Meta-analysis of left prefrontal repetitive transcranial magnetic stimulation (rTMS) to treat depression
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Authors' objectives
To assess the effect of left prefrontal repetitive transcranial magnetic stimulation (rTMS) on depression.

Searching
PsycINFO (from 1887 to April 2002), MEDLINE (from 1966 to April 2002), Current Contents (April 2002) and two prior meta-analyses (see Other Publications of Related Interest nos.1-2) were searched for reports published in the English language. The search terms were stated.

Study selection

Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion if the participants and outcome assessors were blinded to treatment allocation.

Specific interventions included in the review
Studies that compared left prefrontal cortical rTMS with sham treatment were eligible for inclusion. In the included studies, rTMS was administered at varying frequencies (10 to 20 Hz, or 1/20, 0.3/10 or 5/20 Hz) and treatment was given for 5 or 10 days. The total daily stimulation dose ranged from 800 to 2,000 (or 800/800, 250/250 or 1,600/1,600) and the motor threshold ranged from 80 to 110%.

Participants included in the review
Studies of patients with depression were eligible for inclusion if the patients had not previously received TMS or sham TMS. In the included studies, the patients continued on stable medication, started treatment with sertraline, or were not receiving any medication. In their discussion, the authors stated that most of the participants had severe depression that had failed to respond to other interventions, but no details were provided.

Outcomes assessed in the review
The inclusion criteria were not explicitly defined in terms of the outcomes. All the studies in the review assessed depression using the Hamilton Rating Scale for Depression (HAM-D).

Data extraction
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

For each study, Hedge's d effect size (ES) and non-parametric variance were calculated using the change in HAM-D scores. For crossover studies, only the pre crossover data were used. The methods used to estimate standard deviations (SDs) of HAM-D scores were described in the text of the review. The authors of 4 studies with missing data were contacted and data were obtained for two of them.
Methods of synthesis
How were the studies combined?
The data were pooled in a meta-analysis and an overall ES and 95% confidence interval were calculated using a fixed-effect model. The pooled correlation and SD between baseline and post-treatment HAM-D scores were estimated. The possibility of publication bias was explored using a funnel plot. The methods of Rosenthal and Orwin were used to estimate the number of non significant studies required to change significant findings to non significant (fail-safe N).

How were differences between studies investigated?
In the meta-analysis, statistical heterogeneity was tested using the Q statistic.

Results of the review
Twelve RCTs (230 patients) were included.

The pooled correlation between baseline and post-treatment HAM-D scores was 0.46 (SD=0.33) for 3 RCTs with adequate data.

The pooled ES showed a significantly greater effect for rTMS compared with sham rTMS (ES 0.53, 95% CI: 0.24, 0.82); no significant heterogeneity was detected (Q=10.65, d.f.=11, P=0.47). The mean change in HAM-D score was 7.24 with rTMS compared with 3.58 with sham rTMS (P=0.0025); no significant heterogeneity was detected (Q=10.65, d.f.=11, P=0.47).

The funnel plot, which was asymmetrical, suggested the possibility of publication bias.

Between 20 and 55 studies showing no positive effect of rTMS would be required to change the significant finding to non significant; the fail-safe N was 55.1 using Rosenthal's method and 20.0 using Orwin's method.

Authors’ conclusions
Left prefrontal rTMS reduces depression.

CRD commentary
The review question was clear in terms of the study design, intervention and outcomes. The inclusion criteria were broadly defined in terms of the participants, with no defined criteria required for the diagnosis of depression. Several relevant sources were searched and the search terms were stated. By limiting the included studies to those in English, some relevant studies may have been omitted. No attempt was made to locate unpublished studies, thus raising the possibility of publication bias. The methods used to select the studies, assess validity and extract the data were not described; hence, any efforts made to reduce errors and bias cannot be judged. There was no assessment of study validity, however, only double-blind RCTs were included.

Few details of the included studies were presented. In particular, no details of the patients' characteristics (e.g. age, gender and severity of depression) were given, or the timing of the outcome assessment. This makes it difficult to assess the generalisability of the results. The data were combined in a meta-analysis and statistical heterogeneity was assessed. While the studies were found to be statistically homogeneous, the authors stated that the populations were clinically heterogeneous. This suggests that a meta-analysis may not have been appropriate, or that some exploration of the effect of population characteristics on the results would have been worth considering.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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