

Snips from the journals

## Non-invasive brain stimulation – a new way forward for psychiatric disorders?

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### Repetitive transcranial magnetic stimulation and deep brain stimulation – the future of brain circuit-based therapies? (1,2)

Repetitive transcranial magnetic stimulation (rTMS) is the focal application of a localized, pulsed magnetic field to the cerebral cortex, resulting in the induction of a small electrical currents that stimulate nerve cells in the region of the brain involved in mood regulation and depression. Similar to electroconvulsive therapy (ECT), it is non-invasive, however unlike ECT it does not involve use of an anaesthetic, seizure induction or loss of consciousness. The Professional Practice Guidelines (PPG 16) of the Royal Australian and New Zealand College of Psychiatrists as well as the Interventional procedures guidance [IPG542] of the National Institute of Clinical Excellence (NICE) of the United Kingdom both list depression as the primary clinical indication for rTMS. The PPG 16 also states that there is accumulating evidence for use of rTMS in obsessive compulsive disorder, but given the wide variety of treatment targets and paradigms used in different studies, it is still difficult to make an overall conclusion. The guideline highlights that the evidence for use of rTMS in schizophrenia is less substantive, with lack of multi-centre trials, but may be considered for patients with persistent auditory hallucinations despite optimal medication, to be delivered with specialist training.

### Cost effectiveness of rTMS after a single failed antidepressant medication trial (3)

Voigt et al. used the lifetime Markov stimulation model to compare the direct costs and quality adjusted life years (QALYs), between rTMS and medication therapy, among a group of patients who were newly diagnosed with major depressive disorder and who had failed to benefit from one pharmacotherapy trial. The results of this model showed that based on comparison of lifetime direct treatment costs and QALYs, rTMS achieved better outcomes with lower cost, compared to antidepressant medication trials across the lifespan of adults with major depressive disorder, in the context of current costs of treatment. The authors suggest that the findings of this

model support the use of rTMS in adults with MDD, who have failed to respond to a single trial of anti-depressant medication.

### A newer form of rTMS that can be delivered in three minutes (4)

Blumberger et al. described intermittent theta burst stimulation (iTBS) as a newer form of rTMS that can be delivered in 3 min, as opposed to the 37.5 min standard 10 Hz treatment session. They conducted a randomized, multicentre, non-inferiority clinical trial on patients diagnosed with a treatment-resistant major depressive episode or those who could not tolerate at least two antidepressants in the current episode. Participants were treated with 10 Hz rTMS or iTBS to the left dorsolateral prefrontal cortex, administered over 5 days a week for 4-6 weeks. The Hamilton Rating Scale for Depression (HRSD-17) score was used as the primary outcome measure, with a non-inferiority margin of 2.25 points. They reported that iTBS (n=193) was non-inferior to 10 Hz rTMS (n=192) for the treatment of depression. Both groups had low dropouts, similar side-effect, safety, and tolerability profiles.

### Long-term deep brain stimulation of the ventral anterior limb of the internal capsule for treatment-resistant depression (5)

Deep brain stimulation (DBS) for depression is currently an experimental treatment and is reported to reduce depressive symptoms in approximately 40%-60% of patients with treatment-resistant depression (TRD). However, studies on safety and long-term efficacy are limited.

This research group previously studied DBS of the ventral anterior limb of the internal capsule (vALIC), which resulted in a response (i.e.,  $\geq 50\%$  symptom reduction) in 10 of 25 patients with TRD after an optimisation period of upto 1 year. This article reports on the follow-up of these patients during the subsequent 1-year maintenance phase (5). The aims were to assess the response rate to DBS after the maintenance phase,



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approximately 2 years after DBS implantation, analyse changes in severity of depression, and record occurrence of any adverse events during this period.

A total of 18 of the original 25 study participants completed the 2-year follow-up or maintenance phase. During this period, the participant scores of the Hamilton Depression Rating Scale and the Montgomery Ashberg Depression Rating Scale did not change, but the rate of self-reported depressive symptomology decreased slightly. Participants who were non-responders to DBS during the first year of follow-up did not respond during the second year of follow up either. The authors conclude that DBS for TRD had continued efficacy 2 years after surgery, with symptoms remaining stable after optimisation as rated by clinicians, and with improvement of patient ratings.

### Non-surgical brain stimulation techniques as alternative or add-on treatments for adults with major depressive episodes (7)

Personalising treatment of treatment resistant depression without major risks of adverse events remains a major hurdle (7). A systematic review with pairwise and network meta-analysis carried out by Mutz et al. examined the comparative clinical efficacy and acceptability of non-surgical brain stimulation for the acute treatment of major depressive episodes in adults (7). Studies that had looked in to at least two of the following treatments were included in the systematic review: Transcranial direct current stimulation (tDCS), theta burst stimulation, transcranial magnetic stimulation (rTMS, accelerated, priming, deep, or synchronized), electroconvulsive therapy (ECT), magnetic seizure therapy, or sham therapy. The review included 113 randomized trials, with a total of 6750 patients with either major depressive disorder or bipolar depression.

The authors report that the quality of the evidence was typically of low or unclear risk of bias (94 out of 113 trials, 83%). In their network meta-analysis, 10 out of 18 treatment strategies, i. e., bitemporal ECT, high dose right unilateral ECT, priming transcranial magnetic stimulation, magnetic seizure therapy, bilateral rTMS, bilateral theta burst stimulation, low frequency right rTMS, intermittent theta burst stimulation, high frequency left rTMS and tDCS were associated with higher response compared with sham therapy. All treatment strategies were at least as acceptable as sham therapy. Network meta-analytic estimates of comparisons of active interventions found that bitemporal ECT and high dose right unilateral ECT were associated with an increased response, compared to the other therapies.

Mutz et al. highlighted that the above findings provide evidence for non-surgical brain stimulation techniques to be considered as alternative or add-on treatments for adults with major depressive episodes.

### Conflicts of interest

None declared.

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