



Statement on Repetitive Transcranial Magnetic Stimulation for Depression

Position statement CERT03/17

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REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION FOR DEPRESSION

1. INTRODUCTION

Transcranial magnetic stimulation (TMS) is a non-invasive technique used to stimulate neuronal tissue. This technique involves placement of an electromagnetic coil to deliver a rapidly changing magnetic field which alters the electrical properties of the cortical neurons. Repetitive Transcranial Magnetic Stimulation (rTMS) is a relatively new treatment modality for psychiatric disorders where the stimulus train is repeated at pre-set intervals. This method has been well established in neuroscience research experiments and also in clinical application for neurological conditions. Additionally it has been used as an investigative tool in neuronal diseases.

2. PUTATIVE MECHANISM OF ACTION

Like most other antidepressant treatments that are available in clinical practice, the precise mechanism of action is not yet fully understood. Several studies suggest that large scale brain networks are altered in patients with depression, and degree of the change in their connectivity predicts the severity of depression. Repetitive stimulation of focal nodes of these networks can result in reorganisation of connectivity patterns in the brain due to brain's inherent plasticity (use-dependent strengthening of existing pathways). Many studies suggest that rTMS indeed results in changes in regional brain activity and metabolism, and applying rTMS at Dorsolateral Prefrontal Cortex (DLPFC) can enhance this region's connectivity with other regions that are crucial for regulating emotional processing. At a physiological level, the effects of rTMS are frequently reported to be similar to long-term potentiation (LTP) or long-term depression (LTD) of 'stimulated' neurons which in turn implicates changes in synaptic plasticity.

3. CLINICAL GUIDANCE AND APPROVALS

The most recent NICE interventional procedure guidance (IPG542) on rTMS for depression published in December 2015 recommends that rTMS may be used for depression with normal arrangements for clinical governance and audit. This

document replaces previous guidance on transcranial magnetic stimulation for severe depression (interventional procedure guidance 242).

- The evidence on repetitive transcranial magnetic stimulation for depression shows no major safety concerns. The evidence on its efficacy in the short-term is adequate, although the clinical response is variable. Repetitive transcranial magnetic stimulation for depression may be used with normal arrangements for clinical governance and audit.
- During the consent process, clinicians should, in particular, inform patients about the other treatment options available, and make sure that patients understand the possibility the procedure may not give them benefit

There are similar guidelines from other national bodies (e.g. APA, RANZCP) that appraised TMS favourably in the treatment of depression.

4. INDICATIONS

NICE recommends rTMS for the treatment of depression. The evidence cited in the IPG comes from RCT's and meta-analysis of patients with primary depressive disorder and treatment resistant depression (TRD). The definition used for TRD in the published data is where patients have limited or no improvement with conventional treatments (antidepressant medication, psychological therapy or a combination of these). rTMS could also be considered in patients with severe depression who do not want to consider, or have contraindications to the use of electroconvulsive therapy (ECT).

5. OVERVIEW OF RTMS ADMINISTRATION

rTMS treatment is an outpatient procedure and does not require sedation or general anaesthesia. The intensity of rTMS is usually set as a percentage of the patient's motor threshold (MT), defined as the minimum stimulus strength required to induce a small involuntary muscle contractions (usually in the thumb). The coil is placed on the left DLPFC using 5cm rule, F3 (International 10-20 system of EEG electrode placement) or neuro-navigation technique. There are various treatment protocols followed by different treatment centres but the most widely used is the FDA based standard parameters, which include

an intensity of 120% of MT, total of 3000 pulses for each session, lasting 37.5 minutes (high frequency, 10 pulse/second in a 4 second train with a 26 second pause between trains). Treatment with rTMS usually involves daily sessions, 5 days a week for 4-5 weeks and possibly longer (Rossi 2009). There are no pre-treatment restrictions or special preparations by patients. Patients sit in a comfortable chair throughout the treatment duration and ear plugs are provided to minimise the noise generated by the coil.

6. SAFETY AND ADVERSE EFFECTS

The international scientific community has evaluated the available evidence in administration of rTMS in both clinical and research setting and has developed a standard safety protocol (Rossi et al., 2009). International studies have reported rTMS as generally a safe treatment modality.

The potential side effects of rTMS include discomfort at the site of stimulation and scalp discomfort, transient headache, neck pain, facial twitching during treatment. Rare side effects include local erythema, tinnitus, vertigo, seizure induction, transient acute hypomania, syncope, transient hearing changes and transient cognitive changes. Recent NICE guidance (IPG 542) concluded that evidence on rTMS for depression showed no major safety concerns.

7. EFFICACY

Efficacy of rTMS treatment for major depressive disorder (MDD) and treatment resistant depression (TRD) has been well established over the recent years. Many systematic review and meta-analysis of randomized, double-blind and sham-controlled rTMS trials for treating MDD have shown rTMS to be effective as augmentation therapy or as a monotherapy with benign tolerability profile (Berlim, et al. 2013, Gross et al. 2007, Schutter 2009). The NNT (Number Needed to Treat) is around 5 for treating depression (Dell'Osso et al., 2011), OR (odds ratio) =3.4 (Gaynes et al 2012).

The NICE IPG refers to four systematic reviews; one a meta-analysis of RCT's where rTMS used to treat depression, one where rTMS and ECT were used in depression and TRD, one involving TRD patients only and the fourth where rTMS was compared to ECT in major depressive disorder. The guidance referred to one

non randomised trial of rTMS in TRD and one case series reporting on relapse after six month follow up in an active rTMS arm of a randomised sham-controlled trial.

8. RTMS ALONG WITH OTHER TREATMENTS

There are no contraindications for concomitant use of rTMS and neurotropic medications; however clinicians should be aware of medications which reduce seizure threshold as there may be a theoretical risk of inducing seizure during stimulation for these patients. rTMS can be safely used in combination with psychological interventions. There are no reported studies on using ECT and rTMS simultaneously. A meta-analysis (Slotema et al 2010) found that rTMS was not as effective as ECT hence it should not be considered as a replacement to ECT.

9. PATIENT CHARACTERISTIC

Assessment of patients should be done by a trained clinician before administering the treatment. Most studies involve working age adults hence there is limited safety and efficacy data in child and adolescent populations and pregnant women. NICE recommends 'during the consent process clinicians should ...inform patients about the other treatment options available ...and the possibility the procedure may not give them benefit.'

10. TRAINING AND ACCREDITATION

There should be a protocol in place in each treatment unit which is approved by the local trust, health board or equivalent governance process. There should also be procedures and policies to ensure the smooth running of the unit. A clear role and responsibility for prescribing clinicians and treating clinician should be established. A qualified rTMS practitioner or equivalent with adequate training and competencies can administer the rTMS and monitor for side effects during the treatment. The rTMS practitioner should have the competencies as detailed in the RCPsych ECT Handbook. A qualified nurse should be in overall charge of the treatment and a named consultant identified to provide medical support.

Once established, the College will look to develop a national training programme for TMS practitioners which will include assessment of competencies and accreditation for rTMS centres along similar lines as ECTAS accreditation.

11. FUTURE DIRECTIONS

Neuromodulation is an emerging new therapeutic field for treatment of neuropsychiatric conditions. Over the last decade rTMS has been used widely for the treatment of depression and is now an established safe and effective treatment option for depression and treatment resistant depression. We envisage more treatment centres will be established in future as a result of the updated guidance from NICE.

12. REFERENCES

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