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Transcranial magnetic stimulation (TMS) safety: a practical guide for psychiatrists

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Rohan Taylor Health Education & Training Institute, Gladesville, NSW, Research Fellow, School of Psychiatry and Black Dog Institute, University of New South Wales, Randwick, NSW; Psychiatry Registrar, Concord Centre for Mental Health, Concord, NSW, Australia

Veronica Galvez Psychiatrist, School of Psychiatry, University of New South Wales, Randwick, NSW; Black Dog Institute, University of New South Wales, Randwick, NSW, Australia

Colleen Loo Professor of Psychiatry, School of Psychiatry, University of New South Wales, Randwick, NSW, and; Black Dog Institute, University of New South Wales, Randwick, NSW, and; Psychiatrist, St George Hospital, Kogarah, NSW, and; Psychiatrist, The Wesley Hospital, Kogarah, NSW, Australia

Abstract

Objectives: Repetitive transcranial magnetic stimulation (rTMS) is increasingly being utilised as a treatment option for depression, and with this comes a need for a practical review of safety issues intended for clinicians. This article provides an overview of the current literature regarding safety issues with rTMS for depression, and provides recommendations for clinical practice.

Conclusions: Overall, rTMS is a well-tolerated treatment with common side effects (such as headache or local pain at the site of stimulation) being mild. Severe adverse effects, such as seizures, hearing impairment or mania, are uncommon. Certain populations, including adolescents, pregnant women, older adults and those with metal/electronic implants, require special consideration when prescribing and monitoring treatment courses. With adequate assessment and monitoring processes, rTMS can be administered safely in a large proportion of depressed patients.

Keywords: rTMS, transcranial magnetic stimulation, depression, safety, adverse effects

Repetitive transcranial magnetic stimulation (rTMS) is increasingly being used in clinical practice in Australia for the treatment of depression. Current RANZCP (Royal Australian and New Zealand College of Psychiatrists) clinical practice guidelines for mood disorders endorse the use of rTMS for patients with non-psychotic depression who have failed one or more trials of standard antidepressant medications or psychological therapy.[1] In this context, it is timely to provide a brief, practical review of safety issues for clinicians to ensure that rTMS practice adheres to high standards of safety and professionalism. When administered within recommended treatment guidelines, rTMS is a very safe and well-tolerated treatment with generally mild side effects and only rare serious adverse effects (see Table 1).

rTMS stimulation parameters and safety

Analogous to electroconvulsive therapy (ECT), rTMS treatment protocols comprise a variety of different parameters that can impact upon the efficacy and safety of treatment – these include the intensity of the stimulus (relative to patient motor threshold), pulse frequency (number of pulses per second), the duration of the stimulus train and time interval between trains. Guidance regarding safe treatment parameters can be found in the international consensus guidelines from 1998, with an update in 2009.[2,3] Numerous trials and years of clinical practice have helped to establish these parameters for safe practice, with the aim of diminishing seizure risk.

Common side effects

The most common side effects to occur during a course of rTMS are local pain during stimulation at the site of

Corresponding author:
Rohan Taylor, Black Dog Institute, University of New South Wales, Hospital Road, Randwick, NSW 2031, Australia.
Email: rohan.taylor@unsw.edu.au

stimulation, headache and neck pain.[4] Pain is thought to be due to stimulation of superficial nerves or facial muscles, neck pain related to prolonged uncomfortable positioning during treatment and headache may relate to local scalp stimulation or changes in cerebral blood flow.[4] While these side effects are common, they are typically not severe with (<2%) of patients in clinical trials discontinuing treatment due to pain.[3] In general, pain at the site of stimulation typically improves over the course of treatment and headache may be eased with the use of simple analgesia (such as paracetamol).[4] Higher frequency treatment, and higher intensity relative to threshold, are more likely to produce local pain, and a switch from high-frequency to low-frequency treatment protocols may be warranted if these pose a significant barrier to treatment.

Serious adverse effects

Serious adverse events are typically of low incidence and the risk is diminished when adequate safety precautions are followed.

Seizures

Overall, the incidence of seizures is very low and thought to be equivalent to the incidence of spontaneous seizures with antidepressant therapy (0.1–0.6%).[5] Importantly, the risk of seizures appears increased with the use of high frequency and more intensive treatment protocols.[4] Other factors to take into account that can increase the risk of seizures are pre-existing neurological conditions, adolescents, substance use and changes in concurrent medications during the rTMS course, which may reduce seizure threshold.[6] It is essential that all services offering rTMS are well-equipped to deal with first response to seizures, ensuring there are clear protocols and staff are trained to manage these situations. Immediate actions include ceasing treatment and ensuring the patient is not injured (by removing the machinery or other objects from close proximity promptly), and placing the patient in the recovery position on cessation of seizure activity. Status epilepticus has not been a demonstrated side effect of rTMS to date, nor do patients seem to be at an increased risk of further seizures.[3]

Hearing impairment

Hearing protection is mandatory due to the loud clicking noise that is produced with each transcranial magnetic stimulation (TMS) pulse (due to rapid mechanical deformation of the TMS stimulation coil). Without hearing protection, transient changes in auditory threshold have been demonstrated in humans, and permanent hearing damage has been demonstrated in rabbits.[7] However, when adequate protection is used, most studies have reported no change in hearing after a course of rTMS.[4]

Affective switch and psychosis

Overall, the risk of inducing a manic or hypomanic switch appears low, with rates being statistically no greater in active than sham conditions in one review.[8] Nevertheless, the use of mood-stabilising medication in patients with bipolar disorder or who have a prior history of manic switching with antidepressant medication is recommended, and the risk of manic switch should be discussed with these patients before embarking upon a treatment course. There have also been case reports of patients developing new onset psychotic symptoms, but the incidence of these outcomes appears to be very low.[9]

Other

Finally, it is worth noting the rare event of rTMS precipitating a retinal tear – in one documented case report of this occurrence, this appeared to be related to coil placement excessively anterior to the dorsolateral prefrontal cortex during one treatment session, possibly arising from poor treatment technique.[10]

Metals and electronic devices

rTMS presents a potential problem for patients with metal implants or electronic devices due to the induction of eddy currents in conducting substances within the vicinity of the magnetic field. Cochlear implants and metallic devices in close contact to the discharging TMS coil are absolute contraindications, though recommendations on the precise safe distance between the TMS coil and metal or implanted electronic devices vary.[3] Preferentially there should be >10 cm between the TMS coil and any metal/electronic device, with device manufacturers recommending at least 30 cm distance.[11] In general, extreme caution should be exercised when considering treatment for patients in this scenario, with due consideration of the risk/benefit ratio.

Cognition

While the potential for cognitive impairment is a significant concern for individuals considering ECT, patients and clinicians can be reassured that the evidence suggests rTMS does not have an adverse impact on cognition.[12]

Special populations

Although specific studies in older populations treated with rTMS are scarce, current evidence suggests that the antidepressant efficacy of rTMS is not necessarily reduced in older patients, and there are not additional safety concerns.[13] However, older populations and those with pre-frontal atrophy may need higher stimulation parameters and a higher number of sessions to achieve a meaningful clinical benefit.

At present, there are a limited number of studies investigating the use of rTMS in pregnant patients, reflecting a common issue regarding evidence-based interventions

Table 1. Adverse effects and contraindications

Common side effects	Local pain, headache and neck pain – all generally mild, discontinuation rates due to these symptoms are low.
Severe adverse effects	Seizures – very low incidence; risk increased with high-frequency treatment and more intense treatment protocols; pre-existing neurological conditions, adolescent patients, substance use and concurrent medication changes may all impact seizure threshold. Hearing impairment – risk managed with adequate hearing protection. Affective switch and psychosis – very low risk; increased risk in those with BPAD, past manic switch or psychotic symptoms.
Contraindications	Cochlear implants or metallic/electronic implants in close contact with TMS coil (need to be at least >10 cm from coil) represent absolute contraindications.

BPAD: bipolar affective disorder; TMS: transcranial magnetic stimulation.

Table 2. Procedures to ensure safe administration of rTMS course

Before commencing rTMS course	***Before and during each treatment session***	***After each rTMS session***
Complete structured safety screen (e.g. TASS developed by Keel et al. 2001[18]).	Any changes in medication since last session?	Check tolerability after each session.
Consider the possibility of pregnancy.	Any side effects since last session?	
Ensure risk/benefit ratio is appropriate.	Use hearing protection for both patient and treater.	Ensure patient is well prior to leaving clinic.
Establish individual patient motor threshold.		
Psychiatrist to administer/supervise first treatment session – check for tolerability and safety.		

TASS: transcranial magnetic stimulation adult safety screen; rTMS: repetitive transcranial magnetic stimulation.

for this group. An open-label study treating depressed pregnant patients ($n = 30$) followed up mothers and children and later found no major abnormalities longitudinally, other than a perception of language delay (though this was also observed in a matched sample of children of depressed mothers who had remained untreated during pregnancy).[14,15] Though current evidence is limited to case series, the theoretical risk of rTMS is thought to be low (due to the rapidly dissipating magnetic field and the distance of the foetus from the coil). A thorough discussion of the risks and benefits of treatment (with rTMS or alternatives) should inform treatment decisions.

A review of studies utilising TMS for a broad range of conditions (in those under 18 years of age) showed that rTMS was generally well tolerated, with minor side effects at rates similar to those seen in adult populations.[16] Of note, two subjects of 322 enrolled children and adolescents (0.62%) experienced a seizure, and two subjects had syncope (0.62%), with no other major adverse events described. This review provides some evidence for the safety of rTMS in this population, albeit tempered by the need for larger sample sizes to further quantify the risk of low-frequency events, and the need for longer-term follow-up periods.

Staff safety

While acute exposure to electromagnetic fields produced during rTMS is minimal, the safety of chronic exposure for staff over many years is unclear. Mollerlokken et al. measured the intensity of magnetic fields produced at various distances from the TMS coil, and found that in close proximity (<20 cm) these values exceeded the recommended safe occupational limits in Europe for acute exposure.[17] They recommended that operators avoid exposure within 40 cm of the coil – treatment should be paused if there is a need to adjust the coil during a treatment session. Typically, staff administering rTMS are within the treatment room but at several metres from the stimulating coil.

Assessment and monitoring

Before commencing a course of rTMS treatment, a comprehensive psychiatric and medical history must be

obtained, and relevant physical examination performed (see Table 2). As demonstrated in this review, there are very few absolute contraindications to rTMS. Nevertheless, a structured safety screen (such as that developed by Keel et al.[18]) is a worthwhile addition to any TMS clinic procedure. The risk/benefit ratio should be carefully considered before recommending a treatment course in certain groups (pregnant women, adolescents, patients with implanted electronic devices and patients with pre-existing neurological conditions). In order to enhance the collection of data relating to safety (and efficacy) outcomes, we advise clinicians providing rTMS of the formation of the CARE network – this network aims to coordinate the collection of relevant clinical data for widespread quality improvement and allow for pooling of a large, naturalistic dataset for analysis.[19]

Disclosure

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