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## 精神疾病認知及功能缺損的新近研究發展

### Recent Advancements in Cognitive and Functional Impairments in Mental Illness

時間：114 年 6 月 28 日(星期六) 13:30~17:30  
地點：臺北榮民總醫院 致德樓第十樓會議室

13:30-13:40	<b>Opening Remarks</b>	白雅美教授 Ya-Mei Bai
	座長：劉慕恩 主任 (Mu-N Liu) 胡力予 主任 (Li-Yu Hu)	
13:40-14:10	探討循環內皮前驅細胞在情緒疾病認知缺損的角色 Explore the role of circulating endothelial progenitor cells in the cognitive deficit in mood disorders	劉英杰主任 Ying-Jay Liou
14:10-14:40	利用多模式神經造影來研究精神疾病之認知功能缺損 Multimodal Neuroimaging to Investigate Cognitive Impairment in Neuropsychiatric Disorders	楊凱鈞主任 Kai-Chun Yang
14:40-15:10	重度憂鬱症緩解期的持續性認知功能障礙及腦刺激治療之潛在應用 Persistent Cognitive Deficits in Euthymic Major Depressive Disorder and the Emerging Role of Brain Stimulation Therapies	鄭佳洵醫師 Jia-Shyun Jeng
15:10-15:30	<b>Coffee Break</b>	
	座長：蘇東平 教授 (Tung-Ping Su) 蔡世仁 主任 (Shih-Jen Tsai)	
15:30-16:20	MDSI 治療的新紀元: Esketamine New Era for MDSI Treatment: Focusing on Esketamine	陳牧宏主任 Mu-Hong Chen
16:20-17:10	以隨機對照試驗及真實世界研究的觀點探討長效針劑在 Maudsley 治療 What's new updates on longer dosing interval Injection for psychiatric care in Maudsley Prescribing Guidelines? - from RCTs to RWEs	Dr. David Taylor (英國)
17:10-17:30	<b>Panel Discussion &amp; Closing Remarks</b>	All

## Explore the role of circulating endothelial progenitor cells in the cognitive deficit in mood disorders

### 探討循環內皮前驅細胞在情緒疾病認知缺損的角色

**Ying-Jay Liou, Ya-Mei Bai, Po-Hsun Huang**

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**Background:** Major depressive disorder (MDD) and bipolar disorder (BD) are associated with endothelial dysfunction (ED). Circulating endothelial progenitor cells (cEPCs) play a vital role in endothelial health, and their quantity and functional characteristics are often seen as indicators of ED. Since cognitive impairment is a key symptom of both MDD and BD and is linked to microvascular dysfunction, we investigated the relationship between cEPC indices and cognitive deficits in individuals with mood disorders.

**Methods:** We recruited MDD and BD patients and healthy controls. cEPC counts and functions (adhesion, apoptosis) were measured using flow cytometry and in vitro assays. Cognitive functions were assessed using Digit Symbol Substitution Test (DSST), Perceived Deficits Questionnaire-Depression (PDQ-D), 2-back, Go/No-Go, and Wisconsin Card Sorting Test (WCST), evaluating various cognitive domains. Statistical analyses explored associations between cEPC parameters and cognitive measures.

**Results:** In MDD, higher counts of cEPCs were associated with worse objective and subjective cognitive dysfunction; lower adhesion of cEPCs significantly correlated with a greater number of errors in working memory, as measured by the 2-back task, and in executive function, assessed through the WCST. In contrast, a lower percentage of apoptotic cEPCs was linked to poorer response inhibition, evidenced by an increased number of commission errors in both the 2-back and Go/No-Go tasks in BD.

**Conclusion:** The studies indicate a complex role of cEPCs in cognitive function related to mood disorders. These findings suggest that the functional properties of cEPCs may contribute to cognitive impairment in both MDD and BD, highlighting the need for further research in this area.

## **Multimodal neuroimaging to investigate cognitive impairment in neuropsychiatric disorders**

### **利用多模式神經造影來研究精神疾病之認知功能缺損**

**Kai-Chun Yang**

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Cognitive impairment is a critical factor in neuropsychiatric disorders, significantly impacting functional outcomes independent of other clinical variables and representing a major unmet therapeutic need. Neuroimaging offers a powerful means to investigate the in vivo relationships between brain structure, function, neurochemistry, and cognition. While neuroimaging research has yielded valuable insights, translating these findings into clinically useful biomarkers remains a challenge. This presentation advocates for a multimodal strategy that integrates neuroimaging with peripheral biological markers and rigorous cognitive assessments to enhance our understanding of cognitive impairments. This approach aligns with the moving beyond single-region analyses to examine brain networks/circuits alterations in neuroscience. Specifically, we will explore the advantages of multimodal approaches that investigate various targets belong the same pathophysiological pathways but have to be examined via different tools. I will present our recent work for this field and discuss the potential of these techniques to elucidate the mechanisms underlying cognitive impairment in neuropsychiatric disorders, as well as the associated challenges and future directions. Ultimately, multimodal neuroimaging holds immense promise for advancing our understanding of these debilitating impairments and paving the way for more effective treatment strategies.

## **Persistent cognitive deficits in euthymic major depressive disorder and the emerging role of brain stimulation therapies**

### **重度憂鬱症緩解期的持續性認知功能障礙及腦刺激治療之潛在應用**

**Jia-Shyun Jeng**

鄭佳洵

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A well-documented but sometimes neglected aspect of Major Depressive Disorder (MDD) is persistent cognitive deficiencies, even after mood symptoms have subsided. This review summarizes current research on cognitive impairments in euthymic MDD and assesses the potential of brain stimulation therapy to mitigate them.

Studies show that cognitive impairment remains after clinical remission, including verbal memory, inhibitory control, information processing speed, and executive functioning. Importantly, these cognitive problems may be trait-like vulnerabilities or “scar effects” from previous episodes and are independent of depressed symptom intensity. Clinical factors include age of onset, number of depressive episodes, and hospitalization history affect cognitive impairment severity.

Non-invasive brain stimulation methods including TMS, TBS, and tDCS are being investigated for improving cognitive performance in MDD. Applied to the left dorsolateral prefrontal cortex, TMS may improve attention, inhibition, cognitive flexibility, and memory. TBS and tDCS investigations also have yielded promising outcomes, but larger, well-controlled trials are needed. Brain stimulation and cognitive training tend to synergistically improve cognitive control and function.

Conclusion, euthymic MDD cognitive abnormalities are clinically important targeted intervention. These unmet demands may be addressed by brain stimulation therapies, which are showing promise in cognitive enhancement. Future research should optimize stimulation techniques, identify patient subgroups who will benefit, and integrate cognitive rehabilitation frameworks to improve long-term outcomes.

## **New era for MDSI treatment focusing on Esketamine**

### **MDSI 治療的新紀元 : Esketamine**

**Mu-Hong Chen**

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**Background:** Major Depressive Disorder (MDD) significantly affects millions worldwide and is associated with high rates of suicidal ideation and behavior. Traditional antidepressants often take weeks to show effects, which can be critical for individuals experiencing severe depressive symptoms and suicidal thoughts. Spravato (esketamine) offers a novel therapeutic option, with rapid action and a unique mechanism that may be beneficial for patients with MDD and suicidal ideation.

**Methods:** In a multi-center, double-blind clinical trial, participants diagnosed with MDD and experiencing suicidal thoughts were treated with Spravato administered intranasally, alongside an oral antidepressant. The study aimed to evaluate the efficacy and safety of Spravato over a specified treatment period. Assessments included standardized scales to measure depressive symptoms and suicidal ideation from baseline to week 4.

**Results:** The results indicated a significant reduction in suicidal ideation among participants receiving Spravato compared to those receiving a placebo. Improvement in depressive symptoms was observed within the first 24 hours, with many patients reporting a notable decrease in their feelings of despair and hopelessness. The safety profile of Spravato was consistent with previous studies, with mild to moderate side effects typically resolving shortly after administration.

**Conclusion:** Spravato represents a promising treatment option for patients with MDD who exhibit suicidal ideation. Its rapid onset of action can provide immediate relief for individuals at risk, potentially mitigating the risk of suicide. Further research is essential to fully understand the long-term effects and benefits of Spravato in this vulnerable population, but the initial findings highlight its potential as a critical intervention in the management of severe depression.

## **What's new updates on longer dosing interval injection for psychiatric care in Maudsley Prescribing Guidelines? - from RCTs to RWEs**

**以隨機對照試驗及真實世界研究的觀點探討長效針劑在 Maudsley 治療指引中的最新進展**

**David Taylor**

*Maudsley Hospital and King's College, London, United Kingdom*

**Background:** Schizophrenia is a chronic mental disorder characterized by delusions, hallucinations, and cognitive impairments that significantly impact daily functioning. Although antipsychotic medications are effective in managing symptoms, adherence to treatment can be challenging due to the frequency of dosing and side effects. Invega Trinza® and Invega Hafyera® are long-acting injectable formulations designed to improve treatment adherence and provide sustained symptom control for patients with schizophrenia.

**Methods:** Clinical trials evaluating Invega Trinza® and Invega Hafyera® involved adult patients diagnosed with schizophrenia who had previously been stabilized on oral paliperidone or risperidone. Participants received intramuscular injections of either Invega Trinza® every three months or Invega Hafyera® every six months. The primary endpoints assessed included the reduction of schizophrenia symptoms measured by standardized scales such as the Positive and Negative Syndrome Scale (PANSS) and overall safety and tolerability over a defined study period.

**Results:** Both Invega Trinza® and Invega Hafyera® demonstrated significant efficacy in reducing symptoms of schizophrenia compared to placebo, with sustained effects observed throughout the dosing intervals. Participants reported improved adherence due to the extended release formulation, effectively resulting in fewer injections needed per year. The safety profiles were consistent with those of other paliperidone formulations, with the most common side effects being weight gain, sedation, and extrapyramidal symptoms, which were generally manageable.

**Conclusion:** Invega Trinza® and Invega Hafyera® offer valuable long-acting treatment options for individuals with schizophrenia, addressing the challenge of medication adherence while providing robust symptom control. Their extended dosing intervals can enhance the quality of life for patients by reducing the frequency of injections and thus improving overall treatment satisfaction. Continued research is warranted to further explore the long-term effectiveness and tolerability of these long-acting formulations, aiming to optimize schizophrenia management in diverse patient populations.