INPLASY PROTOCOL

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

Conflicts of interest:
None declared.

Therapeutic effect of repeated transcranial magnetic stimulation with different stimulation methods for post-stroke cognitive impairment：a Meta-Analysis

Chen, TB[1]; Lv, SP[2].

Review question / Objective: **To evaluate and compare the effects of intermittent theta burst stimulation and high-frequency repetitive transcranial magnetic stimulation on the patients with post-stroke cognitive impairment.**
Condition being studied: **Post-stroke cognitive impairment (PSCI) is a major source of morbidity and mortality after stroke worldwide. Repetitive transcranial magnetic stimulation (rTMS), as a noninvasive brain stimulation technique, modulates cortical excitability and synaptic structure and function to promote functional recovery in stroke patients.High-frequency rTMS and intermittent theta burst stimulation (iTBS) are two different methods of transcranial magnetic stimulation, which have been widely used in the clinical treatment of PSCI patients in recent years.Thus, we will evaluate and compare the effects of iTBS and high-frequency rTMS on the patients with PSCI.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 May 2023 and was last updated on 23 May 2023 (registration number INPLASY202350086).

INTRODUCTION

Review question / Objective: **To evaluate and compare the effects of intermittent theta burst stimulation and high-frequency repetitive transcranial magnetic stimulation on the patients with post-stroke cognitive impairment.**

Rationale: **At present, a large number of clinical studies have shown that rTMS can promote the recovery of cognitive function and activities of daily living in PSCI**

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patients, but the treatment modes used in these studies are different, among which 10Hz rTMS and iTBS are the most widely used modes. Moreover, most of these studies were single-center experiments, with small sample sizes and some differences in experimental design. Therefore, Meta-analysis was used to systematically review the efficacy and safety of different modes of rTMS in patients with PSCI, in order to provide evidence-based basis for its clinical application.

Condition being studied: Post-stroke cognitive impairment (PSCI) is a major source of morbidity and mortality after stroke worldwide. Repetitive transcranial magnetic stimulation (rTMS), as a noninvasive brain stimulation technique, modulates cortical excitability and synaptic structure and function to promote functional recovery in stroke patients.High-frequency rTMS and intermittent theta burst stimulation (iTBS) are two different methods of transcranial magnetic stimulation, which have been widely used in the clinical treatment of PSCI patients in recent years.Thus, we will evaluate and compare the effects of iTBS and high-frequency rTMS on the patients with PSCI.

METHODS

Search strategy: We will searched both Chinese(CNKI,Wanfang,VIP and CBM) and English(PubMed,Embase, Cochrane Library and Web of Science)databases for randomized controlled trials (from database inception until May, 2023).According to the combination of subject words and free words, the search terms are as follows:Stroke, Apoplexy, Cerebrovascular, CVA, Brain Vascular Accident, Brain Ischemia, Ischemic Encephalopath, Brain Infarction, Cerebral Hemorrhage, Cerebrum Hemorrhage, Intracerebral Hemorrhage, Cognitive Dysfunction, memory, Attention, Executive function, Transcranial Magnetic Stimulation, rTMS, intermittent theta burst stimulation, iTBS.

Participant or population: Patients with cognitive deficits after stroke.

Intervention: High-frequency repetitive transcranial magnetic stimulation or intermittent theta burst stimulation.

Comparator: Sham stimulation or placebo or blank control.

Study designs to be included: Randomized controlled trials (RCT) .

Eligibility criteria: Patients with PSCI (as diagnosed by a doctor,or using any recognised diagnostic criteria)will be included.

Information sources: We will searched both Chinese(CNKI,Wanfang,VIP and CBM) and English(PubMed,Embase, Cochrane Library and Web of Science)databases for randomized controlled trials (from database inception until May, 2023).

Main outcome(s): Montreal Cognitive Assessment Scale(MoCA) and Mini-Mental State Examinatio(MMSE).

Additional outcome(s): Modified Barthel Index (MBI) and P300 event-related potential (latency, amplitude).

Data management: Two researchers independently screened the literature, extracted and cross-checked the data. In case of disagreement, the third researcher participated in the discussion and resolved. Data extraction was carried out using the data extraction table established in advance.

Quality assessment / Risk of bias analysis: Two reviewers independently assessed the bias of the included studies according to the Cochrane Handbook for Systematic Reviews of Interventions, and disagreements were resolved by discussing with the third reviewer. The assessment items included selection bias,

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performance bias, detection bias, attrition bias, reporting bias, and other biases. Each item was rated as "high", "low", or "unclear".

Strategy of data synthesis: We used RevMan 5.4 to perform the meta-analysis.We used the Cochrane Q statistic to qualitatively determine whether heterogeneity existed among the included studies (test level α=0.05), while the I^2 statistic to quantitatively determine the magnitude of heterogeneity. If P≥0.1 and I^2≤50%, the heterogeneity was considered to be insignificant and we selected the fixed-effects (FE) model. Conversely, we selected the random-effects (RE) model.The results for the continuous variables were expressed as standardized mean differences (SMDs) with 95% confidence intervals (CIs).

Subgroup analysis: In this meta-analysis, the subgroup analysis includes comparison between iTBS and HF-rTMS.

Sensitivity analysis: Sensitivity analysis was performed by sequential deletion tests to test the stability of the main results. That is,after the deletion of any one study, the combined results of the remaining literature are not significantly different from those that would have passed the sensitivity analysis if it had not been deleted.

Country(ies) involved: China.

Keywords: Stroke;cognitive impariment; repeated transcranial magnetic stimulation; intermittent theta burst stimulation.

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