The way out of dilemma in treatment of brain injury

Host: 陳元皓、李旭東

Location: 生物醫學科學研究所 B1A會議室
Institute of Biomedical Sciences (IBMS) B1A room

Time: Sep. 11, 16:35-17:50

Participate Societies: Taiwan Neurotrauma Society (台灣神經創傷學會)

An important medical concept of chronic pathological change of brain had been recognized from soldier back to US form Iraq which suffered from blast explosion. The epidemiology of repeated combat- or traffic accident- related mild to moderate brain injury should be clarified. On the other hand, the repeated concussion related to professional athletic injury (ex. football player or boxer related injury), which may induced the permanent brain parenchyma injury had been attracted the attention in these years.

Moreover, chronic traumatic encephalopathy (CTE) was conceptualized as a neurological disorder affecting some active and retired boxers who had tremendous exposure to neurotrauma in the 20th century. However, the field have asserted definitively that CTE is a delayed-onset and progressive neurodegenerative disease in recent years, which had been proved by research groups in the USA with statement indicated that these symptoms may appear in midlife or decades after exposure or repeat concussion injury. Most prominently, the mechanisms underlying traumatic axonal injury, microglial activation, amyloid-beta accumulation, and progressive tau pathology are not yet known. In addition, the role of injury to dendritic spine cytoskeletal structures, vascular reactivity impairments, and microthrombi are intriguing and subjects of ongoing inquiry that need to be further investigated. Then the frontier of clinical therapy for TBI to ameliorate the above pathological change are also discussed.

Therefore, in this nanosymposium, we want to highlight the importance of CTE related to repeat or series TBI, which induced the neuronal circuit transmission impairment and other sequelae that became the challenges of the clinical therapy. The topic of this nanosymposium will include the evidence base of CTE, the neurotransmission impact by TBI, cell therapy for brain injury and hyperbaric therapy for TBI patients.

The symposium is host by Taiwan Neurotrauma Society in hopes to improve treatment methods within the realms of neuro-trauma pathophysiology and treatment, to promote extensive research and cooperation between researchers and clinician.

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The Neuropathology of Chronic Traumatic Encephalopathy

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Taipei City 114 Taiwan (R.O.C.)

Abstract

Chronic traumatic encephalopathy (CTE) wildly discussed for a while. However, the understanding of CTE progressed slowly due to that it can only be confirmed after completed the postmortem brain examination. Until recently, CTE has been understood as a neurodegenerative disease and characterized by abnormal p-tau protein accumulation. The first systemically pathologic classification showed in 2011, by Dr. Omalu. He proposed the Omalu criteria for the neuropathological diagnosis of CTE as four “emerging histo-morphological phenotypes.” Although it was a considerable step of the pathologic criteria to follow, there were still some unclear details, such as how CTE distinguished the other mimic diseases. In 2013, the McKee criteria emerging for the neuropathological diagnosis of CTE, which provided the solution for it and becomes the most popular criteria nowadays. Most of the updated pathology criteria of CTE mainly based on this fantastic work. Here, we tried to briefly summarize the changed and update pathologic criteria used in the Chronic Traumatic Encephalopathy.

Selected recent publications:

Li YF, Thom M, Jacques TS. Novel therapeutic targets in epilepsy: oxidative stress and iron metabolism. Neuropathology and applied neurobiology. 2020.

Wang CY, Lin JC, Li YF, Yang CW. Alpha-fetoprotein producing pancreatic neuroendocrine tumor. QJM : monthly journal of the Association of Physicians. 2020.

(Conference Paper) Y.-F, T. Jacques. Using models of cell-cell interactions in the focal cortical dysplasia (FCD) to unravel the cellular diversity in developmental cortical lesions. . Brain Pathol. 2019;Suppl 1:3-198.

(Conference Paper) Y.-F. Li AF, J.C. Pickles, A. Virasami, F. Sceirf, S.R. Picker, M. Tisdall, A. Avery, A. R. Fairchild, J.C. Pickles, H. Cross, D. Hargrave, T. Jacques. (Oral Abstract) Identifying cellular diversity in developmental cortical lesions using models of cell-cell interactions in the focal cortical dysplasia. Neuropathol Appl Neurobiol. 2018;44 Suppl 1:5-49.

Hueng DY, Tsai WC, Chiou HY, Feng SW, Lin C, Li YF, et al. DDX3X Biomarker Correlates with Poor Survival in Human Gliomas. International journal of molecular sciences. 2015;16(7):15578-91.

Hueng DY, Li YF, Sytwu HK. Atypical meningiomas. Journal of neurosurgery. 2014;120(3):781.

Transplantation of a Novel Stem Cell Sheet for Cerebral Reconstruction

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Department of Neurology, Tri-Service General Hospital & Graduate Institute of Medical Sciences, National Defense Medical Center, Taiwan

Ph.D. in Neuroscience, King's College London, London, UK

M.D. School of Medicine, National Defense Medical Center, Taipei, Taiwan, Republic of China

Abstract

Brain damage causes neurological damage which usually cannot be fully recovered. Traumatic brain injury, stroke and neurodegenerative diseases all involve brain tissue loss. Reconstruction of lost brain tissue is therefore an important task in the field of tissue engineering.

We devised a novel co-culture model, using human brain neural stem cells (NSCs) and human cerebral microvascular endothelial cells, to form a cell sheet construct for building neurovascular tissue in the brain. In the pre-clinical animal efficacy verification, we used a rat model of surgical brain trauma to conduct NSC sheet transplantation, combined with molecular biology techniques, neuropathological anatomy, and interventional drugs for exploring angiogenesis mechanisms. Neurobehavioral assessments revealed that the rats in the treatment group performed significantly better than the control group.

Our innovative cell sheet technology directly treats the lesions by transplantation, avoiding the obstacle of blood-brain barrier. In addition, NSC-engineered cell sheet transplantation for cortical damage avoids brain tissue damage which may happen during injection, and the extracellular matrix in the cell sheet provides a scaffold essential for tissue reconstruction.

Selected recent publications:

Chung-Hsing Chou & Michel Modo (2020, May). Characterization of Gene Expression Changes in Human Neural Stem Cells and Endothelial Cells Modeling a Neurovascular Microenvironment. *Brain Res Bull*. 2020 May;158:9-19.

Chung-Hsing Chou & Michel Modo (2016, Jul). Human neural stem cell induced endothelial morphogenesis requires autocrine/paracrine and juxtacrine signaling. *Scientific Reports*, 6:29029.

Chung-Hsing Chou, Hueng-Chuen Fan, and Dueng-Yuan Hueng (2015, Nov). Potential of Neural Stem Cell-Based Therapy for Parkinson's Disease. *Parkinson's Disease*. Volume 2015, Article ID 571475.

Chung-Hsing Chou, John D. Sinden, Pierre-Olivier Couraud, Michel Modo (2014, Sep). In Vitro Modeling of the Neurovascular Environment by Coculturing Adult Human Brain Endothelial Cells with Human Neural Stem Cells. *PLoS ONE*, 2014; 9(9): e106346.

The Role of Hyperbaric Oxygen Therapy in Traumatic Brain Injury

Chung-Kan Peng (彭忠衍)
Associate professor, Department of Internal Medicine, National Defense Medical Center, Taipei, Taiwan

Director of Division of Pulmonary Medicine and Critical Care Medicine, Department of Internal Medicine, Tri-Service General Hospital, Taipei, Taiwan

Director of Sleep Medicine Center, TSGH, Taipei, Taiwan

Attending physician of Undersea and Hyperbaric Medicine Center, Taipei, Taiwan

MD., PhD., National Defense Medical Center, Taipei, Taiwan

Abstract

Traumatic brain injury (TBI) is in a common health issue which causes public and family problems. In the USA approximately 0.56% of the population suffers a head injury, with a case fatality rate of about 40% for severe injuries each year and 2% of the population live with long-term disabilities following head injuries. Here, we consider hyperbaric oxygen therapy (HBOT- by using a pressurized chamber of > 1.4 absolute atmospheres) as the adjunctive therapy to neurosurgery for reducing brain swelling, improving brain tissue hypoxia and avoiding neuronal cell death. HBOT for TBI is still controversial or not approved by the US Food and Drug Administration because of a lack of solid clinical evidence supporting the standard use of HBOT. More studies are indicated to provide another intensive care regimen which may reduce patient death and disability by using HBOT in the future.

Selected recent publications:

Chung-Kan Peng, Kun-Lun Huang, Chin-Pyng Wu, Yao-Kuang Wu, I-Shiang Tzeng, Chou-Chin Lan. Phosphodiesterase-4 Inhibitor Roflumilast Attenuates Pulmonary Air Emboli-Induced Lung Injury. J Surg Res. 2019; 241:24-30.

Chung-Kan Peng, Chin-Pyng Wu, Jr-Yu Lin, Shih-Chi Peng, Chien-Hsing Lee, Kun-Lun Huang, Chih-Hao Shen. Gas6/Axl signaling attenuates alveolar inflammation in ischemia-reperfusion-induced acute lung injury by up-regulating SOCS3-mediated pathway. PLoS One. 2019; 14 (7):e0219788.

Yu-Ling Dai, Chin-Pyng Wu, Gee-Gwo Yang, Hung Chang, **Chung-Kan Peng**,* and Kun-Lun Huang*. Adaptive Support Ventilation Attenuates Ventilator Induced Lung Injury: Human and Animal Study. Int J Mol Sci. 2019; 20(23).

Hong-Jie Jhou, Po-HuangChen, Chin Lin, Li-YuYang, Cho-Hao Lee, **Chung-Kan Peng**. High-flow nasal cannula therapy as apneic oxygenation during endotracheal intubation in critically ill patients in the intensive care unit: a systematic review and meta-analysis. Sci Rep. 2020; 10(1):3541.

Remote effect of TBI in Dopamine system: Reward, Reinforcement and Executive Dysfunction

Yuan-Hao Chen (陳元皓）MD, PhD.,

Executive Dean

National Defense Medical Center, Taipei, Taiwan

Neurosurgeon, Professor

Department of Neurological Surgery

Tri-Service General Hospital, Taipei, Taiwan

Abstract

After brain concussion especially repeated high energy impaction may induce long term damage of brain parenchyma , which referred as chronic encephalopathy. The pathologic finding had proved that significant Tau protein deposit in the affected area, but the interesting finding on contrast to these traditional finding were published by Dr. Crane of Washington university in JAA neurology at 2016. 1589 patients with TBI and loss of conscious underwent autopsy after , the major pathologic finding their data indicated that TBI with LOC is associated with risk for Lewy body accumulation, progression of parkinsonism, and PD, but not dementia, AD, neuritic plaques, or neurofibrillary tangles. These statements highlight the major impact of brain by TBI were neurotransmission system especially dopamine system. In this topic, I will go through our series studies which indicated that the releasing pattern between mesocortical limbic system and nigrostriatal system were different:1).The results from functional assay were compatible to the anatomic difference of dopaminergic origination between shell and core portion: revealed in dopamine project from different original areas; the shell portion dopaminergic project come from VTA while the projects to core portion originate from substantia nigra pars compacta. 2). The functional eChem difference revealed that frequency dependent augmentation release is found in shell portion physiologically while under desensitization condition, the phenomena could be found in core portion also. 3). Brain Injury could suppressed the dopaminergic transmission in mesocortical limbic system which resulted in impairments in reward system and behaviors and nicotin-induced CPP could not be induced in TBI animal. 4)Then force exercise could ameliorate the deficit of cortico-striatal synaptic plasticity and motor function resulted from dopamine transmission impaired by 6-OHDA lesioning. The dopamine neuron injury by 6-OHDA were also rescued partially by regular exercise.

Selected recent publications:

Eagle YK Huang, TT Kuo, JJ Tsai, PF Tsui, YC Chou, TH Tsai, HI Ma, YH Chiang, YH Chen. Remote Effects on the Striatal Dopamine System after Fluid Percussion Injury. Behavioural Brain Research, 267:156-172, 2014

Eagle YK Huang, TT Kuo, JJ Tsai, PF Tsui, YC Chou, TH Tsai, HI Ma, YH Chiang, YH Chen.Amantadine ameliorates dopamine-releasing deficits and behavioral deficits in rats after fluid percussion injury. Plos One , Volume 9 (Issue 1) , January 2014, e86354

Chen YH, Huang EY, Kuo TT, Miller J, Chiang YH, BJ Hoffer. Impact of traumatic brain injury on dopaminergic transmission. Cell Transplant. 2017, Vol. 26(7) 1156-1168, doi: 10.3727/096368917X694787.

Chen YH, Huang EY, Kuo TT, Hoffer BJ, Miller J, Chou YC, Chiang YH. Dopamine release in the nucleus accumbens is altered following traumatic brain injury. Neuroscience. 2017 Apr 21;348:180-190. doi: 10.1016/j.

YH Chen, TT Kuo, JH Kao, Eagle YK Huang, TH Hsieh, YC Chou , BJ Hoffer. Exercise Ameliorates Motor Deficits and Improves Dopaminergic Functions in the Rat Hemi-Parkinson's Model. Scientific Reports. 2018; 8:3973 DOI:10.1038/s41598-018-22462-y

YH Chen ,BJ Lin ,TH Hsieh, TT Kuo, J Miller, YC Chou, Eagle YK Huang, BJ Hoffer. Differences in Nicotine Encoding Dopamine Release between Striatum and Shell portion of the Nucleus Accumbens. Cell Transplantation. 2019 Mar;28(3):248-261. doi: 10.1177/0963689718775382. Epub 2018 May 28.

iPSC technology for Parkinson's disease transplantation therapy: Challenges and breakthroughs

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Assistant Research Fellow, Neuroscience Center, Hualien Tzu Chi Hospital, Taiwan.

Ph.D., National Chung Hsing University, Taiwan

Abstract

Parkinson's disease (PD) is one of the most serious neurodegenerative disease. Dopaminergic neuron (DA neuron) loss in substantia nigra is the major cause of PD, but there is still no therapy strategy to regenerate DA neurons or attenuate the degeneration process yet. Induced Pluripotent stem cells (iPSCs) are reprogrammed from various kinds of somatic cell types and have abilities to self-renew and differentiate into every kinds of somatic cells *in vitro*. Thus, iPSC become the considerable promise for PD transplantation therapy. The development of protocols to convert iPSC into midbrain dopaminergic neuron (mDA) promoted the cell therapy for PD. Clinical trials with the cGMP mDA for PD cell therapy were started around the world. In this speech, I will introduce the current status of this field, discuss the challenges and risks. In addition, I will share some of our research works, highlight the possible future directions to improve the iPSC-based technologies for PD clinical treatments.

Selected recent publications:

Yu SJ, Wang YC, **Chang CY**, Hsieh W, Chen S, Yang CS, Lin SZ, Wang Y. NanoCsA improves the survival of human iPSC transplant in hemiparkinsonian rats. Brain Res 2019;1719:124-132.

Lin CY, Wu CL, Lee KZ, Chen YJ, Zhang PH, **Chang CY**, Harn HJ, Lin SZ, Tsai HJ. Extracellular Pgk1 enhances neurite outgrowth of motoneurons through Nogo66/NgR-independent targeting of NogoA. Elife 2019;8.

Chang CY, Ting HC, Su HL, Jeng JR. Combining Induced Pluripotent Stem Cells and Genome Editing Technologies for Clinical Applications. Cell Transplantation. 2018; 27(3):379-392.

Chang CY, Chen SM, Lu HE, Lai SM, Lai PS, Shen PW, Chen PY, Shen CI, Harn HJ, Lin SZ, Hwang SM, Su HL. N-butylidenephthalide attenuates Alzheimer's disease-like cytopathy in Down syndrome induced pluripotent stem cell-derived neurons. Scientific Reports. 2015; 5:8744.

Chen SM, Lee MS, **Chang CY**, Lin SZ, Cheng EH, Liu YH, Pan HC, Lee HC, Su HL. Prerequisite OCT4 Maintenance Potentiates the Neural Induction of Differentiating Human Embryonic Stem Cells and Induced Pluripotent Stem Cells. Cell Transplantation. 2015;24(5):829-44.

Recent advances in pain research
疼痛研究的最新進展

Host: Jen-Kun Cheng (鄭仁坤)、Chi-Chao Chao (趙啟超)

Location:生物醫學科學研究所 B1B會議室
Institute of Biomedical Sciences (IBMS) B1B room

Time: Sep. 11, 16:35-17:50

Participate Societies: Taiwan Neurological Society (台灣神經學學會)、Taiwanese society of Biological Psychiatry and Neuropsychopharmacology (台灣生物精神醫學暨神經精神藥理學會)

Pain is a vital sensation to the human body and it can transmit harmful stimulus signals to the brain, thereby avoiding danger. Pain management is an important topic in both clinical and basic research. Physicians and neuroscientists work together to understand the mechanism of neuropathic pain and search for novel targets for controlling pain. In this nanosymposium, we will present the use of stem cell exosomes in neuropathic pain, the discovery of biomarkers for pain diagnosis and treatment, the impact of chronic pain on cognition and emotion, and the change of neuronal plasticity underlying the development of chronic pain.

Stem Cell Exosome for Neuropathic Pain

Jen-Kun Cheng (鄭仁坤)

Discipline Director of Anesthesiology, MacKay Medical College, New Taipei City, Taiwan.

M.D., Ph.D., MacKay Memorial College/Hospital

Abstract

Nerve injury–induced neuropathic pain is difficult to treat. We have demonstrated the analgesic effects of intrathecal minocycline, gabapentin, cannabinoid receptor agonists and $Ca_V3.2$ blockers in the L5/6 spinal nerve ligation (SNL) pain model.

Recently, we used exosomes derived from human umbilical cord mesenchymal stem cell (UCMSC) as a cell-free therapy for nerve injury–induced pain in rats. Isolated UCMSC exosomes range in size from 30 to 160 nm and contain CD63, HSP60, and CD81 exosome markers. After SNL, single intrathecal injection of exosomes reversed SNL–induced mechanical and thermal hypersensitivities of right hindpaw of rats at initial and well-developed pain stages. Moreover, continuous intrathecal infusion of exosomes achieved excellent preventive and reversal effects for SNL–induced pain. In immunofluorescent study, lots of Exo-green-labelled exosomes could be found majorly in the ipsilateral L5 spinal dorsal horn, dorsal root ganglion (DRG), and peripheral axons, suggesting the homing ability of UCMSC exosomes. They also appeared in the central terminals or cell bodies of $IB4^+$, $CGRP^+$, and $NF200^+$ sensory neurons. In addition, exosome treatment suppressed SNL–induced upregulation of c-Fos, CNPase, GFAP, and Iba1. All these data suggest that the analgesic effects of exosomes may involve their actions on neuron and glial cells. Exosomes also inhibited the level of TNF-a and IL-1b, while enhanced the level of IL-10, brain-derived neurotrophic factor (BDNF) and glial cell line–derived neurotrophic factor (GDNF) in the ipsilateral L5/6 DRG of SNL rats, indicating anti-inflammatory and pro-neurotrophic abilities. Protein analysis revealed the content of vascular endothelial growth factor C (VEGF-C), angiopoietin-2, and fibroblast growth factor-2 (FGF-2) in the exosomes. In summary, intrathecal infusion of exosomes from UCMSCs may be considered as a novel therapeutic approach for nerve injury–induced pain.

Selected recent publications:

Sheng-Jie Shiue, Ruey-Horng Rau, Han-Shiang Shiue, Yi-Wei Hung, Zhi-Xiang Li, Kuender D. Yang, **Jen-Kun Cheng***. Mesenchymal stem cell exosomes as a cell-free therapy for nerve injury-induced pain in rats. **Pain** 2019 Jan; 160(1):210-223.

S. J. Shiue, H. Y. Peng, C. R. Lin, S. W. Wang, R. H. Rau, **Jen-Kun Cheng***. Continuous intrathecal infusion of cannabinoid receptor agonists attenuates nerve ligation-induced pain in rats. **Regional Anesthesia and Pain Medicine 2017** Jul/Aug; 42(4):499-506.

Yen-Ling Kuo*****, **Jen-Kun Cheng***, Wen-Hsien Hou, Yu-Cheng Chang, Po-Hao Du, Jhao-Jun Jian, Ruey-Horng Rau, Jung-Hui Yang, Cheng-Chang Lien, Meei-Ling Tsaur. K^+ channel modulatory subunits KChIP and DPP participate in Kv4-mediated mechanical pain control. **Journal of Neuroscience 2017** Apr. 37(16):4391-4404.

Chau-Fu Cheng, **Jen-Kun Cheng**, Chih-Yang Chen, Ruey-Horng Rau, Yu-Cheng Chang, Meei-Ling Tsaur. Nerve growth factor-induced synapse-like structures in contralateral sensory ganglia contribute to chronic mirror-image pain. **Pain 2015** Nov. 156(11):2295-309.

Y. L. Chen, M. L. Tsaur, S. W. Wang, T. Y. Wang, Y. C. Hung, C. S. Lin, Y. F. Chang, Y. C. Wang, S. J. Shiue, **Jen-Kun Cheng***. Chronic intrathecal infusion of mibefradil, ethosuximide and nickel attenuates nerve ligation-induced pain in rats. **British Journal of Anaesthesia 2015** Jul; 115(1):105-11.

New biomarkers in acute and chronic pain

Ping-Heng Tan (譚炳恆教授)
Director of General Anesthesiology, Chi Mei Medical Center, Tainan, Taiwan

PhD, National Sun Yat-Sen University

MD., School of Medicine, National Defense Medical Center

Abstract

A number of neuronal circuits are involved in pain transmission. Pain is not only a matter of neurons. The tissue around them plays an important role, too. Other cells—such as skin, immune, or glia cells, to name just a few—participate in the pathogenesis and also the resolution of pain. Nor is there a simple one-way street from the periphery to the brain. More precisely, pain is associated with excessive inflammation in both the peripheral and central nervous system which may contribute to the initiation and maintenance of persistent pain. Pain reflects a loss of homeostasis and/or the establishment of a new homeostatic set point. Although blocking inflammatory response may help pain relief for a short period, restoring their normal function through pro-resolution approaches is probably the best way. In some instances, these endogenous resolution pathways may have failed to turn on or have been inefficient when they did turn on. The strategy then is to provide the mediators exogenously or engineer new ways to turn on these pathways so as to facilitate normal resolution of a pain state. Simply measuring pain is not adequate for diagnosis and management of pain. The development of biomarkers of acute and chronic pain is also essential. In this presentation, I will discuss increasing knowledge of endogenous mechanisms that mediate the resolution of inflammation and pain and present our new findings in the endogenous resolution mediators and biomarkers of inflammatory pain that may provide opportunities for pain modification.

Selected recent publications:

Liu CC, Gao YJ, Luo H, Berta T, Xu ZZ, Ji RR, Tan PH (2016) Interferon alpha inhibits spinal cord synaptic and nociceptive transmission via neuronal-glial interactions. Sci Rep. 6:34356. doi: 10.1038/srep34356.

Liu CC, Cheng JT, Hung KC, Chia YY, Tan PH (2016) Lentiviral vector-encoded microRNA-based shRNA-mediated gene knockdown of NMDA receptors in skin reduces pain. Brain Behav 7(1):e00587:1-11.

Alex Tseng CC, Chia YY, Liu CC, Feng KM, Tan PH (2017) The N-methyl-D-aspartate (NMDA) receptor in skin, dorsal root ganglion and spinal cord: an ideal target gene for RNA interference therapy for pain relief. Neuropsychiatry 7(3):640-5.

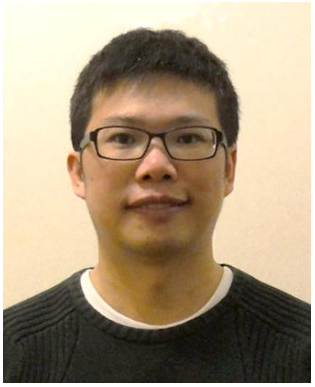
Berta T, Qadri Y, Tan PH, Ji RR (2017) Targeting dorsal root ganglia and primary sensory neurons for the treatment of chronic pain. Expert Opin Ther Targets 21(7):695-703. doi: 10.1080/14728222.2017.1328057.

Liu CC, Cheng JT, Li TY, Tan PH (2018) Integrated analysis of microRNA and mRNA expression profiles in the rat spinal cord under inflammatory pain conditions. Eur J Neurosci 46(11):2713-2728.

Nociceptive processing in the human brain

Ming-Tsung Tseng (曾明宗)

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



PhD, National Taiwan University

MD., National Taiwan University

Abstract

Pain is an inherently multi-faceted experience that includes sensory-discriminative, emotional, and motivational components. The perception of pain is variable across individuals, which depends on individuals' cognitive state when they evaluate afferent nociceptive information, as well as their cognitive modulation of pain processing. By using functional magnetic resonance imaging, we revealed that there is a distinct signature for the encoding of a painful experience in the human brain, and this encoding process involves a strong affective component. Vigilance-related enhancement in the parieto-thalamic attention network allows the prefrontal cortex to estimate the relative intensity differences between noxious stimuli. Moreover, aversive prediction error-related networks interact with pain-processing circuits to underlie stimulus expectancy effects on pain. These cognitive evaluation and modulation mechanisms not only play an adaptive and protective role by providing sensory-discriminative information of painful stimuli for humans to cope with potentially life-threatening situations, but enhance neuroscientific knowledge about top-down cognitive modulation of nociception. They may also serve as the neural basis to decipher the neural mechanisms underpinning the cognitive dysfunctions associated with pain processing in patients with chronic pain in the future.

Selected recent publications:

Shih YW, Tsai HY, Lin FS, Lin YH, Chiang CY, Lu ZL, **Tseng MT**. Effects of positive and negative expectations on human pain perception engage separate but interrelated and dependently regulated cerebral mechanisms. *J Neurosci.* 2019;39:1261-1274.

Yang SL, Wu TW, **Tseng MT.** Vigilance-related attention systems subserve the discrimination of relative intensity differences between painful stimuli. *Pain.* 2018;159:359-370.

Tseng MT, Kong Y, Eippert F, Tracey I. Determining the neural substrate for encoding a memory of human pain and the influence of anxiety. *J Neurosci.* 2017;37:11806-11817.

Tseng MT, Kong Y, Chiang MC, Chao CC, Tseng WY, Hsieh ST. Brain imaging signatures of the relationship between epidermal nerve fibers and heat pain perception. *Neuroimage*. 2015;122:288-97.

Neural Plasticity in Chronic Pain

Wei-Ta Chen (陳韋達), M.D., Ph.D.

Professor of Neurology & Staff Neurologist, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
School of Medicine, National Yang-Ming University, Taipei, Taiwan
Director, Taiwan Headache Society & Taiwan Neurological Society

Abstract

Chronic pain is a group of disorders most disabling in the world. While headache and body pain may be physiological in the acute setting, they can evolve into chronic and pathological forms. The mechanism underlying such a transition has been the subject of intense studies. Using physiological and imaging methods, researchers have identified a number of different forms of neural plasticity associated with pain chronification, including peripheral and central sensitization, and alterations in the endogenous mechanisms of pain modulation. Although these changes have been proposed to contribute to headache and pain chronification, the causal relationship and clinical correlation remain to be confirmed in large longitudinal studies. In this review, we provide a narrative overview of recent advances and clinical implications on the neural plasticity associated with common chronic pain conditions, including primary headaches and fibromyalgia.

Selected recent publications:

Chen WT, Yu CH, Sun CW*. Altered near-infrared spectroscopy response to breath-holding in patients with fibromyalgia. ***J Biophotonics*** 2019;12:e201800142.

Chen WT*, Hsiao FJ, Ko YC, Liu HY, Wang PN, Fuh JL, Lin YY, Wang SJ. Comparison of somatosensory cortex excitability between migraine and "strict-criteria" tension-type headache: a magnetoencephalographic study. ***Pain*** 2018;159:793–803.

Hsiao FJ, Wang SJ, Lin YY, Fuh JL, Ko YC, Wang PN, Chen WT*. Somatosensory gating is altered and associated with migraine chronification: a magnetoencephalographic study. ***Cephalalgia*** 2018;38:744-53.

Liu HY, Chou KH, Lee PL, Fuh JL, Niddam, DM, Lai KL, Hsiao FJ, Lin YY, Chen WT*, Wang SJ*, Lin CP. Hippocampus and amygdala volume in relation to migraine frequency and prognosis. ***Cephalalgia*** 2017;37:1329-36.

Liu HY, Fuh JL, Lin YY, Chen WT*, Wang SJ*. Suicide risk in patients with migraine and comorbid fibromyalgia. ***Neurology*** 2015;85:1017-1023 (Editorial highlight)

Neurotechnology
神經影像技術—朱士維

Host: Shi-Wei Chu (朱士維)

Location: 生物醫學科學研究所 B1C會議室
Institute of Biomedical Sciences (IBMS) B1C room

Time: Sep. 11, 16:35-17:50

Participate Societies: Taiwanese Society for Computational Neuroscience (台灣計算神經科學學會)、 Taiwan Magnetic Resonance Society (台灣磁共振學會)

Since Cajal established the neuron doctrine by observing stained neurons under an optical microscope, many innovative neurotechnologies have played a key role in facilitating the advancement of neuroscience. In this nanosymposium, we will report novel imaging methods, including magnetic resonance imaging, synchrotron x-ray imaging and optical imaging, with a special emphasis on their applications toward monitoring brain activity and constructing structural and functional connectomes.

Sub-Cellular Whole Brain Mapping with Synchrotron X-rays

Yeukuang Hwu (胡宇光)
Distinguished Scientists, Professor

Institute of Physics, Academia Sinica

Brain Research Center, National Tsing Hua University, Taiwan

Ph D., University of Wisconsin-Madison, Physics

Abstract

The complexity and sheer mass of the complete neural networks in an animal brain is beyond the current technology to describe and analyze. Comprehensive mapping of neural networks in the brain is therefore a formidable but very exciting challenge. Could x-ray techniques be the tool of choice to challenge the animal brain circuitry mapping? Is the overall performance adequate, however?

We present an effective strategy based on recent advances to put synchrotron x-ray tomography into this competitive race. The approach reaches three critical objectives: (1) three-dimensional (3D) imaging with high and isotropic spatial resolution; (2) fast image taking and processing, as required for comprehensive whole-brain mapping within a reasonable time, and (3) multi-scale resolution, to zoom into specific regions of interest. The current performance: 0.3 μm lateral resolution isotropic in all 3 dimensions and image acquisition speed of $1mm^3$/min in high throughput microtomography; 20 nm resolution with $(50\ \mu m)^3$/min speed of nanotomography, is orders-of-magnitude faster than the competing 3D imaging techniques. We tested the strategy by mapping large populations of metal-labeled neurons and their connections in two animal models, *Drosophila* and mouse. Its speed notably allowed full 3D mapping of the *Drosophila* brain in a few days.

These positive results instigated two additional directions for further improved: an even better spatial resolution and higher probe depth, both are relevant to the high brightness synchrotron radiation and new nanofabrication facilities. An ongoing project also aims to improve the heavy metal staining efficiency and specificity. With these improvements in place and the newly initiated SYNAPSE (Synchrotron for Neuroscience – an Asia Pacific Strategic Enterprise) consortium with 6 synchrotron facilities, the combined data acquisition and processing power, we are confident that a human brain can be mapped within 3 years.

Selected recent publications:

Chin, H, et al. (2020) A Synchrotron X-ray Imaging Strategy to Map Large Animal Brains. *Chinese J. Phys.* 65: 24-32.

Chang, W L, et al. (2020) The Making of a Flight Feather: Bio-architectural Principles and Adaptation. *Cell* 179(6): 1409-1423.

Chu, L A, et al. (2019) Rapid single-wavelength lightsheet localization microscopy for clarified tissue. *Nat. Comm.* 10:47620.

Lu C H, et al. (2019) Lightsheet localization microscopy enables fast, large-scale, and three-dimensional super-resolution imaging. *Commun. Biol.* 2:177.

Hwu Y, Margaritondo G, Chiang A S (2017) Q&A: Why use synchrotron x-ray tomography for multi-scale connectome mapping. *BMC Biology* 15:122.

Faster, deeper, higher-resolution optical imaging of brain

Shi-Wei Chu (朱士維)

Professor, Department of Physics and Molecular Imaging Center, National Taiwan University
Director for Innovative Technology, Brain Research Center, National Tsing Hua University
Vice director, Center for Teaching and Learning Development, NTU
Director for Innovative Education, NTU D.School

Ph.D., National Taiwan University

Abstract

Brain is one of the most important organs in our body, but it is functionally the least understood one. It is composed of millions of neurons, whose interconnection, i.e. connectome, determines its function. Since the days of Cajal, optical microscopy has been a vital tool for physiology, and neuroscientists have accumulated significant amount of information on structures and functions of isolated neurons. However, to understand the emergent properties of a brain, functional observation of complicated neuronal networks is necessary. No existing tool can capture whole-brain emergent properties at single neuron or even synapse resolution. To understand functional connectome, an imaging system that can cover a whole brain *in vivo* with spatial resolution of micrometers (neuron) to nanometers (synapse) as well as temporal resolution in sub-seconds (calcium) to milliseconds (action potential) is highly desirable, leading to the request of volumetric imaging with high speed, deep penetration, and dendritic level resolution. In this talk, I report our recent progresses on *Drosophila* brain imaging, including world-record 20-nm resolution across a whole brain, three-photon imaging penetrating through a living fly brain, and all-optical physiology platform based on a 100-kHz tunable acoustic lens.

Selected recent publications:

C. Huang, K.-J. Hsu, H.-Y. Lin, and **S.-W. Chu***, "Novel Optical Microscopies to Unravel Brain Function," AAPPS Bulletin (2020) **Invited Focus article, selected as Cover Image**

C. Huang, C.-Y. Tai, K.-P. Yang, W.-K. Chang, K.-J. Hsu, C.-C. Hsiao, S.-C. Wu, Y.-Y. Lin*, A.-S. Chiang*, and **S.-W. Chu***, "All-optical volumetric physiology for connectomics in dense neuronal structures" *iScience* 22, 133-146 (2019)

K.-J. Hsu, Y.-Y. Lin, Y.-Y. Lin, K. Su, K.-L. Feng, S.-C. Wu, Y.-C. Lin, A.-S. Chiang, **S.-W. Chu***, "Millisecond two-photon optical ribbon imaging for small-animal functional connectome study" *Opt. Lett.* 44, 3190-3193 (2019). **Editor's pick**

H.-Y. Lin, L.-A. Chu, H. Yang, K.-J. Hsu, Y.-Y. Lin, K.-H. Lin, **S.-W. Chu***, A.- S. Chiang, "Imaging Through the Whole Brain of Drosophila at λ/20 Super-Resolution," *iScience* 14, 164-170 (2019).

K.-J. Hsu, Y.-Y. Lin, A.-S. Chiang, **S.-W. Chu***, "Optical properties of adult Drosophila brains in one-, two-, and three-photon microscopy," *Biomed. Opt. Exp*. 10, 1627-1637 (2019).

Mapping the connectomics of human brain

Ching-Po Lin (林慶波)
Distinguished Professor, Institute of Neuroscience,
National Yang-Ming University

PhD, National Taiwan University

Abstract

The human brain comprises a complex neural network, known as the human connectome, with a broad range of regional microscale cellular morphologies and macroscale global properties, together forming an efficient system for processing and integration of multimodal information. Plenty of evidences have shown that mapping the connections may be great helpful to understand the normal variability as well as mental disorders. It may also be crucial for pursuing new generation algorithm of artificial intelligent and thus has the so-called 21st century of the brain.

Due to the limit of available techniques, neuroscientists exhibited little interest in the connections for centuries, till modern non-invasive neuroimaging techniques invented in 1990s. The structural connections as well as related neural activities were thus attracted people's attentions and thus open the prolog of human brain connectome. Opportunely, Prof. Lin caught up the tide for his PhD thesis and found the Brain Connectivity Lab, BcLab, dedicated to drive modern neuroimaging methods for brain connectomics studies, after move to National Yang-Ming University in 2004.

By studying the direction-dependent water molecular diffusivity and blood oxygen level coherence, brain structural and functional connectivity could be mapped through modern MRI techniques and thus open a window to explore functional anatomy on the basis of its structural substrates. Meanwhile, the complexity of higher brain systems emerged another challenge to explain the rich functionalities that arises from a relatively fixed structure. To facilitate human brain study, BcLab dedicated to drive technical developments and strive to optimize these methods under human brain study regulations for decades. Accordingly, reliable and efficient neuroimaging protocols were established to promises further brain connectomics studies, including clarifying human brain functions and assisting clinical services including neurosurgical plan, neurodegenerative prediction, signatures for psychiatric disorders.

Hereby, within this lecture, modern imaging technologies for mapping human brain connectome and the connectomics of brain disorders will be discussed. Meanwhile, technical limitation of these non-invasive tools will also be highlighted.

Selected recent publications:

Chih-Chin Heather Hsu, Edmund T. Rolls*, Chu-Chung Huang, Shin-Tai Chong, Chun-Yi Zac Lo, Jianfeng Feng*, Ching-Po Lin* (2020) Connections of the human orbitofrontal cortex and inferior frontal gyrus. *Cerebral Cortex* (in press)

Chen-Yuan Kuo, Pei-Lin Lee, Sheng-Che Hung, Li-Kuo Liu, Wei-Ju Lee, Chih-Ping Chung, Albert C. Yang, hih-Jen Tsai, Pei-Ning Wang, Liang-Kung Chen, Kun-Hsien Chou*, Ching-Po Lin (2020) Large-scale structural covariance networks predict age in middle-to-late adulthood: a novel brain aging biomarker. *Cerebral Cortex* (in press)

Chu-Chung Huang, Qiang Luo, Lena Palaniyappan, Albert C Yang, Chia-Chun Hung, Kun-Hsien Chou, Chun-Yi Zac Lo, Mu-En Liu, Shih-Jen Tsai, Deanna M. Barch, Jianfeng Feng*, Ching-Po Lin*, Trevor W. Robbins (2020) Transdiagnostic and Illness-specific Functional Dysconnectivity Across Schizophrenia, Bipolar Disorder and Major Depression. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* (in press)

Yi-Chia Kung, Chia-Wei Li, Shuo Chen, Chia-Ju Sharon Chen, Chun-Yi Zac Lo, Bharat Biswal, Changwei W. Wu*, Ching-Po Lin* (2019) Instability of Brain Connectivity during Non-rapid Eye Movement Sleep Reflects Altered Properties of Information Integration. *Human Brain Mapping* 40(11): 3192-3202

Chun-Yi Zac Lo, Tsung-Wei Su, Chu-Chung Huang, Chia-Chun Hung, Wei-Ling Chen, Tsuo-Hung Lan, Ching-Po Lin*, Ed Bullmore (2015) Randomization and resilience of brain functional networks as systems-level endophenotypes of schizophrenia. *Proceedings of the National Academy of Sciences* 112(29): 9123-9128

Predicting chemo-brain in breast cancer survivors using functional and structural connectome features and machine-learning

Jun-Cheng Weng (翁駿程)

Associate Professor and Associate Chairman, Department of Medical Imaging and Radiological Sciences, Chang Gung University;

Director, Medical Imaging Research Center, Institute for Radiological Research, Chang Gung University and Chang Gung Memorial Hospital at Linkou;

Joint Appointment Associate Professor, Bachelor Program in Artificial Intelligence, Chang Gung University;

Joint Appointment Associate Research Fellow, Department of Psychiatry, Chang Gung Memorial Hospital at Chiayi.

Ph.D., National Taiwan University

Abstract

Breast cancer is the leading cancer among women worldwide, and a high number of breast cancer patients are struggling with psychological and cognitive disorders. In this study, we aim to use machine-learning models to discriminate between chemo-brain subjects and healthy controls (HCs) using connectomes (connectivity matrices) and topological coefficients. Nineteen postchemotherapy breast cancer (BC) survivors and 20 female HCs were recruited for this study. Subjects in both groups received resting-state functional magnetic resonance imaging (rs-fMRI) and generalized q-sampling imaging (GQI). Logistic regression (LR), decision tree classifier (CART), and xgboost (XGB) were the models we adopted for classification. In connectome analyses, LR achieved an accuracy of 79.49% with the functional connectomes and an accuracy of 71.05% with the structural connectomes. In the topological coefficient analysis, accuracies of 87.18%, 82.05%, and 83.78% were obtained by the functional global efficiency with CART, the functional global efficiency with XGB, and the structural transitivity with CART, respectively. The areas under the curves (AUCs) were 0.93, 0.94, 0.87, 0.88, and 0.84, respectively. Our study showed the discriminating ability of functional connectomes, structural connectomes, and global efficiency. We hope our findings can contribute to an understanding of the chemo brain and the establishment of a clinical system for tracking chemo brain.

Selected recent publications:

Jun-Cheng Weng, Tung-Yeh Lin, Yuan-Hsiung Tsai, Man Teng Cheok, Yi-Peng Eve Chang, Vincent Chin-Hung Chen*, “An autoencoder and machine learning model to predict suicidal ideation with brain structural imaging”, Journal of Clinical Medicine, 2020 Feb; 9(3), 658.

Vincent Chin-Hung Chen, Kai-Yi Lin, Yuan-Hsiung Tsai, **Jun-Cheng Weng***, “Connectome analysis of brain functional network alterations in breast cancer survivors with and without chemotherapy”, PLoS One, 2020 May; 15(5), e0232548.

Vincent Chin-Hung Chen, Tung-Yeh Lin, Dah-Cherng Yeh, Jyh-Wen Chai, **Jun-Cheng Weng***, “Predicting chemo-brain in breast cancer survivors using multiple MRI features and machine-learning”, Magnetic Resonance in Medicine, 2019 May; 81(5), 3304-3313.

Chao-Yu Shen, Vincent Chin-Hung Chen, Dah-Cherng Yeh, Shu-Ling Huang, Xuan-Ru Zhang, Jyh-Wen Chai, Yen-Hsun Huang, Ming-Chih Chou, **Jun-Cheng Weng***, “Association of functional dorsal attention network alterations with breast cancer and chemotherapy”, Scientific Reports, 2019 Jan; 9(1), 104.

Tsung-Yuan Li, Vincent Chin-Hung Chen, Dah-Cherng Yeh, Shu-Ling Huang, Cheng-Nan Chen, Jyh-Wen Chai, Clayton Chi-Chang Chen, **Jun-Cheng Weng***, “Investigation of chemotherapy-induced brain structural alterations in breast cancer patients with generalized q-sampling MRI and graph theoretical analysis”, BMC Cancer, 2018 Dec; 18(1), 1211.

Detection and manipulation of brain activities
偵測並操控大腦的活動

Host: Wan-Chen Lin (林宛蓁)

Location: 跨领域大楼
Interdisciplinary Research Building for Science and Technology (IRB)
Time: Sep. 11, 16:35-17:50

Participate Societies: Taiwan Neuroscience Society (台灣基礎神經科學學會)、Taiwanese Society of Biomedical Engineering (中華民國生物醫學工程學會)

The brain operates through numerous neural circuits to command a variety of functions. Each circuit is formed by several types of neurons, and a specific function is often accomplished via the synergistic actions of multiple circuits. A grand challenge for neuroscience is to dissect the composition, connectivity, and operation mechanisms of these circuits, as well as their causal relationships with behavior and functions. The key to exploring this subject lies in the precise detection and manipulation of neuronal activities in the brain. Several revolutionary breakthroughs have been achieved in recent years, this nanosymposium will introduce novel techniques, including optogenetics, sonogenetics, in vivo fluorescent imaging, multichannel electrode recording, and lightsheet microscopy.

LightSheet Fluorescent Imaging at Expanded Space to Approach EM Resolution

Bi-Chang Chen (陳壁彰)

Associate Research Fellow, Research Center for Applied Sciences, Academia Sinica, Taiwan

PhD, The University of Texas at Austin

Abstract

Electron microscopy (EM) has imaged densely labeled brain tissue at nanometer-level resolution over near-millimeter-level dimensions but lacks the contrast to distinguish specific proteins and the speed to readily image multiple specimens. Conversely, optical imaging techniques provide much important information in understanding life science especially cellular structure and morphology. However, the resolution of optical imaging is limited by the diffraction limit to ~200 nm. With the invention of super-resolution microscopic techniques enables biologists to visualize nano-sized fluorophores that are beyond the diffraction limit. These techniques do not physically violate the Abbe limit of resolution but exploit the photoluminescence properties and labelling specificity of fluorescence molecules to achieve super-resolution imaging

Instead of sweating on the super-resolution techniques to pursuit high spatial resolution, expansion microscopy (ExM) is invented to bypass the optical diffraction limit by physically expanding the samples to ~4 times larger than original with swellable polymers. Furthermore, applying the swellable hydrogel concept, with exchange of certain monomer component, we could also obtain ~10 times in size change of both cell culture and *Drosophila* brain. In order to image such expanded samples, we use lightsheet microscopy, a separate excitation lens perpendicular to the widefield detection lens to confine the illumination to the neighborhood of the focal plane. By combining intrinsic optical sectioning with widefield detection, lightsheet microscopy allows fast imaging speed to record multi-megapixel imaging of selected plane in a single exposure of the camera. By manipulating sample space, we wish to approach electron microscopic resolution with lightsheet fluorescent detection to investigate 3D subcellular morphologies and protein connectomics in several mm-scale samples.

Selected recent publications:

Chang, B.-J., Tang, W.-C., Liu, Y.-T., Tsai, Y.-C., Tsao, C., Chen, P., **Chen, B.-C.** (2020) Two-beam interference lattice lightsheet for structured illumination microscopy *J. Phys. D: Appl. Phys.* 53:044005

Tsai, Y.-C., Tang, W.-C., Low, C. S. L., Liu, Y.-T., Wu, J.-S.; Lee, P.-Y., Lin, Y.-L., Kanchanawong, P., Gao, L., **Chen, B.-C.** (2020) Rapid High Resolution 3D Imaging of Expanded Biological Specimens with Lattice Lightsheet Microscopy, *Methods*, 174:11-19

Chu, L.-A., Lu, C.-H., Yang, S.-M., Liu, Y-T, Feng, K.-L., Tsai, Y.-C., Chang, W.-K., Wang, W.-C., Chang, S.-W., Chen, P.; Lee, T.-K., Hwu, Y.-K., Chiang, A.-S., **Chen, B.-C.** (2019) Rapid single-wavelength lightsheet localization microscopy for clarified tissue, *Nature Communications*, 10: 4762

Lu, C.-H., Tang, W.-C., Liu, Y.-T., Wu, F. C. M., Chen, C. Y., Tsai, Y. C., Yang, S.-M, Kuo, C.-W., Okada, Y., Hwu, Y.-K., Chang, S.-W., Chen, P., **Chen, B.-C.** (2019) Lightsheet localization microscopy enables fast, large-scale, and three-dimensional super-resolution imaging. *Communications Biology*, 2:177

Gao, L., Tang,W.-C., Tsai, Y.-C., **Chen, B.-C.** (2019) Lattice light sheet microscopy using tiling lattice light sheets *Optics Express*, 27:1497-1506

Chronic Massive Parallel Neural Recording with Microwire Bundle-CMOS Integration

Yu-Wei Wu (吳玉威)
Assistant Research Fellow, Institute of Molecular Biology, Academia Sinica, Taiwan

PhD, University College London

Abstract

Multi-channel neural recordings of brain activity are a powerful technique that is increasingly uncovering new aspects of neural communication, computation, and prosthetic interfaces. However, while silicon CMOS devices continue to scale rapidly in number and power in planar geometries, this scaling has not been followed for large-scale mapping along three dimensions. Here, we present a new strategy to interface CMOS-based devices with a three-dimensional microwire array, providing the link between rapidly developing electronics, and high-density neural interfaces. The system consists of a bundle of insulated and spaced microwires perpendicularly mated to a commercial large-scale CMOS microelectrode array, such as a camera chip. The modular nature of the design enables a variety of microwire types and sizes to be integrated with different types of silicon-based arrays, allowing channel counts to be scaled from a few dozen to thousands of electrodes using the same fundamental platform. This system has excellent recording performance, demonstrated via single unit and local-field potential recordings in isolated retina, and in the motor cortex and striatum of awake moving mice. This concept links the rapid progress and power of commercial multiplexing, digitization and data acquisition hardware together with a three-dimensional neural interface.

Selected recent publications:

Obaid A*, Hanna M*, **Wu YW*** (co-first author), Kollo M*, Racz R, Angle MR, Muller J, Wray W, Franke F, Blackbill N, Chichilinsky EJ, Hierlemann A, Ding JB, Schaefer AT, Melosh NA (2020) Massively parallel microwire arrays integrated with CMOS chips for neural recording *Science Advances* 6(12): eaay2789

Wu YW*(co-corresponding author), Gordleeva S, Tang X, Shih PY, Dembitskaya Y, Semyanov A* (2019) Morphological profile determines frequency of spontaneous calcium events in thin astrocytic processes. *Glia* 67(2):246-262

Du K*, **Wu YW***(co-first author), Lindroos R, Liu Y, Rózsa B, Katona G, Ding JB, Kotaleski JH (2017) Cell-type specific inhibition of the dendritic plateau potential in striatal spiny projection neurons. *PNAS* 114(36): E7612-E7621.

Guo L*, Xiong H*, Kim JI*, **Wu YW***(co-first author), Lalchandani RR, Cui Y, Shu Y, Xu T, Ding JB (2015) Dynamic rewiring of neural circuits in the motor cortex in mouse models of Parkinson's disease. *Nature Neuroscience* 18(9):1299-309

Wu YW, Kim JI, Tawfik VL, Lalchandani RR, Scherrer G, Ding JB (2015) Input- and cell type-specific Endocannabinoid-Dependent LTD in the striatum. *Cell Reports* 10(1):75-87

In vivo voltage imaging reveals coordinated membrane potential dynamics of hippocampal interneurons during sharp wave ripple oscillation

Tsai-Wen Chen (陳摘文)
Assistant Professor, Institute of Neuroscience, National Yang-Ming University, Taipei, Taiwan

PhD, University of Göttingen

Abstract

Hippocampal sharp wave ripples (SWR) are transient (~50ms), high frequency (~120-200Hz) field oscillation events that can be detected in the CA1 area during sleep and quite awake states *in vivo*. During SWR, patterns of neuronal activation reflecting prior experiences are 'replayed' in precise sequences. Manipulations that target SWR events impact memory performances, suggesting an important role of SWR in memory function. The neuronal firing during SWR is thought to be paced by temporally precise activation of local inhibitory interneurons. Indeed, specific sub-types of CA1 interneurons are known to participate in SWR oscillations. Furthermore, blockade of inhibitory synaptic transmission disrupts ripple oscillations both *in vitro* and *in vivo*. To understand how coordination between specific interneurons contribute to brain's rapid network dynamics, we developed imaging technology to record membrane potential dynamics at kilohertz temporal resolution in specific CA1 interneurons in awake, head-fixed mice. A novel genetically encoded fluorescent voltage indicator 'Voltron' was targeted to specific subtypes of interneurons through virus injection. Fluorescence signals related to supra- and sub- threshold membrane potential were imaged using a custom high speed microscope with a large field of view. In this talk, I will discuss our efforts in analyzing the dynamics of hippocampal interneurons during awake SWR events.

Selected recent publications:

Chen T-W, Wardill T, Sun Y, Pulver S, Renninger S, Baohan A, Schreiter E, Kerr R, Orger M, Jayaraman V, Looger LL, Svoboda K, Kim D (2013) Ultrasensitive fluorescent proteins for imaging neuronal activity. ***Nature***, 499 (7458) 295-300

Dana H, **Chen T-W**, Hu A, Shields B, Guo C, Looger L, Kim D, Svoboda K (2014) Thy1-GCaMP6 transgenic mice for neuronal population imaging *in vivo* ***PloS One,*** *9 (9)*

Li N, **Chen T-W**, Guo Z, Gerfen C, Svoboda K (2015) A motor cortex circuit for motor planning and movement. ***Nature***, 519 (7541) 51-56.

Chen T-W, Li N, Daie K, Svoboda K (2017) A map of anticipatory activity in the mouse motor cortex. ***Neuron,*** 94 (1-14)

Abdelfattah A, Kawashima T, Singh A, Novak O, Liu H, Shuai Y, Huang Y-C, Grimm J, Patel R, Friedrich J, Mensh B, Paninski L, Macklin J, Podgorski K, Lin B-J, **Chen T-W**, Turner G, Liu Z, Koyama M, Svoboda K, Ahrens M, Lavis L, Schreiter E (2019) Bright and photostable chemigenetic indicators for extended in vivo voltage imaging, **Science**, 365 (6454) 699-704

Sonogenetic modulation of cellular activities using an engineered auditory-sensing protein

Yu-Chun Lin (林玉俊)
Associate Professor, Institute of Molecular Medicine and Department of Medical Science, National Tsing Hua University, Taiwan

PhD, TungHai University

Abstract

Approaches that can non-invasively stimulate target cells buried are highly desirable for basic research and clinical therapy. We report herein a sonogenetic approach that can non-invasively manipulate target cell activities in the deep tissues by ultrasound stimulation. This system requires an ultrasound-responsive protein derived from an engineered auditory-sensing protein prestin. Heterologous expression of mouse prestin containing two parallel amino acid substitutions, N7T and N308S, that frequently exist in prestins from echolocating species endowed transfected mammalian cells with the ability to sense ultrasound. Ultrahigh ultrasound sensitivity of prestin(N7T, N308S) makes it possible to evoke cellular calcium responses by a short pulse of ultrasound (3 seconds) under low acoustic pressure in vitro. Moreover, pulsed ultrasound can also non-invasively stimulate target neurons expressing Prestin(N7T, N308S) in deep regions of mouse brains. Our study delineates how an engineered auditory-sensing protein can cause mammalian cells to sense ultrasound stimulation. Moreover, owing to the great penetration of low-frequency ultrasound (~150 mm in depth), our sonogenetic tools will serve as new strategies for non-invasive therapy in deep tissues.

Selected recent publications:

Lian YL*, Chen KW*, Chou YT, Ke TL, Chen BC, **Lin YC#,** Chen L#. (2020) PIP3 depletion rescues myoblast fusion defect in human rhabdomyosarcoma cells. ***Journal of Cell Science*** 133, jcs240325.

Wu CY*, Fan CH*, Chiu NH, **Lin YC#,** Yeh CK#. (2020) Targeted delivery of engineered auditory sensing protein for ultrasound neuromodulation in the brain. ***Theranostics*** 10(8):3546-3561.

Huang YS*, Fan CH*, Hsu N*, Chiu NH, Wu CY, Guo V, Chiang YC, Hsu WC, Chen L, Lai CPK, Yeh CK#, **Lin YC#.** (2020) Sonogenetic modulation of cellular activities using an engineered auditory-sensing protein. ***Nano Letters*** 20(2):1089-1100

Hong SR*, Wang CL*, Huang YS, Chang YC, Chang YC, Pusapati GV, Lin CY, Hsu N, Cheng HC, Chiang YC, Huang WE, Shaner NC, Rohatgi R, Inoue T#, **Lin YC#** (2018) Spatiotemporal manipulation of ciliary glutamylation reveals its roles in intraciliary trafficking and Hedgehog signaling. ***Nature Communications*** 9, 1732

Fan CH*, Huang YS*, Huang WE*, Lee AA*, Ho SY, Kao YL, Wang CL, Lian YL, Ueno T, Wang TSA, Yeh CK, **Lin YC.#** (2017) Manipulating cellular activities using an ultrasound-chemical hybrid tool. ***ACS Synthetic Biology*** 6: 2021-2027.

Nanosymposium (I)-5

Understanding human cognition through intracranial recordings and functional neuroimaging

人類認知的神經基礎：透過「顱內電生理」和「功能性腦造影」來了解認知運作的動態歷程

Host: Shih-Wei Wu (吳仕煒)

Location: 分子生物研究所 Institute of Molecular Biology (IMB)

Time: Sep. 11, 16:35-17:50

Participate Societies: Taiwan Society of Cognitive Neuroscience (台灣認知神經科學學會)、Taiwan Society for Stereotactic Functional Neurosurgery and Radiosurgery (台灣立體定位功能性神經外科及放射手術學會)

To understand the human brain in action, we must be able to characterize the complex dynamics of neural activity during cognitive computations. Standard technology such as functional magnetic resonance imaging (fMRI), however, lacks the temporal resolution to address this question. Recently, intracranial neurophysiological recording in epilepsy patients have offered a unique and timely opportunity because it directly measures electrical signals at the level of neuronal populations, therefore providing the appropriate temporal and spatial scales. In this symposium, we will present recent advances in combining these two techniques to understand human cognitive functions.

Neural Computations underlying biases in decision making

Shih-Wei Wu (吳仕煒)

Associate Professor
Institute of Neuroscience
National Yang-Ming University, Taipei, Taiwan

PhD, New York University, New York, USA

Abstract

Decades of research from experimental psychology and behavioral economics suggest that human decision making systematically deviates from standard models in economics. Such deviations are often labeled as 'biases' in decision making. In neuroscience, although tremendous progress has been made in understanding the neural mechanisms for decision making, characterizing the neural architecture that contributes to decision biases is a unique area of research that is currently lacking in our understanding of decision making in general and its neurobiological basis. In this talk, I will present a series of fMRI and intracranial electrophysiology studies that aimed to investigate the neurocomputational basis of decision bias. In particular, we focused on studying three important biases—base-rate neglect, context-dependent probability estimation, and loss aversion. These biases –despite their differences—all highlight the importance of context in affecting how decision makers evaluate different sources of information. At the neural level, we found that a key signature shared between these biases is individual differences. That is, brain regions implicated in the valuation of reward and punishment and the estimation of uncertainty quantitatively represent individual differences in decision biases. These findings suggest that variations in brain activity across individuals are simply not noise. Rather, they systematically reflect something unique about a particular individual, whether it be how well she can estimate the probability of uncertain events or how sensitive she is to potential monetary losses when making risky financial decisions.

Selected recent publications:

Yang Y-Y, **Wu S-W** (in press) Base-rate neglect and neural computations for decision under uncertainty. *Proceedings of the National Academy of Sciences, USA.*

Lin W-H, Gardner JL, **Wu SW** (2020) Context effects on probability estimation. *PLOS Biology* 18:e3000634.

Farashahi S, Ting C-C, Kao C-H, **Wu S-W**, Soltani A (2018) Dynamic combination of sensory and reward information under time pressure. *PLOS Computational Biology* 14(3): e1006070.

Wu S-W, Delgado MR, Maloney LT (2015) Gambling on visual performance: Neural correlates of metacognitive choice between visual lotteries. *Frontiers in Neuroscience*, 9:314.

Ting C-C, Yu C-C, Maloney LT, **Wu S-W** (2015) Neural mechanisms for integrating prior knowledge and likelihood in value-based probabilistic inference. *Journal of Neuroscience*, 35:1792-1805.

The retrieval of context variability in episodic memory: behavioral and ERP studies

Shih-kuen Cheng (鄭仕坤)
Professor, Institute of Cognitive Neuroscience, National Central University, Taiwan

PhD, University College London

MD., Nickelodeon University

Abstract

Human beings make a vast number of decisions everyday consciously or unconsciously and a great number of decisions rely on memory processes. The choice of a particular alternative is to a great extent subject to and biased by what information is or is not retrieved from memory. Most theories of decision-making considered the retrieval of the memory of a past decision and its context as an all-or-none process and the decision-maker is viewed as a passive rememberer who exerts no control over the retrieval cues in a decision-making context. However, many studies have shown that people can actively vary the way a retrieval cue is processed contingent on the characteristics of the sought-for information. The current study aimed to fill out this gap by investigating the roles of retrieval orientation and strategic retrieval in memory-guided decision-making. Specifically, we focused on the retrieval of encoding context variability and its influences on decision-making under risk.

Across behavioral and ERP experiments, we found that when the targets of retrieval were the encoding context variability per se, participants indeed could retrieve their memories of encoding variability. However, it was only when the participants were prompted to search for items that were encoded in a constant condition that the retrieved variability information could be utilized. The encoding context variability information seems to be of little use if participants were prompted to retrieve items from varied contexts. In addition, increasing the times of exposure could enhance the capacity to retrieve the memory of encoding context variability. However, the enhancement from repetition could only be observed when the retrieval targets were items that were paired with constant contexts.

Selected recent publications:

Liu, T.-L., Chen, N.-F., & **Cheng, S.-k.*** (2017) Selective Rehearsal is affected by the emotionality of the Encoding Context in Item-Method Directed Forgetting: An Event-Related Potential Study. *Biological Psychology, 123,*15-24.

Chen, N.-F., Lo, C.-M., Liu, T.-L., & **Cheng, S.-k*.** (2016) Source Memory Performance is modulated by Transcranial Direct Current Stimulation over the Left Posterior Parietal Cortex, *NeuroImage, 139,* 462-469.

Liu, T.-L., Han, Y.-J., & **Cheng, S.-k.*** (2015). An ERP study of the dissociation between recollection- and familiarity-related prestimulus encoding activities. *Chinese Journal of Psychology, 57(4),* 1-14.

Han, Y.-J, Huang, S.-c, Lee, C.-Y., & **Cheng, S.-k.*** (2014). The modulation of semantic transparency on recognition memory for Chinese two-character words. *Memory & Cognition, 42,* 1315-1324.

Kuo, Y.-C., Lee, C.-Y., Chen. M.-C., Liu, T.-L., & **Cheng, S.-k.*** (2014). The impact of spectral resolution on the mismatch response to Mandarin Chinese tones: An ERP study of cochlear implant simulations. *Clinical Neurophysiology, 125,* 1568-1575.

Using SEEG to investigate language processing in the brain

Wen-Jui Kuo (郭文瑞)

Institute of Neuroscience, National Yang-Ming University

Ph.D., National Chung Cheng University

Abstract

More than 50% of languages in the world are tone languages. Tone languages use pitch patterns to distinguish words. For example, in Mandarin Chinese, the syllable /ma/ could mean “mother” when pronounced with a high tone (Tone 1), or “horse” with a falling-rising tone (Tone 3). Therefore, usage of lexical tone is a common practice in human languages rather than exceptional or deviant. Lexical tone has acoustic and articulatory properties distinct from segment (i.e., vowel or consonant). Lexical tone processing creates neural activity patterns distinct from those for processing segment, including higher activities in the right auditory cortex and the right inferior frontal gyrus. In our previous studies, for example, we demonstrated that phonological processing to implement Mandarin lexical tone for production highly correlates with the right inferior frontal gyrus. However, the picture about how it interplays with other language areas in the left hemisphere remains to be elucidated. In this talk, we would like to present you the results of our recent studies in which we used a novel fMRI imaging sequence (10 Hz sampling rate) and SEEG to pin down the possible connections.

Selected recent publications:

Claire H. C. Chang, Stanislas Dehaene, Denise H. Wu, Wen-Jui Kuo, Christophe Pallier. 2020. Cortical encoding of linguistic constituent with and without morphosyntactic cues. Cortex (in press).

Fa-Hsuan Lin, Yun-Fei Liu, Hsin-Ju Lee, Claire H. C. Chang, Iiro P. Jaaskelainen, Jyh-Neng Yeh, Wen-Jui Kuo. 2019. Differential brain mechanisms during reading human vs. machine translated fiction and news texts. Sci Rep. 2019 Sep 13; 9(1): 13251.

Lee SR, Lin FH, Kuo WJ. The neural mechanism underpinning balance calibration between action inhibition and activation initiated by reward motivation. Sci Rep. 2017 Aug 29;7(1):9722.

Stereo-EEG: the route to the field of neuroscience

Cheng-chia Lee (李政家)

Neurosurgery Department, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan

PhD, National Yang-Ming University

MD, National Yang-Ming University

Abstract

The effects of epilepsy are felt in multiple aspects of the person's life, including physical and mental health, cognitive function, educational achievements, vocational prospects, and family and peer relations. The successful treatment in patients with refractory epilepsy is the identification and localization of a potential surgical target.

In the past decades, intracranial EEG (iEEG), including subdural grid EEG and stereotactic EEG (sEEG), was used for precise EEG recording. Taipei Veterans General Hospital (TPE-VGH) is the only one center that can perform invasive presurgical evaluation of epilepsy using sEEG. Epilepsy surgery team in TPE-VGH have had the first case of sEEG implantation in 2014. The team also used data from SEEG to explore spreading of seizure activities in the patients with temporal lobe epilepsy, MR negative epilepsy, and epilepsy with migration disorders. The epilepsy surgery team provides good quality of presurgical evaluation and outstanding outcome of epilepsy surgery. In 2015, the team earned the award of "18th National Biotechnology and Medical Care Quality".

More recently, by collaborations with cognitive neuroscientists, several cognitive function including language functions were investigated based on the sEEG recording. Language about lexical tone processing in the brain is a good example. In Mandarin Chinese, there are four tones to distinguish word meaning. By comparing the intracranial EEG recorded under different task demands, the results indicated that EEG recordings from the frontal, temporal, and supramarginal electrodes showed differential responses to different cognitive demands. This is important because we can calculate correlation between electrodes from different brain areas to show how they work in concert to implement a cognitive function. We believe the sEEG is a route can take us on the route to the field of neuroscience.

Selected recent publications:

Chou CC, Lee CC*, Lin CF, Peng SY, Hsiao FJ, Yu HY, Chen C, Chen HH, Shih YH: Cingulate gyrus epilepsy: Semiology, invasive EEG, and surgical approaches. Neurosurgery Focus 2020 (in press)

Lee CC, Hsu SPC, Lin CJ, Wu HM, Chen YW, Luo YH, Chiang CL, Hu YS, Chung WY, Shiau CY, Guo WY, Pan DHC, Yang HC: Epidermal growth factor receptor mutations: association with favorable local tumor control following Gamma Knife radiosurgery in patients with non–small cell lung cancer and brain metastases. JNS 2019 Jun 21:1-8 [Epub ahead of print]

Lee CC, Yang HC, Lin CJ, Chen CJ, Wu HM, Shiau CY, Guo WY, Pan DHC, Liu KD, Chung WY, Peng SJ: Intervening nidal brain parenchyma and risk of radiation-induced changes after radiosurgery for brain arteriovenous malformation: a study using unsupervised machine learning algorithm. World Neurosurgery 2019 May;125:e132-e138

Lee CC, Wang WH, Yang HC, Lin CJ, Wu HM, Chen CJ, Chen YW, Chou CC, Liu YT, Chung WY, Shiau CY, Guo WY, Pan DHC, Sanford PC Hsu: Gamma Knife radiosurgery for cerebral cavernous malformation. Scientific Reports 2019 Dec 24;9(1):19743

Lee CC, Hung SC, Chen HH, Chen H, Wu HM, Lin CP, Peng SY: Structural connectivity in children after total corpus callosotomy. Epilepsia 2020 (revision)

Modern concept of Functional Mapping

Jimmy Ming-Jung Chuang, M.D. (莊銘榮)

Attending Staff, Assistant Professor of Neurosurgery Department, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan

Research fellow and clinical research associate, Lebonheur children's hospital and St Jude children's research hospital, Memphis, USA

Abstract

The goals of neurosurgery is to resect pathological brain tissue and to minimize postoperative functional deficit. It becomes necessary to perform presurgical functional mapping and assess the risk of neurological impairments following surgery on an individual basis. Intraoperative cortical stimulation mapping (ICSM) is the conventional clinical standard-of-care for functional mapping. However, there are several limitations for ICSM including electrically-induced seizures、time-consuming、not always guaranteed and requires patient cooperation that makes functional mapping in young, uncooperative, and developmentally delayed patients quite challenging. Given the limitations of CSM, other functional mapping approaches have been developed, including functional magnetic resonance imaging (fMRI), Magnetoencephalography (MEG), transcranial magnetic stimulation (TMS) and high gamma electrocorticography (hgECoG). Many studies revealed that multi-modality functional mapping approach using fMRI, hgECoG, and TMS can complement, or in some cases even replace ICSM given the complementary nature of these modalities and their ability to assess different aspects of neurophysiological task-specific activation.

Therefore, these methods can be used in conjunction with ICSM or as an alternative, when the latter is deemed impractical.

Selected recent publications:

Oral presentation, The 2016 Annual Meeting of Taiwan Neurosurgical Society, Dec 1-4, 2016, Chiayi, Taiwan : Modern Strategy for Glioma adjacent to Language-eloquent area

Poster presentation, The 2017 Annual Meeting of Organization Human Brain Mapping , June 25-29, Vancouver Canada: Receptive language mapping with magnetoencephalography under sedation in pediatric patient for resection of supratentorial tumors in the language area.

Poster presentation, The 2017 Annual Meeting of World Federation of Neurosurgical Society, Aug 20-25, Istanbul Turkey: Three-Dimensional reconstructed image-based presurgical planning for EC-IC Bypass

Oral presentation, The 2017 Annual Meeting of World Federation of Neurosurgical Society, Aug 20-25, Istanbul Turkey: Contribution of intraoperative electrostimulation mapping for GBM surgery in and around motor cortex

Oral presentation, The 2018 Annual Meeting of World Federation of Neurosurgical Society,

Aug 2 0-25, Istanbul Turkey: Investigating comprehension of narrative speech using functional MRI

Circadian rhythm and sleep: The rhythm matters!
生理時鐘和睡眠：晝夜節奏的重要性!

Host: Po-See Chen (陳柏熹)

Location: 細胞與個體生物研究所
Institute of Cellular and Organismic Biology (ICOB)

Time: Sep. 11, 16:35-17:50

Participate Societies: Taiwan Neurological Society (台灣神經學學會)、Taiwanese society of Biological Psychiatry and Neuropsychopharmacology (台灣生物精神醫學暨神經精神藥理學會)

The 2017 Nobel Prize in Biomedicine was awarded for the discovery of genes that control circadian rhythm in the living body. Such a circadian clock cooperates with the external environment (such as lights) and integrates the operation of various organs at a regular rhythm. Ultradian rhythm is another rhythm in sleep, which controls the switch between rapid eye movement and non-rapid eye movement, and processes memory, emotion and energy; when disturbed by light or the pace of modern life can cause sleep disorders. Thus, a good day and night rhythm is absolutely essential for a healthy life. In this nanosymposium, we will share our studies on sleep disorders in the elderly and shift workers and how light regulates circadian rhythm.

Sun rise, sun down: Light and circadian rhythm

Tsung-Hua Lu (呂宗樺)
Attending psychiatrist, Department of Psychiatry, National Cheng Kung University Hospital

MD., Chung Shan Medical University

Abstract

The science of circadian rhythm has been under researching since 1990. The circadian rhythm is also called the “biological clock.” This physiological phenomenon is showed in nearly all the organisms, such as sleep, eating and endocrine secretion. It affects our behavior pattern and vice versa. The key factors to regulate the rhythm is the “light”, that is, the sun light in the earth with a 24-hours cycle. The melatonin, which is a “sleep promoting neuro-transmitter” from pineal body, is inhibited by light via a specific neuro-circuit. As a result, human keep awake in daytime and asleep in nighttime. The importance of circadian rhythm is that it integrates all the body systems in the specific regularity, which can promote physiological health. As a result, any disturbance in light exposure could change the circadian rhythm.

Selected recent publications:

Tsung-Hua Lu, Lan-Ting Lee, Shuo-En Hsu, Kao Chin Chen, I Hui Lee, Tzung Lieh Yeh, Po See Chen; Yen Kuang Yang. The Correlations of Baseline Autonomic Nervous System Function and Hostility Score with Change Ratio of Treatment Response in Generalized Anxiety Disorder. International journal of child development and mental health. Vol 7 No 1 (2019): January - June 2019

Tsung-Hua Lu, Po See Chen, Kao Chin Chen, I Hui Lee, Yen Kuang Yang. Poor Sleep in Medicated Patients with Remitted Depressive Disorder: A Naturalistic Study. Taiwanese Journal of Psychiatry (Taipei) 2020; 34: 42-46.

Sleep Well, Live Well: Sleep Duration and Heart Rate Variability in the Older Adults

Hsi-chung Chen (陳錫中)
Clinical Associate Professor, College of Medicine, National Taiwan University, Taiwan
Attending Physician, Department of Psychiatry & Center of Sleep Disorders, National Taiwan University Hospital

M.D., National Yang-Ming University
Ph.D., National Yang-Ming University

Abstract

Heart rate variability is used as a marker of autonomic modulation of the heart. Lower Heart rate variability is indicative of dysregulation of cardiac autonomic function and a predictor of poor health status . Aging per se is accompanied with diminishing cardiac autonomic function Hence, it is important to explore factors that might further contribute to diminished cardiac autonomic control among the older adults. Extreme sleep duration is a risk indicator for cardiovascular morbidities and mortalities. Because attenuated cardiac autonomic control is one of the important pathophysiological indicators for cardiovascular diseases, impaired cardiac autonomic function may mediate the relationship between extreme sleep duration and cardiovascular morbidities/ mortalities. Sleep duration in the older adults is determined by sleep length, sleep phase and hypnotics use. Thus, it is interesting to investigate how these sleep parameters correlate with Heart rate variability. In this lecture, I will review previous evidence on the adverse impact of long sleep duration in older adults. I will also describe our effort in several community elderly cohorts to examine the relationship between extreme sleep duration and adverse physiological indicators, including heart rate variability. Finally, I will introduce our recent works on the relationship between the sleep phase, hypnotics use with heart rate variability.

Selected recent publications:

Chen, HC, Hsu, NW, & Chou, P (2017). The association between extreme sleep duration and cardiac autonomic control in community-dwelling older adults: The Yilan Study, Taiwan. *Journals of Gerontology. Series A: Biological Sciences and Medical Sciences, 72*(7), 929-936.

Chang, SW, **Chen, HC**, & Chou, P (2018). The Association between Earlier Bedtime and Cardiac Vagal Control in Community-Dwelling Older Adults: The Shi-Pai Sleep Study, Taiwan. *Neuropsychiatry (London), 8*(3), 893-904.

Tang, IT, Hsu, N., Chou, P, & **Chen, HC**. (2020). The Association between Various Characteristics of Hypnotics and Cardiac Autonomic Control in Community-dwelling Older Adults: The Yilan Study, Taiwan. *Sleep Medicine*. doi: 10.1016/j.sleep.2020.03.026

REM sleep behavior disorder and dementia

Wei-Pin Hong (洪煒斌), Taiwan

Department of Neurology, National Cheng Kung University Hospital, Tainan, Taiwan.

MD., College of Medicine, Kaohsiung Medical University.

Abstract

REM sleep behavior disorder is the dream-acting out behavior during rapid eye movement (REM) sleep. The clinical course can be acute or chronic. In acute cases, toxin, medication (TCA, MAOI, SSRI, caffeine), alcohol withdrawal are considered. In chronic course, it is believed as synucleinopathy, which may further develop neurodegenerative disease such as Parkinson disease, multiple system atrophy, dementia with Lewy bodies, and pure autonomic failure later. Polysomnography illustrates submental or limbs electromyographic atonia in REM sleep. The differential diagnoses include arousal disorders, other parasomnia, panic disorders, and nocturnal seizures. It is primarily in older man. The manifestation of RBD in younger persons should alarm the clinicians about medication related or narcolepsy or structural problems. In this talk, I will review the relationship between RBD and dementia.

Selected recent publications:

Wei-Pin Hong, Chin-Wei Huang, Ying-Che Huang, Poh-Shiow Yeh. Altered Mental Status Related to Carbamazepine-Induced Cardiac Conduction Dysfunction: A Case Report and Literature Review. Taiwan Geriatr Gerontol. 2015; 10(2): 116-122

Dementia and topographical disorientation through questionnaire on everyday navigational ability. Wei-Pin Hong, Ming-Chyi Pai. The 14th International Conference on Alzheimer’s & Parkinson’s disease, Lisbon, Portugal. 2019.03.

Working is a part of Life: Shift work sleep disorder

Huan-Jan Lin (林煥然)
Neurology department, E-DA hospital/I-shou University, Taiwan

Sleep Center, E-DA cancer hospital/I-shou University, Taiwan

M.D., Kaohsiung Medical University, Taiwan

Abstract

In the highly developing society, about one in five employees need to work in some forms of shift. Shift work is associated with numerous negative health consequences, including sleep disturbances, medical and psychiatric comorbidities. A substantial percentage of shift workers develop shift work disorder, a circadian rhythm sleep disorder characterized by excessive sleepiness, insomnia, or both as a result of shift work.

In addition to adverse health consequences and diminished quality of life at the individual level, shift work disorder incurs significant costs to employers through diminished workplace performance and increased accidents and errors. Since shift work will remain a vital component of the modern economy, finding a solution to deal with the dilemma became imperative

In my speaking, I will briefly review the prevalence, diagnostic criteria, treatment strategy and organizational recommendation of shift work sleep disorder, according to the updated scientific evidences.

Selected recent publications:

Huan-Jan Lin, Jen-Hao Yeh, Meng-Tsang Hsieh, Chung-Yao Hsu Continuous positive airway pressure with good adherence can reduce risk of stroke in patients with moderate to severe obstructive sleep apnea: An updated systematic review and meta-analysis. Sleep Medicine Reviews (article in press)

Yu-Hsuan Liu, Huan-Jan Lin Cefepime Induced Encephalopathy Presented with Asymmetric Generalized Periodic Discharges in Electroencephalogram: A Case Report. E-Da Medical Journal 2019;6(1):13-16

Huan-Jan Lin, Jung-chi Tsou, Hung-Chang Kuo Acute-Onset Painful Restless Legs Syndrome after Ischemic Stroke: A Case Report. E-Da Medical Journal 2017;4(4):19-22

Huan-Jan Lin, Te-Yu Hung, Yi-Jung Hsieh, Jing-Jane Tsai, Chin-Wei Huang Spontaneous and stimulus-induced rhythmic periodic or ictal discharges (SIRPIDs) with rhythmic eye blinking and ocular dipping in a post-anoxic comatose patient: a case report Neurol Sci. 2016 Dec;37(12):2027-2030.