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Review

A review of the efficacy of transcranial magnetic stimulation (TMS) treatment for depression, and current and future strategies to optimize efficacy

Colleen K. Loo [a,*], Philip B. Mitchell [b]

[a] *School of Psychiatry, University of NSW, Psychiatrist, Black Dog Institute and South Eastern Sydney Illawarra Area Health Service, Australia*
[b] *School of Psychiatry, University of NSW, Psychiatrist, Black Dog Institute, Australia*

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Abstract

Background: There is a growing interest in extending the use of repetitive transcranial magnetic stimulation (rTMS) beyond research centres to the widespread clinical treatment of depression. Thus it is timely to critically review the evidence for the efficacy of rTMS as an antidepressant treatment. Factors relevant to the efficacy of rTMS are discussed along with the implications of these for the further optimization of rTMS.
Method: Clinical trials of the efficacy of rTMS in depressed subjects are summarized and reviewed, focusing mainly on sham-controlled studies and meta-analyses published to date.
Results: There is a fairly consistent statistical evidence for the superiority of rTMS over a sham control, though the degree of clinical improvement is not large. However, this data is derived mainly from two-week comparisons of rTMS versus sham, and evidence suggests greater efficacy with longer treatment courses. Studies so far have also varied greatly in approaches to rTMS stimulation (with respect to stimulation site, stimulus parameters etc) with little empirical evidence to inform on the relative merits of these approaches.
Limitations: Only studies published in English were reviewed. Many of the studies in the literature had small sample sizes and different methodologies, making comparisons between studies difficult.
Conclusions: Current published studies and meta-analyses have evaluated the efficacy of rTMS as given in treatment paradigms that are almost certainly suboptimal (e.g of two weeks' duration). While the data nevertheless supports positive outcomes for rTMS, there is much scope for the further refinement and development of rTMS as an antidepressant treatment. Ongoing research is critical for optimizing the efficacy of rTMS.

Keywords: Transcranial magnetic stimulation; Depression; Efficacy

* Corresponding author. Black Dog Institute, Prince of Wales Hospital, Barker St, Randwick. NSW 2031, Australia. Tel.: +61 02 93823721; fax: +61 02 93828208.
E-mail address: colleen.loo@unsw.edu.au (C.K. Loo).

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1. Introduction

There is a considerable interest worldwide in the use of subconvulsive repetitive transcranial magnetic stimulation (rTMS) for the treatment of depression. rTMS has excited the interest of clinicians and been highly acceptable to patients (Walter et al., 2001), because of its ability to stimulate focal areas of brain cortex non-invasively using magnetic fields. Unlike ECT, it does not involve a general anaesthetic or seizure. In some countries, e.g. Canada and Israel, rTMS is approved for the clinical treatment of depression. In Australia, the Royal Australian and New Zealand College of Psychiatrists Position Statement on TMS (2003) recognizes the need for further research into TMS but cautiously allows for its clinical use to treat depression in limited circumstances, with recommended caveats, including that the patient sign a consent form acknowledging that "the most efficacious manner of administering rTMS has not yet been established".

The International Society for Transcranial Stimulation Consensus Statement on the use of rTMS is mainly concerned with advising on safety and procedural issues in whatever context rTMS is used (Belmaker et al., 2003). There has been a debate on the advisability of broadening the use of rTMS to clinics beyond research centres, with discussion of associated regulatory issues (e.g. Fitzgerald, 2003a; Sachdev, 2003). Apart from considerations of safety, adequate regulatory safeguards and the limitations of current therapeutic options in treatment resistant depression, a critical appraisal of the efficacy of rTMS as a treatment for depression is central to this debate. This article evaluates the efficacy outcomes reported so far in clinical trials of rTMS, and discusses the potential of future strategies to optimize the efficacy of rTMS.

2. Studies of the efficacy of rTMS in depression

Given the relatively large number of published rTMS treatment trials but relatively small sample sizes in each (see Table 1 for summary of sham-controlled trials), it is perhaps most constructive to begin by reviewing the seven published meta-analyses (including a Cochrane Review) (McNamara et al., 2001; Holtzheimer et al., 2001; Burt et al., 2002; Kozel and George, 2002; Martin et al., 2003; Aarre et al., 2003; Couturier, 2005).

The earliest meta-analysis (McNamara et al., 2001) only included five controlled studies and excluded the only negative depression trial for rTMS published at the time (Loo et al., 1999), yielding unsurprisingly, a positive result for rTMS compared to a sham control.

Holtzheimer et al. (2001) identified 12 controlled rTMS depression trials, 11 of which involved rTMS to the left dorsolateral prefrontal cortex and seven of which involved a parallel design. The latter distinction is important as the blinding of subjects in crossover studies is questionable, given the difference in scalp sensation with active and sham rTMS (Loo et al., 2000). They calculated the weighted mean effect sizes (based on the difference in outcome between