid plaques that primarily result from the accumulation of the amyloid-β peptide (Aβ). The production of Aβ is mediated by sequential proteolysis of amyloid precursor protein (APP) by β- and γ-secretase, and different forms of the peptide have been implicated as essential determinants of AD pathology. Previous studies have demonstrated that the level of phosphatidylinositol-4,5-bisphosphate [PI(4,5)P2] in the membrane may potentially modulate Aβ production. Given that PI(4,5)P2 is produced by type 1 phosphatidylinositol-4-phosphate 5-kinases (PIP5Ks), we sought to determine whether the level of PIP5K type Iα (PIP5K1A) can affect production of Aβ by modulating the lipid composition of the membrane. Using a HEK-derived cell line that constitutively expresses yellow fluorescent protein-tagged APP (APP-YFP), we demonstrated that overexpression of PIP5K1A results in significant enhancement of non-amyloidogenic APP processing and a concomitant suppression of the amyloidogenic pathway, leading to a marked decrease in secreted Aβ. Using immunofluoroscence microscopy, we further discovered that cells overexpressing PIP5K1A exhibit a significant redistribution of APP-YFP from endosomal compartments to the cell surface. Our findings suggest that PIP5K1A may play a critical role in governing Aβ production by modulating membrane distribution of APP, and as such, the pathway may be a valuable therapeutic target for AD.

投稿學會：無	編號:14

Role of NADPH oxidase 2 in the BDNF dysregulation and memory deficits after systemic inflammation

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Abstract

Background: Sepsis has been reported to increase the risk of cognitive impairment. Following systemic inflammation, a corresponding neuroinflammation including glia activation and excessive pro-inflammatory factors are rapidly induced in brain, possibly affecting the crucial brain capability. BDNF represents one of the major mediators of neuroplasticity. We wanted to evaluate one of the most interesting hypotheses: NOX2 plays a role in the involvement of the neurotrophic factor BDNF dysregulation and cognitive deficient after systemic inflammation.

Methods: Mice with deficits of NOX regulatory subunit/NOX2 organizer p47^{phox} (*p47$^{phox-/-}$*) and wild-type (WT) mice were used. Lipopolysaccharide (LPS) intraperitoneal injection was used to induce systemic inflammation. Spatial learning and memory were compared among treatment groups using the radial-arm maze task. Brain tissues were evaluated for the transcript levels of proinflammatory cytokines, while immunofluorescence staining and immunoblotting were used to determine the damaged neurons and the levels of BDNF.

Results: Cognitive impairment following systemic inflammation was significantly attenuated in the *p47$^{phox-/-}$* mice compared with the WT mice. We found that the levels of BDNF in astroglia and neurons were significantly reduced within 10 days after the LPS injection in parallel with glia activation and increased cytokines in brains. We further revealed that *p47^{phox}* deletion could reduce glia activation, BDNF downregulation, and cognitive deficits, compared to those in WT-type mice following LPS injection.

Conclusions: Our results suggest that alteration of BDNF could be related to excessive neuroinflammation, subsequently involved in developing cognitive impairment. NOX2 might play a role in the pathogenesis of the development of cognitive deficits after systemic inflammation in a mouse model.

Keywords: sepsis; nicotinamide adenine dinucleotide phosphate oxidase; diphenyleneiodonium; lipopolysaccharide; cognition; neuroinflammation; brain-derived neurotrophic factor

投稿學會：臺灣基礎神經科學學會 | 編號:15

FKBP51 regulates anxiety susceptibility involving regulation of hippocampal neuroinflammation and GABA synthesis after transient peripheral inflammation

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Abstract

FK506-binding protein 51 (FKBP51) encoded by the *Fkbp5* gene is a negative feedback co-chaperone of glucocorticoid receptor (GR) and has been linked to many stress-related mental disorders. Peripheral inflammation has been suggested as a pathogenic inducer for anxiety disorder, but the role of FKBP51 in the inflammation-associated anxiety remained unknown. In this study, we used *Fkbp5*-knockout (*Fkbp5*-KO) mice applied to a single intraperitoneal injection of lipopolysaccharide (LPS) to study the role of FKBP51 in the inflammation-induced behavioral and neurochemical changes. We found that LPS injection induced *Fkbp5* gene expression in both liver and hippocampus, suggesting the induction of peripheral and central stress responses. *Fkbp5* deletion did not affect LPS-induced transient sickness, but significantly increased anxiety-like behaviors on 7 days after the LPS injection. *Fkbp5*-KO attenuated LPS-induced neuroinflammation, as indicated by decreasing LPS-induced hippocampal TNFα and IL-6 gene expressions. LPS-injected *Fkbp5*-KO mice also had lower TSPO levels by whole-brain [18F]FEPPA neuroimaging for glial activation compared with WT mice. In addition, LPS induced a delayed upregulation of GR on day 7 in the hippocampus, and this response was diminished in *Fkbp5*-KO mice. Interestingly, LPS injection induced a *Fkbp5*-dependent elevation of hippocampal glutamic acid decarboxylase 65 (GAD65), the GABA synthesizing enzyme, whereas $GABA_A$ receptor, serotoninergic $5HT_{1A}$ receptor or excitatory NMDA receptor subunits were not affected. However, *Fkbp5*-dependent GAD65 upregulation was not affected in the synthetic glucocorticoid dexamethasone-induced stress model. In sum, these results suggest that FKBP51 mediates neuroinflammation-induced stress adaptation and upregulation of GABAergic neurotransmission in hippocampus.

投稿學會：台灣基礎神經科學學會 | 編號:16

Efficient Generation of Functional Microglia-like Cells from Human Induced Pluripotent Stem Cells by Defined Transcription Factors

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Abstract

Human induced pluripotent stem cells (hiPSCs) are a powerful tool for *in vitro* research to model human disease pathogenesis, including neurological disorders. Different methodologies to generate primitive neurons from hiPSCs as normal or disease model have been reported. However, increasing evidences show that microglia, the immune cells of the central nervous system (CNS), also play critical roles in CNS physiology and pathology. Thus, introducing microglia into a mono-culture of only neurons can provide a more complete model for neurological research. Here, we established a novel approach to enable rapid differentiation of microglia-like cells from hiPSCs. Briefly, we carried out a screening using several transcription factors involved in microglial development, and identified co-expression of two genes to be sufficient to convert hiPSCs into induced microglia (iMG) within 10 days. High-level expression of the main microglial markers in iMG cells was confirmed by RT-qPCR, immunocytochemistry and flow cytometry analyses. Quantification also revealed that our protocol yielded iMG cells of high purity. Whole transcriptome analysis demonstrated that iMG cells are similar to human fetal and adult microglia but not human monocytes. Moreover, the iMG cells exhibited physiological functions including LPS/IFNγ-induced inflammatory responses, phagocytosis of microspheres or fibrillar Aβ and ADP/ATP-evoked Ca2+ influx and cell migration. When co-cultured with hiPSC-derived neurons (iNs), iMG cells migrated toward and surrounded laser-injured iN clusters, further suggesting that our iMG cells were capable to sense their environments and act as scavengers. Taken together, we established a protocol to rapidly convert hiPSCs into iMG, and provided a feasible method for production of "disease in a dish" models, which will facilitate human cell-based platform for novel drug screening and evaluation for neurological diseases.

投稿學會：台灣神經罕見疾病學會	編號:17

Impairment of Proteasome and Autophagy Leads to Ubiquitin and P62 Aggregates Underlying the Pathogenesis of Globoid Cell Leukodystrophy

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Abstract

Impairment of the ubiquitin-proteasome-system (UPS) and autophagy causing cytoplasmic aggregation of ubiquitin and p62 have been implicated in the pathogenesis of most neurodegenerative disorders, yet, they have not been fully elucidated in leukodystrophies. The relationship among impairment of UPS, autophagy, and globoid cell leukodystrophy (GLD), one of the most common demyelinating leukodystrophies, is clarified in this study. We examined the ubiquitin and autophagy markers in the brains of twitcher mice, a murine model of infantile GLD, and in human oligodendrocytes incubated with psychosine. Immunohistochemical examinations showed spatiotemporal accumulation of ubiquitin- and p62-aggregates mainly in the white matter of brain and spinal cord at disease progression. Western blot analysis demonstrated a significant accumulation of ubiquitin, p62,and LC3-II in insoluble fraction in parallel with progressive demyelination and neuroinflammation in twitcher brains. In vitro study validated a dose- and time-dependent cytotoxicity of psychosine upon autophagy and UPS machinery. Inhibition of autophagy and UPS exacerbated the accumulation of insoluble ubiquitin, p62, and LC3-II proteins mediated by psychosine cytotoxicity as well as increased cytoplasmic deposition of ubiquitin- and p62-aggregates, and accumulation of autophagosomes and autolysosomes. Further, the subsequent accumulation of reactive oxygen species and reduction of mitochondrial respiration led to cell death. Our studies validate the impairment of proteasome and autophagy underlying the pathogenesis of GLD. These findings provide a novel insight into pathogenesis of GLD and suggest a specific pathomechanism as an ideal target for therapeutic approaches.

投稿學會：台灣基礎神經科學學會 | 編號:18

Epigenetic regulation of *WNT3A* enhancer during regeneration of injured cortical neurons

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Abstract

Traumatic brain injury (TBI) disrupts normal function of the brain and everyone is at risk of TBI, especially elderly adults. Approximately 70 million individuals worldwide reported suffer from TBI. However, there is currently no effective therapy to promote neuronal survival and regeneration upon TBI due to limited regenerative potential of damaged brain neurons. We thus aim to identify candidate regeneration-associated genes (RAGs) from injured cortical neurons. Based on our RNA-seq data, a number of *WNT* genes are among the most promising RAGs. Among several recombinant WNT proteins, WNT3A showed the most promoting effect via *in vitro*, *ex vivo* and *in vivo* TBI models. To further investigate the mechanism by which injury-inducing WNT3A expression is regulated, chromatin immunoprecipitation-sequencing (ChIP-seq) of histone H3 lysine 27 acetylation (H3K27ac) and tri-methylation of histone H3 at lysine 4 (H3K4me3) modifications were performed. The aggregated ChIP-seq signals of H3K27ac aligns to distal regions rather than proximal promoter region of *WNT3A*. Thus, we hypothesized that *WNT3A* gene might be regulated by novel enhancer. A putative enhancer region was predicted and divided into 10 sub-regions, e1 to e10. Our analysis showed that active enhancer marks, H3K27ac and H3K4me1 signals, at e5 and e7 were elevated during neuronal regeneration. Chromosome conformation capture (3C) analysis reveals a reduced e5-e7 interaction with concomitant increase of e7 and *WNT3A* promoter during neuronal regeneration. Together, our findings demonstrate an enhancer regulation of *WNT3A* transcription during neuronal regeneration.

投稿學會： 無	編號:19

Synthesis of Positron Emission Tomography Images through Deep Learning

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Abstract

Positron emission tomography (PET), an imaging modality used to accurately localize diseases and qualitatively characterize the function and status of organ, requires administration of intravenous radioactive tracer. The desire to minimize radiation risk never goes away. To this end, the need to estimate or synthesize realistic PET images is certain. Deep learning algorithms, having been intensively developed and extensively applied to images synthesis and to spatial resolution enhancement, is our algorithm of choice. In this work, we synthesized PET images using T1-weighted magnetic resonance imaging (MRI) images through deep learning with a 77-subject MRI and PET dataset from Taipei Veterans General Hospital. These images underwent spatial normalization, white and gray matter extraction, SUVr calculation and then value normalization. We exploited two dimensional U-Net of its contraction-expansion architecture and skipped connection characteristic. The image quality was evaluated using quantitative measures such as mean absolute error (MAE), peak-signal-to-noise-ratio (PSNR) and structural similarity index (SSIM). Our technique achieved high image quality in testing images. Histogram showed that the distribution of real and synthesized PET images was similar and that joint histogram revealed high correlation between them. Moreover, synthesized PET images also revealed significant difference in SUVr between Alzheimer's group and non-Alzheimer's group, including mild cognitive impairment group, subjective cognitive decline and control group. Our work demonstrated the potential benefit of the synthesized PET scans for multi-modality analysis in Alzheimer's disease.

投稿學會：中華民國生物醫學工程學會 | 編號:20

Development of High-resolution Multiple-contrast MRI for Imaging Postmortem Fetal Brain at 3T

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Abstract

Proper developmental processes of mammalian brain including the control of cell number, growth, differentiation, migration, and forming synapse and connectivity underlies the function and plasticity of mature brains. Particularly, how the complicated structure and function of the human brain forms from the fetal brain that is simpler in structure with unknown function poses the most challenging topic. Since magnetic resonance imaging (MRI) is an excellent noninvasive approach in studying brain structures, we aim to establish a dedicated MRI system platform and imaging methods for acquiring high-resolution multiple-contrast fetal brain images. Many efforts have been carried out in optimizing the MRI system hardware and software to obtain exceptionally high-spatial-resolution images for postmortem fetal brain, including gradient system optimization, pulse sequence design, RF coil design, RF chain improvement, and sample holder design. We have successfully obtained postmortem fetal brain images with 100-μm isotropic spatial resolution at 3T. The imaging sequences with multiple MRI tissue contrasts, such as T1 and T2 relaxation time, susceptibility, and diffusion, have been developed in routine data acquisition framework. Advanced diffusion MRI techniques for mapping structural connectivity, such as diffusion tensor imaging and high-angular resolution diffusion imaging, have been developed and the fiber tractography on postmortem fetal brain could reveal primary fiber bundles, including callosal fibers and thalamocortical pathways. With high spatial resolution and a variety of MRI contrasts, it could be possible to gain more insights into the complex tissue microstructures in fetal brain, especially in marginal zone, superficial subplate and deep subplate areas, and uncover the change of cortical structures, morphology, and neural fiber connections during brain development.

投稿學會：台灣認知神經科學學會 | 編號:21

Intrinsic cross frequencies coupling oscillation revealed with Holo-Hilbert spectral analysis in human

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Abstract

Recent studies have emphasized the importance of applying the individualized stimulation, and this relies on precise quantification of the signal measured from the participant (e.g. the oscillation measured by EEG). Previous electrical stimulation studies have shown that the facilitation brought by the stimulation can be further improved by matching the frequency of the external stimulation to the individualized intrinsic oscillation. However, the analytical method they incorporated has limited their capabilities to exploit the nonlinear parts (e.g. amplitude modulation (AM) / frequency modulation (FM)) of the signal, which are proposed to be critical signatures of the neural communications. In the present study, we aimed to quantify the intrinsic oscillation with the Holo-Hilbert spectral analysis (HHSA; Huang et al., 2016; Nguyen et al., 2019), which is able to simultaneously estimate the AM and FM of the signal. Specifically, resting state electroencephalography (EEG) was applied to HHSA. The result shows that in addition to the alpha peak detect by conventional Fourier based method, the amplitude of the dominating alpha is also modulating by the frequency around delta frequency (~ 2 Hz). Moreover, the distinct AM frequency is observed for Eye Open (EO) and Eye Closed (EC) trials. These findings shed a light into different aspect of resting state EEG, which remains poorly understood. In light of the additional AM frequency measured by the HHSA, it may provide better predictions regarding individual's response to the external stimulation and revelations of the underlying mechanism of the interaction of external and intrinsic oscillation. Furthermore, this information can be applied for customizing parameters of brain stimulation tailored for the individual to improve the efficacy.

投稿學會：台灣認知神經科學學會 | 編號:22

Motor inhibitory control as a function of grip force and its electrophysiological dynamics were revealed with Holo-Hilbert Spectrum Analysis

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Abstract

Response inhibition has been widely explored by the stop-signal paradigm in a laboratory setting. However, the mechanism underlying the differentiation between attentional capture and motor inhibition processes is still unclear. A modified version of the stop signal task was used in this study to control and eliminate potential attentional capture effect from the motor inhibition index. Furthermore, EEG was recorded during the task and analyzed with a newly developed nonlinear analytical method, namely: Holo-Hilbert Spectrum Analysis (HHSA). With HHSA, nonlinear EEG characteristics were decomposed into the fast waves (carrier frequencies) wherein envelope modulates the carrier frequencies. Therefore, HHSA provides a comprehensive and high-dimensional representation of carrier and envelop frequency occurred in EEG. Twenty participants performed the task with EEG recording coupled with force measurement that provides a finer estimate of inhibitory control process. The results demonstrate that the non-canceled force and force rate increased as a function of stop signal delay, offering new objective indices for gauging the dynamic inhibitory process. The early N1 component complements the existing N2 component as a novel motor inhibition index. The HHSA results showed that theta (3.5-7Hz)/beta (14-28Hz), alpha (7-14Hz)/beta, theta/lower gamma (28-56Hz) and alpha/lower gamma modulation may serve as an electrophysiological index of inhibitory control in the level of cross frequency couplings. Moreover, delta (0.5-3.5Hz)/theta modulation was also found to be associated with error detection. Thus, the effective EEG/ERPs indices of motor inhibition can be established with force measures and HHSA methods, these extend our understanding of the dynamic electrophysiological mechanisms of human motor control.

投稿學會：台灣基礎神經科學學會 | 編號:23

Musicians and non-musicians' dissonance/consonance perception: separate and joint analyses of event-related potential (ERP) and functional Magnetic Resonance Imaging (fMRI)experiments of the same design

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Abstract

Musician's sensibility of detecting tonal differences between two musical notes is extraordinary. The perception of musical tonality can be either consonant or dissonant, depending on pitch relationship between intervals. Previous studies suggested that musician and nonmusician may have different reliance upon discerning two intervals from the perspective of frequency ratio (Western tonal theory) or the frequency difference (psychoacoustics). In this study, electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) are used with jittered event-related design to obtain a finer brain activity in response to tonal dissonance/consonance. Thirty-two musicians and thirty nonmusicians judged dissonance and consonance at 20 sounds of pitch interval and roughness orthogonally mixed across frequency range from 100Hz to 500Hz for behavioral. The results of fifteen musicians and fourteen nonmusicians are collected for EEG experiments, and fourteen musicians and seventeen nonmusicians for fMRI experiments. Behavior findings supported previous evidence for an association between musician with pitch interval and nonmusician with roughness, the EEG results further demonstrated that manipulation of tonal differences increased interaction effect between groups at N1 amplitude across F3, FZ, F4, FC3, FCZ, FC4, C3, CZ, C4, CP3, CPZ, and CP4 channels. The fMRI results using ANOVA and MVPA searchlight also indicated the functional dissociations between musicians and non-musicians in the frontal lobe including Medial Prefrontal Cortex (MPFC), Medial Frontal Gyrus (MFG), Superior Frontal Gyrus (SFG), and in the temporal lobe, such as primary auditory cortex. Furthermore, the representational similarity analysis (RSA) was used to identify spatio-temporally corresponding brain regions for dissimilarity matrix designed on different frequency properties across stimuli and 12-channels ERP, postulating top-down driven consonance/dissonance judgments processing in musicians, and bottom-up processing for non-musicians. Together, these results suggest that musicians and non-musicians rely upon pitch intervals and sensory roughness, respectively, for consonance/dissonance perception. To our knowledge, this is the first study to combine multi-modal data across the pitch interval and roughness spectrum. Our results further support the brain plasticity as a result of musical training in consonance perception.

投稿學會：台灣認知神經科學學會 | 編號:24

Over- and underreaction in detecting regime shifts and the neurocomputational substrates for estimating probability of change

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Abstract

In dynamic environments where technology, markets, competitors and even narratives change regularly, many decisions are tightly associated with our ability to estimate and detect changes. Previous studies on judgment and decision making had established that people can over-react and under-react to potential changes in response to system that generates the signals.

In a probability estimation task, subjects had to estimate change from one regime – red -- to the other – blue – based on the signals they receive. The signals were generated from one of the regimes, which always started from the red regime but can shift to the blue regime based on some transition probability. We investigated the impact of transition probability and signal diagnosticity -- the relative ratio of red to blue balls – on change detection.

We replicated the systematic biases shown in previous studies: compared with the ideal Bayesian solution, subjects (n=30) tended to overreact to a new sample by giving larger estimates on the probability of regime-shift in noisy (low signal diagnosticity) but stable environments (small transition probability). By contrast, subjects tended to underreact in environment that is unstable and signal is precise Further, we fit a quasi-Bayesian model that incorporate free parameters to separately estimate sensitivity to transition probability and signal diagnosticity under different environmental conditions. We found that sensitivity to both transition probability and signal diagnosticity are a decreasing function of their respective dimensions, consistent with a "system- neglect" model in which people respond primarily to the signal and secondarily to the system that generates the signal.

Preliminary fMRI results showed that intraparietal sulcus, anterior insula and pre-supplementary motor area positively correlated with probability estimate on shift, while VMPFC negatively correlated with it. We also found that IPS and VMPFC represent both subjective transition probability and signal diagnosticity estimated from the quasi-Bayesian model.

投稿學會：台灣認知神經科學學會 | 編號:25

Interactive effects of timescale and formant frequency on frequency-sweep elicited mismatch negativity: an electroencephalography study

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Abstract

Speech comprehension across languages depends on rapidly encoding the dynamic pitch variations in frequency sweeps. However, whether cortical processing of pitch variations operate according to linguistically functional timescale is less examined. In the present study, an auditory oddball paradigm was used to examine unattended processing of pitch variations at different levels of linguistically important timescales and frequency regions. Frequency sweeps with varying fundamental/formant frequencies (fundamental frequency [F0] vs. first formant frequency [F1]) and timescales (local vs. global) representing linguistic functions in Mandarin Chinese were employed. Mismatch negativities (MMNs) were calculated by subtracting event-related potentials to identical upward/downward frequency sweeps serving as a standard in one block and as a deviant in another block. Larger MMN amplitudes were elicited by tone sweeps with F0 pitch variations than those with F1 pitch variations at the local timescale. A reversed MMN pattern was obtained when the pitch contour fluctuated at the global timescale. Importantly, the interactive effects of MMN responses between F0/F1 frequencies and timescales reflected the distinct linguistic functions of F0 and F1 pitch contours in tonal language. An interhemispheric asymmetry of MMN topography was observed that corresponded to timescales of sweep contours commensurate with processing of lexical tones and intonational contours. Our findings suggest that the human brain can, at the pre-attentive cortical level, disentangle different levels of pitch contours which signal functionally relevant timescales in language.

投稿學會：台灣認知神經科學學會 | 編號:26

Collaboration and deception in strategic interaction: an fMRI hypercanning study

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Abstract

In various social events, people sometimes face the challenge of whether to misinform/cheat others for one's own benefit or face-keeping. Despite the fact that fMRI has once been dubbed the 'next possible lie detector?', there are surprisingly not many studies addressing social/non-social lying. Part of the reasons might be the difficulty to create contexts where cheatings naturally arise. Even so, the extant neuroimaging studies and meta-analyses both suggest the involvement of default mode network (DMN), including brain regions (i.e., temporal parietal junction, TPJ) related to theory of mind (TOM) and moral reasoning, and self-related processing (i.e., rostral anterior and posterior cingulate cortex, rACC and PCC). In addition, almost all previous fMRI studies deployed univariate or region-of-analysis methods, with few recent exceptions utilizing connectivity and multivariate analysis approaches.

In the present study, we ran a hyperscanning fMRI experiment of the strategic game (33 pairs, n=66), where participants either collaborated or competed for the trial reward (NT $200 and $150, respectively). In the collaboration case ($200), the dyad split the reward if they succeeded in guessing the right treasure box (e.g., the receiver followed the sender's left/right signal), whereas in the competition condition ($150), either the sender or the receiver took the money (e.g., the sender suggested the right box, and the receiver chose the left one and won). Trials were fixed in the '$200/sender-$150/sender-$200/receiver-$150/receiver' unit arrangements.

Complying with the literature, the results in the competition condition showed higher precuneus activations in the bluffing than in the truth-telling trials. Moreover, functional connectivity between the rTPJ and the precuneus/PCC was higher than those in the collaboration interactions. Most strikingly, the percentage of participants bluffing in the competition condition was negatively correlated with the rTPJ-rACC and rTPJ-PCC connectivity, among others, indicating the heightened detachment between the self-processing regions and the TOM regions while the participants were bluffing. To sum up, these results reveal the neural substrate underpinning social deception, including internal conflicts among moral self, projected self, and the present value.

投稿學會：台灣認知神經科學學會 | 編號:27

Past and current subjective-value signals in the human orbitofrontal cortex (OFC): A stereo-electroencephalography (sEEG) study

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Abstract

There is extensive evidence suggesting that the orbitofrontal cortex (OFC) represents the subjective value (SV) of options essential for value-based decision-making. A growing body of research further indicates that the OFC encodes relative SV depending on the temporal context of experience. However, these findings are mainly based on single-unit electrophysiology in non-human primates and have not been widely reported in humans. In this study, we investigated value representations in the human OFC using stereo-electroencephalography (sEEG). Subjects implanted with multi-contact depth electrodes performed a Becker-DeGroot-Marschack auction task on snack food items to elicit and estimate the subjective value of rewards. The event-related high-gamma power (80-150 Hz) was extracted and regressed against the SV in the current trial and the SV in the previous trial. For all the subjects, there were contacts in OFC showing value-related signals. There were more OFC contacts showing positive correlation to the current SV after the stimulus onset in comparison to those showing positive correlation to the previous SV. There were more OFC contacts showing negative correlation to the previous SV after the stimulus onset in comparison to those showing negative correlation to the current SV. On the other hand, the OFC contacts showing positive correlation to the previous SV before the stimulus onset were outnumber that showing positive correlation to the current SV. The OFC contacts showing negative correlation to the current SV before the stimulus onset were outnumber that showing negative correlation to the previous SV. In summary, we found evidence that high-gamma activity in the human OFC encodes current as well as previous SV for food rewards. The results provide support to the hypothesis that OFC computes relative value that is sensitive to the temporal context of experience.

投稿學會：台灣認知神經科學學會 | 編號:28

The role of information lifespan and rate of information flow on decision making

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Abstract

In many decisions we face, collecting more information is beneficial to making better choices but comes at a cost of time and energy. Previous research showed that people tend to collect less information than they should. In this study, we investigated two potential causes of such suboptimal behavior—information lifespan and rate of information flow. We found that information lifespan, but not rate of information flow, affected cost-benefit tradeoff decisions. Under extremely short lifespan, subjects collected even less information. Unexpectedly, speed-accuracy tradeoff (SAT)—an important aspect of performance essential to cost-benefit tradeoff decisions—was affected in opposite ways: SAT was impacted by rate of information flow but not information lifespan. This contradicted the common belief that longer information lifespan leads to better SAT performance. Together, these findings point to dissociable impacts of duration and rate of information on human decision making and suggest distinct computational demands between SAT and cost-benefit tradeoff decisions.

投稿學會：台灣基礎神經科學學會 | 編號:29

High gamma activity in the human prefrontal and insular cortices represent monetary gains and losses during decision making

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Abstract

Many decisions we face involve choosing between options that carry potential gains and losses. Decades of research from psychology show that people are loss averse — that "losses loom larger than gains". Human fMRI studies showed that many brain regions, including the ventromedial prefrontal cortex (VMPFC), orbitofrontal cortex (OFC) and ventral striatum, represent information about monetary gains and losses during decision making. It remains controversial, however, whether these regions simultaneously represent gains (positive) and losses (negative). In this study, we attempted to address this issue using human intracranial electrophysiology. In a mixed-gamble task, human subjects (n=18) on each trial faced a 50/50 lottery of a potential monetary gain or loss and had to decide whether to play the lottery. As part of treatment plan attempting to identify epileptogenic zone, multi-contact depth electrodes were implanted in different brain regions including the OFC, dorsal-to-mid cingulate cortex, amygdala and insula. These four brain regions, with a total of 221 contacts across subjects, were the focus of this study. Behaviorally, we replicated loss aversion in the patient population. Lambda, the ratio of sensitivity to changes in losses to gains inferred from choice behavior was around 1.5, suggesting that subjects were mildly loss averse. Neurally, we found evidence for gain and loss representations in high-gamma activity. However, most contacts represent either gains or losses; very few contacts represent both gain and loss information. Together, these results suggest that gains and losses are more likely to be represented by different populations of neurons in these regions rather than by the same neurons.

投稿學會：台灣認知神經科學學會 | 編號:30

Individual difference in social interaction pattern modulated brain activities in STS, insula, and cingulate cortex during coordination task

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Abstract

Lots of studies have explored the neural mechanism underlying specific social interaction such as cooperation or competition. However, people may behave differently when interacting with each other in the same task. In this study, we focus on how people collaborate with their partners so that we could catch up various interaction patterns among different dyads, which is more in line with real life. Thus, we designed a coordination task, which requires subjects to convey their intention to their partners and try to coordinate well to get more rewards. The rewards received by both subjects in each trial depends on their final decisions. However, the rewards are always unequal. Only one can receive the higher reward, otherwise both of them get nothing. That means subjects in a pair need to coordinate well to earn more rewards eventually. If they insist to get higher reward, then neither side wins. We separated subjects from each dyad according to their overall rewards. Subject with higher overall reward was classified as Dominant group, and the other was classified as Non-dominant group. In order to find out dyads' behavior patterns, we used "coordinate success rate" to investigate how well they coordinate with each other. In addition, an "alternating index" were used to describe their behavioral patterns how often subjects in a pair take turns to get the higher reward. The results showed that there is positive correlation between two behavioral indicators. Combined with the fMRI results, we found that there are several diverse brain activities correlated with two behavioral indicators in each group. In the Non-dominant group, the activities of STS, insula, and cingulate cortex are positively correlated with the coordinate success rate. However, the results showed the opposite in the Dominant group. Furthermore, distinct patterns of correlation between alternating index and brain activity were also found in two groups. In conclusion, the present study demonstrated that despite engaging in the same task, participants with different performances showed different brain activity patterns. The better Non-dominant groups coordinated with their partners, the higher brain activities in social cognition related regions, but Dominant group showed reversed pattern.

投稿學會：台灣認知神經科學學會 | 編號:31

Brain Activity in Processing Static and Dynamic Facial Expressions

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Abstract

Cognition and recognition human facial expressions are essential in identifying emotions of others and considered as an important factor in social interaction. The present study explores the brain activity in processing two kinds, namely static and dynamic emotional facial expressions. Recognition process when watching emotional faces. In the study, 25 college students (aged 20-25) participated and their functional magnetic resonance imaging (fMRI) data were collected when they view static (images) and dynamic (videos) stimuli that included angry, fear, happy, neutral facial expressions, and non-human face objects. All stimuli were randomly presented in experiment and participants were asked pressed a bottom when they saw non-human face stimuli (i.e., objects). Data were first analyzed in preprocessing using SPM and then analysis were conducted by comparing static and dynamic facial expressions. The results found differences in active brain areas in viewing static images versus dynamic videos. The areas for dynamic stimuli were more active than static images at right middle frontal gyrus, right precentral gyrus, left posterior cingulate and left middle occipital gyrus. The areas for object stimuli were more active than fear, happy and neutral face stimuli at left precentral gyrus and left posterior cingulate. The significant difference also found at brain regions of precentral gyrus in comparing each type of non-human objects with angry, fear, happy and neutral faces. Taken together, results suggested middle frontal gyrus, precentral gyrus, posterior cingulate and middle occipital gyrus are involved in and more active for viewing dynamic than in viewing static faces/object stimuli.

投稿學會：台灣認知神經科學學會 | 編號:32

Self-awareness impacts individual variations in perceiving appetitive cues

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Abstract

Being aware of long-term goals enables individuals to resist their temptation and further enhance their self-control ability. Although previous studies have provided supportive evidence, researchers also found remarkable individual variations in this self-awareness enhancing effect. In the current study, we recruited 41 chronic dieters who aimed to achieve long-term dieting goals to examine how self-awareness influences individuals' perception of tempting cues, and what individual differences might contribute to individual variations in the self-awareness enhancing effect. These participants were randomly assigned into two groups, in which one group received awareness manipulation of their dieting goals, whereas another group received no such manipulation before fMRI scanning. All participants then underwent a food-cue reactivity task in the scanner, which is commonly used to examine how appetitive food cues are represented in the brain. We were interested in using intersubject representation similarity analysis (IS-RSA) to test whether similarity in participants' self-reported sensitivity to external appetitive food cues were associated with similarity in brain spatial representations of food cues, and whether self-awareness manipulation enhanced this association. Our results showed that, in the awareness group, similarity in the self-reported sensitivity to external appetitive cues were associated with similarity in brain representations in the fronto-parietal executive control network, whereas no such association was found in the non-awareness group. Lastly, we used meta-analytic decoding to explore which psychological processes might be most likely engaged in this self-awareness enhancing effect. We found that self-awareness enhancing effect revealed stronger associations with executive control, conflict, cognitive control, and error monitoring than non-awareness effect. Our results demonstrated that by using IS-RSA, researchers can have a new understanding of how self-awareness impacts the representation of temptation in the brain.

投稿學會：臺灣生物精神醫學暨神經精神藥理學學會 | 編號:33

Combined Plasma CCL11 and Cotinine Levels to Predict Alcohol Dependence

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Abstract

Alcohol consumption is usually difficult to define if one were dependent. Stress is one of the factors which may play a role in alcohol use. In this study, we reported the inflammatory factor, C-C motif chemokine ligand 11 (CCL11; also called eotaxin-1) of a neurodegenerative biomarker, predicted alcohol dependence when considered smoking status.

This study was conducted in the alcohol detoxification ward of Taipei City Psychiatric Center after obtaining the approval from Research Ethics Committee (REC No: EC1070102-R2). A population of 98 alcohol dependent patients fulfilling the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria for alcohol dependence and alcohol withdrawal syndrome verified by at least 2 boarded psychiatrists, and 121 age-and gender-matched non-alcohol dependent normal controls were recruited. A diagnosis of delirium tremens (DTs) were made among the alcohol dependent patients according to the DSM-IV-TR criteria, which included disturbance of consciousness, severe alteration in cognition or perceptual disturbance that is not better accounted for by a preexisting, established, or evolving neurocognitive disorder. The blood plasma was collected and analyzed for CCL11 and cotinine levels with enzyme-linked absorbent assay (ELISA).

The average ages were 45 and 43 years old between alcohol dependent patients and controls respectively. The alcohol dependent patients had significantly higher tobacco smoking in pack/year smoking, smoking daily, and plasma nicotine metabolite cotinine concentration than the controls ($P<0.001$, respectively). The plasma CCL11 level was significantly higher in alcohol dependent patients than the controls ($P <0.001$). The alcohol dependent patients with delirium tremens (DTs) had more severe anxiety symptom score rated by Beck Anxiety Inventory (BAI) ($P=0.033$), but lower plasma CCL11 levels ($P=0.07$) than non-DTs. The plasma CCL11 was significantly correlated with the Severity of Alcohol Dependence Questionnaire (SADQ) total score (Spearman's $r=0.556$, $P<0.0001$). The plasma CCL11 combine the cotinine level predicted alcohol dependence (AUC=0.91, $P<0.0001$).

In summary, inflammatory plasma CCL11 is correlated with the severity of alcohol dependence. Plasma CCL11 combine cotinine levels may be a novel indicator to predict alcohol dependence.

投稿學會：台灣基礎神經科學學會 | 編號:34

The gain-loss frequency and long-term outcome reassessed in the Soochow gambling task: Evidence from an internet addiction cases/internet gaming disorder cases study

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Abstract

Objective The present experiment is an extension of Lin et al (2019) and examined the mechanisms of internet addiction, specifically, how behaviors of internet addiction are affected by gain-loss frequency and long-term outcomes (expected value). Namely, we tested the differences in the decision patterns between the participants with internet addiction and non-internet addiction in the Soochow gambling task (SGT, Chiu et al., 2008).

Method The 23 participants were diagnosed as internet gaming disorder, also, the 38 participants of the control group were diagnosed as non-internet addiction by a psychiatrist. Both groups were asked to complete IGT first (Lin et al., 2019) and then SGT. All participants of both groups were the same as that of Lin et al., (2019) study.

Results and Discussion The results of the experiment in the SGT are consistent with the previous studies (Chiu et al., 2008) that the participants prefer to choose bad decks and were affected by gain-loss frequency rather than long-term outcomes. Notably, there are no significant differences between the IA and control groups. According to the results, there are three possibilities. First, the performances between the IA and control groups do not differ significantly in the SGT. Second, the mechanisms of internet addiction are complex and cannot only be evaluated by gain-loss frequency and long-term outcomes. Finally, the present experiment has its limitations and cannot distinguish the characters of these two groups due to some confounding (e.g. following stage of IGT).

Conclusion Gain-loss frequency is very dominant to affect decision-makers including the cases with the internet addition in an uncertain situation. At present, there is not convinced evidence to reveal the differences in decision patterns between the IA and control groups for the gain-loss frequency and long-term outcome.

投稿學會：台灣神經罕見疾病學會 | 編號:35

Characterization of *Dlgap2* mutant, a mouse model of autism spectrum disorder

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Abstract

Autism spectrum disorders (ASDs) are characterized by impaired communication, reciprocal social interaction, restricted repetitive behavior or interests and cognitive dysfunctions. Recently, a deletion of approximately 2.4Mb at 8p23 terminal region in a Taiwanese autistic boy has been identified. Among genes mapped in this region, DLGAP2 might be involved in the pathogenesis of ASDs. In order to elucidate the function of DLGAP2, we generated *Dlgap2* gene knockout mice and characterized their phenotypes. In the open field and prepulse inhibition (PPI) test, no obvious difference was noticed in homozygous (Homo) and heterozygous (Het) *Dlgap2* mutant mice, suggesting the locomotor activity and sensorimotor gating property were not affected by the mutation of *Dlgap2* gene. Notably, impaired short-term recognition memory in the novel object recognition test and defect in spatial memory in the water maze test were observed in the Homo mice, indicating the impairment of hippocampal function in these mutants. We then examined the dendritic features of the hippocampal neurons, including the granule cells in the dentate gyrus (DG) and pyramidal neurons in the Cornu Ammonis 1 (CA1) regions. In the Homo mice, the dendritic complexity was reduced in the DG neurons which is in line with the functional defects in these mice. The morphology of hippocampal neurons in the Het mice was comparable to that in the wildtype mice. DLGAP2 is a postsynaptic scaffold protein, highly expressed in the hippocampus. Here we demonstrated the importance of DLGAP2 by showing impaired hippocampal function and reduced dendritic complexity in hippocampal neurons in homozygous *Dlgap2* mutant mice. Mutation of DLGAP2 gene might be related to the cognitive impairments of ASDs.

投稿學會：台灣神經罕見疾病學會 | 編號:36

Vacuolar ATPase Subunit Gene *ATP6V1B2* Variation Causes Complex Brain Malformation and Hearing Impairment

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Abstract

ATP6V1B2 encodes the B2 subunit of the vacuolar ATPase, which is responsible for acidification of intracellular organelles. Mutations in ATP6V1B2 gene have been reported in dominant deafness-onychodystrophy (DDOD) and Zimmerman Laband Syndrome (ZLS). Both syndromes presented with multi-system malformation, including intellectual disability, nail hypoplasia and hearing impairment. Recently, epilepsy has been associated with ATP6V1B2 mutations but brain malformation was not described. Here, we reported a case severe intellectual disability, epilepsy caused by complex brain malformation (microcephaly, agenesis of corpus callosum, cortical dysgyria and hindbrain hypoplasia) caused by de novo missense single nucleotide variant (c.C1097G, p.Pro366Arg) in *ATP6V1B2* gene identified by whole exome sequencing technology. The variant p.Pro366Arg located in the nucleotide binding domain, which is likely to affect the ATP hydrolysis activity.

Using immunofluorescent microscopy, the mutant locates to the lysosome similar to the wild type ATP6V1B2. Immunoprecipitation assay demonstrated that the mutant decreased binding to the A subunit of the V1 complex (ATP6V1A) compared to wild type ATP6V1B2. In addition, our preliminary data demonstrate that expressing the mutant ATP6V1B2 interferes with neuronal differentiation of stem cells.

Taken together, our finding expanded the phenotypic spectrum of ATP6V1B2 to include complex brain malformation. The functional experiment support the mutant affected the assembly of vacuolar ATPase complex on lysosome and perhaps also interfere with normal neuronal differentiation.

投稿學會：台灣神經罕見疾病學會 | 編號:37

Astrocytic *Epm2a* / laforin deficiency disrupts perineuronal astrocyte processes and synaptic integrity in Lafora disease animal and cell models

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Abstract

Lafora disease (LD) is caused by mutations in *Epm2a* to induce adolescence-onset myoclonic epilepsy and neurodegeneration. *Epm2a* encodes laforin, a dual-specificity phosphatase with a carbohydrate-binding module that interacts with glycogen to prevent glycogen hyperphosphorylation and mediates glycogen degradation. Laforin deficiency caused by *Epm2a* mutations induces formation of Lafora bodies (LBs), composed of insoluble polyglucosan accumulation, and glycogen metabolism dyshomeostasis. The lack of laforin in astrocytes has been shown to impair surface expression of glutamate transporter 1 (GLT1), which is mainly expressed on perineuronal astrocyte processes (PAPs) to maintain glutamate homeostasis at excitatory synapses. However, the role of astrocytic laforin in astrocyte-neuron interactions remained largely unknown. In this study, we used *Epm2a* heterozygous (*Epm2a*-Het) mutant mice, a LD mouse model, to perform comparative hippocampal transcriptome analysis, and found that GLT1-related genes are reduced. Q-PCR and Western blotting validation were performed in the hippocampus of *Epm2a*-Het mice, suggesting a possible cascade mechanism involved in the regulation of glutamate homeostasis. We further generated a GFAP promoter-driven *Epm2a* shRNA (pCDH-GFAPpro-EGFP-sh*Epm2a*) to direct astrocyte-specific *Epm2a* knockdown (*Epm2a*-asKD) in primary glia-neuron (GN) mix culture as a LD cell model. *Epm2a*-asKD induces LB formation and cell death, GLT1 downregulation, withdrawal of both GLT1-labeled PAPs and MAP2-labeled dendrites, and reduction of vGluT1/PSD-95-labeled excitatory synapses in the GN mix culture. Therefore, our results suggest that astrocytic *Epm2a* deficiency leads to the disruption of perineuronal astrocyte processes and the loss of excitatory synapses, which may contribute to the pathogenesis of LD-associated hyperexcitation and neurodegeneration. (MOST107-2321-B-010-009-MY3; MOST107-2811-B-010-010).

投稿學會：台灣神經罕見疾病學會 | 編號:38

Study on the function of phosphorylated paxillin at serine 119 in the developing brain

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Abstract

Receiving physical and chemical stimuli from the environment can trigger the recruitment of signaling proteins through critical mediators such as paxillin. Paxillin is a multifunction adaptor protein serving as a signaling mediator in signal transduction of cell migration. Neural paxillin is found at focal adhesion sites and plays a critical role in regulating endocytosis to facilitate neurite initiation. The paxillin family genes, paxillin, Hic-5, and leupaxin, can translocate into the nuclei of nonneural cells and alter their gene expression. Stage-dependent neural development requires precise gene regulation to determine neural fate. Whether neural paxillin has nuclear functions during brain development and, if so, what these functions are, is unclear. To investigate the genetic networks regulated by neural paxillin, I will use chromatin immunoprecipitation sequencing to identify the binding region of genes and their associating partners. I will then determine the existence of brain-specific phosphorylation sites that modulate the nuclear functions of neural paxillin by comparing the phosphorylation status of different organs through liquid chromatography with tandem mass spectrometry (LC-MS/MS). I will investigate the upstream and downstream signaling pathways regulated by these brain-specific phosphorylation sites through a pharmacological approach and genetic modification. Finally, I will explore the molecular mechanisms of nuclear translocation of neural paxillin through brain-specific phosphorylation. In sum, I will discuss the critical contribution of neural paxillin to controlling the transcriptional activity of certain genes during brain development. I will also explore how the brain-specific modulation of paxillin can induce nuclear translocation at a critical time point of neural development.

Keywords: paxillin, nucleus, genetic regulation, brain development

投稿學會：台灣神經罕見疾病學會 | 編號:39

Efficient in Utero Gene Transfer to the Mammalian Inner Ears by the Synthetic Adeno-Associated Viral Vector Anc80L65

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Abstract

Sensorineural hearing loss is one of the most common sensory disorders worldwide. Recent advances in vector design have paved the way for investigations into the use of adeno-associated vectors (AAVs) for hearing disorder gene therapy. Numerous AAV serotypes have been discovered to be applicable to inner ears, constituting a key advance for gene therapy for sensorineural hearing loss, where transduction efficiency of AAV in inner ear cells is critical for success. One such viral vector, AAV2/ Anc80L65, has been shown to yield high expression in the inner ears of mice treated as neonates or adults. Here, to evaluate the feasibility of prenatal gene therapy for deafness, we assessed the transduction efficiency of AAV2/Anc80L65-eGFP (enhanced green fluorescent protein) after microinjection into otocysts in utero. This embryonic delivery method achieved high transduction efficiency in both inner and outer hair cells of the cochlea. Additionally, the transduction efficiency was high in the hair cells of the vestibules and semicircular canals and in spiral ganglion neurons. Our results support the potential of Anc80L65 as a gene therapy vehicle for prenatal inner ear disorders.

投稿學會：台灣神經罕見疾病學會 | 編號:40

Growth hormone rescue cerebellar degeneration in SCA3 transgenic mice

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Abstract

Spinocerebellar ataxia type 3 (SCA3) is a fatal neurodegenerative disease for which no identified effective treatment or prevention methods exist. However, low-dose growth hormone (GH) therapy, as a potential off-label use, may deter the progress of SCA3. SCA3 15Q and SCA3 84Q transgenic mice harboring a YAC transgene that expresses the human ATXN3 gene with a pathogenic expanded 15 CAG repeat and 84 CAG repeat motif, respectively, were recruited. SCA3 15Q transgenic mice were considered as the healthy control group, whereas low-dose GH- and PBS-treated SCA3 84Q transgenic mice were considered as the study and sham groups, respectively. The SCA3 84Q transgenic mice were administered intraperitoneal injections of GH or PBS weekly from the postnatal age of 9 months to 18 months. After 9 months of GH treatment in the SCA3 84Q transgenic mice, all locomotor functions including rotarod test, behavior box analysis were restored. The GH-treated SCA3 84Q mice revealed more preserved Purkinje cells/cerebellar cortex and less ataxin-3 aggregation, DNA oxidative, cell apoptosis compared with the PBS-treated SCA3 84Q mice. GH therapy may be one of the potential off-labeled using in the alleviation of SCA3 progression.

投稿學會：台灣神經罕見疾病學會 | 編號:41

Curcumin Analog JM17 Enhance the Degradation of Poly-Q Aggregation in cell Models of Spinocerebellar Ataxia-3

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Abstract

Polyglutamine (polyQ)-expanded mutant ataxin-3 protein, which is prone to misfolding and aggregation, leads to cerebellar neurotoxicity in spinocerebellar ataxia type 3 (SCA3), an inherited polyQ neurodegenerative disease. Although the exact mechanism is unknown, the pathogenic effects of mutant ataxin-3 are associated with dysregulation of transcription, protein degradation, mitochondrial function, apoptosis, and antioxidant potency. An activator of Nrf1 and Nrf2, JM17, a curcumin analog, developed by Alllianz Pharmascience Ltd., has been shown to ameliorate the toxicity of mutant Huntingtin protein in Huntington's disease model (R6/2-1J) and improve motor coordination and activity as well as the shrinkage of cortex and striatum volume. It is well known that the pathogenesis in both of diseases are caused by abnormal aggregation of polyQ mutant protein in nuclei of specific neurons to induce the neurodegeneration diseases. Thus, in this study, we investigated the impact of JM17 on cell viability, mitochondrial respiratory function, protein aggregation, and oxidative stress in SCA3 cells. Treatment with JM17 decreased the levels of mitochondrial and cellular total reactive oxygen species and increased HO-1, NQO1, SOD1 and SOD2 protein expression in SCA3 cells. JM17 also diminished mutant ataxin-3 proteins expression and protein aggregation. Moreover, JM17 enhanced the mitochondrial respiration by measuring oxygen consumption the basal respiratory rate, indicating oxidative phosphorylation, as well as maximum oxidative phosphorylation and ATP production, maximum uncoupled capacity in SCA3 cells. Notably, JM17 slightly upregulated Nrf2 transcription activity and nuclear Nrf2 proteins expression. In summary, our study provides that the JM17 has the potential for improving mitochondrial function and antioxidant potency in SCA3.

Keywords: Oxidative stress; mutant ataxin-3; mitochondrial respiratory function; JM17; Nrf2.

投稿學會：台灣神經罕見疾病學會 | 編號:42

From peptide probes to therapeutic peptides for neurodegenerative diseases

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Abstract

Protein misfolding and aggregation play an important role in different neurodegenerative diseases including Amyotrophic Lateral Sclerosis (ALS) and Huntington's disease (HD). In the past decade, our group has been focusing on delineating the roles of TAR DNA-binding protein (TDP-43) and mutant Huntingtin protein (mHTT) in ALS and HD. Since 2010, we reported the first amyloidogenic properties of the TDP-43 C-terminal peptide fragments and disclosed their seeding properties. Given the valuable knowledge learned from these amyloidogenic polypeptides, we chemically-synthesized a series of photocontrollable probes deduced from the TDP-43 peptide fragments as a unique tool for the study of ALS in 2017. Our probe allows spatiotemporal control of amyloidogenic nanofibril formation in the living cells. We also found these photoinduced neurotoxic aggregates impaired the nucleocytoplasmic transport in ALS, which sheds light on the early pathogenesis of neurodegenerative diseases. With the inspiration of the physiochemical properties of TDP-43 peptide fragments, we further developed amphiphilic peptides against mHTT aggregation in Huntington's disease in 2019. We demonstrated the positively-charged amphiphilic peptide conformationally transformed the oligomers and aggregates of mHTT, ameliorate mHTT-induced neurological deterioration in both cell and HD mouse models, and rescue the memory deficit through intranasal administration. Recently, we also found the complex of negatively-charged amphiphilic peptides with chitosan suppressed the mHtt inclusion body formation and reduced mHTT neuron toxicity.

投稿學會：台灣神經罕見疾病學會 | 編號:43

Development of small molecule agonists targeting TRKB for Alzheimer's disease treatment: virtual screening, molecular modeling and Tau/Aβ cellular models

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Abstract

Brain-derived neurotrophin factor (BDNF) is a member of neurotrophin family which participates in neuronal health. The binding of matured BDNF to its high-affinity tropomycin-related kinase receptor B (TRKB) induces dimerization of TRKB which subsequently activates signaling cascades critical for neuronal survival, development and synaptic plasticity. These effects make BDNF-TRKB pathway a potential therapeutic target of neurodegenerative diseases such as Alzheimer's disease (AD), since reduced BDNF levels were found in AD brains. While clinical application of BDNF has been limited because of poor blood-brain barrier penetration and low plasma stability, small-molecule BDNF mimetics that selectively target the TRKB receptor provide a strategy to overcome these limitations. Previously, administration of 7,8-dihydroxyflavone (7,8-DHF), a TRKB specific agonist, significantly improved spatial memory and minimized dendrite loss in the hippocampus of AD mice. In addition, a novel synthetic chalcone-coumarin hybrid LM-031 delayed AD progression by targeting HSPB1 to reduce Tau misfolding and activating NRF2 and CREB pathways to suppress apoptosis and promote neuron survival. In this study, virtual screening was carried out to find analogous compounds of 7,8-DHF and LM-031 to expand chemical space of potential agonists. BDNF has been shown to bind to leucine-rich motif (LRM) and the second Ig-like (Ig-2) domain (or d5 domain) in the extracellular domain of TRKB. In molecular modeling, docking conformation between potential agonists and 7,8-DHF with TRKB d5 domain (PDB 1hcf) was compared. Also, *E. coli*-expressed complete extracellular domain (including LRM and d5) of TRKB was purified and applied on surface plasmon resonance (SPR) to confirm the binding of potential agonists to TRKB. Moreover, we tested these compounds on our ΔK280 tau_{RD}-DsRed and Aβ-GFP SH-SY5Y AD cell models, to examine the molecular mechanisms of these compounds. Combining modeling computation, SPR and AD cellular experiments results, the derived compounds could be possible therapeutic candidates in AD, while still need more experiments to verify.

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Functional Characterization of *PIAS1* Gene Variants in Huntington's Disease

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Abstract

Huntington's disease (HD) and spinocerebellar ataxia type 3 (*SCA3*) are polyglutamine (PolyQ)-related diseases with a CAG-trinucleotide-repeat expansion in the *huntingtin* and *ataxin-3* genes, respectively. The length of CAG-trinucleotide-repeat is the major determiner of the age of onset (AO) of polyQ-related diseases. Deviation from the average AO suggests the presence of genetic modifier(s). We first conducted exome screening of 583 genes, which have been implicated in proteinopathies, of 500 patients (140 HD and 360 SCA3). Five *PIAS1* gene variants associated with the late AO of HD and SCA3 were identified. PIAS1 is known to regulate the JAK/STAT signaling by repressing the transcriptional activity of STAT1 in the interferon signaling pathway. It possesses the function of a E3 SUMO ligase and stabilizes the interaction between the E2 SUMO conjugating enzyme and the substrates. This is of great interest because both protein clearance pathways (the ubiquitin proteasome system and autophagy) label target proteins with ubiquitin for degradation. The extent of SUMO labeling therefore is associated with protein stability. To determine the contribution of *PIAS1* gene variant on the accumulation of the disease-causing protein (i.e., the polyQ-expanded HTT, mHTT), expression constructs of *PIAS1* (wild type or variant) were transfected along with the expression construct of mHTT (i.e., Q_{25} and Q_{109}-HTT_{EX1}) into HEK293T cells. Results of a filter-trap assay revealed that PIAS1 variants significantly reduced the accumulation of insoluble mHTT, when compared with wildtype PIAS1. Furthermore, using the GST-pull down assay and baits comprising of GST-Q_{25}-HTT_{EX1} or GST-Q_{43}-HTT_{EX1}, we observed that a PIAS1 variant (PIAS1-V3) had a lower ability to interact with both HTT and mHTT than wild type. Based on the above findings, we generated a HD mouse model (R6/2) expressing PIAS1-V3 to evaluate the biological impact of PIAS1 variants *in vivo*. Characterization of this HD mouse model will provide evidence to validate our clinical finding and reveal the underlying mechanism.

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The protective role of Translin associated factor X (TRAX) in Huntington's disease (HD)

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Abstract

TRAX was first discovered as a binding partner of Translin identified using a yeast two-hybrid system. Both TRAX and Translin are highly enriched in the brain. The heteromeric complex composed of TRAX and Translin shows nucleic acid binding activity, plays a role in dendritic RNA trafficking in neurons and suppresses the microRNA-mediated RNA silencing at activated synapses by degrading pre-miRNA in neurons. TRAX is also known to interact with an activator of DNA-PK (C1D) during DNA damage and the C terminus of the A_{2A} adenosine receptor ($A_{2A}R$). Our laboratory recently discovered that TRAX ameliorates the H_2O_2-induced DNA damage and primary neurons during $A_{2A}R$ activation.

Huntington's disease (HD) is an inherited neurodegenerative disease. This devastating disease is caused by a CAG repeat expansion (>36) mutation in the exon 1 of *huntingtin*, which encodes an elongated polyglutamine (polyQ) repeat in mutant Huntingtin protein (mHTT). Accumulation of mHTT gives rise to aggregates in nucleus, cytosol, and neurite that lead to neuronal loss in HD brains. We discovered that the mRNA and protein levels of TRAX and Translin were significantly increased in the striatum of R6/2 HD mice when compared with those of WT. Down-regulation of TRAX by intrastriatal delivery of AAV harboing TRAX shRNA in the striatum of HD mice (R6/2) accelerated HD disease progression. TRAX downregulation suppressed the expression of DARPP-32 and increased sizes of mHTT aggregates in the striatum of HD mice. These data indicate that TRAX plays a protective role in HD. To gain insights into how TRAX functions *in vivo*, we have identified the miRNAs/mRNAs that were modulated by TRAX downregulation in the striatum of HD mice by RNA sequencing. The role of these TRAX-regulated miRNA/mRNA in HD pathogenesis will be discussed.

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Treadmill training increases the motor activity and neuron survival of the cerebellum in a mouse model of spinocerebellar ataxia type 1

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Abstract

Spinocerebellar ataxia (SCA) type 1 (SCA1) is a rare autosomal dominant disorder that is characterized by worsening of disordered coordination, ataxia of the trunk, and other neurological symptoms. Physical activity improves both mobility and the daily living activities of patients with SCA. Intervention with daily regular treadmill exercise may slow the deterioration of cerebellar neurons in SCA1. Therefore, the signal changes and performance of cerebellar neurons after exercise in SCA1 was investigated in this study. We employed a transgenic mouse model of SCA1, generated by amplifying the cytosine-adenine- guanine trinucleotide repeat expansions, and the mice underwent 1 month of moderate daily treadmill exercise for 1 hour. The rotarod test revealed that the motor function of the SCA1 mice that underwent training was superior to that of the control SCA1 mice, which did not undergo training. Moreover, the cerebellar pathology revealed preserved Purkinje neurons stained by carbindin with an increase of the neuronal Per Arnt Sim domain protein 4, a key regulation in the structural and functional plasticity of neurons, in the excised SCA1 mice relative to the controls. The mechanism was related to an increase of phosphorylation of ribosomal protein S6, a downstream target of the mammalian target of rapamycin pathway, but not to autophagy activation. This study determined that regular treadmill exercise may play a crucial role in the viable support of cerebellar neurons in SCA1.

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Insulin-like growth factor-1 (IGF-1) as a potential therapy for the spinal cerebellar ataxia type III

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Abstract

Spinocerebellar ataxia type 3 (SCA3),also known as Machado-Joseph disease (MJD), is the most common polyglutamine (polyQ) disease in the world, mainly because of the excessive accumulation of polyQ mutant proteins, ataxin-3, which leads to the increase in protein aggregation, oxidative stress and cerebellar neurotoxicity. Our previous study showed that low dose of growth hormone (GH) restored the locomotor, preserved more Purkinje cell/cerebellar cortex and less ataxin-3 aggregation in the SCA3 transgenic mice. Although GH treatment has a protective effect on neurons, it used in non-GH deficiency syndrome patient is still a safety issue. Thus we apply GH-downstream molecular: insulin-like growth factor-1 (IGF-1), which not only easily passes through the cerebral blood barrier, but also has neuroprotection. Here, we performed intraperitoneal injection of IGF-1 (50 mg/kg) or saline (as placebo group) in SCA3 transgenic mice weekly from the postnatal age of 9 months to 18 months. The current progress of the study found that after 9 months of IGF-1 treatment in the MJD 84Q mice, most of the locomotor functions including rotarod test, open field test and catwalk analysis were restored. Moreover, cerebellar immunochemistry stain also revealed more preserved Purkinje cell/cerebellar cortex and less ataxin-3 aggregation. Furthermore, IGF-1 treated mice had higher cerebral mitochondrial respiratory function, higher phosphorylation activity, more ATP production and better electron delivery system, indicated IGF-1 treatment might improve mitochondrial function.

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ERK activation precedes Purkinje cell loss in mice with Spinocerebellar ataxia type 17

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Abstract

Spinocerebellar ataxia type 17 (SCA17) is one subtype of autosomal dominant cerebellar ataxia group caused by the CAG/CAA expansion in the TATA-binding protein (TBP) gene. The clinical features are progressive ataxia, spasticity, chorea, Parkinsonism and cognitive impairment. Cerebellar atrophy, Purkinje cell loss and gliosis are the neurological hallmarks of SCA17 disease, which ultimately lead to ataxia and behavioral disorders. We have established the SCA17 transgenic mice to study how abnormal TBP aggregates could induce the SCA17 pathology. In this study, we focused the analysis of mice at 4-8 week-old, the disease onset initiation age. We found that a reduction of Purkinje cell count, mutant TBP aggregation in the Purkinje cell nuclei and the activation of microglia appeared in the 4 week-old SCA17 transgenic mice. The degeneration of Purkinje cells occurs since 6 weeks old. The presence of astrogliosis and Bergmann's gliosis was also observed since then. The activated ERK was identified in the reactive astrocytes and Bergmann's glial cells. Simultaneously, SCA17 transgenic mice showed abnormal motor coordination. Furthermore, the expression of Bax/Bcl2 ratio, active caspase-3 and cleaved PARP were significantly increased in the 6- and 8- week-old SCA17 transgenic mice. The gait abnormalities and motor incoordination in the 6 week-old SCA17 mice are corresponded to the neurological pathogenesis. Our study suggests that the activation of ERK in astrocytes and Bergmann glia may contribute to the elevated gliosis and the neuronal apoptosis in the SCA17 mouse cerebellum. Further, we identified a potential GSK3 inhibitor PHA-767491, also known as Cdc7/CDK inhibitor, which has a neuroprotective effect by inhibiting the neuroinflammation in the protein aggregation diseases, AD and SCA17 models. PHA-767491 reduced the active glial cells in both the SCA17 primary and organotypic slice cultures. In addition, PHA-767491 improved the gait abnormalities and reduced inflammation in the SCA17 transgenic mice. From the above data, we suggest that inhibition of the neuroinflammatory pathways might be a potential therapeutic strategy for the SCA17 disease.

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AMPK activation disrupts the nuclear import pathway in motor neurons and contributes to amyotrophic lateral sclerosis

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Abstract

The degeneration of motor neurons is a key event in amyotrophic lateral sclerosis (ALS). Mislocalization of TAR DNA-binding protein 43 (TDP-43) from the nucleus to the cytoplasm is an early event and a hallmark of ALS. We previously reported that abnormal AMPK activation mediates TDP-43 mislocalization in motor neurons. In the present study, we demonstrated that aberrant AMPK activation reduced the interaction between importin-α and TDP-43, and blocked the importin-α-mediated nuclear import of TDP-43. Intriguingly, the interaction between importin-α and its exportin (CAS) was also suppressed during AMPK activation, suggesting an impairment in the function of importin-α. We next examined whether abnormal AMPK activation affects the importin-α-mediated transport of proteins other than TDP-43. We performed a comparative proteomic analysis of importin-α complexes harvested by immunoprecipitation. GO analysis from proteomic results suggested that the protein translation machinery is affected during AMPK activation. AMPK activation also altered the cellular localization of many substrates of importin-α. Collectively, our findings suggest that abnormal AMPK activation affects the cellular distribution of many proteins by impairing the importin-α-mediated nuclear import, and contributes to the degeneration of motor neurons.

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Association of visual motor coordination and social cognition in schizophrenia

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Abstract

Patients with schizophrenia have difficulties in social cognitive domains including emotion recognition and mentalization, and in sensorimotor processing and learning. The relationship of social cognitive deficits with sensorimotor function in patients with schizophrenia remained largely unexplored. We hypothesized that visual motor processing impairments may decelerate information processing and affects various domains of social cognition. Thus, we examined the association of nonverbal emotion recognition, mentalization, and visual motor processing in schizophrenia. The study examined mentalization using the Chinese version of Theory of Mind (CToM) and emotion recognition using the Diagnostic Analysis of Nonverbal Accuracy 2-Taiwan version (DANVA-2-TW), basic motor function by Finger Tapping Test (FFT), and sensorimotor processing and learning using a joystick tracking task for visual motor coordination in 34 individuals with chronic schizophrenia in the community and 42 healthy controls. Patients with schizophrenia had significantly worse performance than healthy controls in both facial and prosodic emotion recognition and mentalization. Their emotion recognition ability was positively associated with mentalization. Both visual motor coordination and learning was also significantly worse in patients with schizophrenia. Both emotion recognition (mainly in prosodic modality, happy and sad emotions) and mentalization were positively associated with the visual motor learning capacity while controlling for basic motor function and visual motor coordination in patients with schizophrenia. The visual motor learning capacity had a significant positive association with social cognitive functions in schizophrenia. The relationship may provide a new direction for restoration of social cognitive function in schizophrenia by enhancing visual motor coordination and learning capacity. The future study for exploring the fundamental neural mechanism and the potential effect of visual motor coordination training is warranted.