

New treatment for patients with serious depression goes on trial

Personalised form of brain stimulation said to be rapid-acting, with fewer side effects

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In a first for South-east Asia, Singapore researchers are studying a personalised form of magnetic brain stimulation that can potentially help more people with treatment-resistant depression.

It involves mapping a person's brain using scans to locate a precise spot to target during the stimulation.

In Transcranial Magnetic Stimulation (TMS), which is already offered in Singapore, doctors stimulate a spot that is connected to a deep part of the brain that has been consistently implicated in depression.

Standard TMS, which is done without the brain-mapping, offers those diagnosed with treatment-resistant depression around a 30 per cent chance of getting well

enough to not qualify for a depression diagnosis.

It delivers stimulation to the same spot of the brain for all patients.

As the layout and location of the brain networks are different for each person, the personalised version uses functional magnetic resonance imaging (fMRI) to pinpoint the exact spot unique to each patient, and stimulate it to treat their depression disorder as accurately as possible.

An artificial intelligence algorithm is used to clearly outline individual brain networks from the fMRI data, said Associate Professor Thomas Yeo, a brain scientist who is from the Centre for Sleep and Cognition at the Yong Loo Lin School Of Medicine at the National University of Singapore (NUS Medicine) and the co-principal investigator for the trials.

A high-precision robot arm is al-

so used to target the stimulation.

The personalised TMS treatments are more intensive than the standard procedure – 50 sessions are conducted over five days, instead of a minimum of 30 sessions over 30 days. Each personalised TMS session is 10 minutes long, while a standard TMS session can be 30 to 60 minutes long.

The Institute of Mental Health (IMH) is collaborating with NUS Medicine for two concurrent trials on personalised TMS, funded by separate parties. The trials started in March 2024 and will last for three years. The two trials will recruit a total of 90 patients, of whom 55 will undergo personalised TMS while the rest will be assigned to standard TMS.

Singapore is the first country in South-east Asia to conduct the clinical trials of personalised TMS, which is modelled after the personalised TMS approved for use in the US, known as the Stanford Accelerated Intelligent Neuromodulation Therapy protocol.

"In the US (study), about 80 to 90 per cent of the patients get well

with personalised TMS after one week. We will see whether it works in Asia," said Dr Tor Phern Chern, a senior consultant at the Mood and Anxiety department and Head of Neurostimulation Service at IMH, at a media briefing on April 12.

Dr Tor said that one day of 10 personalised TMS sessions is equivalent to six weeks of standard TMS, so it is like getting 7½ months of TMS in five days. Whether this removes the need for individualisation is a question that one of the trials will attempt to answer.

Trial participants do not have to pay for the treatment. Temasek Foundation and the National Medical Research Council are funding the trials, each with a grant of \$1 million.

So far, two patients here have completed the personalised TMS, with positive results.

The first one, in particular, had a very good outcome. She was diagnosed with depression and had suicidal thoughts.

Over the years, she had tried multiple types of antidepressants, none of which worked for her. She

responded partially to the current gold standard treatment for treatment-resistant depression known as electroconvulsive therapy (ECT) but could not tolerate it due to the side effects. ECT can cause cognitive side effects such as confusion or memory loss. Standard TMS did nothing for her.

After five days of personalised TMS, her symptoms mostly went away, and she was able to enjoy a vacation for the first time in many years, said Dr Tor, the principal investigator for the trials.

Currently, aside from optimising or switching medications, ECT and standard TMS are also recommended as options for those with treatment-resistant depression.

ECT is a treatment that involves applying direct electric currents to the head to trigger a seizure. It is done with the patient under general anaesthesia.

TMS uses magnetic pulses, which are converted to electrical energy in the brain cells, to stimulate them. There is no seizure, little or no side effects, and possibly only slight discomfort.

For Singapore citizens, each session of ECT costs around \$480, while each session of standard TMS costs around \$130. These are non-subsidised rates.

TMS is cleared by the US Food and Drug Administration to treat depression in patients who have not responded to standard medicines, and for obsessive-compulsive disorder.

"(TMS) is not a magic cure that gets rid of depression," said Dr Tor.

"We don't change the brain, we are modulating and exercising the brain, and once you stop... eventually the effects wear off. The treatment lasts for, on average, about 26 weeks – half a year," he added, referring to personalised TMS.

In comparison, the effects of standard TMS last for about three months.

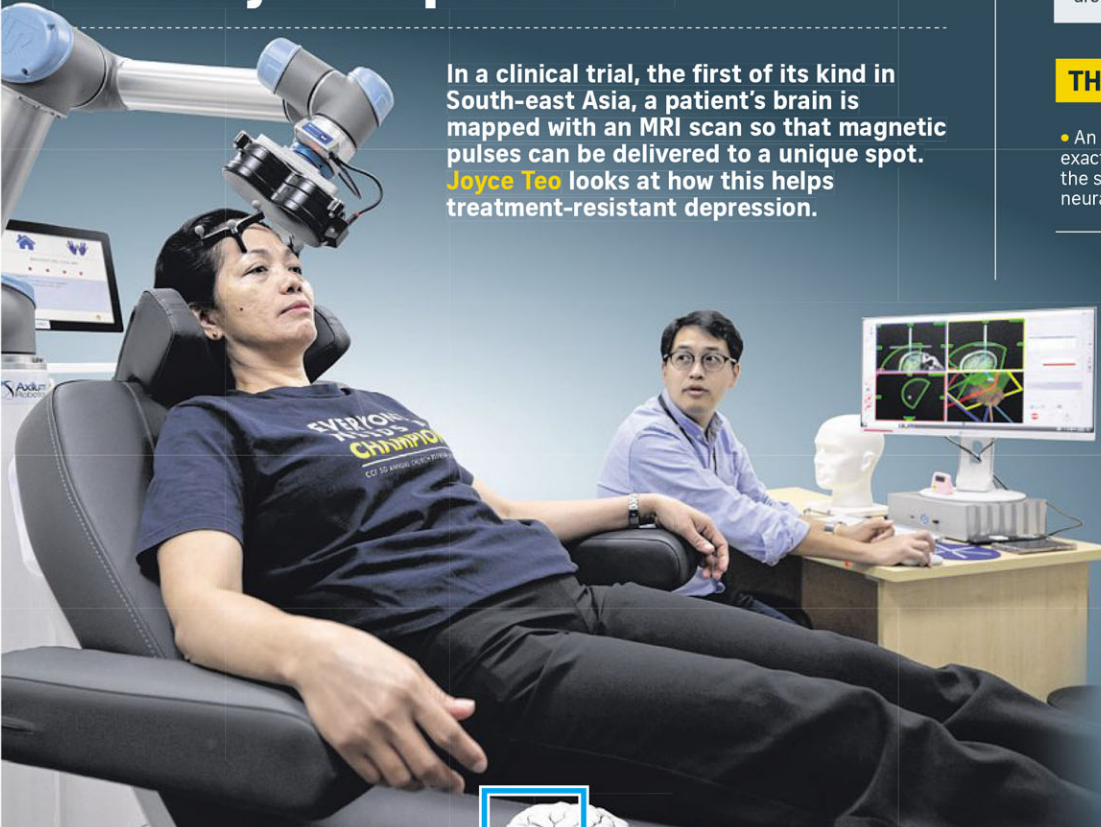
In the future, personalised TMS may be explored in the treatment of other conditions like obsessive-compulsive disorder, autism and post-traumatic stress disorder, said Dr Tor.

He said the rapid-acting personalised TMS treatment can be a game changer. "Currently, we think of depression as a chronic disease; you will see a psychiatrist and you expect to see them for months, for years," said Dr Tor.

"Imagine if depression is seen more as an acute condition, where there was an episode of depression... We treat the individual and treatment is acute – days to weeks, rather than months to years."

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A personalised treatment for major depression



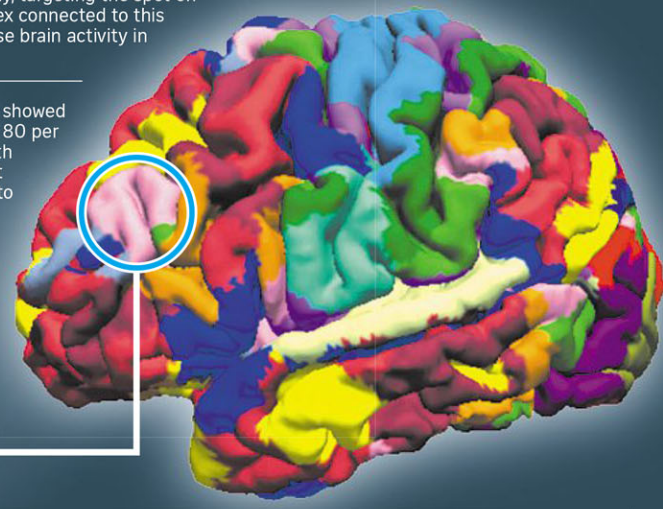
In a clinical trial, the first of its kind in South-east Asia, a patient's brain is mapped with an MRI scan so that magnetic pulses can be delivered to a unique spot. **Joyce Teo** looks at how this helps treatment-resistant depression.

CURRENT TREATMENT

- Transcranial Magnetic Stimulation (TMS) is used to stimulate a patient's prefrontal cortex, but as the brain is not mapped, the application of magnetic pulses is less targeted. The pulses are delivered to the same spot of the brain for all participants.
- One in three patients becomes well enough to no longer qualify for a depression diagnosis.

THE NEW TREATMENT METHOD

- An MRI scan provides a personalised map that helps locate the exact area of the prefrontal cortex that is thought to modulate the subgenual anterior cingulate cortex (sgACC). Abnormal neural activity in the sgACC is linked to depression.
- As the sgACC is too deep for magnetic pulses to penetrate directly, targeting the spot on the prefrontal cortex connected to this region can normalise brain activity in the sgACC.
- Studies in the US showed that approximately 80 per cent of patients with treatment-resistant depression went into remission, which means they no longer qualified for a depression diagnosis.

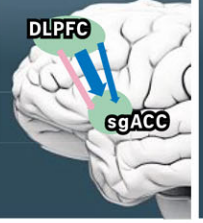


Area of mapped brain where magnetic pulses are applied

DEPRESSION LINK DEEP IN THE BRAIN

NORMAL MOOD

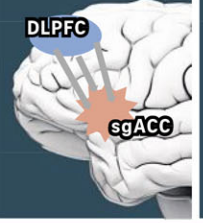
An area known as dorsolateral prefrontal cortex (DLPFC) is highly connected with a deep part of the brain, the sgACC, which is consistently implicated in depression. Normally, the DLPFC inhibits the sgACC and mood is well regulated.



DLPFC
sgACC

DEPRESSION

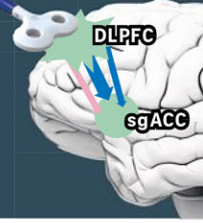
When a person is diagnosed with major depressive disorder, the area in the prefrontal cortex becomes less active and fails to inhibit the deep part of the brain. This causes cognitive impairment and negative thoughts.



DLPFC
sgACC

HOW TMS WORKS

TMS stimulates this part of the prefrontal cortex to reactivate the inhibitory connections to the deep part of the brain. This normalises mood regulation.



DLPFC
sgACC

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