# INPLASY PROTOCOL

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Corresponding author: Min Cheol Chang

wheel633@ynu.ac.kr

Author Affiliation: Yuengnam Univ.

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**Conflicts of interest:** 

None declared.

# Effect of Repetitive Transcranial Magnetic Stimulation on Post-stroke Dysphagia: Meta-analysis of Stimulation Frequency, Stimulation Site, and Timing of Outcome Measurement

Hsiao, MY<sup>1</sup>; Choo, YJ<sup>2</sup>; Liu, IC<sup>3</sup>; Mathieu, BR<sup>4</sup>; Chang, MC<sup>5</sup>.

Review question / Objective: Dysphagia is one of the most frequent sequelae after stroke. It can result in various complications, such as malnutrition, dehydration, aspiration pneumonia, and poor rehabilitation outcomes. Repetitive transcranial magnetic stimulation (rTMS) is reported to improve dysphagia after stroke; however, the details remain unclear. We evaluated the following rTMS parameters on post-stroke dysphagia: stimulation frequency (high frequency [≥3 Hz] or low frequency [1 Hz]), stimulation site (ipsilesional mylohyoid cortex or contralesional mylohyoid cortex), and outcome measurement timing (immediately, 3 weeks, and 4 weeks after the rTMS session).

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 April 2022 and was last updated on 01 April 2022 (registration number INPLASY202240005).

### INTRODUCTION

Review question / Objective: Dysphagia is one of the most frequent sequelae after stroke. It can result in various complications, such as malnutrition, dehydration, aspiration pneumonia, and poor rehabilitation outcomes. Repetitive transcranial magnetic stimulation (rTMS) is

reported to improve dysphagia after stroke; however, the details remain unclear. We evaluated the following rTMS parameters on post-stroke dysphagia: stimulation frequency (high frequency [≥3 Hz] or low frequency [1 Hz]), stimulation site (ipsilesional mylohyoid cortex or contralesional mylohyoid cortex), and outcome measurement timing

(immediately, 3 weeks, and 4 weeks after the rTMS session).

Condition being studied: Dysphagia is a frequent consequence of stroke and has a high incidence ranging from 29% to 81%. Dysphagia after stroke can cause malnutrition, dehydration, and aspiration pneumonia, which result in prolonged hospitalization and poor clinical outcomes, as well as a threefold increase in mortality. In addition, about half of the stroke patients with dysphagia are reported to experience anxiety or a feeling of panic during eating and deterioration of selfesteem and social participation. Therefore, the treatment of post-stroke dysphagia is essential to stroke rehabilitation. Several studies have reported that rTMS can improve dysphagia after stroke and to date, several meta-analyses have reported a positive therapeutic effect of rTMS on poststroke dysphagia. However, it remains a subject of debate as most of the previous studies have not analyzed the outcomes according to stimulation frequency, stimulation site, and timing of outcome measurement. Additionally, in some studies different outcome measurements were analyzed together for the meta-analysis. Due to the aforementioned issues, the results of previous meta-analysis studies may be less reliable. In our study, we evaluated the effect of rTMS on post-stroke dysphagia following rTMS parameters: stimulation frequency (high frequency or low frequency), stimulation site (ipsilesional mylohyoid cortex or contralesional mylohyoid cortex), and outcome measurement timing (immediately, 3 weeks, and 4 weeks after the rTMS session).

# **METHODS**

Participant or population: Patients with dysphagia symptoms after stroke.

Intervention: Repetitive transcranial magnetic stimulation.

**Comparator: Sham stimulation.** 

Study designs to be included: Randomized controlled trials were included.

Eligibility criteria: The inclusion criteria for this meta-analysis were as follows: (1) all patients with ischemic or hemorrhagic stroke with definitive evidence on magnetic resonance imaging or computed tomography; (2) all patients with dysphagia symptoms after stroke; (3) patients with no neurological diseases other than stroke or no other swallowing disorders; (4) the experimental group received rTMS, and the control group received sham stimulation; (5) the statistical combination of results are available for conducting meta-analysis (for being included for meta-analysis, a result measurement tool in each included study should have been used in two or more separated studies).

Information sources: The PubMed, SCOPUS, Embase, and Cochrane Library databases were systematically searched for relevant studies published between January 01, 1980, and December 13, 2021. The keywords used for the search were 'dysphag\*,' 'swallow\*,' 'deglutition,' 'pharyng\*,' 'oropharyng\*,' 'cerebral vascular accident,' 'stroke,' 'brain infarction,' 'brain hemorrhage,' 'cerebrovascular,' 'CVA,' 'hemiplegic,' 'hemiplegia,' 'transcranial magnetic stimulation,' 'non-invasive brain stimulation,' 'neurostimulation.'

Main outcome(s): The effect according to the follow-up period after rTMS was confirmed with the following evaluation tool; Penetration-Aspiration Scale, Standardized Swallowing Assessment.

# Quality assessment / Risk of bias analysis:

The methodological qualities of the studies included in this meta-analysis were evaluated using the Cochrane Collaboration Handbook. Adequate sequence generation, blinding, incomplete outcome data, allocation concealment, selective outcome reporting, and other potential sources of bias were determined. Risk of bias was evaluated based on the domains of the Cochrane Handbook 5.1 Assessment Tool. Studies were divided into

the following categories based on the bias levels: low risk, high risk, or unclear risk.

Author 5 - Min Cheol Chang. Email: wheel633@gmail.com

Strategy of data synthesis: After eliminating duplicate publications, two independent reviewers (YJC and MCC) evaluated potentially eligible studies to be included in the meta-analysis. Articles were screened for eligibility based on their titles and abstracts, and any disagreement was resolved by consensus. After primary screening, the two reviewers (YJC and MCC) independently scrutinized the full text of the eligible articles. Subsequently, data including the first author's name, year of publication, sample size, demographic data, protocol for rTMS treatment, and outcome measures (mean values and standard deviations), were independently extracted from each eligible article. In cases where data were only available in graph form and we were unable to obtain the original datasets from the corresponding authors, the data were extracted directly from the graphs. In addition, if some data were missing from the published articles, the corresponding authors of the original studies were contacted for the required information.

Subgroup analysis: Not applicable.

Sensitivity analysis: The studies were excluded one by one, and then the metaanalysis was performed in the remaining studies.

Language: English.

Country(ies) involved: Republic of Korea.

Keywords: Repetitive transcranial magnetic stimulation; Dysphagia; Stroke; Metaanalysis.

### Contributions of each author:

Author 1 - Ming-Yen Hsiao. Email: myferrant@gmail.com Author 2 - Yoo Jin Choo. Email: cyj361@hanmail.net Author 3 - I-Chun Liu.

Email: jacy50521@gmail.com

Author 4 - Boudier-Revéret Mathieu.

Email: mathieu.boudier-reveret@umontreal.ca