Review: repetitive transcranial magnetic stimulation is of unknown effectiveness in people with depression


QUESTION: Is repetitive transcranial magnetic stimulation more effective than sham treatment in people with depression?

Design
Systematic review and meta-analysis.

Data sources
The reviewers searched Medline, Embase, PsychLit, Cochrane Controlled Trials Register, Cochrane Depression, Neurosis and Anxiety review group trials register to 2002 and contacted authors for further information.

Study selection
Eligible studies were randomised controlled trials comparing repetitive transcranial magnetic stimulation versus a sham intervention in people with depressive disorder or bipolar disorder (in depressed phase), with or without psychosis (DSM-IV or ICD-10 criteria).

Data extraction
Data were extracted using a standard form, and coded for methodological quality on the adequacy of randomisation, allocation concealment, intention to treat analysis, blinding of outcome assessment and confounding factors. The primary outcome measure was symptom severity (determined by Hamilton rating scale for depression or the Beck Depression Inventory).

Main results
14 studies met the inclusion criteria. The methodological quality of the studies was low. Mean age of participants ranged from 41.8 to 60.9 years. 13 studies included people with major depressive disorders only. 13 studies compared left-sided high frequency repetitive transcranial magnetic stimulation versus sham treatment. The remaining study compared right sided, low frequency repetitive transcranial magnetic stimulation versus sham treatment. Repetitive transcranial magnetic stimulation reduced depression on the Hamilton Depression scale compared with sham treatment after 2 weeks of treatment but not after a further 2 weeks (12 studies in meta-analysis; standardised mean difference after 2 weeks treatment: -0.35, 95% CI -0.66 to -0.04); (standardised mean difference after a further 2 weeks: -0.33, 95% CI -0.84 to 0.17). Outcomes on the Beck Depression Inventory were not significant at any time point.

Conclusions
Existing trials are of low quality and provide inadequate evidence about effects of repetitive transcranial magnetic stimulation in people with depression.

COMMENTARY
Transcranial magnetic stimulation (TMS) is a relatively safe non-invasive method to focally stimulate the brain. Repetitive TMS (rTMS) induces sustained effects such that “fast” rTMS (> 1 Hz) has an activating effect while “slow” (< 1 Hz) has an inhibitory effect. Using rTMS to modulate neuronal circuitry in neuropsychiatric disorders has attracted much research, particularly for treating depression.

This Cochrane Collaboration supported review is the most comprehensive meta-analysis of rTMS for depression to date. The authors included 14 studies, however, they acknowledge that many of the published trials are of variable quality. Most trials have few participants, unclear standards of randomisation and blinding, and use differing methods to administer rTMS to heterogeneous populations.

As with most previous reviews and meta-analyses, the general conclusion is that rTMS has a modest antidepressant effect compared to placebo rTMS but the evidence does not yet support routine use. One important limitation to the interpretation of this meta-analysis is that the authors have not taken into account that some placebo or “sham” forms of rTMS, in which a real coil is used angled away from the scalp, actually have an effect upon the underlying cortex. Thus the analysed trials should be further subdivided into those using activating or non-activating sham rTMS.

The conclusion is not too surprising, as the optimal parameters for administration of rTMS for depression have not been established. For example, which brain regions should be stimulated, for how long, and at what frequency? Clearly, more research is warranted into the novel antidepressant effects of rTMS. It is worth noting that something similar can be said of electroconvulsive therapy (ECT), probably the most powerful antidepressant treatment available and in use for 60 years. The possibility of rTMS as an alternative to ECT has also been proposed and some recent trial data suggest that rTMS may be as effective as ECT in non-psychotic major depression.

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