IMH Research News

A publication brought to you by the Research Division, Institute of Mental Health | Feb – Apr 2021

Accelerating the treatment of depression

Major Depressive disorder (MDD) is the leading cause of disability in the world and treatment resistant depression (TRD), defined not responding adequately to at least one adequate antidepressant trial, is a major challenge for mental health care systems as up to 50% of MDD patients meet that criteria. In addition, standard treatment of depression takes weeks to months for a proper trial, resulting in long delays in getting timely and effective treatments to our patients.

The Department of Mood & Anxiety (DMA) is hence running 3 simultaneous treatment trials for patients with treatment resistant depression to receive 3 different novel antidepressant treatments that not only have a mechanism of action distinct from standard serotonin, norepinephrine or dopamine modulators but also potentially have a faster onset of action (1 week compared with 2-3 months).

1. Accelerated repetitive transcranial magnetic (rTMS) stimulation

a. rTMS is a novel treatment for TRD and has been US FDA approved since 2008. It uses magnetic pulses to stimulate the brain and induce functional and structural changes to the brain to treat depression. Standard treatment is a daily session over 4 to 6 weeks.

b. The long duration of treatment makes it challenging for patients to access the treatment, so we developed an accelerated version of the treatment that delivers 4 treatments a day instead of 1 and completes a standard course in just 1 week rather than 4.

2. Accelerated theta burst magnetic (TBS) stimulation

a. A standard rTMS course takes 20 to 40 minutes, a significant time requirement for patients. TBS takes only 3 minutes to deliver an equivalent treatment and was US FDA approved to treat TRD in 2018. However standard treatment with TBS still requires daily treatments for 4-6 weeks, a significant burden for patients.

b. We developed an accelerated TBS trial where patients get 5 TBS treatments a day rather than 1 and a complete course within 1 week rather than 4 or 5.

3. Oral ketamine treatment

a. Ketamine is a glutaminergic antagonist that has robust antidepressant properties if given intravenously for patients with TRD. The onset of antidepressant effects can be as rapid as 24 hours.

b. However intravenous treatments are difficult to administer in the outpatient psychiatric setting, so we embarked on a multinational study of oral ketamine for TRD patients.

c. Subjects get 5 days of oral ketamine and if they respond well, they can be further enrolled for a 3-month maintenance trial.

All 3 trials mentioned above are actively enrolling subjects so please approach me or Dr Tan Xiaowei if there are potential subjects interested in participation.

Dr Tor Phern Chern

Dr Tan Xiaowei

Contributed by:

Dr Tor Phern Chern
Senior Consultant, Department of Mood and Anxiety
Institute of Mental Health

Deconstructing Heterogeneity in Schizophrenia Through Cognitive Subtypes

Cognitive impairment is a core feature in schizophrenia and is of importance due to its associations with clinical and functional outcomes. The delineation of individuals with schizophrenia using cognitive performance could lead to better understanding and refinement of this condition, mapping of specific biological mechanisms and personalised clinical treatments.

Using cognitive performance data from 767 individuals with schizophrenia, we found 4 distinct subtypes of cognitive performance in schizophrenia; a 'less-impaired' cognitive subtype, 2 subtypes with 'intermediate cognitive impairment' differentiated by executive function, and a 'globally impaired' cognitive subtype. The 4 subtypes were replicated in another independent cohort and showed stability across time. Additionally, we found that the 4 cognitive subtypes were associated with clinical symptomatology, such as negative symptoms, in schizophrenia.

Our findings suggest that the 4 cognitive subtypes represent distinct meaningful profiles, rather than a severity continuum of cognitive performance. Further work to elucidate the neurobiology of the 4 cognitive subtypes would be useful in identifying individuals who might benefit from targeted treatment, such as cognitive remediation, consequently, improving clinical and functional outcomes.

More information about the study can be found at
https://doi.org/10.1093/schbul/sbaa157

Contributed by:

Mr Keane Lim
Research Psychologist, Research Division
Institute of Mental Health