Non-invasive brain stimulation for Parkinson's disease: a systematic review and meta-analysis of the literature
Fregni F, Simon D K, Wu A, Pascual-Leone A

CRD summary
This review concluded that transcranial magnetic stimulation shows a significant modest positive effect, and that electroconvulsive therapy may also have a significant effect, on the motor function of patients with Parkinson's disease. These conclusions should be regarded with some caution, mainly because of a lack of information on the included studies.

Authors' objectives
To evaluate the efficacy of transcranial magnetic stimulation (TMS) and electroconvulsive therapy (ECT) for motor dysfunction treatment in patients with Parkinson's disease.

Searching
MEDLINE, EMBASE, SciELO and the Cochrane Library were searched for studies published between 1980 and January 2005; the search terms were reported. In addition, references of systematic reviews, retrieved papers, the CRISP database and conference abstracts were screened and experts were contacted. The studies had to be published in a book, journal, proceeding or indexed abstracts, and in English, German, Italian, French, Spanish or Portuguese.

Study selection
Study designs of evaluations included in the review
Prospective studies (both controlled and uncontrolled) evaluating treatment effects were eligible; case reports and case series were excluded.

Specific interventions included in the review
Studies evaluating TMS or ECT were eligible for inclusion. Some of the included TMS studies were compared with sham treatment. Stimulation sites and parameters varied. The number of sessions ranged from 1 to 14 in the TMS studies and from 4 to 9 in the ECT studies.

Participants included in the review
Studies of patients with Parkinson's disease were eligible. The mean age of the participants was 63 years in the TMS studies and 69 years in the ECT studies. The ratio of men to women was 1.3:1 and 1.1:1 in the two study groups and the disease duration was 6.6 years (TMS) and 13.8 years (ECT), respectively.

Outcomes assessed in the review
Studies of TMS had to use the Unified Parkinson's Disease Rating scale (UPDRS); ECT studies could also use other continuous clinical scales to evaluate motor symptoms in Parkinson's disease. In addition, the studies had to report the mean and standard deviation (SD), or a parameter that allowed them to be deduced, of the motor function before and after treatment. The review reported effects at different follow-up dates.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection. Authors were contacted if the mean and SD of the outcome measures could not be deduced from the included studies.

Assessment of study quality
The authors did not formally assess validity but they indicated that some of the controlled trials were double-blind.
Data extraction
One reviewer extracted and a second one checked the extracted data. Any discrepancies were resolved through consensus or referral to a third reviewer where necessary. Where overlapping series of data were published, the study with the largest sample was used. The data were extracted on the mean and SD of the motor section (Part III) of the UPDRS (or other clinical scale for ECT studies) at baseline and after treatment, separately for the intervention and placebo groups (if the study included a sham control group). For studies that used more than one active group (i.e. different doses of TMS), each group was considered as a separate study in the analysis.

Standardised mean differences (Cohen's d) were calculated for continuous outcome measures based either on the pre-treatment and post-test values of one group within each study, or a comparison of the mean chances in pre-treatment to post-treatment for studies that included a sham control group. Post-treatment values were based on assessment immediately following treatment. A separate analysis based on longer term follow-up (up to 2 months) was also carried out.

Methods of synthesis
How were the studies combined?
Pooled effect sizes and their 95% confidence intervals (CIs) were estimated using random-effects and fixed-effect meta-analyses. Publication bias was assessed using the Begg modified funnel plot.

How were differences between studies investigated?
Clinical and statistical heterogeneity (Q statistic) were assessed. The influence of each study on the pooled results was evaluated and meta-regression was carried out on a number of variables.

Results of the review
Seventeen studies (n=273) were included, at least eight of which were controlled studies.

For TMS, the pooled standardised mean difference for before and after treatment was 0.62 (95% CI: 0.38, 0.85; based on 12 studies, 18 datasets); no significant heterogeneity was detected (p=0.11). The results for the 8 double-blind controlled studies only were similar. A comparison of standardised mean differences for before and after treatment between TMS and sham treatment groups showed a pooled effect size of 1.19 (95% CI: 0.44, 1.94; based on 8 studies). There was statistical evidence of heterogeneity (p<0.0001). The pooled weighted mean difference in the UPDRS scores before and after treatment was 5.90, which was equivalent to over 20% improvement in motor function compared with baseline. Where reported, the number of TMS-treated patients ranged from 7 to 21.

For ECT, the pooled effect size was 1.68 (95% CI: 0.79, 2.56; based on 5 studies); there was significant heterogeneity (p=0.012). The number of participants in each study was not reported, but only 49 patients in total were included.

There was no indication of publication bias for the TMS studies.

Authors' conclusions
TMS can exert a significant but modest positive effect on motor function across applied stimulation sites and parameters. ECT may also have a significant effect on motor function of patients with Parkinson's disease.

CRD commentary
The review stated a clear question and inclusion criteria. The search was thorough, encompassed published and unpublished material, and a number of languages were considered; this reduces publication and language bias. The individual study results were only reported for one group of the included studies, making it difficult to evaluate the pooled result. In addition, validity was not formally assessed so the quality of the included studies remained unclear. This was a particular problem as a variety of study designs were included. The reviewers only reported a procedure to reduce errors and bias for the data extraction but not for other stages of the review. The statistical analyses appeared thorough. The clinical significance of the established effect was discussed. Overall, the conclusions should be regarded
with some caution.

**Implications of the review for practice and research**

Practice: The authors did not state any specific implications for practice.

Research: The authors stated that studies need to assess the efficacy of new methods of brain stimulation, such as transcranial direct current stimulation or cortical/epidural stimulation, in patients with Parkinson's disease. Furthermore, a study should assess the suitability of patients for more invasive, cortical stimulation and future studies should compare the efficacy of different types of motor cortex stimulation.

**Funding**

Harvard Medical School Scholars in Clinical Science Program, grant numbers NIH K30 HL04095-03 and K24 RR018875.

**Bibliographic details**


**Original Paper URL**

http://jnnp.bmj.com/cgi/content/full/76/12/1614

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Electroconvulsive Therapy; Motor Skills Disorders /etiology /therapy; Parkinson Disease /therapy; Radiation; Severity of Illness Index; Treatment Outcome

**AccessionNumber**

12005004728

**Date bibliographic record published**

31/08/2007

**Date abstract record published**

31/08/2007

**Record Status**

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.