



臺灣生物精神醫學 暨神經精神藥理學學會



2025 TSBPN SPRING CONGRESS Mar.22, 2025

主辦單位:臺灣生物精神醫學暨神經精神藥理學學會(TSBPN) 共同主辦單位:台灣恩覺失調症研究學會(TSSR)

Contents

議程2
教育演講:思學生調疔的藥物之現今與未來
秋月便時·心見入明征的朱初之死了兴不不 田人之田魯生調应茲物公成也引
玩了之心見入調症朱初石療相引
利工业兴资展十心見大调症架初
專題討論:思覺失調症新藥開發研究在台灣
思覺失調症負性症狀的自動評估系統及嶄新治療的發展
思覺失調症與相關認知疾患之新藥開發:基於 NMDA 受體之調控13
Cognitive Impairment in Patients with Schizophrenia17
Leveraging Population Pharmacokinetics to Optimize Clinical Outcomes of
Long-Acting Injectable Antipsychotics23
New Horizon in Treating Anxiety27
rTMS 認證課程-基礎課程
重覆經顧磁刺激 rTMS 治療 憂鬱症原理、機轉、安全性
TBS 原理與機轉
rTMS 於神經科應用
A Comparison of iTBS and 10Hz rTMS in Treatment-resistant Depression40
rTMS 認證課程-思覺失調症的治療應用
Enhancing Visual Working Memory in Schizophrenia: Effects of Frontoparietal Theta
tACS in Low-performing Patients43
Focused Ultrasound Stimulates the Prefrontal Cortex and Prevents MK-801-Induced
Psychiatric Symptoms of Schizophrenia in Rats46
Effects of Online High-definition Transcranial Direct Current Stimulation over Left
Dorsolateral Prefrontal Cortex on Predominant Negative Symptoms and EEG
Functional Connectivity in Patients with Schizophrenia: a Randomized, Double-blind.
Controlled Trial50

2025 臺灣生物精神醫學暨神經精神藥理學學會春季會

Date : 2025/03/22

Vanue	스바리	三谷 3 花	司欧	命 張口	
venue.		区 才下 5支	ES Pr	日 時代 「	- U) TOL

Ó

 $\left(\right)$

0

Time	Торіс	Speaker	Moderator
8:30-8:50	報到	Dia 14 3	
8:50-9:00 教育	Opening 新講・田學生調症藥物之祖今朗未來(Corporate Breakfage	限相 _量	₹ 埋事長
TXP.			
9:00-9:30	現今之忠覺失調症樂物治療指引	趙乂麟醫師	白雅美教授
9:30-10:00	新上市與發展中思覺失調症藥物	莊暘安醫師	李朝雄 教授
10:00-10:20	Coffee Break & 海報展示		
	專題討論:思覺失調症新藥開發研究在台灣		
10:20-10:50	思覺失調症負性症狀的自動評估系統及嶄新治療的發展 Development of auto-assessing system and novel treatment for negative symptoms of schizophrenia	劉智民醫師	謝明憲醫師
10:50-11:20	思覺失調症與相關認知疾患之新藥開發:基於 NMDA 受 體之調控 New drug development for schizophrenia and related cognitive disorders: based on NMDAR regulation	藍先元 教授	沈武典 教授
11:20-11:40	Coffee Break & 海報展示		
11:40-12:20	Cognitive Impairment in Patients with Schizophrenia	Yusuke Iwata MD. PhD.	陳柏熹 理事長
12:20-12:50 (Room 1001)	Leveraging Population Pharmacokinetics to Optimize Clinical Outcomes of Long-Acting Injectable Antipsychotics	梁志頌 醫師	謝明憲醫師
12:20-12:50 (Room 1002)	New horizon in treating anxiety	楊凱鈞醫師	陳柏熹 理事長
	rTMS認證課程-基礎課程		
13:00-13:30	重覆經顱磁刺激rTMS治療憂鬱症原理、機轉、安全性	鄭智銘醫師	楊延光 教授
13:30-14:00	TBS原理與機轉	李正達 教授	蘇東平教授
14:00-14:30	rTMS於神經科應用	呂明桂 教授	黃尚堅主任
14:30-15:00	A comparison of iTBS and 10Hz rTMS in treatment-resistant depression	林清華教授	黃條來 教授
15:00-15:20	Coffee Break		
	rTMS認證課程-思覺失調症的治療應用		
15:20-15:50	Enhancing visual working memory in schizophrenia: effects of frontoparietal theta tACS in low-performing patients	王俊凱主任	黃名琪 教授
15:50-16:20	Focused Ultrasound Stimulates the Prefrontal Cortex and Prevents MK-801-Induced Psychiatric Symptoms of Schizophrenia in Rats	潘怡如主任	林式穀 教授
16:20-16:50	Effects of online high-definition transcranial direct current stimulation over left dorsolateral prefrontal cortex on predominant negative symptoms and EEG functional connectivity in patients with schizophrenia: a randomized, double-blind, controlled trial	張勳安教授	毛衛中主任
16:50-17:00	Exams for training certification	李正達 教授	
17:00-17:10	Closing	陳柏嘉	理事長
	土 新 単 ய ・ 室 高 主 初 朝 仲 歯 学		



教育演講 思覺失調症的藥物 之現今與未来



Yu-Lin Chao, MD PhD 趙又麟醫師 Director, Department of Psychiatry, National Yang Ming Chiao Tung University Hospital

Dr. Yu-Lin Chao graduated from National Yang Ming University and completed his psychiatric residency training at Taipei Veterans General Hospital. After obtaining his Board-Certified Psychiatrist qualification, he served in Eastern Taiwan, working at Yu-Li Veterans Hospital for over two years before continuing his practice at Hualien Tzu Chi General Hospital for 15 years. Dr. Chao earned his PhD from the Institute of Medical Science at Tzu Chi University and has been an officially appointed Assistant Professor since 2014. His clinical expertise spans child and adolescent psychiatry, geriatric psychiatry, and forensic psychiatry. He became a Board-Certified Forensic Psychiatrist in 2020. His research focuses on developing animal models of psychosis and investigating genetic and genomic regulations, particularly microRNAs, in different brain regions following electroconvulsive treatment. Additionally, Dr. Chao is interested in identifying relevant biomarkers in human exosomes that reflect the status of mental disorders and treatment responses.

Psychopharmacological Treatment Guidelines of Schizophrenia at a glance

Authors :

Yu-Lin Chao MD, PhD (趙又麟醫師)

Affiliation :

Department of Psychiatry, National Yang Ming Chiao Tung University Hospital Abstract :

The psychopharmacological treatment of schizophrenia is continuously evolving, with guidelines from different regions being periodically updated to reflect new evidence and therapeutic advancements. This brief review introduces the treatment principles and key recommendations from the latest guidelines issued by the American Psychiatric Association (APA), the National Institute for Health and Care Excellence (NICE), the World Federation of Societies of Biological Psychiatry (WFSBP), and the Japanese Society of Neuropsychopharmacology (JSN). Additionally, the evidence-based rationale behind these guidelines and region-specific considerations are discussed. Recent advancements in the use of long-acting injectable (LAI) antipsychotics for various clinical applications in schizophrenia treatment are also addressed. Finally, the advantages and limitations of treatment guidelines are examined, emphasizing that professionals should regard guidelines as a tool rather than a rigid rule.



Professor Ya Mei Bai, M.D.,Ph.D. 白雅美 教授醫師 Taipei Veterans General Hospital. National Yang-Ming Chao-Tung University

Professor Ya Mei Bai, M.D., Ph.D. is Director of Department of Psychiatry, Taipei Veterans General Hospital, Taiwan, full Professor in the Department of Psychiatry and Institute of Brain Science at the National Yang-Ming Chao-Tung University; Deputy Director, Faculty of Medicine, National Yang-Ming Chao-Tung University; Chief of Department of Psychiatry, National Yang-Ming Chao-Tung University, and Deputy Chairman and Board Member of Institutional Review Board, Taipei Veterans General Hospital. She is the Council of the international college of Neuropsychopharamcology (CINP), and the Council of Asian College of Neuropsychopharmacology (AsCNP). Prof. Bai is past President of Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology (TSBPN).

Prof Bai's main clinical and academic interests include neuro-inflammatory research in schizophrenia, depressive disorder and bipolar disorder; psychopharmacological treatment and safety studies by clinical cohort study, psycho-epidemiology big data study, and neuro-imaging study. She has published more than 400 papers in the international journals, and listed as the World's Top 2% Scientists 2021, 2022,2023,2024 of the most-cited scientists in various disciplines by Standford University, and in the top 1% of 2021 scholars writing about Mood Disorders over the past 10 years by Expertscape's PubMed-based algorithms. Prof. Bai has received many honors and awards including Dr. Paul Janssen Research Award of Schizophrenia, Research Award of bipoalr disorder, GSK depression and anxiety research Award, Travel Award of European College of Neuropsychopharmacology (ECNP) and Japan biological and neuropsychopharmacological association. Prof Bai is also the devoted in medical education, and has been voted by the medical students as the Distinguished Teacher of National Yang-Ming Chao-Tung University for more than 10 years.

Email: ymbi@mail2000.com.tw



Yang-An Chuang, MD-PhD 莊暘安醫師 Department of Psychiatry, China Medical University Hospital

Dr. Yang-An Chuang received his M.D. degree from National Yang-Ming University, followed by psychiatric residency training at Yuli Veterans Hospital, where he gained extensive clinical experience in the diagnosis and treatment of psychiatric disorders. After obtaining board certification as a psychiatrist, he continued as an attending psychiatrist before pursuing further graduate studies in the United States. He earned a Master's degree in Biotechnology from Columbia University and subsequently completed his Ph.D. in Biochemistry, Cellular, and Molecular Biology (Neuroscience) at the Johns Hopkins University School of Medicine in 2020. His doctoral research, conducted under the mentorship of Drs. Paul Worley and Richard Huganir, focused on how aberrant synaptic mechanisms impact on neurological disorders. From 2020 to 2022, he remained at Johns Hopkins as a postdoctoral fellow in Dr. Worley's laboratory, where he investigated the molecular pathophysiology of neurodegenerative diseases. In 2023, Dr. Chuang returned to Taiwan and joined the Department of Psychiatry at China Medical University Hospital as a research psychiatrist. His research has been published in high-impact, peer-reviewed journals, including Nature Cell Biology, Neuron, and Molecular Cell, reflecting his ongoing commitment to advancing the understanding of psychiatric and neurodegenerative disorders.

E-mail: yc2579@gmail.com

新上市與發展中思覺失調症藥物

Newly marketed and developing drugs targeting on schizophrenia

Authors :

Yang-An Chuang, MD-PhD 莊暘安醫師

Affiliation :

中國醫藥大學附設醫院精神醫學部

Department of Psychiatry, China Medical University Hospital

Abstract:

The development of antipsychotic medications has undergone significant transformations since the 1950s, beginning with the introduction of chlorpromazine. Traditional antipsychotics primarily targeted dopamine D₂ receptors, effectively managing the positive symptoms of schizophrenia but often leading to substantial side effects. Recent advancements have focused on developing medications with novel mechanisms of action to enhance efficacy and tolerability. A notable recent approval is Cobenfy (xanomeline and trospium chloride), sanctioned by the U.S. Food and Drug Administration in September 2024. Cobenfy is the first antipsychotic drug approved to treat schizophrenia that targets cholinergic receptors, offering a new approach distinct from traditional dopamine receptor antagonists. Other innovative antipsychotics have emerged, such as lumateperone and cariprazine, which offer alternative mechanisms and improved side effect profiles. Additionally, promising novel therapeutic agents are under investigation, including the GlyT1 inhibitor iclepertin, which aims to address cognitive impairments associated with schizophrenia by modulating glycine levels to enhance NMDA receptor function. Other-class agents like LK00764, a TAAR1 agonist, and mesdopetam (IRL-790), a dopamine D₂/D₃ receptor antagonist, are also being explored for their potential benefits in treating various aspects of schizophrenia and related disorders. These developments signify a shift towards more targeted and potentially effective treatments for schizophrenia, addressing both positive and negative symptoms while aiming to reduce adverse effects.



Chau-Shoun LEE, M.D., Ph.D. 李朝雄醫師 Professor and chief, Department of Medicine, MacKay Medical College

Director, Department of Medical Education and senior attending psychiatrist, MacKay Memorial Hospital

Associate editor, International Journal of Gerontology

Standing councilor, Taiwanese College of Psychiatry ; Taiwanese Society of Biological

Psychiatry and Neuropsychopharmacology

Councilor, Taiwanese Academia of Psychiatric Epidemiology; Taiwan Association of Medical Screening; Taiwan Society of Addiction

Best teaching staff in MacKay Memorial Hospital, 2014-2021

Professor Wen-Ho Chang Research Award (2015) & Paul Janssen Research Award (2021), TSBPN

Dr Chau-Shoun Lee graduated from College of Medicine, National Taiwan University, and received his psychiatric residency training in National Taiwan University Hospital. After completing the training and acquiring Board Certified psychiatrist qualification, he served as a Chief in Department of Psychiatry, Lotung Pohai Hospital in Ilan area. During 1995 to 1998, he ever worked as a consultation psychiatrist in National Cheng Kung University Hospital and then went to work in Ilan once again. He is now the director of Department of Medical Education, Mackay Memorial Hospital and also the professor and chief in Department of Medicine, Mackay Medical College. Dr Lee's main clinical and academic interests include bipolar disorder, alcohol use disorder, stress-related disorders, psychiatric epidemiology and neuro- psychopharmacology. In 2008 he completed the PhD degree at the Institute of Preventive Medicine, National Taiwan University, where he had trainings in posttraumatic stress disorder and genetic epidemiology. Thereafter, he began to participate in genome wide association study and pharmacogenetics research in bipolar disorders. He had an important publication on trends of common mental disorder in Taiwan in the Lancet 2013. Another distinguished article, as to the genetic biomarker for lithium maintenance treatment in bipolar disorder, was published in the New England journal of Medicine. After 2013, several reports have been published on neurobiology and neuropharmacology about the blue light impact on depression and methylone effect on mental disorders. Over the past 5 years he has reviewed articles for international and domestic journals, such as Psychological Medicine and the Lancet Psychiatry.

E-mail: csleepsych@gmail.com and cslee@mmc.edu.tw







Chih-Min, Liu MD, PhD 劉智民醫師 Attending Physician and Associated Professor, Department of Psychiatry, National Taiwan University Hospital, and College of Medicine, National Taiwan University

Dr. Chih-Min Liu is engaged in studying the etiological factors and developing novel treatment for major psychiatric disorders, especially schizophrenia. As the leader of integrated team of Genomic medicine of Psychiatric Disorders in National Taiwan University Hospital, we have collected the blood sample and neuropsychological tests, niacin skin test of about 3600 families of schizophrenia and conducted a series of molecular genetic studies of schizophrenia through international collaborations. We have collaborated with Psychiatric Genomic Consortium-Asian (PGC-Asian) and reported the GWAS of East-Asian schizophrenia with 208 significant associations in 176 genetic loci for schizophrenia published in Nature Genetics 2019. The samples also engaged in the PGC-3 schizophrenia and identified 287 distinct genomic loci significantly associated with schizophrenia published in Nature 2022.

We have collected the event-related potentials, DSI data of schizophrenia. We hope to clarify the complex relationship between the genotypes and phenotypes in the complex disorder as schizophrenia. We also focus upon the study of early stage of schizophrenia, including first-episode schizophrenia (FES), first-episode psychosis (FEP) and ultra-high risk prodrome (UHR).

We have collaborated with Professor Tseng in Institute of Medical Device and Image, National Taiwan University Medical College for many years. We have collected the white matter integrity data of the whole-brain 45 tracts, using DSI and Tract-based Automatic Analysis (TBAA), of 340 schizophrenia patients at different stages and 70 pre-schizophrenia patients (FEP and UHR), all of these patients have detail clinical, neuropsychological data and their DNAs are available. We have published our research results in several high-impact journals.

In recent years, I have a collaboration with NTU, NHRI and National Chiao Tung University to develop a novel molecule, RS-D7, which is an inhibitor of d-amino acid oxidase (DAO), an NMDA receptor modulator. We demonstrated this molecule has treatment effects upon the negative symptoms and cognitive symptoms in the schizophrenia mouse model. In an open label clinical trial, we showed the molecule seems to have treatment effect on negative symptoms of schizophrenia using its parent drug. We have applied several patents for this molecule.

E-mail: cmliu1968@ntu.edu.tw

Development of auto-assessing system and novel treatment for negative symptoms of schizophrenia

Authors :

Chih-Min Liu¹, Yi-Hsuan Chan², Ming-Yang Ho^{2,3}, Yufeng Jane Tseng^{2,3}, Yu-Li Liu⁴, Wen-Sung Lai⁵, Chung-Ming-Sun⁶, Hai-Gwo Hwu¹

Affiliation :

¹ Department of Psychiatry, National Taiwan University Hospital and College of Medicine, National Taiwan University, Taipei, Taiwan

² Graduate Institute of Biomedical Electronics and Bioinformatics, National Taiwan University, Taipei, Taiwan

³ Department of Computer Science and Information Engineering, National Taiwan University, Taipei, Taiwan

⁴ Center for Neuropsychiatric Research, National Health Research Institutes, Miaoli, Taiwan

⁵ Department of Psychology, National Taiwan University, Taipei, Taiwan

⁶ Department of Applied Chemistry, National Yang-Ming ChiaoTung University, Hsinchu, Taiwan Abstract :

Traditional assessments of schizophrenia's negative symptoms, including expression (EXP) and motivation/pleasure (MAP) domains, are subjective and time-consuming. We developed an automated system leveraging generative AI (GenAI) and ensemble learning (EL) for more objective and efficient evaluations. We conducted audio- and video-recorded interviews with schizophrenia patients using a semi-structured protocol based on the Clinical Assessment Interview for Negative Symptoms. The EL model processed the visual and audio data for EXP assessment, while GenAI analyzed the interview transcripts for MAP assessment. The EXP assessment demonstrated moderate to substantial reliability and the MAP assessment showed good reliability. The system underscoring its potential to improve the consistency and efficiency of negative symptom assessment.

We found d-amino acid oxidase (DAO) gene acts as a hub gene in schizophrenia genetic pathology. The DAO degrades d-serine, which is a co-agonist of NMDA receptor. NMDA hypofunction contributes to the pathophysiological mechanism of schizophrenia. We identified a novel molecule, named as RS-D7, which a metabolite of a known drug, has potent DAO inhibition through drug repurposing. Animal studies showed RS-D7 could rescue the anhedonia and cognitive deficits of schizophrenia mouse models. RS-D7 has been shown no toxicity on major organ systems in animal models. A open-label drug trial using the parent drug of RS-D7 for the treatment of negative symptoms of schizophrenia showed significant improvement of negative symptoms after 8-week treatment. We transferred the patent and technology of RS-D7 to a commercial company. We expect that it will bring the hope for the treatment of primary negative symptoms and cognitive deficits of schizophrenia in the future.



Ming H. Hsieh, MD, PhD 謝明憲醫師 Attending Psychiatrist and Clinical Associate Professor Department of Psychiatry, National Taiwan University Hospital

ERP-Lab director, Department of Psychiatry, National Taiwan University Hospital

E-mail: hsiehmingh@ntu.edu.tw

Dr. Ming H. Hsieh graduated from School of Medicine, National Taiwan University, and received his psychiatric residency training in National Taiwan University Hospital. He engaged in the work of event related potential study of schizophrenia since 1998, and had been to Psychiatry Department of UCSD as a research scholar under the mentorship of Prof. David Braff and Prof. Gregory A. Light from 2003 to 2004. Dr. Hsieh followed Professor Hai-Gwo Hwu in academic research, and his 2013 PhD dissertation was on brain electrophysiology: 'Application of Event-related Potentials in Schizophrenia Research '.

Dr. Hsieh's major research fields are auditory event-related potentials: P50, MMN (mismatch negativity) and Gamma ASSR in patients with psychiatric disorders. He is interested in how these preattentional, automatic information processing differentiated in different population. Besides schizophrenia, the ERP-Lab at Department of Psychiatry, NTUH also recruits subjects of other psychiatry disorders, for example, suspected pre-psychotic state, autistic spectrum disorders, ADHD, etc.

1. Hsieh MH, Chien YL, Gau SS: Mismatch negativity and P3a in drug-naïve adults with attention-deficit hyperactivity disorder. Psychological Medicine 2021 1-11

2. Shen C-L, Chou T-L, Lai W-S, Hsieh MH*, Liu C-C, Liu C-M, Hwu HG: P50, N100, and P200 auditory sensory gating deficits in schizophrenia patients. Frontiers in Psychiatry 2020, 11:868. (Corresponding Author)

3. Chen TC, Hsieh MH, Lin YT, Chan PS, Cheng CH: Mismatch negativity to different deviant changes in autism spectrum disorders: A meta-analysis. Clinical Neurophysiology 2020, 131:766-777.

4. Hsieh MH, Lin YT, Chien YL, Hwang TJ, Hwu HG, Liu CM, Liu CC: Auditory event-related potentials in antipsychotic-free subjects with ultra-high-risk state and first-episode psychosis. Frontiers in Psychiatry 2019, 10: 223.

5. Huang WL, Liu CY, Liu HM, Liu CM, Hsieh MH*: Sex as a moderating factor in

the relationship between hippocampal volume and sensory gating in schizophrenia patients. Clinical EEG and Neuroscience 2019, 50(4):227-230. (Corresponding Author) 6. Chien YL, Hsieh MH, Gau SS: P50-N100-P200 sensory gating deficits in adolescents and young adults with autism spectrum disorders. Progress in Neuropsychopharmacology & Biological Psychiatry 2019, 95:109683

7. Hsieh MH*, Liu HH: Points that need attention in auditory N100 gating research in schizophrenia. Clinical Neurophysiology 2019, 130(1):196. (First and Corresponding Author)

8. Huang WL, Liu CY, Liu CM, Liu HM, Yang CY, Hwang TJ, Hsieh MH*, Hwu HG: Association between mismatch negativity and voxel-based brain volume in schizophrenia. Clinical Neurophysiology 2018, 129: 1899-1906. (Corresponding Author)



Hsien-Yuan Lane, MD, PhD 藍先元醫師 Director, Center for Addiction and Mental Health, China Medical University Hospital, Taichung, Taiwan Director & Professor, Graduate Institute of Biomedical Sciences, China Medical University, Taichung, Taiwan

Dr. Lane obtained his M.D. in Taipei Medical College (now Taipei Medical University) and his doctorate in Graduate Institute of Life Sciences, National Defense Medical Center, Taiwan. He received his psychiatric residency training in Taipei City Psychiatric Center. Currently he is the Director of Center for Addiction and Mental Health, China Medical University Hospital and Director & Professor of Graduate Institute of Biomedical Sciences & Department of Psychiatry at China Medical University Medical College, Taichung, Taiwan. He has been devoted to translational studies, especially those on several NMDA-enhancing agents for treatment of various mental disorders. Dr Lane's group leads in clinical trials to show the efficacy of the pivotal DAAO inhibitor (sodium benzoate in their trials) for treatment of schizophrenia, encouraging further development of novel compounds and lending support to glutamate hypothesis of schizophrenia. He is a fellow and the winner of 2016 CNS Drug Innovation Award of the International College of Neuropsychopharmacology (CINP).

E-mail: hylane@gmail.com

New drug development for schizophrenia and related cognitive disorders: based on NMDAR regulation

Authors :

Hsien-Yuan Lane

Affiliation :

Center for Addiction and Mental Health, China Medical University Hospital, Taichung, Taiwan.

Graduate Institute of Biomedical Sciences & Department of Psychiatry, China Medical University Medical College, Taichung, Taiwan

Abstract :

Current drug treatments of schizophrenia have limited efficacy and significant side effects for many patients (Lin SK & Lane, Schizophr Res 2024), highlighting the need to develop new therapies (Etchecopar-Etchart et al., EClinicalMedicine 2024). NMDA receptor (NMDAR) dysfunction is implicated in several mental disorders, including schizophrenia (Lin et al., Mol Psychiatry 2014, Schizophrenia [accepted]; Lane & Lin, Int J Neuropsychopharmacol 2023). For enhancing NMDAR activity to treat schizophrenia, NMDAR co-agonists (including glycine, D-serine) were examined in clinical trials, albeit with unsatisfactory results. Alternatively, inhibition of glycine transporter-I, showed promising potential in treating schizophrenia (Lane et al., Arch Gen Psychiatry 2005; Chang et al., J Psychopharmacol 2020; Fleischhacker et al., Lancet Psychiatry 2021). However, these strategies have failed in the treatment of clozapine-resistant patients (Lane et al., Biol Psychiatry 2006; Harrison, Biol Psychiatry 2018).

For improving the treatment of mental disorders, dual modulation of NMDAR and oxidative stress is a promising approach against treatment-resistant mental disorders. This speech reviews the current status of clinical trials on NMDAR and/or redox modulation for the treatment of mental disorders.

Another promising route to strengthen NMDAR activity is inhibition of D-amino acid oxidase (DAAO) for slowing D-serine degradation (Kuo et al., CNS Drug 2022; Liang et al., Front Psychiatry 2024). Initially, we found that sodium benzoate, a pivotal DAAO inhibitor, was more efficacious than other NMDAR enhancers. In the first trial, sodium benzoate improved cognitive function of patients with schizophrenia (Lane et al., JAMA Psychiatry 2013). Consequently, benzoate also improved clinical symptoms of clozapine-resistant patients (Lin et al., Biol Psychiatry 2018). Moreover, sodium benzoate has been found to target at other pathways, such as the antioxidants (Lane et al., Psychiatry Clin Neurosci 2023) and follicle-stimulating hormone/estradiol (Lin et al., JAMA Netw Open 2021). In addition, benzoate also improved cognitive function of patients with Alzheimer's disease (Lin et al., Biol Psychiatry 2014) or late-life depression (Lin et al., Int J Neuropsychopharmacol 2022;

Cheng et al., Neuropharmacology 2023).

If these findings can be reconfirmed, modulation of NMDAR and redox may instill hope for the treatment of mental disorders. Nonetheless, more novel compounds are needed for better treatment (Lin CH & Lane, Schizophr Res 2024; Sehatpour & Kantrowitz, Biol Psychiatry 2025).



Winston W. Shen, M.D. 沈武典醫師 Attending and Professor, Department of Psychiatry, Wan Fang Medical Center and College of Medicine, Taipei Medical University

Professor Winston W. Shen graduated from Taipei Medical College in 1970, and received his psychiatric residency trainings in Taipei City Psychiatric Center (TCPC), University of Nebraska and University of New Mexico. After having completed the trainings in 1975, he was certified for psychiatry specialty and added qualification in addition medicine by the American Board of Psychiatry and Neurology as well as certified in psychiatry by the Taiwanese Board of Psychiatry. He was appointed as professor of psychiatry at Saint Louis University, USA. Since 2000, he has been appointed as professor at Taiwan Medical University. Besides his involvement in the Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology (TSBPN), Dr. Shen is also active in the World Psychiatric Association (WPA) and the Asian Federation of Psychiatric Association (AFPA). He is the editor-in-chief of the Taiwanese Journal of Psychiatry (www.e-tjp.org) and editor of the Bulletin of the AFPA (www.afpa.asia/en/bulletin.htm).

E-mail: Winston W. Shen < Shenwinw@gmail.com >

Yusuke IwataMD. PhD. Organization: Graduate Faculty of Interdisciplinary Research Faculty of Medicine Clinical Medicine (Neuropsychiatry) Associate Professor Address: Department ofNeuropsychiatry, School ofMedicine, YamanashiUniversity 1110 Shimokatou,Chuo, Yamanashi, 409-3898 E-mail:yiwata@yamanashi.ac.jp Degree: Doctor of Medicine, Keio University Research Projects: DAAO Inhibition and Glutamate in Schizophrenia

2020.12 -2021.12

Public Interest Incorporated Foundation for the Promotion of Advanced Medicine Research

Effects of Sodium Benzoate on Glutamate and Glutathione Levels in the Brain of Patients with Schizophrenia

2019.4 -2022.3 □ Effects of DAAO inhibitor on brain glutamate levels of patients with schizophrenia

2019.4 -2020.3
Inokashira Hospital Grants for psychiatry research
Awards:
Paul Janssen Award
October 2019, Japanese Society of Clinical Neuropsychopharmacology
Publication:
A Trajectory of Long-Term Antipsychotic Medication Dosage in Inpatients with Severe
Behavioral and Psychological Symptoms of Dementia: A Retrospective Study.
Tada T, Suzuki T, Iwata Y, Kubota M, Watanabe K, Sakurai H.
Pharmacopsychiatry. 2024 Jun 25.

Clozapine treatment and astrocyte activity in treatment resistant schizophrenia: A proton magnetic resonance spectroscopy study.

Torres-Carmona E, Nakajima S, Iwata Y, Ueno F, Stefan C, Song J, Abdolizadeh A, Koizumi MT, Kambari Y, Amaev A, Agarwal SM, Mar W, de Luca V, Remington G, Gerretsen P, Graff-Guerrero A.

Schizophr Res. 2024 Aug;270:152-161.

descSPIM: an affordable and easy-to-build light-sheet microscope optimized for tissue clearing techniques.

Otomo K, Omura T, Nozawa Y, Edwards SJ, Sato Y, Saito Y, Yagishita S, Uchida H, Watakabe Y, Naitou K, Yanai R, Sahara N, Takagi S, Katayama R, Iwata Y, Shiokawa T, Hayakawa Y, Otsuka K, Watanabe-Takano H, Haneda Y, Fukuhara S, Fujiwara M, Nii T, Meno C, Takeshita N, Yashiro K, Rosales Rocabado JM, Kaku M, Yamada T, Oishi Y, Koike H, Cheng Y, Sekine K, Koga JI, Sugiyama K, Kimura K, Karube F, Kim H, Manabe I, Nemoto T, Tainaka K, Hamada A, Brismar H, Susaki EA. Nat Commun. 2024 Jun 12;15(1):4941.

Elevated intrinsic cortical curvature in treatment-resistant schizophrenia: Evidence of structural deformation in functional connectivity areas and comparison with alternate indices of structure.

Torres-Carmona E, Ueno F, Iwata Y, Nakajima S, Song J, Mar W, Abdolizadeh A, Agarwal SM, de Luca V, Remington G, Gerretsen P, Graff-Guerrero A.

Schizophr Res. 2024 Jul;269:103-113.

Impaired Glycosylation of Gastric Mucins Drives Gastric Tumorigenesis and Serves as a Novel Therapeutic Target.

Arai J, Hayakawa Y, Tateno H, Murakami K, Hayashi T, Hata M, Matsushita Y, Kinoshita H, Abe S, Kurokawa K, Oya Y, Tsuboi M, Ihara S, Niikura R, Suzuki N, Iwata Y, Shiokawa T, Shiomi C, Uekura C, Yamamoto K, Fujiwara H, Kawamura S, Nakagawa H, Mizuno S, Kudo T, Takahashi S, Ushiku T, Hirata Y, Fujii C, Nakayama J, Shibata S, Woods S, Worthley DL, Hatakeyama M, Wang TC, Fujishiro M. Gastroenterology. 2024 Aug;167(3):505-521.e19.

Disease Progression Patterns of Brain Morphology in Schizophrenia: More Progressed Stages in Treatment Resistance.

Sone D, Young A, Shinagawa S, Tsugawa S, Iwata Y, Tarumi R, Ogyu K, Honda S, Ochi R, Matsushita K, Ueno F, Hondo N, Koreki A, Torres-Carmona E, Mar W, Chan N, Koizumi T,

Kato H, Kusudo K, de Luca V, Gerretsen P, Remington G, Onaya M, Noda Y, Uchida H, Mimura M, Shigeta M, Graff-Guerrero A, Nakajima S.

Schizophr Bull. 2024 Mar 7;50(2):393-402.

Psychological distress among early medical residents: A 2-year longitudinal cohort study over seven years in Japan.

Watanabe S, Uemura T, Iwata Y, Yagasaki H, Itakura J, Suzuki T.

Compr Psychiatry. 2023 Nov;127:152425. doi: 10.1016/j.comppsych.2023.152425. Epub 2023 Sep 20.

Depression and Associated Factors Among the Elderly Population in an Urban Tertiary Geriatric Hospital in Bangladesh.

Tabassum T, Suzuki T, Iwata Y, Ishiguro H.

Gerontol Geriatr Med. 2023 Jul 28;9:23337214231178145

Cortical thinning in relation to impaired insight into illness in patients with treatment resistant schizophrenia.

Kim J, Song J, Kambari Y, Plitman E, Shah P, Iwata Y, Caravaggio F, Brown EE, Nakajima S, Chakravarty MM, De Luca V, Remington G, Graff-Guerrero A, Gerretsen P.

Schizophrenia (Heidelb). 2023 Apr 29;9(1):27.

Infant coronary artery bypass grafting completely under surgical microscope.

Iwata Y, Takeuchi T, Konuma T, Obase K, Eishi K.

JTCVS Tech. 2021 Aug 20;10:441-443. doi: 10.1016/j.xjtc.2021.08.023. eCollection 2021 Dec.

A valuable echocardiographic indicator for the optimal tightness of bilateral pulmonary artery banding.

Koshiyama H, Takeuchi T, Katagiri J, Iwata Y.

Gen Thorac Cardiovasc Surg. 2022 Feb;70(2):116-123.

Glutathione Levels and Glutathione-Glutamate Correlation in Patients With Treatment-Resistant Schizophrenia.

Iwata Y, Nakajima S, Plitman E, Truong P, Bani-Fatemi A, Caravaggio F, Kim J, Shah P, Mar W, Chavez S, Remington G, Gerretsen P, De Luca V, Sailasuta N, Graff-Guerrero A.

Schizophr Bull Open. 2021 Mar 8;2(1):sgab006. doi: 10.1093/schizbullopen/sgab006. eCollection 2021 Jan.

Successful Introduction of Paliperidone Palmitate for Pregnant Woman With Schizophrenia: Case Presentation and Literature Review.

Iwata Y, Aruga Y, Ohtsuki M, Inoue M, Yasuda K, Hirata T, Uemura T, Suzuki T. J Clin Psychopharmacol. 2021 Mar-Apr 01;41(2):210-212.

Glutamatergic Neurometabolite Levels in Patients With Ultra-Treatment-Resistant Schizophrenia: A Cross-Sectional 3T Proton Magnetic Resonance Spectroscopy Study. Iwata Y, Nakajima S, Plitman E, Caravaggio F, Kim J, Shah P, Mar W, Chavez S, De Luca V, Mimura M, Remington G, Gerretsen P, Graff-Guerrero A.

Biol Psychiatry. 2019 Apr 1;85(7):596-605.

Neurometabolite levels in antipsychotic-naïve/free patients with schizophrenia: A systematic review and meta-analysis of 1H-MRS studies.

Iwata Y, Nakajima S, Plitman E, Mihashi Y, Caravaggio F, Chung JK, Kim J, Gerretsen P, Mimura M, Remington G, Graff-Guerrero A.

Prog Neuropsychopharmacol Biol Psychiatry. 2018 Aug 30;86:340-352.

Threshold of Dopamine D2/3 Receptor Occupancy for Hyperprolactinemia in Older Patients With Schizophrenia.

Iwata Y, Nakajima S, Caravaggio F, Suzuki T, Uchida H, Plitman E, Chung JK, Mar W, Gerretsen P, Pollock BG, Mulsant BH, Rajji TK, Mamo DC, Graff-Guerrero A. J Clin Psychiatry. 2016 Dec;77(12):e1557-e1563.

Lack of association between dopaminergic antagonism and negative symptoms in schizophrenia: a positron emission tomography dopamine D2/3 receptor occupancy study.

Fervaha G, Caravaggio F, Mamo DC, Mulsant BH, Pollock BG, Nakajima S, Gerretsen P, Rajji TK, Mar W, Iwata Y, Plitman E, Chung JK, Remington G, Graff-Guerrero A. Psychopharmacology (Berl). 2016 Oct;233(21-22):3803-3813. doi: 10.1007/s00213-016-4415-6. Epub 2016 Aug 24.

Cognitive Impairment in Schizophrenia: Clinical Course, Assessment, and Treatment Strategies

Authors :

Yusuke Iwata, MD, PhD

Affiliation :

Department of Neuropsychiatry, School of Medicine, Yamanashi University

Abstract : Cognitive impairment is a core feature of schizophrenia, profoundly affecting patients' functional outcomes. Despite the co-occurrence of cognitive deficits with psychosis, current antipsychotic treatments do not effectively improve cognitive function. This presentation focused on the clinical course of cognitive impairment, its assessment, and potential treatment strategies.

Cognitive deficits in schizophrenia encompass multiple domains, including processing speed, working memory, verbal learning, and reasoning. These impairments are evident before the onset of psychosis, persist throughout the disease course, and contribute significantly to functional disability. While some longitudinal studies suggest stability of cognitive impairment over time, others indicate potential deterioration, particularly in institutionalized elderly patients.

Assessment tools such as the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) and Brief Assessment of Cognition in Schizophrenia (BACS) provide structured evaluations of cognitive function. However, cognitive symptoms remain underdiagnosed in routine clinical practice due to the lack of standardized assessment criteria in diagnostic guidelines.

Treatment approaches for cognitive impairment in schizophrenia include cognitive remediation therapy, non-invasive brain stimulation (e.g., repetitive transcranial magnetic stimulation, transcranial direct current stimulation), and pharmacological interventions targeting non-dopaminergic systems. Notably, NMDA receptor modulators, such as glycine transporter inhibitors and d-amino acid oxidase inhibitors, have been investigated for their potential to enhance cognitive function. While some agents show promise, their effect sizes remain modest, and clinical applicability is limited. Additionally, muscarinic receptor agonists and trace amine-associated receptor 1 (TAAR1) agonists are emerging as potential candidates for improving cognitive outcomes.

Despite increasing research efforts, the long-term trajectory of cognitive impairment in schizophrenia remains controversial. Further longitudinal studies are needed to clarify the progression of cognitive deficits and their interaction with other symptom domains. Developing effective treatments to mitigate cognitive decline is crucial for improving the quality of life in individuals with schizophrenia.

Po-See Chen, MD, PhD 陳柏熹醫師



Department of Psychiatry & Institute of Behavioral Medicine College of Medicine and Hospital National Cheng Kung University, Tainan, Taiwan

Dr. Po-See Chen is Professor at the National Cheng Kung University, Department of Psychiatry and Institute of Behavioural Medicine. He holds a PhD rom the National Cheng Kung University and a MD from the Kaohsiung Medical University, Taiwan. Dr. Chen's research interest and clinical practice focuses on the mood disorders and schizophrenia. After received his psychiatry residency training in NCKU, he extended his research to the field of brain images at the Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, N.C., USA. After that, he studies in the effect of mood stabilizer valproate on glia at the neurobiology laboratory/ neuropharmacology group, NIEHS/NIH, USA. Dr. Chen now has a major translational focus that seeks to use knowledge of the fundamental mechanisms regulating emotion to develop personalized treatment strategies for mood disorders. He uses animal models, pharmacogenomics, microbiota, metabolomics, neuroimage, neuromodulation and digital phenotyping to develop precision medicine in treating mood disorders.

E-mail: chenps@mail.ncku.edu.tw



Chih-Sung Liang 梁志頌醫師 Current Position: 1. Director of Department of Education & Research, Beitou Branch, Tri-Service General Hospital, National Defense Medical Center 2. Attending psychiatrist 3. Assistant professor

Email: lcsyfw@gmail.com

I am currently serving as the Director of the Department of Education & Research and an Assistant Professor at the Beitou Branch, Tri-Service General Hospital, National Defense Medical Center. Our hospital is a psychiatric teaching hospital. As both a practicing psychiatrist and academic researcher, I have dedicated my career to advancing psychiatric epidemiology and evidence-based medicine.

My research interests focus primarily on evidence synthesis and big data research in psychiatry, with particular emphasis on geriatric psychiatry, child and adolescent psychiatry, and brain stimulation. I have been fortunate to contribute significantly to the field through publications in leading medical journals including BMJ, Lancet, and JAMA, where I've explored various aspects of psychiatric care and treatment outcomes.

My recent work includes research on psychedelic therapies for depression, mortality rates in different types of dementia, and the effectiveness of brain stimulation techniques. I find great satisfaction in synthesizing complex medical evidence and translating research findings into practical clinical applications.

In my role as Director of Education & Research, I am committed to enhancing the quality of medical education and research in our institution. I work closely with international collaborators on various research projects, aiming to improve our understanding of psychiatric conditions and their treatments. My approach combines rigorous scientific methodology with practical clinical applications, as I believe this integration is crucial for advancing psychiatric care.

Leveraging Population Pharmacokinetics to Optimize Clinical

Outcomes of Long-Acting Injectable Antipsychotics

Authors :

Chih-Sung Liang

Affiliation :

Tri-Service General Hospital Beitou Branch

Abstract :

I will introduce the basic concept of population pharmacokinetics (POP-PK). Besides, I will focus on optimizing long-acting injectable antipsychotic therapy suing the data from POP-PK studies. POP-PK modeling integrates patient-specific factors and drug concentration data to understand pharmacokinetic variability across populations. Therefore, we could understand how individual patient characteristics influence drug exposure, and how this knowledge can be applied to personalize LAI dosing strategies.



Ming H. Hsieh, MD, PhD 謝明憲醫師 Attending Psychiatrist and Clinical Associate Professor Department of Psychiatry, National Taiwan University Hospital

ERP-Lab director, Department of Psychiatry, National Taiwan University Hospital

E-mail: hsiehmingh@ntu.edu.tw

Dr. Ming H. Hsieh graduated from School of Medicine, National Taiwan University, and received his psychiatric residency training in National Taiwan University Hospital. He engaged in the work of event related potential study of schizophrenia since 1998, and had been to Psychiatry Department of UCSD as a research scholar under the mentorship of Prof. David Braff and Prof. Gregory A. Light from 2003 to 2004. Dr. Hsieh followed Professor Hai-Gwo Hwu in academic research, and his 2013 PhD dissertation was on brain electrophysiology: 'Application of Event-related Potentials in Schizophrenia Research '.

Dr. Hsieh's major research fields are auditory event-related potentials: P50, MMN (mismatch negativity) and Gamma ASSR in patients with psychiatric disorders. He is interested in how these preattentional, automatic information processing differentiated in different population. Besides schizophrenia, the ERP-Lab at Department of Psychiatry, NTUH also recruits subjects of other psychiatry disorders, for example, suspected pre-psychotic state, autistic spectrum disorders, ADHD, etc.

1. Hsieh MH, Chien YL, Gau SS: Mismatch negativity and P3a in drug-naïve adults with attention-deficit hyperactivity disorder. Psychological Medicine 2021 1-11

2. Shen C-L, Chou T-L, Lai W-S, Hsieh MH*, Liu C-C, Liu C-M, Hwu HG: P50, N100, and P200 auditory sensory gating deficits in schizophrenia patients. Frontiers in Psychiatry 2020, 11:868. (Corresponding Author)

3. Chen TC, Hsieh MH, Lin YT, Chan PS, Cheng CH: Mismatch negativity to different deviant changes in autism spectrum disorders: A meta-analysis. Clinical Neurophysiology 2020, 131:766-777.

4. Hsieh MH, Lin YT, Chien YL, Hwang TJ, Hwu HG, Liu CM, Liu CC: Auditory event-related potentials in antipsychotic-free subjects with ultra-high-risk state and first-episode psychosis. Frontiers in Psychiatry 2019, 10: 223.

5. Huang WL, Liu CY, Liu HM, Liu CM, Hsieh MH*: Sex as a moderating factor in

the relationship between hippocampal volume and sensory gating in schizophrenia patients. Clinical EEG and Neuroscience 2019, 50(4):227-230. (Corresponding Author) 6. Chien YL, Hsieh MH, Gau SS: P50-N100-P200 sensory gating deficits in adolescents and young adults with autism spectrum disorders. Progress in Neuropsychopharmacology & Biological Psychiatry 2019, 95:109683

7. Hsieh MH*, Liu HH: Points that need attention in auditory N100 gating research in schizophrenia. Clinical Neurophysiology 2019, 130(1):196. (First and Corresponding Author)

8. Huang WL, Liu CY, Liu CM, Liu HM, Yang CY, Hwang TJ, Hsieh MH*, Hwu HG: Association between mismatch negativity and voxel-based brain volume in schizophrenia. Clinical Neurophysiology 2018, 129: 1899-1906. (Corresponding Author)



Kai-Chun Yang, MD, PhD 楊凱鈞醫師 Chief, Section of Psychosomatic Medicine, Department of Psychiatry, Taipei Veterans General Hospital Taipei, Taiwan.

Associate Professor, Psychiatric Division, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan.

Dr. Yang completed his psychiatry residency at Taipei Veterans General Hospital (TVGH) from 2005 to 2009. He subsequently earned his PhD in Clinical Neuroscience from the Karolinska Institute (2013-2017), under the mentorship of Drs. Sjoerd J. Finnema, Lars Farde, Christer Halldin, and Akihiro Takano. His doctoral thesis explored "PET studies on the mechanisms of action of antidepressant and antipsychotic drugs." During his PhD, Dr. Yang developed innovative PET imaging paradigms that enhanced sensitivity for measuring serotonin release and quantifying phosphodiesterase 10A.

Since joining TVGH as an attending psychiatrist in December 2017, Dr. Yang's research has focused on utilizing molecular imaging to elucidate the pathophysiology of neuropsychiatric disorders, with a specific emphasis on associated cognitive impairments. For example, he has investigated the interactions between clinical features and dopamine transporter availability in relation to cognitive deficits in individuals who attempted suicide via carbon monoxide intoxication. Furthermore, he has explored the interactions between dopamine transporter availability and peripheral markers of dopamine or glutamate system, and their impact on cognitive impairments in patients with schizophrenia.

Dr. Yang's research also encompasses multimodality imaging, combining molecular imaging with MRI techniques such as resting-state fMRI and MR spectroscopy. He aims to further advance neuropsychiatric research by exploring the potential of simultaneous PET/MRI applications, seeking to uncover novel insights into the underlying mechanisms of these disorders.

E-mail: kcyang2@gmail.com Publications: https://scholar.google.com.tw/citations?user=YxxHdWwAAAAJ&hl=en

New horizon in treating anxiety

Authors :

Kai-Chun Yang, MD, PhD

Affiliation :

Department of Psychiatry,

Taipei Veterans General Hospital and National Yang Ming Chiao Tung University, Taipei, Taiwan

Abstract :

Anxiety disorders present a significant burden on individuals and society, necessitating the development of more effective treatments. While current approaches include pharmacological interventions like selective serotonin reuptake inhibitors and psychological therapies such as cognitive behavioral therapy, a substantial portion of patients experience suboptimal responses. This highlights the heterogeneous nature of anxiety, likely stemming from diverse targets within brain circuits. Consequently, treatments with varied mechanisms of action may be crucial for managing this complexity.

A recent network meta-analysis on generalized anxiety disorder (GAD) treatment efficacy supports this view, revealing a broad spectrum of potential pharmacological agents. However, the approval of novel anxiolytics in the past decade has been limited. Agomelatine, a melatonergic agonist and 5-HT2C antagonist, stands out, having been approved for GAD alongside its indication for depressive disorder.

This presentation will delve into agomelatine's unique mechanism, exploring its potential implications for understanding anxiety pathophysiology and its role in clinical management. Ultimately, personalized interventions, tailored to specific anxiety subtypes and individual brain circuit vulnerabilities, are essential for enhancing treatment efficacy and alleviating the societal impact of anxiety disorders.

Po-See Chen, MD, PhD 陳柏熹醫師



Department of Psychiatry & Institute of Behavioral Medicine College of Medicine and Hospital National Cheng Kung University, Tainan, Taiwan

Dr. Po-See Chen is Professor at the National Cheng Kung University, Department of Psychiatry and Institute of Behavioural Medicine. He holds a PhD rom the National Cheng Kung University and a MD from the Kaohsiung Medical University, Taiwan. Dr. Chen's research interest and clinical practice focuses on the mood disorders and schizophrenia. After received his psychiatry residency training in NCKU, he extended his research to the field of brain images at the Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, N.C., USA. After that, he studies in the effect of mood stabilizer valproate on glia at the neurobiology laboratory/ neuropharmacology group, NIEHS/NIH, USA. Dr. Chen now has a major translational focus that seeks to use knowledge of the fundamental mechanisms regulating emotion to develop personalized treatment strategies for mood disorders. He uses animal models, pharmacogenomics, microbiota, metabolomics, neuroimage, neuromodulation and digital phenotyping to develop precision medicine in treating mood disorders.

E-mail: chenps@mail.ncku.edu.tw

rTMS認證課程 基礎課程





Chih-Ming, Cheng, MD 鄭智銘醫師 Attending Psychiatrist, Department of Psychiatry, Taipei Veterans General Hospital, Taiwan Instructor, Division of Psychiatry, Medical School, National Yang-Ming Chiao-Tung University, Taipei, Taiwan. Deputy Secretary-General Taiwanese Society of Geriatric

Deputy Secretary-General, Taiwanese Society of Geriatric Psychiatry, Taiwan.

Dr. Chih-Ming Cheng graduated from National Yang-Ming University and completed his psychiatric residency at Taipei Veterans General Hospital (VGHTPE). He finished his geriatric psychiatry fellowship at VGHTPE after completing his medical training and becoming a Board Certified Psychiatrist. During his residency training, he followed in the footsteps of Profs. Tung-Ping Su and Ya-Mei Bai, actively attending many international congresses and receiving awards for best poster, travel support, winner of the young psychiatrist and young investigator, CINP student encouragement award, and CINP research fellowship. In academic research, he followed Professor Tung-Ping Su, Professor Ya-Mei Bai, Professor Cheng-Ta Li, Dr. Chia-Fen Tsai, and Dr. Mu-Hong Chen. Dr. Cheng has been a member of the Functional Neuroimaging and Brain Stimulation Lab at VGHTPE since his Postgraduate Year Residency (PGY) Training program (2012), and he has thirteen years of clinical trial experience (new antidepressants, rTMS, esketamine, IV low-dose ketamine). His scientific interests include brain stimulation in treatment-resistant depression, as well as epidemiology in mental illnesses. Dr. Cheng is a doctoral candidate at the Institute of Brain Science, College of Medicine, National Yang-Ming Chiao-Tung University and has published about seventy peer-reviewed articles, including JAMA psychiatry, Molecular Psychiatry, American Journal of Geriatric Psychiatry, International Journal of Geriatric Psychiatry, Psychiatry and Clinical Neurosciences, Neurology as well as the co-editor for Progress in Brain Research volume 278&281, Treatment-Resistant Depression (Elsevier).

E-mail: vdodaco@gmail.com

重覆經顧磁刺激 rTMS 治療 憂鬱症原理、機轉、安全性

Abstract :

Transcranial magnetic stimulation (TMS) is a non-invasive neuromodulation technique that has gained significant attention in neuroscience and clinical applications. It utilizes electromagnetic fields to induce electrical currents in targeted brain regions, thereby modulating neuronal activity. When applied repetitively, known as repetitive transcranial magnetic stimulation (rTMS), this method has been widely studied for its potential in treating neuropsychiatric disorders, particularly depression.

The mechanism by which rTMS exerts its effects on the brain extends beyond local stimulation. It induces widespread neural network changes, influencing functional connectivity and neurotransmitter release. Research suggests that rTMS modulates subcortical structures, including dopamine pathways, and alters structural and functional connections between brain regions. These neuroplastic effects may contribute to its therapeutic benefits, though further studies are required to elucidate the precise mechanisms involved. Additionally, rTMS has been hypothesized to promote the release of neurotrophic factors such as brain-derived neurotrophic factor (BDNF), which may facilitate long-term synaptic plasticity.

High-frequency rTMS, typically applied to the left dorsolateral prefrontal cortex (DLPFC), has demonstrated significant antidepressant efficacy in numerous clinical trials and meta-analyses. The mechanism of action involves increasing local cortical excitability and altering inhibitory circuits. Since its initial development in the 1980s and subsequent clinical applications in the 1990s, rTMS has evolved into a widely accepted therapeutic modality for major depressive disorder. Ongoing research continues to explore its broader applications in other neuropsychiatric conditions, including anxiety disorders, obsessive-compulsive disorder (OCD), and neurodegenerative diseases.

The growing body of evidence supports the notion that rTMS represents a valuable tool in modern psychiatry and neuromodulation, with future directions focused on optimizing treatment parameters, understanding its neurophysiological effects, and expanding its clinical applications.



Yen Kuang Yang, MD 楊廷光醫師 Distinguished Professor, Department of Psychiatry, Institute of Behavioral Medicine, Department of Psychology National Cheng Kung University, Tainan, Taiwan Superintendent, Tainan Hospital, Ministry of Health and Welfare, Tainan, Taiwan

Dr Yen Kuang Yang graduated from Kaohsiung Medical University, and received his psychiatry residency training in National Taiwan University Hospital and National Cheng Kung University (NCKU) Hospital. After completing the training and acquired board certified psychiatry qualification in Taiwan, he served as a consultant responsibility for psychiatric acute wards, clinical drug trials, clinics for substance abuse, home care services, day care treatment, psychiatric community rehabilitation forensic psychiatry programs at National Cheng Kung University and Hospital(NCKUH) and Dou-Liou Branch. He was the president of the Taiwanese Society of Schizophrenia Research (2017-19) and the Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology (2018-21). He also served as the superintendent at NCKUH Dou-Liou Branch (2017-2020), the deputy superintendent at NCKUH (2019-20) and the superintendent of Tainan Hospital, Ministry of Health and Welfare, Tainan (2020-24). Dr Yang's main clinical and academic interests include neuroimaging, neuropsychopharmacology and behavioral medicine. In 2000, he worked as a visiting fellow in Duke University for Psychiatry, NC, USA, where he had trainings in biological psychiatry and program of clinical drug trial. Currently, he has reviewed articles for many international journals and published more than 300 peerreviewed papers. He is now the associate editor of the Taiwanese Journal of Psychiatry (Taiwan), the Clinical Psychopharmacology and Neuroscience (South Korea) and the International Journal of Child Development and Mental Health (Thailand).

Cheng-Ta Li, M.D., Ph.D 李正達教授

現職:

台北榮民總醫院精神部主治醫師 國立陽明大學醫學系及腦科學研究所教授 台北榮民總醫院智慧醫療中心大腦健康組組長 台北榮民總醫院精神部情緒精準醫療中心主任 國立中央大學認知神經科學研究所教授 台灣精神醫學會常務理事 暨 腦神經刺激小組召集人



台灣生物精神醫學會暨藥理學會理事 暨 腦神經刺激專家委員會主任委員 衛生福利部食藥署醫療器材諮議會審查委員;科技部傑出研究獎審查委員

學經歷:

國立陽明大學醫學系;國立陽明大學腦科學研究所博士 美國國家衛生研究院分子造影研究員

代表獎項:

第21 屆國家新創精進獎(2024)康健雜誌年度好醫師(2025)
第20 屆國家新創獎(2023) AsCNP 亞洲生物神經精神藥理學會臨床科學獎(2023)
台港民總醫院醫師創新獎(2022)
台灣精神醫學會精神健康社會倡議獎(2021)
永信李天德基金會青年醫藥科技獎(2020)
台灣生物精神醫學暨藥理學會張文和創會理事長獎(2020)
科技部創新創業競賽創業潛力獎(2019)
科技部新創團隊獎暨 CES 台灣代表隊(2018)
台北榮民總醫院醫師創新獎(2017);榮台聯大最佳論文獎(x4)
宏基基金會龍騰微笑創業創新競賽獎(2016)
台灣精神醫學會保羅揚森論文獎/禮來雙極疾患研究論文獎(x3)
台灣精神醫學會最佳聲報(x4);台灣生物精神醫學暨藥理學會最佳聲報(x3)

代表著作: Total SCI papers > 200

- <u>Cheng-Ta Li</u>^{*} et al. Efficacy of Prefrontal Theta-Burst Stimulation in Refractory Depression: A Randomized Sham-Controlled Study. *Brain*, 2014
- <u>Cheng-Ta Li</u> et al. Prefrontal Glucose Metabolism in Medication-Resistant Major Depression. *British Journal of Psychiatry*, 2016
- 3. Cheng-Ta Li* et al. Effects of prefrontal theta-burst stimulation on brain function in treatment-

resistant depression: A randomized sham-controlled neuroimaging study. *Brain Stimulation*. 2018

- <u>Cheng-Ta Li*</u> et al. Antidepressant Efficacy of Prolonged Intermittent Theta Burst Stimulation Monotherapy for Recurrent Depression and Comparison of Methods for Coil Positioning. *Biological Psychiatry*, 2020
- 5. <u>Cheng-Ta Li</u>*, et al. Global Cognitive Dysfunction and Beta-Amyloid Neuropathology in Late-Life and Treatment-Resistant Depression. *Psychological Medicine*. 2021

Rapid Antidepressant Effects & Mechanisms of Theta Burst Stimulation (TBS) Cheng-Ta Li, M.D., Ph.D. TPVGH and NYMCTU

Abstract

Theta-burst stimulation (TBS) is an updated form of repetitive transcranial magnetic stimulation (rTMS) and could also be utilized to treat treatment-resistant depression (TRD). In my presentation, I will first show you the basic concepts of TBS from early science paper and motor cortical experiments. The second part of my talk will show you that many factors have been shown to have an impact on the TBS outcomes. For example, intermittent TBS (iTBS) seems to have better antidepressant efficacy than continuous TBS (cTBS). We conducted several sham-controlled studies, indicating iTBS in a prolonged manner (piTBS: 1800 pulses; 80% active motor threshold) over 2 weeks is an effective treatment. Blumberger et al. indicated that iTBS (600 pulses; 120% resting motor threshold) over 6 weeks is non-inferior to 10Hz rTMS in treating depression. Accelerated protocols may explain the success of antidepressant effects in shorter time, since the SNT (1800 pulses/session, 10 sessions/day, intersessional intervals: 54 minutes) has been found to have rapid antidepressant effects over 1-2 weeks. However, some other studies provided no support that accelerated protocols always come along with better clinical efficacy. Other parameters, such as stimulation strength and intersessional intervals, may also play a role. For example, recent studies have shown that subthreshold iTBS (i.e., < 100% motor threshold of the stimulation strength) have better effects than suprathreshold iTBS (i.e., $\geq 100\%$ motor threshold). Later in my presentation, I will show you neural mechanisms and molecular basis of iTBS for treating depression, using data from our clinical studies. We mainly found that the applied rhythm is critically involved in the antidepressant effects of non-invasive brain stimulation, glutamate and GABA all play a role in the antidepressant mechanisms of prefrontal iTBS. Normalization of theta-gamma connections is involved in the neural mechanisms of iTBS. Finally, we conducted animal studies and found that iTBS involves a normalization of long-term potentiation and depression (LTP and LTD) in the prefrontal cortex. A review of brain mechanisms of prolonged iTBS for explaining its rapid antidepressant effects would be provided.

Biosketch for Professor Tung-Ping Su, MD Jan. 2025



Professor Tung-Ping Su graduated from National Defense Medical Center, Taipei, Taiwan in 1971 and had completed dual residency training in Taiwan and the US. He did clinical fellowship at the NIMH. Dr. Su is currently Professor and Attending physician of the Department of Psychiatry, Cheng-Hsin General Hospital and Professor Emeritus of National Yang Ming Chia Tung University, Taiwan. Dr. Su was the previous president of Asian Society of Neuropsychopharmacology (AsCNP) and Vice Superintendent of Taipei Veterans General Hospital. His interests are studying treatment refractory mood disorders in association with brain imaging. Dr. Su introduced rTMS therapy to Taiwan depressed patients and was one of the pioneers conducting clinical trials of ketamine on depression in the Asian populations and is the recipient of the "Academic Achievement Award" from the Taiwanese Society of Psychiatry and of APA "Kun-Po Soo award". Over the past few years, he has focused on exploring the relationship between depression and parkinsonism in the elderly and built a normative dataset for striatum dopamine transporter concentration by Trodate-SPECT for clinical referential use. He had published more than 345 papers in SCI and wrote several book chapters.



Ming-Kuei Lu, MD, PhD 呂明桂醫師 Director, Division of Parkinson's Disease and Movement Disorders, Department of Neurology, China Medical University Hospital Associate Professor, College of Medicine, China Medical University

Dr. Lu graduated from China Medical University and received his neurological resident training at China Medical University Hospital, Taichung, Taiwan. He has served as an attending physician in the Department of Neurology, China Medical University Hospital since 2004. In addition to the clinical experience, he pursued his Ph.D. training focusing on clinical electrophysiology in Frankfurt. His major research interests include clinical neurophysiology and movement disorders, focusing on Parkinson's disease and essential tremor. He has published several research articles and educational materials regarding this field. He is currently a faculty of the Medical College at China Medical University and an active member of Taiwan Neurological Society, Taiwan Society of Clinical Neurophysiology and Taiwan Movement Disorder Society.

E-mail: mklu@mail.cmu.edu.tw

Application of rTMS in neurological disorders

Authors :

Ming-Kuei Lu, MD. PhD.

Affiliation :

¹Division of Parkinson's Disease and Movement Disorders, Department of Neurology, China Medical University Hospital

²Graduate Institute of Biomedical Sciences, College of Medicine, China Medical University

Abstract :

Repetitive transcranial magnetic stimulation (rTMS) has been applied in several neuropsychiatric disorders with notable benefits. Recent studies show its effectiveness, mechanisms, and optimal strategies in disease conditions such as stroke, Parkinson's disease (PD), multiple sclerosis (MS), epilepsy, and chronic pain. For stroke rehabilitation, rTMS has been widely used to enhance motor recovery by modulating cortical excitability. High-frequency rTMS (\geq 5 Hz) applied to the ipsilesional hemisphere and low-frequency rTMS (\leq 1 Hz) to the contralesional hemisphere have shown promising results in improving motor function and reducing spasticity.

In PD, rTMS has been investigated for alleviating motor symptoms, cognitive dysfunction, and depression. High-frequency stimulation over the primary motor cortex (M1) and the dorsolateral prefrontal cortex (DLPFC) has demonstrated benefits in bradykinesia, gait disturbances, and non-motor symptoms.

For MS, rTMS has been used to manage fatigue, cognitive impairment, and spasticity. Recent trials suggest that rTMS over the M1 and DLPFC can improve motor performance and reduce neuropathic pain.

In epilepsy, inhibitory low-frequency rTMS has been applied over epileptogenic zones, showing the potential to reduce seizure frequency. However, variability in response necessitates further optimization.

Chronic pain management with rTMS, particularly targeting M1 and DLPFC, has gained interest. Studies have reported significant pain relief in conditions like neuropathic pain, fibromyalgia, and migraine.

Advancements in rTMS protocols, including theta burst stimulation (TBS) and individualized targeting using neuroimaging, can enhance the efficacy of rTMS. However, there are challenges such as response variability, optimal dosing, and long-term effects in clinical practice. Overall, rTMS continues to evolve as a promising therapeutic tool for neurological disorders, with ongoing studies refining its clinical applications.



Huang, Shang-Chien MD 黃尚堅醫師 Chair, Department of Psychiatry, Tungs' Taichung MetroHarbor Hospital Assistant professor, Jenteh Junior College of Medicine Executive supervisor of the Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology (TSBPN)

Dr Huang, Shang-Chien graduated from China Medical University in Taichung. After completing the psychiatric residency training and acquired Board Certified Psychiatrist qualification, he served as an executive director of the Taiwanese Society of Addiction. Now serves as the director of the Dementia Center of Tungs' Taichung MetroHarbor Hospital, and also the executive supervisor of the Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology (TSBPN) and the chairman of the Taichung Dementia Association (TDA).

Publication in the past three years :

1.Y Tien, SC Huang. Aripiprazole-Associated Acute Dystonia During Dose Reduction in Patient With Schizophrenia and Dementia: A Case Report. Journal of Clinical Psychopharmacology. (2022) 42(5); 508-509 (corresponding author)(IF=3.152)

2.Y Tien, HP Huang, DL Liao, SC Huang. Dose-response analysis of aripiprazole in patients with schizophrenia in Taiwan. Therapeutic Advances in Psychopharmacology. 2022; 12;1-8 (corresponding author) (IF=4.988)

3.KM Jhang, WF Wang, KN Hsu, SC Huang, etc. A 12-Year Comparison of Alzheimer's Dementia Patients With Their Informants in Taiwan. American Journal of Alzheimer's Disease and other Dementias. (2023) 38(11); (IF=3.400)

E-mail: huangsc190@yahoo.com.tw



Ching-Hua Lin, MD, PhD 林清華醫師 Elegance Psychiatric Clinic, Kaohsiung, Taiwan Kaohsiung Municipal Kai-Syuan Psychiatric Hospital Professor, College of Medicine, Kaohsiung Medical University & National Sun Yat-sen University

Dr. Ching-Hua Lin graduated from Kaohsiung Medical University (MD & PhD) and received his psychiatric residency training in Kaohsiung Municipal Kai-Syuan Psychiatric Hospital (KSPH). After completing the training and acquired Board Certified Psychiatrist qualification, he had his fellowship of mood disorders at University of British Columbia & Toronto University, Canada. He was appointed as the Chief of Adult Psychiatry and has been in charge of managing the psychosomatic ward for inpatients with major depressive disorder or other psychosomatic disorders since 2006. He has about twenty years' experiences in clinical studies of mood trials and is interested in disorders. schizophrenia, psychopharmacology, electroconvulsive therapy, and rTMS. He has published about 100 peer reviewed articles and has reviewed articles for many international journals. Now he is a primary care psychiatrist and in charge of a private psychiatric clinic in Kaohsiung City.

E-mail: chua.lin@msa.hinet.net

A comparison of iTBS and 10Hz rTMS in treatment-resistant depression

Authors :

Ching-Hua Lin

Affiliation :

Elegance Psychiatric Clinic, Kai-Syuan Psychiatric Hospital

Abstract :

Objectives: The goal of this retrospective study was to compare the response/remission rates, time to response/remission, common side effects, and attitude toward rTMS between treatment-resistant depression (TRD) patients receiving the iTBS or the 10 Hz rTMS.

Methods: TRD Patients, who received iTBS (n = 38) or 10 Hz rTMS (n = 58) between May 2019 and August 2023 and at least 5 rTMS sessions entered the analysis. 17item Hamilton Depression Rating Scale (HAMD-17), common side effects, and attitudes toward rTMS were routinely assessed during the treatment period. Response and remission were defined as a HAMD-17 \geq 50% reduction and a HAMD-17 \leq 7, respectively. Survival analysis was used to compare the time to response/remission between the two groups.

Results: The two treatment groups were comparable at baseline variables, dropout rates, post-ECT response/remission rates, and attitudes toward rTMS. There were no statistically significant differences in time to response/remission between these two groups. The iTBS group experienced significantly higher rates of facial twitching than the 10 Hz rTMS group (73.7% vs. 24.1%, p<0.001).

Conclusions: iTBS yielded comparable response/ remission rates and time to response/ remission response/ remission with 10Hz rTMS. However, the iTBS group was more likely to experience more facial twitching during the treatment period. More research is needed in the future.



Tiao-Lai Huang, MD 黃條來 醫師 1. Department of Psychiatry, Chang Gung Memorial Hospital at Kaohsiung 2. Genomic and Proteomic Core Laboratory, Department of Medical Research, Kaohsiung Chang Gung Memorial Hospital

Dr Tiao-Lai Huang graduated from Chang Gung University and received his psychiatric residency training in Chang Gung Memorial Hospital. After completing his training, he served as an attending in Kaohsiung Chang Gung Memorial Hospital since 1999. He is now the professor in Chang Gung Memorial Hospital and also maintains a teaching position at College of Medicine, Chang Gung University as professor.

In the past, he had been the Head of the Department of Psychiatry in Kaohsiung Chang Gung Memorial Hospital (2009/07-2011/09) and the Chief of the Department of General Psychiatry in Kaohsiung Chang Gung Memorial Hospital (2011/10-2013/09). His research interests are consultation and biological psychiatry, including molecular biochemistry, genetics and proteomics. Until now, he had published 137 papers and contributed 7 chapters in books. He developed the lorazepam-diazepam protocol to rapidly relieve catatonia symptoms from patients with mental illness, including schizophrenia, bipolar disorder, major depression and general medical condition.

He is a member of the Society of Psychiatry, R.O.C. (Taiwan) and acts as an Executive Editor of Taiwanese Journal of Psychiatry. He is also the director of Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology (101/09-116/10).

He also received many awards including Dr. Paul Janssen Research Award (2008) and GSK Award (2009) by Taiwan Society of Psychiatry and Travel Award from BP/NP OSAKA (2005). Recently, he is the Vice Head of the Department of Psychiatry in Kaohsiung Chang Gung Memorial Hospital (2017/07-2022/06).

E-mail: a540520@adm.cgmh.com.tw



rTMS認證課程 思覺失調症的治療應用

Jiunn-Kae Wang, MD, MS 王俊凱 醫師 Director, Department of Psychiatry Shuang Ho Hospital Adjunct lecturer, College of Medicine Taipei Medical University Email: 14073@s.tmu.edu.tw



Education

Taipei Medical University (TMU)	Taipei, Taiwan
PhD student of Mind, Brain and Consciousness (GIMBC)	Sep. 2024 - Present
National Yang-Ming University (NYMU)	Taipei, Taiwan
Master of Public Health	Sep. 2006 - Jun. 2008
Bachelor of Medicine	Sep. 1992 - Jun. 1999

Professional experience
Shuang Ho Hospital, TMU
Visiting staff Department of

Visiting staff, Department of Psychiatry Cheng Hsin General Hospital Visiting staff, Department of Psychiatry Taipei Tzu Chi Hospital Visiting staff, Department of Psychiatry Taipei Veterans General Hospital Resident, Department of Psychiatry

Board certification

Psychiatrist, Taiwan Geriatric Psychiatrist, Taiwan New Taipei, Taiwan Apr. 2014 - Present Taipei, Taiwan Jan. 2013 - Mar. 2014 New Taipei, Taiwan May 2005 - Dec. 2012 Taipei, Taiwan May 2001 – Apr. 2005

Since 2004 Since 2010

Publication



https://orcid.org/0000-0003-2907-0355

Enhancing visual working memory in schizophrenia: effects of frontoparietal theta tACS in low-performing patients

Authors :

Jiunn-Kae Wang, MD, MS

Affiliation :

Department of Psychiatry, Shuang Ho Hospital, Taipei Medical University

Abstract :

Cognitive impairments in schizophrenia significantly affect patients' functional outcomes, yet treatment options remain limited. Among these impairments, deficits in visual working memory (VWM) are particularly detrimental. Previous research suggests that transcranial alternating current stimulation (tACS) may enhance cognitive performance, but its effects on schizophrenia-related VWM deficits require further investigation.

This study aimed to examine the efficacy of right frontoparietal theta tACS in improving VWM performance in patients with schizophrenia, particularly those with low baseline performance. We conducted a controlled experiment comparing VWM outcomes across different stimulation conditions. Participants underwent cognitive assessments before and after stimulation, focusing on memory consolidation and retrieval processes.

Our findings indicate that low-performing patients benefited significantly from Retro-cues with improvements primarily observed during the memory maintenance phase. This suggests that their VWM deficits stem from accelerated memory decay rather than retrieval difficulties. Additionally, the facilitatory effects of tACS were not limited to a specific memory stage but reflected an overall enhancement in visual attention. In contrast, high-performing patients did not exhibit improvements, and retrieval cues even led to decreased accuracy, possibly due to interference with their established response strategies.

These results highlight the importance of individualized treatment approaches for cognitive impairments in schizophrenia. While non-invasive brain stimulation techniques like tACS show promise, treatment efficacy varies among patient subgroups. Future research should explore optimal stimulation parameters, long-term effects, and cost-effectiveness. Personalized interventions may offer a more effective strategy for mitigating cognitive deficits and improving functional outcomes in schizophrenia.



Ming-Chyi Huang, M.D. Ph. D Director and Staff Psychiatrist, Taipei City Psychatirc Center, Taipei City Hospital Professor, Department of Psychiatry, School of Medicine, Taipei Medical University EC member and Treasurer, International College of Neuropsychopharmacology (CINP)

Dr. Huang is currently serving as a staff psychiatrist at Taipei City Psychiatric Center (TCPC), also known as Taipei City Hospital, Song-De branch. With nearly 29 years of clinical experience, she specializes in addiction treatment for nearly 20 years. Her clinical and academic interests primarily revolve around biomarkers of neurotoxicity or neuroadaptation in addictive disorders (alccohol, ketamine, and methamphetamine addiction), and she also explores metabolic issues in schizophrenia. Dr. Huang has initiated clinical trials investigating both pharmacotherapy (naltrexone and dextromethorphan) and non-pharmacotherapy (smartphone applications, SoberDiary) for alcohol dependence. Her recent focus lies in characterizing the neurobiology and psychological consequences of chronic ketamine use, along with substance-associated psychosis (ketamine and methamphetamine). Beyond her clinical and administrative responsibilities, Dr. Huang is dedicated to teaching addiction sciences and psychopharmacology to psychiatric trainees of various levels. She has pioneered interdisciplinary medical-legal intervention programs in Taiwan, providing medical interventions for people with substance and alcohol use disorders referred from legal systems. She has published papers 190 peer-reviewed journal papers.

Email: mch@tpech.gov.tw



Yi-Ju Pan, MD 潘怡如醫師 Director, Department of Psychiatry, Far Eastern Memorial Hospital Associate professor, Department of Chemical Engineering and Materials Science, Yuan Ze University

Dr. Pan's primary research focuses on the economic evaluation of healthcare services, diseases, and treatments, with a particular emphasis on mental illnesses such as schizophrenia, bipolar disorder, and depression. Her research methodologies include database and modeling analyses, examining the cost burden of treatment for psychiatric patients and the healthcare utilization, prognosis, treatment patterns, and cost-effectiveness (or cost-utility) analyses for individuals with psychiatric disorders and comorbid physical conditions, including cardiovascular diseases and chronic pain.

Beyond clinical research, Dr. Pan has long been dedicated to suicide prevention, particularly among adolescents and young adults, investigating depressive symptoms and suicide risk factors in these populations. Her work also explores the use (or discontinuation) of psychiatric medications and their potential effects or adverse reactions in various groups, including the elderly, young adults, individuals with sedative-hypnotic abuse, and patients with schizophrenia or dementia. In addition to pharmacological treatments, she examines healthcare utilization patterns, including outpatient, emergency, and inpatient services, and their associations with clinical outcomes, including mortality.

Dr. Pan's recent work extends to developing novel methodological frameworks, incorporating social network analysis, quality-of-life assessments (considering both patients and caregivers), online surveys, and the integration of computer systems and technology to enhance psychiatric treatment and physical health screening.

In recent years, she has focused on exploring non-pharmacological treatments for schizophrenia. In collaboration with Professor Feng-Yi Yang's team at National Yang

Ming Chiao Tung University, she has investigated the application of transcranial ultrasound in schizophrenia animal models. Their findings revealed that low-intensity pulsed ultrasound (LIPUS) stimulation restored balanced levels of brain-derived neurotrophic factor (BDNF) in the hippocampus and medial prefrontal cortex of schizophrenia-model rats, improving cognitive deficits and reducing neuropathology.

Furthermore, using an MK-801-induced schizophrenia rat model, their team demonstrated that LIPUS stimulation of the prefrontal cortex significantly alleviated sensorimotor gating deficits and anxiety-like behaviors. The study also showed that NR1 expression was significantly higher in LIPUS-pretreated animals, providing new evidence of LIPUS's role in modulating NMDA receptor function and c-Fos activity. These findings suggest LIPUS as a promising therapeutic approach for schizophrenia, with the potential to improve both positive and negative symptoms. Dr. Pan's related LIPUS research has been published in leading journals, including Radiology, Cerebral Cortex, Neurotherapeutics, and Brain Stimulation.

E-mail: panyiju0211@gmail.com

Focused Ultrasound Stimulates the Prefrontal Cortex and Prevents MK-801-Induced Psychiatric Symptoms of Schizophrenia in Rats

Authors :

Tsung-Yu Pan^{1,#}, Yi-Ju Pan^{2,3#}, Shih-Jen Tsai^{4,5}, Che-Wen Tsai¹, and Feng-Yi Yang^{*,1} Affiliation:

¹Department of Biomedical Imaging and Radiological Sciences, National Yang Ming Chiao Tung University, Taipei, Taiwan;

²Department of Psychiatry, Far Eastern Memorial Hospital, New Taipei City, Taiwan; ³Department of Chemical Engineering and Materials Science, Yuan Ze University, Taoyuan City, Taiwan;

⁴Department of Psychiatry, Taipei Veterans General Hospital, Taipei, Taiwan;

⁵Division of Psychiatry, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan

Abstract :

Schizophrenia remains a major challenge in psychiatric treatment, with growing evidence linking its pathology to impaired glutamatergic signaling via NMDA receptors. Recent studies suggest that Low-Intensity Pulsed Ultrasound (LIPUS) may offer a promising non-invasive intervention.

Our study investigated the effects of LIPUS on psychiatric symptoms and anxietylike behaviors in a rat model of schizophrenia induced by MK-801. We observed that LIPUS stimulation of the prefrontal cortex significantly improved locomotor activity, sensorimotor gating, and anxiety-related behaviors. Moreover, LIPUS counteracted MK-801-induced downregulation of NR1, a critical NMDA receptor subunit, in the medial prefrontal cortex. Additionally, LIPUS suppressed the excessive activation of c-Fos, a neuronal activity marker, in key brain regions associated with schizophrenia. These findings highlight LIPUS as a potential breakthrough therapy, capable of modulating NMDA receptor function and neural activity. As we seek innovative solutions for schizophrenia, LIPUS may offer a new, non-pharmacological approach to improving patient outcomes.



Shih-Ku Lin, MD 林式穀醫師

Attending Psychiatrist, Department of Psychiatry, Taipei Chang Gung Memorial Hospital

Dr. Shih-Ku Lin graduated from Kaohsiung Medical University in 1981 and completed his psychiatric residency

training at the Taipei City Psychiatric Center (TCPC). After finishing his training and becoming a Board-Certified Psychiatric Specialist, he pursued a fellowship in child psychiatry at the Kansas University Medical Center in 1988. In 1993, he was appointed as the Chief of the Department of Addiction Science at TCPC, a position he held for 11 years. He later chaired the Department of Psychiatry at Taipei City Hospital and Psychiatric Center and also served as an adjunct associate professor at the College of Medicine, Taipei Medical University. Dr. Lin retired from Taipei City Hospital in July 2020 and relocated to Linkou Chang Gung Memorial Hospital.

Since his residency, Dr. Lin has collaborated with Professor Wen-Ho Chang in academic research and participated in founding the Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology (TSBPN). Dr. Lin founded the Taiwanese Society of Addiction and became its inaugural president in 2008.

His research interests include psychopharmacology, with a particular focus on ethnic differences in pharmacokinetics and new drug clinical trials. He currently plays a leading role in the Research on Asian Prescription Pattern (REAP https://reap.asia/index_en.html) consortium, the largest and longest-running international collaborative research project in psychiatry in Asia. In the field of addictive disorders, his research group focuses on alcohol dependence, heroin dependence, methamphetamine-induced psychosis, and ketamine use disorder, encompassing studies ranging from genetics to clinical interventions.

Dr. Lin also has over twenty years of experience in clinical trials, primarily in phase II and III global and regional psychotropic drug development. He has published more than 180 peer-reviewed papers and has reviewed articles for numerous international journals. Currently, he serves as the Vice President of the Asian College of Neuropsychopharmacology (AsCNP) and was the Vice President of the International College of Neuropsychopharmacology (CINP) from 2018 to 2022.

E-mail: sklin@tpech.gov.tw sklintcpc@gmail.com



Hsin-An Chang, MD 張勳安醫師 Chief, Division of Child and Adolescent Psychiatry, Department of Psychiatry, Tri-Service General Hospital, Taipei, Taiwan Professor, School of Medicine, National Defense Medical Center, Taipei, Taiwan

Dr. Hsin-An Chang graduated from School of Medicine, National Defense Medical Center, Taipei, Taiwan, and received his psychiatric residency training in Tri-Service General Hospital. After completing the training and acquired Board Certified Psychiatrist qualification, he serves as an attending psychiatrist in Tri-Service General Hospital. In 2021 he was appointed as the Chief, Division of Child and Adolescent Psychiatry. Currently he serves as the Executive Director of Taiwan Society of Psychophysiology, of Taiwan Clinical TMS Society, and of Asia Pacific Institute of Stress as well as the committee member of Asian Special Interest Council (SIC) under the Clinical TMS Society (CTMSS). He has over 12 years of experience in clinical trials and his research interest includes psychophysiology, psychopharmacology and the application of non-invasive brain stimulation in treating psychiatric disorders. Dr. Chang has published more than one hundred and eighty peer reviewed articles and has reviewed articles for many international journals.

E-mail: chang.ha@msa.hinet.net

Effects of online high-definition transcranial direct current stimulation over left dorsolateral prefrontal cortex on predominant negative symptoms and EEG functional connectivity in patients with schizophrenia: a randomized, double-blind, controlled trial

Authors :

Yeh TC and Chang HA*

Affiliation:

Department of Psychiatry, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

Abstract :

Aims: Schizophrenia, a debilitating mental disorder, is characterized by persistent negative symptoms such as avolition and anhedonia. Currently, there are no effective treatments available for these symptoms. Thus, our study aims to assess the efficacy of online high-definition transcranial direct current stimulation (online HD-tDCS) in addressing the negative symptoms of schizophrenia, utilizing a double-blind, randomized, sham-controlled trial design.

Methods: Fifty-nine patients with schizophrenia were randomized to receive either active HD-tDCS or sham stimulation, targeting the left dorsolateral prefrontal cortex. Outcomes were measured by changes in the Positive and Negative Syndrome Scale Factor Score for Negative Symptom (PANSS-FSNS). Exact low-resolution electromagnetic tomography was used to assess the functional connectivity.

Results: All 59 participants, including 50.84% females with an average age of 43.36 years, completed the trial. In the intention-to-treat analysis, patients receiving active HD-tDCS showed greater improvement in PANSS-FSNS scores compared to those receiving the sham procedure. The differences were 2.34 (95% confidence interval [CI], 1.28-3.40), 4.28 (95% CI, 2.93-5.62), and 4.91 (95% CI, 3.29-6.52) after the intervention, as well as at 1-week and 1-month follow-ups, respectively. A tingling sensation on the scalp was more common in the active group (63.3%) compared to the sham group (10.3%). Additionally, HD-tDCS was associated with a decrease in delta-band connectivity within the default mode network.

Conclusions: High-definition transcranial direct current stimulation was effective and safe in ameliorating negative symptoms in patients with schizophrenia when combined with online functional targeting.

Keywords: clinical psychopathology; psychophysiology; schizophrenia.

Wei-Chung Mao, MD, Ph D 毛衛中 醫師



Director, Department of Psychiatry, Chen Hsin General Hospital, Assistant professor, School of Medicine National Defense Medical Center

Dr. Wei-Chung Mao graduated from the National Defense Medical Center and completed his psychiatry residency training at Tri-Service General Hospital. From 2000 to 2003, he pursued subspecialty training in sleep medicine at the University of California, San Diego.

From March 2003 to August 2017, Dr. Mao served in the Department of Psychiatry at Tri-Service General Hospital, initially as an attending physician and later as the Chief of the Psychosomatic Medicine Division. In September 2017, he transitioned to Cheng Hsin General Hospital, where he assumed roles as an attending physician and the Chief of the Psychosomatic Medicine Division. Since February 2023, Dr. Mao has been serving as the Director of the Department of Psychiatry at Cheng Hsin General Hospital, a position he holds to this day.

Dr. Mao completed his master's and doctoral degrees at the Institute of Brain Science, National Yang Ming Chiao Tung University. His main clinical and academic interests include sleep medicine, neurophysiology, and the neuroimaging of mental disorders. His doctoral dissertation focused on studying auditory hallucinations in patients with schizophrenia and developing an assessment tool for social cognition.

Dr. Mao has actively contributed to the development of the Taiwan Society of Sleep Medicine. As the chairperson of the Board Accreditation Committee for six years, he played a key role in establishing the accreditation system for the Taiwanese Board of Sleep Medicine in 2012.

E-mail: wc.maoi@msa.hinet.net