INPLASY PROTOCOL

To cite: Chen et al. Effects of repetitive transcranial magnetic stimulation on upper-limb and finger function in stroke patients: a systematic review and meta-analysis of randomized controlled trials. Inplasy protocol 202250121. doi: 10.37766/inplasy2022.5.0121

Received: 19 May 2022

Published: 19 May 2022

Corresponding author:
Gengbin Chen

757854757@qq.com

Author Affiliation:
Guangzhou first people's Hospital.

Support: **NSFC, GSTP.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

Effects of repetitive transcranial magnetic stimulation on upper-limb and finger function in stroke patients: a systematic review and meta-analysis of randomized controlled trials

Chen, GB[1]; Lin, T[2]; Wu, MF[3]; Cai, GY[4]; Ding, Q[5]; Xu, JY[6]; Li, WQ[7]; Wu, C[8]; Chen, HY[9]; Lan, Y[10].

Review question / Objective: **P:Adult patients (age ≥ 18 years) diagnosed with stroke based on relevant clinical examination; I:Intervention group with rTMS alone or in combination with other treatments with rTMS; C:Control group received sham treatment or no rTMS; O: Upper extremity function:the Fugl-Meyer Assessment Upper Extremity (FMA-UE); Hand function:box and block test(BBT), nine-hole peg test(NHPT), and Purdue pegboard test(PPT); S:Randomized controlled trials (rather than crossover designs).**
Condition being studied: **In Europe, more than 1 million new cases of stroke are reported each year. The absolute number of stroke patients is expected to increase in the near future due to the progressive aging of the population. Approximately 50-80% of stroke survivors present with upper extremity dysfunction. Recovery of upper extremity function is associated with improvements in activities of daily living and mental health. However, few stroke survivors show full recovery of upper extremity function 6 months after stroke. In addition, rehabilitation has a limited impact on the recovery of hand motor function.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 May 2022 and was last updated on 19 May 2022 (registration number INPLASY202250121).

INTRODUCTION

Review question / Objective: **P:Adult patients (age ≥ 18 years) diagnosed with stroke based on relevant clinical examination; I:Intervention group with rTMS alone or in combination with other treatments with rTMS; C:Control group received sham treatment or no rTMS; O: Upper extremity function:the Fugl-Meyer**

Assessment Upper Extremity (FMA-UE); Hand function:box and block test(BBT), nine-hole peg test(NHPT), and Purdue pegboard test(PPT); S:Randomized controlled trials (rather than crossover designs).

Rationale: Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive, painless treatment modality that modulates cortical excitability. TBS is a new modality of repetitive transcranial magnetic stimulation. Many studies have investigated the efficacy of transcranial magnetic stimulation for post-stroke rehabilitation. In addition, several literature reviews and meta-analyses have attempted to synthesize the available evidence on transcranial magnetic stimulation for the treatment of upper extremity dysfunction after stroke. Previous reviews did not assess the effects of variables, such as baseline injury level, hemispheric stimulation, etc. However, these factors are known to influence the efficacy of transcranial magnetic stimulation. Furthermore, previous meta-analyses have not systematically explored the effects of various recovery factors in different periods (acute, subacute, and chronic) of stroke, nor have they clearly delineated the subsequent effects of transcranial magnetic stimulation interventions in the upper extremities and hands. Therefore, in this meta-analysis, the effects of transcranial magnetic stimulation on upper limb recovery in stroke patients at different periods were discussed in terms of stimulation hemisphere, number of stimulation sessions, and baseline injury level. In addition, the short-, medium- and long-term effects of transcranial magnetic stimulation intervention on upper limb and hand dysfunction after stroke were analyzed, and finally, the meta-analysis of transcranial magnetic stimulation for post-stroke hand dysfunction was updated.Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive, painless treatment modality that regulates cortical excitability. Numerous studies have investigated the efficacy of rTMS for post-stroke rehabilitation. In addition, several literature reviews and meta-analyses have attempted to synthesize the available evidence on the efficacy of rTMS for upper extremity dysfunction after stroke. Previous reviews have not assessed the effect of variables such as baseline injury level, hemispheric stimulation, etc. However, these factors are known to influence the efficacy of rTMS. Furthermore, previous meta-analyses have not systematically explored the effects of various recovery factors during different periods of stroke (acute, subacute, chronic), nor have they clearly delineated the follow-up effects after transcranial magnetic stimulation interventions in the upper limb and hand. Therefore, in this meta-analysis, the effects of transcranial magnetic stimulation on the recovery of the upper extremity were discussed in terms of stimulation hemisphere, number of stimulation sessions, and the degree of baseline injury in patients with different periods of stroke. Furthermore, the short-, medium-, and long-term effects of transcranial magnetic stimulation intervention on upper limb and hand dysfunction after stroke were analyzed, and finally, the meta-analysis of transcranial magnetic stimulation for hand dysfunction after stroke was updated.

Condition being studied: In Europe, more than 1 million new cases of stroke are reported each year. The absolute number of stroke patients is expected to increase in the near future due to the progressive aging of the population. Approximately 50-80% of stroke survivors present with upper extremity dysfunction. Recovery of upper extremity function is associated with improvements in activities of daily living and mental health. However, few stroke survivors show full recovery of upper extremity function 6 months after stroke. In addition, rehabilitation has a limited impact on the recovery of hand motor function.

METHODS

Search strategy: A comprehensive literature search was conducted in three electronic databases (PubMed, Web of Science, and Embase) to identify relevant studies published in English. The search terms for each database were modified so

that the primary keywords included, but were not limited to, "stroke," "repetitive transcranial magnetic stimulation," "upper extremity," and "hand." The last search was conducted on February 12, 2022. In addition, references listed in the included articles and reference lists from previous systematic evaluations were manually screened to retrieve additional eligible studies.

Participant or population: Adult patients (age ≥ 18 years) diagnosed with stroke based on relevant clinical examination

Intervention: Intervention group with rTMS alone or in combination with other treatments with rTMS.

Comparator: Control group received sham treatment or no rTMS.

Study designs to be included: Randomized controlled trials (rather than crossover designs).

Eligibility criteria: Inclusion criteria.(1) >5 patients(2) All included peer-reviewed and published English articles(3) PEDro scores >6Exclusion criteria.(1) suffering from other diseases(2) Articles published, such as reviews, meta-analyses or case reports(3) Results were not mean plus standard deviation but median and quartiles.

Information sources: Electronic databases (pubmed, Embase, Web of Science).

Main outcome(s): We investigated (1) The effect sizes of transcranial magnetic stimulation interventions on the upper extremities of patients with acute, subacute and chronic stroke with different baseline injuries (2) The number of treatments for the upper extremity in patients with acute, subacute and chronic stroke with transcranial magnetic stimulation (3)Transcranial magnetic stimulation in patients with acute, subacute and chronic upper limb dysfunction (bilateral, affected and unaffected hemispheres) (4)Transcranial magnetic stimulation for post-stroke fine motor intervention (5)Transcranial magnetic stimulation for fine motor movements in different stroke periods (6) Short-term (0-1 month), mid-term (2-5 months) and long-term (>6 months) effects of transcranial magnetic stimulation on upper limb and hand dysfunction after stroke.

Quality assessment / Risk of bias analysis: The quality of the included studies was assessed independently by two assessors using the PEDro scale. The scale consists of 11 items, and since the first item is not included in the total results, there are 10 scoring quality criteria, each recorded as 1 (meets the criteria) or 0 (does not meet the criteria), and the scores for each item are summed to obtain a total score for each study. The maximum total score for each study was 10/10.Studies with a total score ≤6 were excluded, which indicates high methodological quality.

Strategy of data synthesis: All analyses were performed using StataMP 14.0 software. Effects and corresponding 95% confidence intervals (CIs) were used to compare results. Heterogeneity among included studies was assessed by Cochran's Q test and I2 statistics. A random effects model was used to allow generalization of the results beyond the included studies. p-values <0.05 were considered as a sign of statistical significance. Effect sizes were expressed as standardized mean differences (SMD).

Subgroup analysis: (1) Effect size of transcranial magnetic stimulation intervention in the upper extremity of patients with different baseline injuries in the acute phase of stroke (2) Effect sizes of transcranial magnetic stimulation in the upper extremity of patients with different baseline injuries in the acute phase of sub-stroke (3) Effect sizes of transcranial magnetic stimulation in the upper extremity of patients with different baseline injuries in the chronic phase of stroke (4)The number of treatments of upper extremity in patients with acute stroke with transcranial magnetic stimulation (5)Number of transcranial magnetic stimulation treatments in the upper extremity of patients with subacute stroke (6)Number of

treatments of upper extremity in patients with chronic phase of stroke by transcranial magnetic stimulation (7)The number of stimulated hemispheres (bilateral hemispheres, affected hemispheres, unaffected hemispheres) in patients with upper limb dysfunction in the acute phase of transcranial magnetic stimulation (8) Stimulation hemispheres (bilateral hemispheres, affected hemispheres, unaffected hemispheres) for transcranial magnetic stimulation intervention for upper limb dysfunction in the acute phase of stroke (9)Transcranial magnetic stimulation for upper limb dysfunction in the chronic phase of stroke (bilateral hemispheres, affected hemispheres, unaffected hemispheres) (10) Transcranial magnetic stimulation for fine motor movements after stroke (11)Transcranial magnetic stimulation for fine motor movements in different stroke periods (12)Short-term (0-1 month), medium-term (2-5 months) and long-term (>6 months) effects of transcranial magnetic stimulation after stroke upper limb dysfunction (13)Short-term (0-1month) mid-term (2-5months) long-term (>6months) effects of transcranial magnetic stimulation intervention after stroke hand dysfunction.

Sensitivity analysis: Sensitivity analyses were performed on selected studies to determine the potential impact of outliers on the overall results.

Language: Published in English language.

Country(ies) involved: China.

Keywords: repetitive transcranial magnetic stimulation, stroke, meta-analysis, Hand, Upper limb, review.

Contributions of each author:

Author 1 - Gengbin Chen.
Email: 757854757@qq.com
Author 2 - Tuo Lin.
Author 3 - Manfeng Wu.
Author 4 - Guiyuan Cai.
Author 5 - Qian Ding.
Author 6 - Jiayue Xu.
Author 7 - Wanqi Li.
Author 8 - Cheng Wu.
Author 9 - Hongying Chen.
Author 10 - Yue Lan.