

# INPLASY

## Non-invasive brain neuromodulation techniques for phantom limb pain: a systematic review

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### ADMINISTRATIVE INFORMATION

**Support** - None.

**Review Stage at time of this submission** - Preliminary searches.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY2023110032

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 November 2023 and was last updated on 07 November 2023.

### INTRODUCTION

**Review question / Objective** P: Participants with phantom limb pain; I: non-invasive brain neuromodulation techniques (NIBS); C: Control group received sham treatment or placebo; O: Pain intensity (any pain scale reported in the trial, such as visual analogue scale); S: RCT. The aim is to evaluate the effects of NIBS in the treatment of phantom limb pain to evaluate the effects of non-invasive brain neuromodulation techniques for phantom limb pain.

**Condition being studied** About 50% -80% of amputees will experience PLP. Phantom limb pain (PLP) is characterized as the painful sensation experienced in the missing limb after amputation. PLP is a serious public health problem that can affect the physical, psychological, and functional health of amputees. The current treatment options (pharmacological and behavioral) for PLP are not entirely effective. NIBS is a promising treatment technology and previous studies have found its potential in treating neuropathic pain.

### METHODS

**Participant or population** Participants with phantom limb pain.

**Intervention** Non-invasive brain neuromodulation techniques such as repetitive transcranial magnetic stimulation, transcranial direct current stimulation.

**Comparator** Sham treatment or placebo.

**Study designs to be included** Randomized controlled trial.

**Eligibility criteria** Our inclusion criteria were as follows: i) studies that evaluated any beneficial or adverse effect of the use of noninvasive neuromodulation techniques in the treatment of adults (>18 years old) with a PLP diagnosis. ii) randomized controlled trials (RCTs), including parallel-group and crossover designs, and quasi-experimental (QE) studies; iii) studies with pain

scales (visual analog scale [VAS], numeric rating scale [NRS], McGill Pain Questionnaire, or universal pain score [UPS]) as the primary outcome (and this information had to include mean and standard deviation before and after the intervention). The exclusion criteria were non-English and non-Chinese studies and case-control studies, cohort studies, case series, review articles, conference abstracts, case reports, letters, and editorials. We excluded the studies with full text not available after trying to contact the authors.

**Information sources** Pubmed, Medline, Embase, Web of Science, Wanfang Database, China National Knowledge Infrastructure Database, and China Biomedical Literature Database.

**Main outcome(s)** Pain intensity such as: visual analog scale (VAS) , numeric rating scale (NRS) , Leeds Assessment of Neuropathic Symptoms and Signs Scale (LANSS) , McGill Pain Questionnaire.

**Quality assessment / Risk of bias analysis** To analyze the methodological quality of each individual study, the Physiotherapy Evidence Scale (PEDro) will be used. To analyze the risk of bias of each individual study, the revised Cochrane risk-of-bias tool for randomized trials will be used.

**Strategy of data synthesis** We will use RevMan 5.3 software to synthesize and analyze outcome data. We will calculate the treatment effect of dichotomous data using risk ratio and 95% confidence intervals (CIs), and that of continuous data using standardized mean differences (SMDs) and 95%CIs . We will exam ineheterogeneity using  $I^2$  statistic, and we will undertake statistical pooling on groups of trials which are considered to be sufficiently similar. Where heterogeneity is low or minor ( $I^2 < 50\%$ ), we will utilize a fixed-effect model to pool the data; if heterogeneity is obvious ( $I^2 \geq 50\%$ ), we will not pool the data. Meta-analysis will be carried out based on the sufficient homogeneity regarding on participant characteristics, types of intervention and outcome, and comparability between methods and ability to aggregate data.

**Subgroup analysis** We will carry out subgroup analysis to test the sources of significant heterogeneity based on the different time periods, study quality, and types of intervention and control.

1. Efficacy of NIBS for PLP (subgroup analysis: difference in efficacy between rTMS and tDCS as the intervention method)

2. Efficacy of NIBS for PLP (subgroup analysis: difference in efficacy between stimulation areas of primary motor cortex (M1), primary sensory cortex (S1) and M1+S1)

3. Efficacy of NIBS in treating PLP (subgroup analysis: difference in efficacy between <2 weeks and >2 weeks.

**Sensitivity analysis** We will investigate the sensitivity analysis to test the stability and robustness of study findings based on the sample size of included trials, and study quality.

**Country(ies) involved** China.

**Keywords** non-invasive brain neuromodulation techniques; phantom limb pain; meta-analysis.

**Contributions of each author**

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