

# INPLASY PROTOCOL

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**Corresponding author:**  
Kunpeng Li

xyfyli@163.com

**Author Affiliation:**  
Shanghai University of  
Traditional Chinese Medicine.

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**Conflicts of interest:**  
None declared.

## The Effects of Repetitive Transcranial Magnetic Stimulation on the Cognition in Patients with Stroke: a Systematic Review and Meta-analysis

Li, K<sup>1</sup>; Sun, J<sup>2</sup>; Wu, C<sup>3</sup>; An, X<sup>4</sup>; Wu, J<sup>5</sup>; Zheng, M<sup>6</sup>; Hua, X<sup>7</sup>; Xu, J<sup>8</sup>.

**Review question / Objective:** To evaluate the effects of rTMS on patients with post-stroke cognitive impairment.

**Condition being studied:** Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive approach that can enhance cognitive performance and the utilization of which is a rapidly emerging field with encouraging results. A large number of studies have shown that rTMS can improve the cognitive and memory function of stroke patients. At the same time, rTMS can be used to treat depression by stimulating or inhibiting the cerebral cortex at different frequencies. Currently, several countries including Canada and the United States have approved rTMS for the treatment of depression, either alone or in combination with drugs.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 May 2022 and was last updated on 12 May 2022 (registration number INPLASY202250078).

### INTRODUCTION

**Review question / Objective:** To evaluate the effects of rTMS on patients with post-stroke cognitive impairment.

**Rationale:** Stroke is a global health problem, leading to a variety of adverse consequences such as cognitive

impairment. Cognitive impairment after stroke involves multiple cognitive domains, with attention and executive dysfunction as main symptoms. At the same time, cognitive decline can lead to depression, which seriously affects the physical function, rehabilitation and prognosis of patients. Further, depression can lead to a significant decline in patients'

quality of life, and is closely related to high mortality. Since, the importance of cognitive function training in stroke rehabilitation should be emphasized.

**Condition being studied:** Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive approach that can enhance cognitive performance and the utilization of which is a rapidly emerging field with encouraging results. A large number of studies have shown that rTMS can improve the cognitive and memory function of stroke patients. At the same time, rTMS can be used to treat depression by stimulating or inhibiting the cerebral cortex at different frequencies. Currently, several countries including Canada and the United States have approved rTMS for the treatment of depression, either alone or in combination with drugs.

## METHODS

**Search strategy:** The search string will be built as follows: “randomized controlled trial” AND (“Cognitive Dysfunction” OR “Cognitive Impairment” OR “Mild Neurocognitive Disorder” OR “Cognitive Decline”) AND (“Transcranial Magnetic Stimulation” OR “rTMS”).

**Participant or population:** Patients with stroke.

**Intervention:** Repetitive Transcranial Magnetic Stimulation.

**Comparator:** Sham stimulation.

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

**Eligibility criteria:** The pathological tissue and imaging diagnosis of stroke patients, stroke type, unlimited by installments.

**Information sources:** We will search the following databases for relevant English language literature: PubMed, the Cochrane Library, Embase, EBSCO and SCOPUS. The electronic database search will be

supplemented by a manual search of the reference lists of included articles.

**Main outcome(s):** Cognition assessment results like the scores of Mini-Mental Status Examination (MMSE) scale or Montreal Cognitive Assessment (MoCA) scale.

**Additional outcome(s):** Beck depression rating (BDI) scale; Modified Barthel index (MBI) scale.

**Data management:** Two authors will independently extract data. Any disagreement will be resolved by discussion until consensus is reached or by consulting a third author. The following data will be extracted: author, year of publication, study period, original inclusion criteria, total number of people included in the study, interventions, frequency and time of stimulation.

**Quality assessment / Risk of bias analysis:** Two reviewers will independently assess the quality of the selected studies according to the Cochrane collaboration's tool for randomized controlled trials. Items will be evaluated in three categories: Low risk of bias, unclear bias and high risk of bias. The following characteristics will be evaluated: Random sequence generation (selection Bias); Allocation concealment (selection bias); Blinding of participants and personnel (performance bias); Incomplete outcome data (attrition bias); Selective reporting (reporting bias); Other biases. Results from these questions will be graphed and assessed using Review Manager 5.4.

**Strategy of data synthesis:** Risk ratio (RR) for both fixed and random effects models (weighting by inverse of variance) will be used. A continuity correction will also be used for cells with zero values. Between-study heterogeneity will be assessed using the I<sup>2</sup> statistics. When I<sup>2</sup> < 50%, the heterogeneity was not obvious, and the fixed effect model was used for meta-analysis. Otherwise, random effects model was used for meta-analysis. Results will be

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assessed using forest plots and presented as RRs for the main outcome and secondary outcomes. An influence analysis will be performed to ascertain the results of the meta-analysis by excluding each of the individual studies.

**Subgroup analysis:** We will consider subgroups such as frequency, stimulation site.

**Sensitivity analysis:** After excluding a low-quality study, the combined effect size was re-estimated and compared with the results of the Meta-analysis before exclusion to explore the extent of the effect of the study on the combined effect size and the robustness of the results. If the results did not change significantly after exclusion, it indicates that the sensitivity is low and the results are more robust and credible; on the contrary, if large differences or even diametrically opposite conclusions are obtained after exclusion, it indicates that the sensitivity is high and the robustness of the results is low, and great care should be taken when interpreting the results and drawing conclusions, suggesting the existence of important and potentially biased factors related to the effects of the intervention, and the source of the controversy needs to be further clarified.

**Country(ies) involved:** China.

**Keywords:** Stroke; Repetitive Transcranial Magnetic Stimulation; Cognition; Meta-analysis.

**Contributions of each author:**

Author 1 - Kunpeng Li.

Email: xyfyli@163.com

Author 2 - Jie Sun.

Email: sunjie970815@163.com

Author 3 - Caiqin Wu.

Author 4 - Xufei An.

Author 5 - Jiajia Wu.

Author 6 - Mouxiong Zheng.

Author 7 - Xuyun Hua.

Author 8 - Jianguang Xu.