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# Non-invasive brain stimulation techniques for chronic pain. A Cochrane systematic review and meta-analysis

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**Abstract**

**Purpose**

To evaluate the efficacy of non-invasive brain stimulation techniques in chronic pain.

**Relevance**

Non-invasive brain stimulation techniques aim to induce an electrical stimulation of the brain in an attempt to reduce chronic pain by directly altering brain activity. They include repetitive transcranial magnetic stimulation (rTMS), cranial electrotherapy stimulation (CES) and transcranial direct current stimulation (tDCS). These approaches to pain treatment are relatively novel. It is important to assess the existing literature robustly to ascertain the current level of supporting evidence and to inform future research and potential clinical use.

**Methods**

We systematically searched CENTRAL, MEDLINE, EMBASE, CINAHL, PsycINFO, LILACS, the Cochrane PaPaS Group Trials Register and clinical trials registers for randomised and quasi-randomised studies of rTMS, CES or tDCS that employed a sham stimulation control group, recruited patients over the age of 18 with pain of three months duration or more and measured pain as a primary outcome.

**Analysis**

Two authors independently extracted and verified data and assessed all studies for risk of bias using the Cochrane Risk of Bias Tool [1]. Where possible we entered data into meta-analyses. We excluded studies judged as being at high risk of bias from the analysis.

**Results**

We included 33 trials in the review (involving 937 people)(19 rTMS, eight CES and six tDCS). Only one study was judged as being at low risk of bias.

Studies of rTMS (involving 368 people) demonstrated significant heterogeneity. Pre-specified subgroup analyses suggest that low-frequency stimulation is ineffective. A short-term effect on pain of active high-frequency stimulation of the motor cortex in single-dose studies was suggested (standardised mean difference (SMD) -0.40, 95% confidence interval (CI) -0.26 to -0.54, P < 0.00001). This equates to a 15% (95% CI 10% to 20%) reduction in pain which does not clearly exceed the pre-established criteria for a minimally clinically important difference (> 15%).

For CES (four studies, 133 people) no statistically significant difference was found between active stimulation and sham. Analysis of tDCS studies (five studies, 83 people) demonstrated significant heterogeneity and did not find a significant difference between active and sham stimulation. Pre-specified subgroup analysis of tDCS applied to the motor cortex suggested superiority of active stimulation over sham (SMD -0.59, 95% CI -1.10 to -0.08).

Non-invasive brain stimulation appears to be associated with minor and transient side effects.

**Conclusions**

Single doses of high-frequency rTMS of the motor cortex may have small short-term effects on chronic pain. The effects do not clearly exceed the predetermined threshold of minimal clinical significance. Low-frequency rTMS is not effective in the treatment of chronic pain. There is insufficient evidence from which to draw firm conclusions regarding the efficacy of CES or tDCS. The available evidence suggests that tDCS applied to the motor cortex may have short-term effects on chronic pain and that CES is not effective.

**Implications**

There is a need for further, rigorously designed studies of all types of stimulation before firm conclusion can be drawn regarding the efficacy of non-invasive brain stimulation techniques for chronic pain.

**Keywords**

transcranial direct current stimulation (tDCS), repetitive transcranial magnetic stimulation (rTMS), cranial electrotherapy stimulation (CES), efficacy, chronic pain.

**References**

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