ORIGINAL ARTICLE

Repetitive Transcranial Magnetic Stimulation Protocols for Swallowing Rehabilitation in Unilateral Hemispheric Stroke: A Scoping Review

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ABSTRACT

Background. Stroke is a significant health concern globally, and dysphagia has been a very common complication. Early intervention for managing dysphagia is challenging with a lack of universally accepted treatment protocols. Non-invasive repetitive transcranial magnetic stimulation (rTMS) is emerging as a treatment option for stroke dysphagia. However, there is no standardized rTMS treatment protocol for it, leading to challenges in clinical decision-making.

Objective. To determine available rTMS protocols for unilateral hemispheric stroke dysphagia.

Methods. A scoping review using PubMed, ProQuest, and EBSCOHost databases was conducted using the keywords "dysphagia," "stroke," "repetitive transcranial magnetic stimulation," "conventional therapy," and "swallowing examination." Eligible studies published from inception to April 2020 were appraised using the Oxford Centre for Evidence-Based Medicine and analyzed qualitatively.

Results. Out of 42 articles, five randomized controlled trials met the eligibility criteria. A total of 108 patients with stroke and oropharyngeal dysphagia were randomized into one of the following treatment groups: (1) rTMS (unilateral or bilateral); (2) conventional dysphagia therapy (CDT); and (3) combined intervention (CI) of rTMS and CDT. The CI gave significant improvements in swallowing function and quality of life compared to CDT alone. The bilateral rTMS protocol resulted in more significant improvements than unilateral rTMS.

Conclusion. There are various and heterogeneous treatment protocols involving neuromodulation available for stroke dysphagia. The combination of bilateral excitatory-inhibitory rTMS and CDT seems to result in an optimal outcome for swallowing function among patients with unilateral hemispheric stroke dysphagia.

Keywords: dysphagia, conventional swallowing therapy, transcranial magnetic stimulation, neuromodulation, stroke

** Dr. Leochico and Dr. Biben shared first authorship for this manuscript.*

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INTRODUCTION

According to the National Institute of Neurological Disorders and Stroke (NINDS), stroke occurs when blood supply to the brain is suddenly interrupted due to a blockage or rupture of blood vessels.[1] The National Health Research showed an increase in the prevalence of stroke symptoms in Indonesia from 7.0% in 2013 to 10.9% in 2018.[2] Globally, there were approximately 13.7 million new stroke cases in 2016.[3] Among the various stroke complications, dysphagia is very common with prevalence ranging from 41 to 78% and can lead to serious outcomes like malnutrition, pneumonia, and dehydration.[4–8]

The neurophysiology behind dysphagia recovery after stroke is complex and incompletely understood.[9] Leveraging the process of neuroplasticity that begins shortly after ictus, treatments in the acute and subacute phases of stroke can be highly beneficial.[10] From a practical viewpoint, swallowing evaluation and rehabilitation instituted early post-stroke may help decrease the occurrence of dysphagia-related aspiration pneumonia and duration of hospital stay.[4,8,9]

However, challenges exist in the management of dysphagia especially after acute or subacute stroke. For instance, the lack of universally accepted treatment protocols particularly for subacute stroke dysphagia may be misleading for clinicians, especially those without adequate experience with the different treatment options available.[9] The bulk of relevant studies deals with chronic stroke dysphagia therapy.[11]

An emerging treatment option for stroke dysphagia is the use of non-invasive repetitive transcranial magnetic stimulation (rTMS) either as an adjunct or alternative to conventional dysphagia therapy (CDT), which typically consists of postural changes, altering food volume and speed of feeding, modifying food consistency and viscosity, improving sensory oral awareness, oropharyngeal muscle strengthening exercises, vocal cord exercises, tongue retraction exercises, and various swallowing maneuvers.[12–14]

Studies have indicated that rTMS can improve language, motor, and swallowing functions after stroke.[15] Using either inhibitory (1 Hz) or excitatory (3 Hz and 5 Hz) modes for the contralesional or ipsilesional side of the brain, respectively, rTMS can improve swallowing of patients in the acute, subacute, and chronic phases of stroke.[16–21] High-frequency magnetic stimulation of the ipsilateral hemisphere increases cortical excitability, whereas low-frequency stimulation of the contralesional hemisphere decreases cortical excitability, thereby reducing the inhibition effect from the contralateral hemisphere. Currently, there are no standardized rTMS treatment protocols for patients with dysphagia, especially for the subacute phase when neuroplasticity can be maximized.[10,11,22] Prior studies have employed different rTMS techniques (bilateral versus unilateral; inhibitory versus excitatory) and heterogenous outcome parameters, resulting in difficulties translating research findings into clinical applications.[9,11–14,17,20]

The extent of swallowing recovery post-stroke varies widely, depending on each patient's presentation, including dysphagia severity, presence of dysarthria, and risk of aspiration on videofluoroscopic and clinical swallowing evaluation.[23,24] Nonetheless, the majority of patients with uncomplicated stroke may return to normal swallowing in seven days.[23] On the other hand, patients may have persistent dysphagia and risk of serious complications, such as pneumonia and respiratory distress, with factors such as: advanced age (>70 years), absence of reflex cough after swallowing, chronic obstructive pulmonary disease, severely impaired consciousness, poor functional outcomes, and videofluoroscopic evidence of delayed oral transit, impaired swallowing reflex, and penetration of contrast into the laryngeal vestibule.[5,6,23,25,26] Given that the functional recovery post-stroke generally plateaus beyond 3-6 months,[27–30] it is hypothesized that rTMS may be best introduced during the subacute phase of stroke.

This study, therefore, aimed to review the literature and determine available rTMS protocols (either as a stand-alone therapy or an adjunct to conventional dysphagia therapy) for improving swallowing among patients with stroke. It also aimed to summarize the various treatment and outcome parameters (such as swallowing function and quality of life) used in the rTMS literature that could serve as a quick reference for healthcare providers and aid in their clinical decision-making.

METHODS

We conducted a scoping review to answer our research objective. Our study received an ethical review exemption from the St. Luke's Medical Center – Quezon City Institutional Ethics Review Committee (SL-24169). An online systematic search through PubMed, ProQuest, and EBSCOHost was performed using the keywords "*dysphagia,*" *"repetitive transcranial magnetic stimulation," "stroke," and "swallowing examination"* to include publications from inception until April 2020. The exact search strategies used are presented in Table 1.

The titles and abstracts of the identified articles were then screened for duplicates, relevance to the study objective, and availability of full text. Only randomized controlled trials written in English were included. The remaining articles were then subjected to the following inclusion criteria: (1) Population: adult patients diagnosed with unilateral hemispheric stroke (ischemic or hemorrhagic) by clinical and/or ancillary examinations (e.g., computed tomography, magnetic resonance imaging) and oropharyngeal dysphagia by clinical and/or ancillary examinations (e.g., videofluoroscopy, flexible endoscopic evaluation of swallowing) that lasted longer than two weeks after stroke onset (including subacute and chronic phases of stroke); (2) Intervention: rTMS; (3) Comparator: CDT; and (4) Outcomes: (a) treatment effectiveness based on clinical measures (e.g., functional outcomes of swallowing, quality of life related to swallowing,

Table 1. Search Strategies

Database	Search strategy	Hits	Selected
ProQuest	ab("repetitive transcranial magnetic stimulation" OR "rTMS" OR "bilateral rTMS") AND ab("exercise" OR "traditional dysphagia therapy" OR "conventional dysphagia therapy" OR "rehabilitation" OR "sham") AND ab("dysphagia" OR "swallowing dysfunction" OR "bilateral rTMS" OR "swallowing exercise" OR "swallowing disorder") AND ab("subacute stroke" OR "sub-acute stroke" OR "stroke" OR "cerebrovascular disease")	8	2
PubMed	("repetitive transcranial magnetic stimulation"[Title/Abstract] OR "rTMS"[Title/Abstract] OR "bilateral rTMS"[Title/Abstract]) AND ("exercise"[Title/Abstract] OR "traditional dysphagia therapy"[Title/Abstract] OR "conventional dysphagia therapy"[Title/Abstract] OR "rehabilitation"[Title/Abstract] OR "sham"[Title/Abstract]) AND ("dysphagia"[Title/Abstract] OR "swallowing dysfunction"[Title/Abstract] OR "swallowing disorder"[Title/Abstract]) AND ("subacute stroke"[Title/Abstract] OR "sub-acute stroke"[Title/Abstract] OR "stroke"[Title/Abstract] OR "cerebrovascular disease"[Title/Abstract])	37	3
EBSCOhost	(AB (repetitive transcranial magnetic stimulation) OR AB (rTMS) OR AB (bilateral rTMS)) AND (AB (exercise) OR AB (traditional dysphagia therapy) OR AB (conventional dysphagia therapy) OR AB (rehabilitation) OR AB (sham)) AND (AB (dysphagia) OR AB (swallowing dysfunction) OR AB (swallowing disorder)) AND (AB (subacute stroke) OR AB (sub-acute stroke) OR AB (stroke) OR AB (cerebrovascular disease))	1	0

diet scales, dysphagia symptom scales, or health outcomes related to swallowing) and/or ancillary examinations (e.g., videofluoroscopy, flexible endoscopic evaluation of swallowing), and (b) safety based on occurrences of adverse events. Studies involving dysphagia from causes other than stroke, such as head injury, cancer, or infection, were excluded. We also excluded studies without available full text.

Two authors then independently and critically appraised the full text of each eligible article using the 2011 Oxford Centre for Evidence-Based Medicine criteria,[31] while a third author was needed to achieve consensus for conflicting reviews. The following data were extracted from the included studies: lead author, publication year, sample size, treatment groups and protocols, outcomes of interest, assessment points, and pertinent results. Due to the heterogeneity of treatment methods and outcomes, a meta-analysis could not be performed.

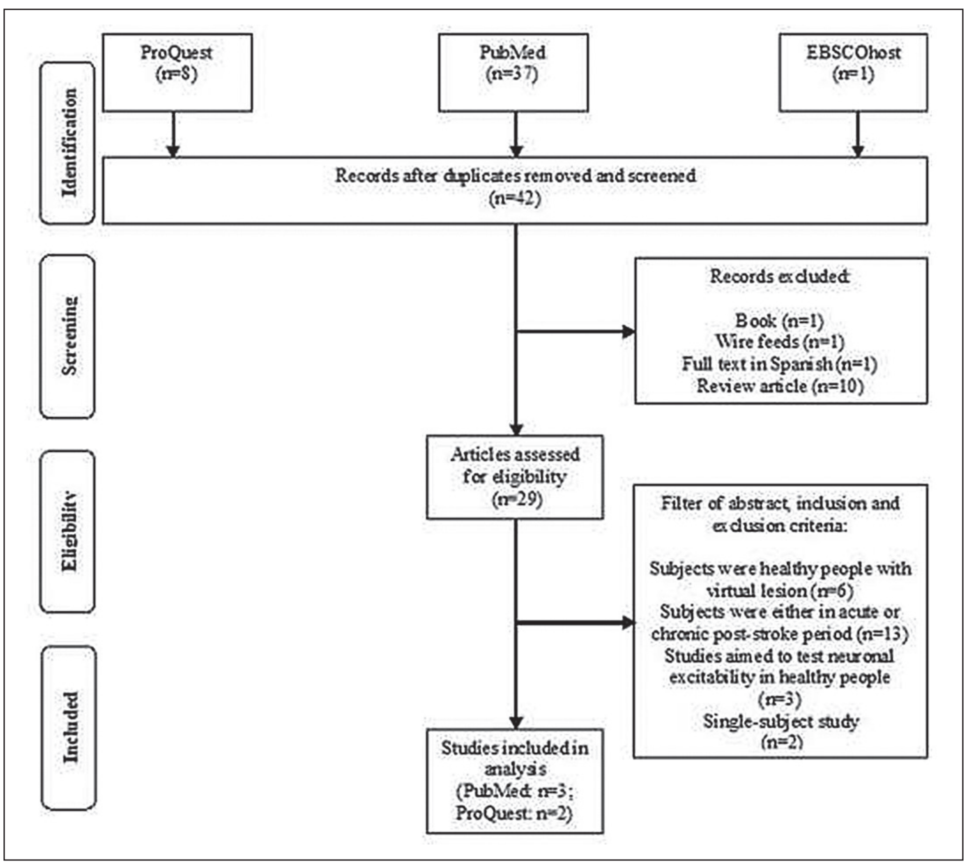

Figure 1. Flow search of studies.

Table 2. Critical Appraisal of Included Studies (n = 5) Based on the 2011 Oxford Center for Evidence-Based Medicine Criteria[22]

Authors	Validity							Appli-cability	Level of evidence
	Year	Study design	Randomized	Similarity	Equal treatment	Lost to follow-up (<20%)	Blinding		
Tarameshlu et al.[12]	2018	RCT	Yes	Yes	Yes	Yes	Yes	Yes	2
Ünlüer et al.[13]	2018	RCT	Yes	Yes	Yes	Yes	Yes	Yes	2
Park et al.[14]	2016	RCT	Yes	Yes	Yes	Yes	Yes	Yes	2
Park et al.[20]	2013	RCT	Yes	Yes	Yes	Yes	Yes	Yes	2
Khedr et al.[17]	2009	RCT	Yes	Yes	Yes	Yes	Yes	Yes	2

RESULTS

A total of 46 abstracts were retrieved from records. After duplicate removal and initial screening, 29 studies were further screened and their full text reviewed. Five studies met the eligibility criteria and were critically appraised. The search flow is depicted in Figure 1, and main characteristics and findings of included studies are presented in Table 2.

The studies were conducted from 2009 to 2019 and included a total of 108 patients. The patients were aged 66.46 ± 5.52 years, mostly females, and with a mean stroke duration of 3.55 ± 1.43 months. They included cases with unilateral hemispheric stroke, oropharyngeal dysphagia that lasted longer than two weeks after stroke onset, and no previous dysphagia rehabilitation. They excluded patients with other neurological diseases, severe aphasia, agitations, altered consciousness, history of seizures, and contra-indications to rTMS (e.g., metal objects in the skull or eye and implanted pacemakers). Two studies employed the inhibitory rTMS mode applied on the intact hemisphere,[12,13] one study employed the excitatory rTMS on the non-intact hemisphere,[17] and two studies employed the excitatory rTMS on both hemispheres.[14,20] The treatments ranged from 5-10 sessions of rTMS and 10-28 sessions of CDT over a period of 2-12 weeks.

The clinical dysphagia assessment tools used in the studies included one or more of the following: Mann Assessment of Swallowing Ability (MASA) (a 24-item tool to assess oropharyngeal dysphagia);[12] Functional Oral Intake Scale (FOIS) (a 7-point ordinal scale to document the functional level of oral intake of food and liquid);[12] Swallowing Ability and Function Evaluation (SAFE) (composed of three subscales to evaluate the oropharyngeal mechanism, and oral and pharyngeal phases of swallowing);[13] Clinical Dysphagia Scale (CDS) (an 8-item tool to predict the aspiration risk of patients and quantify the severity of dysphagia);[14,32] Dysphagia Outcome and Severity Scale (DOSS) (a 7-point scale to systematically rate the functional severity of dysphagia);[14,33] Dysphagia Degree (from grade I as no clinical signs and symptoms to grade IV as the severe form of dysphagia);[17] and nutritional status (classified either as oral feeding, modified oral feeding, non-oral feeding, or modified enteral feeding).[13] Certain videofluoroscopic swallowing study (VFSS) outcomes, such as the Penetration Aspiration Scale (PAS) and Videofluoroscopic Dysphagia Scale (VDS), were also used in some studies.[13,14,17] Lastly, the Swallowing Quality of Life (SWAL-QOL) questionnaire was used in one study.[13] Baseline severe dysphagia was reported among the patients with MASA score of 129.39 ± 6.48,[12] PAS of 6.27 ± 1.73,[13,14,20] and dysphagia degree of 3.65 ± 0.10.[17]

The combination of unilateral contralesional inhibitory rTMS and CDT provided more significant improvements in MASA and FOIS scores compared with either rTMS or CDT alone (Table 3).[12] Both the combined interventions (CI) (i.e., inhibitory rTMS and CDT) and CDT alone groups significantly improved SAFE and VFSS outcomes over time.[13] Meanwhile, the combination of unilateral contralesional excitatory rTMS and CDT provided significant improvements in PAS and VDS over time, but CDT alone did not result in any significant improvement.[20] Single-therapy rTMS did not give any significant difference compared to CDT in swallowing function based on MASA and FOIS scores.[12] The combination of bilateral excitatory rTMS and CDT yielded significant improvements in swallowing function across various outcome measures (i.e., Dysphagia Degree, CDS, DOSS, PAS, and VDS) compared with combined unilateral rTMS and CDT.[14,17] Patients who received the combined unilateral inhibitory rTMS and CDT had a significantly better quality of life parameters (i.e., fear of eating, eating desire, mental health) than those who received CDT alone.[13]

DISCUSSION

The brain is a dynamic structure that is influenced by external factors. The ability of the brain to adapt to changes in its environment or as a result of injury is known as plasticity. The term "neuroplasticity" describes the brain's capacity to adapt its functioning capabilities to different settings. To maximize neuronal resources for functional recovery in the event of a stroke, this may involve modulating neural activation within the remaining network of motor regions.[34]

There are two types of brain plasticity: adaptive and maladaptive. Each type of plasticity is strongly related to the other. Adaptive plasticity in stroke refers to plastic alterations that enhance recovery of an implicated function, whereas maladaptive plasticity occurs when plasticity prevents the recovery from an injury or results in the emergence of

Table 3. Clinically Relevant Data from Included Studies (n = 5)

Lead author of article; characteristics of participants	Treatment group and parameters	Control group/s	Results
Tarameshlu et al.[12] - 18 patients (13: cortical stroke; 5: subcortical); 50% females; range of mean age across groups: 55—75 years; range of mean duration post-stroke: 3—5 months	CI (n=6): rTMS + CDT for 5 consecutive sessions Inhibitory rTMS applied on the intact cerebral hemisphere to the mylohyoid hot spot area: 1200 pulses at 1 Hz, stimulus strength at 120% of RMT for 20 minutes	• CDT alone (n=6): 18 sessions, 3 times a week • rTMS alone (n=6): 5 consecutive days	***MASA*** • The score improved over time in all groups (p<0.001). • Large effect sizes were found in all groups (p<0.001): CDT (d =3.57), rTMS (d=2.67), and CI (d=3.87). • The severity of dysphagia improved over time in all groups (p<0.05) and differed significantly between groups (p=0.03). • The severity of aspiration improved over time in all groups (p<0.05) but did not significantly differ between groups (p=1.0). ***FOIS*** • The median FOIS score improved over time in all groups (p<0.05). • The score was different between groups after treatment in favor of the CI group (p<0.01).
Ünlüer et al.[13] - 28 patients; 43% females; range of mean age across groups: 67—69 years; range of mean duration post-stroke: 101—105 days	CI (n=15): rTMS + CDT for 5 consecutive sessions Inhibitory rTMS applied on the intact cerebral hemisphere to the mylohyoid hot spot area: 1200 pulses at 1 Hz, stimulus strength at 90% of RMT for 20 minutes	• CDT: 3 times a week of in-person therapy for 4 weeks, followed by 2 times a week of home exercise program for 2 months	***Nutritional Status*** • Oral feeding was accomplished by both groups during the 3rd month post-treatment (p=0.999). No differences between groups (p>0.05). ***SAFE*** • The score improved in both groups from baseline to 1 month until 3 months after treatment. No differences between groups at each evaluation time (p>0.05). ***VFSS*** • PAS with liquid and semisolid decreased beginning from post-treatment to 1 month in both groups (p<0.05). No differences were found between groups (p>0.05). • Tongue retraction, swallowing reflex, hyolaryngeal elevation, and residue significantly improved over time (p<0.05), but there were no differences between both groups (p>0.05). ***SWAL-QOL*** • Significantly higher quality of life parameters in CI group than CDT group: fear of eating (p=0.012), eating desire (p=0.006), and mental health (p=0.007).
Park et al.[14] - 33 patients; 30% females; aged 65.9 ± 12.4 years; range of mean duration post-stroke: 4—7 weeks	CDT + bilateral rTMS (n=11) 2 weeks of active rTMS stimulation + CDT at 5 consecutive sessions per week Stimulatory bilateral rTMS to the mylohyoid hot spot area: 500 pulses at 10 Hz rTMS, stimulus strength at 100% of RMT for 10 minutes	• CDT + unilateral ipsilesional rTMS (n=11) 2 weeks of stimulatory rTMS combined with 30 minutes of CDT each day • CDT + sham rTMS (n=11) 2 weeks of sham rTMS combined with 30 minutes of CDT each day	• In the bilateral and unilateral rTMS groups, all CDS, DOSS, PAS, and VDS scores improved over time (p<0.05). • The change in CDS score from immediately post-rTMS treatment to weeks 2 and 3 post-rTMS was significantly higher in the bilateral rTMS group than the other two groups (p<0.05). • There were significantly higher changes in the DOSS, PAS, and VDS scores from immediately post-rTMS to week 2 post-rTMS in the bilateral stimulation group than in the other two groups (p<0.05).
Park et al.[20] - 18 patients; 44.4% females; aged 71.3 ± 7.3 years	rTMS + CDT (n=9) 2 weeks of rTMS stimulation + CDT at 5 consecutive sessions per week Stimulatory rTMS to the intact cerebral hemisphere to the pharyngeal hot spot area: 500 pulses at 5 Hz, stimulus strength at 90% of RMT for 10 minutes	• CDT + sham rTMS stimulation (n=9) 2 weeks of sham rTMS stimulation CDT regimen not described	***VDS*** • VDS significantly improved after treatment (p<0.05) for the rTMS + CDT group. ***PAS*** • PAS significantly improved after treatment (p<0.05) for the rTMS + CDT group.
Khedr et al.[17] - 11 patients with lateral medullary infarct; 100% males; range of mean age across groups: 56—58 years; range of mean duration post-stroke: 5—6 weeks	Active bilateral rTMS + CDT (n=6) 5 consecutive sessions of active bilateral rTMS targeted at oesophageal cortical area, 100 pulses at 3 Hz, 10 trains at 3 Hz stimulus strength at 130% of RMT for 10 minutes	• CDT + sham bilateral rTMS stimulation for 5 consecutive sessions (n=5) CDT regimen not described	Bilateral rTMS produced significantly greater improvements over time in swallowing function (Dysphagia Degree) than sham (p<0.001).

CI: combined intervention; rTMS: repetitive transcranial magnetic stimulation; CDT: conventional dysphagia therapy; RMT: resting motor threshold; MASA: Mann assessment of swallowing ability; FOIS: functional oral intake scale; SAFE: swallowing ability and function evaluation; VFSS: video fluoroscopic swallowing study; PAS: penetration aspiration scale; SWAL-QOL: swallowing quality of life; DOSS: 24 dysphagia outcome and severity scale; VDS: videofluoroscopic dysphagia scale.

an undesirable symptom or disordered function. Cortical excitability modification could promote synaptic plasticity and/or prevent potential post-stroke maladaptive processes.[35]

The motor regions of both hemispheres of a healthy brain have functionally connected neural activity that is evenly balanced in terms of mutual inhibitory control.[36] Better motor performance could result from reducing the effect of brain regions that negatively alter the physiological network architecture and normalizing cortical processing in the afflicted hemisphere. An imbalance of interhemispheric inhibition is the electrophysiological correlate of a maladaptive neuronal activity pattern following stroke.

Transcallosal inhibitory circuit equilibrium between the motor regions in both hemispheres may be impacted by stroke. These stroke-induced alterations are thought to be one factor in the frequent observation that, after ischemia, brain activity is frequently increased in motor regions of the unaffected hemisphere. Additionally, it has been noted that movements of the affected site are linked to a pathological suppression of M1 in the affected hemisphere coming from homologous cortical regions in the unaffected hemisphere. Beyond the loss brought on by injury to corticospinal fibres, such increased inhibition of motor regions in the lesioned hemisphere may also compromise the motor function of the affected side. The degree of the affected functional impairment is positively linked with the amount of transcallosal inhibition that the unaffected hemisphere exerts on the affected hemisphere. Decoupled inhibitory interactions between the motor areas may impede motor recovery and worsen motor function of the affected side following stroke, according to the theory of interhemispheric competition.[37,38]

Furthermore, it has been noted that movements of the affected site are linked to a pathological suppression of M1 in the affected hemisphere coming from homologous cortical regions in the unaffected hemisphere. According to the theory of interhemispheric competition, it has been proposed that externally induced inhibition of M1 in the unaffected (contralesional) hemisphere or facilitation of excitability in M1 in the affected (ipsilesional) hemisphere normalizes the balance of transcallosal inhibition between both hemispheres, leading to improved motor function.

All five studies included in this review showed that the CI of rTMS and CDT showed superiority over CDT alone in providing significant improvements to patients with subacute unilateral hemispheric stroke dysphagia.[12–14,17,20] In particular, two studies showed that CI consisting of excitatory bilateral rTMS provided more significant improvements than CI consisting of unilateral rTMS.[14,17] The advantage of bilateral rTMS could be explained by the fact that control of swallowing comes from bilateral brain hemispheres.[39,40] Therefore, the remaining intact ipsilateral neurons and the contralateral intact hemisphere could be optimized to overcome dysphagia. By applying excitatory bilateral rTMS, this natural process of recovery could be hastened.[17]

The finding that the CI group gave the most considerable improvement might be clarified by looking at CDT as a behavioural swallowing therapy, which could improve relevant strength, endurance, sensory thresholds, timing, tone, and coordination.[41,42] A previous study showed that after a 2-month exercise treatment for dysphagia, CDT showed significant swallowing improvements over time.[43] However, bedside dysphagia exercises seem to only significantly improve the oral, and not the pharyngeal, phase of swallowing. As a possible reason, the pharyngeal phase could be considered partly involuntary so that direct stimulation to the brain through rTMS could be considered more effective than exercise treatment.[43] Furthermore, a study showed that rTMS as a single therapy did not give any significant difference in swallowing function compared to CDT.[12] Consequently, both CDT and rTMS augment each other's potential in improving swallowing function. Previous reviews also showed that CI gave positive effects on swallowing function and quality of life for patients with subacute or chronic stroke dysphagia.[44,45]

Comparison of Different Swallowing Rehabilitation Protocols Involving rTMS

Currently, there are no standardized protocols used for rTMS in patients with dysphagia.[10,11,22] Even though the combination of rTMS and CDT seems to provide the most optimal outcome, the specific rTMS protocol to be applied in the CI remains underinvestigated.

The mechanism of motor impairment and recovery after stroke has been thought to be based on the interhemispheric competition model. Increasing the excitability of the contralesional homotopic area and disinhibiting nearby ipsilesional cortical areas are the two methods used to restore swallowing.[38,46] Inhibition from the contralesional hemisphere, which is thought to be overactive after stroke, can be limited by stimulating the injured hemisphere to restore output from the lesioned side. Suppressing the excitability of the contralesional hemisphere will enhance recovery by reducing transcallosal inhibition (TCI) of the affected hemisphere.

Cortical excitability can be modified using contemporary neurophysiological, non-invasive brain stimulation techniques like rTMS. Cortical excitability can be increased (facilitation) or decreased (inhibition) depending on the stimulation settings, which may lead to plastic changes in the network of sensorimotor areas of the cortex. The idea of interhemispheric competition is mostly used when applying brain stimulation after stroke.[38]

Protocol 1: Unilateral excitatory rTMS targeting the ipsilesional hemisphere

Unilateral excitatory rTMS that targets the ipsilesional hemisphere improves swallowing function by reorganizing the remaining intact ipsilateral neurons (Figure 2).[17,21] Khedr et al.[18] utilized excitatory 3-Hz rTMS to the ipsilesional hemisphere, resulting in brain excitability improvement in 1 and 2 months after treatment, and recovery from oropharyngeal dysphagia. On the other hand, Park et al.[14] reported no significant improvement to the unilateral ipsilesional stimulation group compared to the sham stimulation group. Such conflicting results could be explained by the difficulty in finding a "hot spot" in the ipsilesional hemisphere since the corticobulbar tract might be disunited. Therefore, targeting the contralesional hemisphere seems to be more accessible.[18]

Protocol 2: Unilateral inhibitory rTMS targeting the contralesional hemisphere

Unilateral inhibitory rTMS targeting the intact cerebral hemisphere showed that swallowing function increased over time, and the improvement was significantly larger in the CI group.[12] A single-subject study from Ghelichi et al.,[47] who used the same rTMS utilization protocol, also showed improvement in the MASA score over time. Unilateral inhibitory rTMS targeting the contralesional intact hemisphere provided improvement in swallowing by decreasing transcallosal inhibition from the intact cerebral hemisphere to the damaged one (Figure 3).[21] On the other hand, Ünlüer et al.[13] who used inhibitory rTMS that targeted the intact hemisphere revealed that CI did not give any significant difference in swallowing function when CI was compared to CDT. However, the rTMS group provided more significant improvements in quality-of-life parameters. Oral feeding achieved by the patient at the end of the treatment and the patient's dietary route change could contribute to the improved quality of life. Moreover, it was presumed that CI gave a more positive improvement in the quality of life through placebo effect since many patients preferred to have

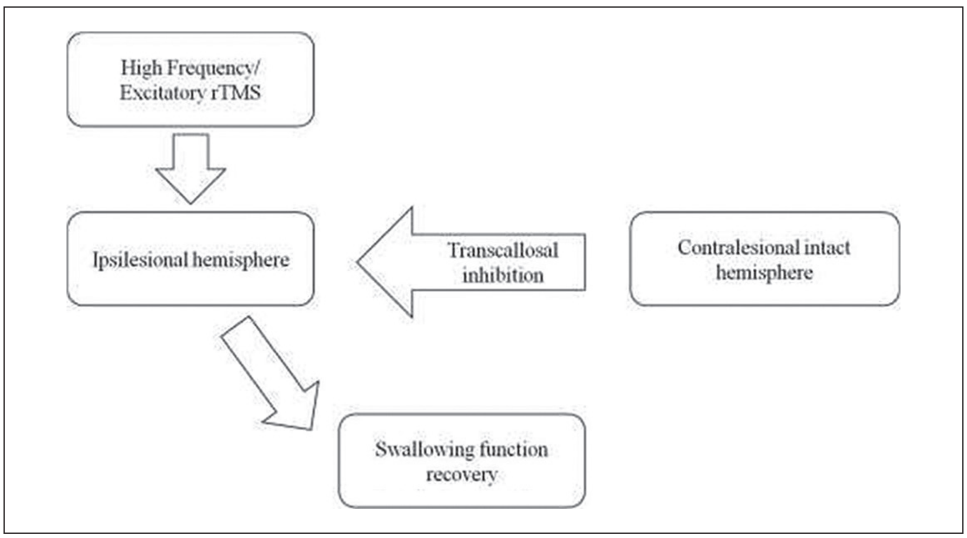

Figure 2. Unilateral excitatory rTMS and swallowing function recovery mechanism.

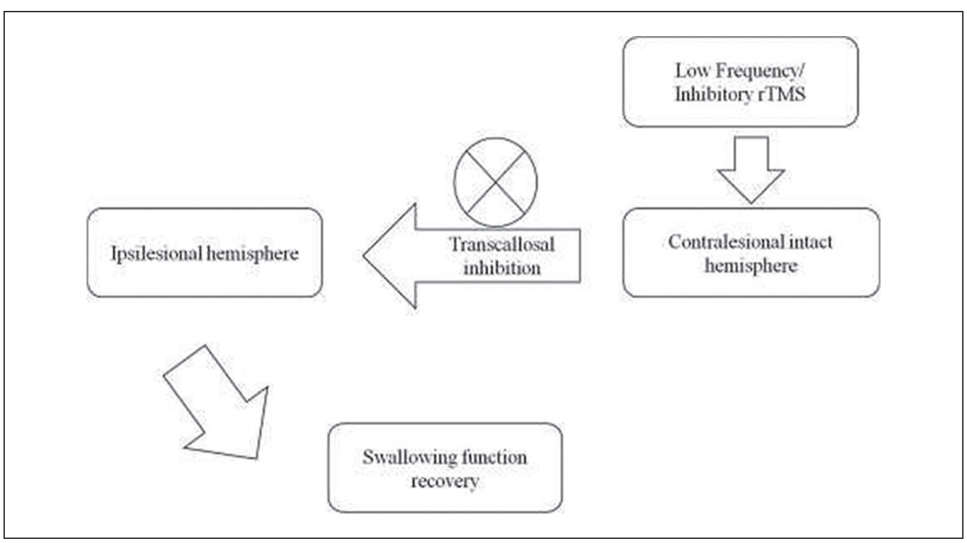

Figure 3. Unilateral inhibitory rTMS and swallowing function recovery mechanism.

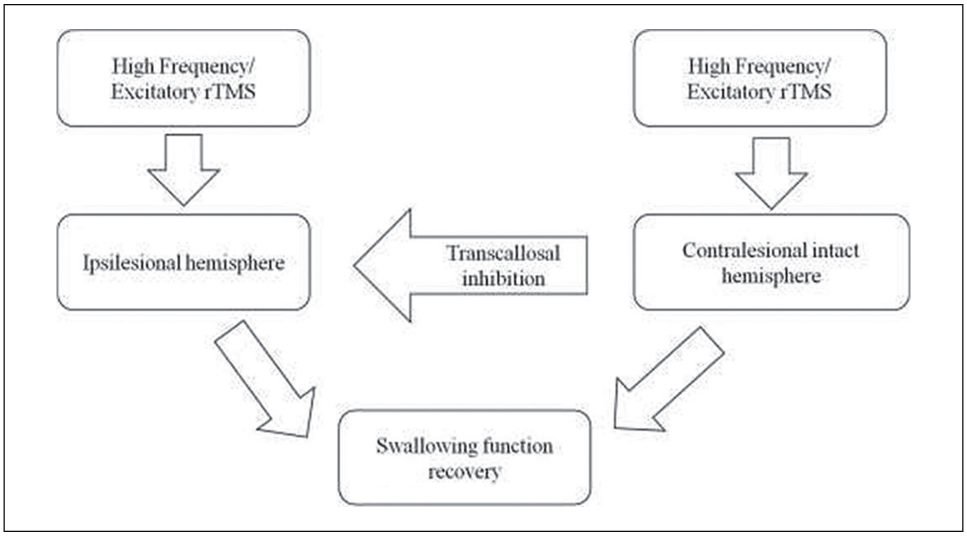

Figure 4. Bilateral excitatory rTMS and swallowing function recovery mechanism.

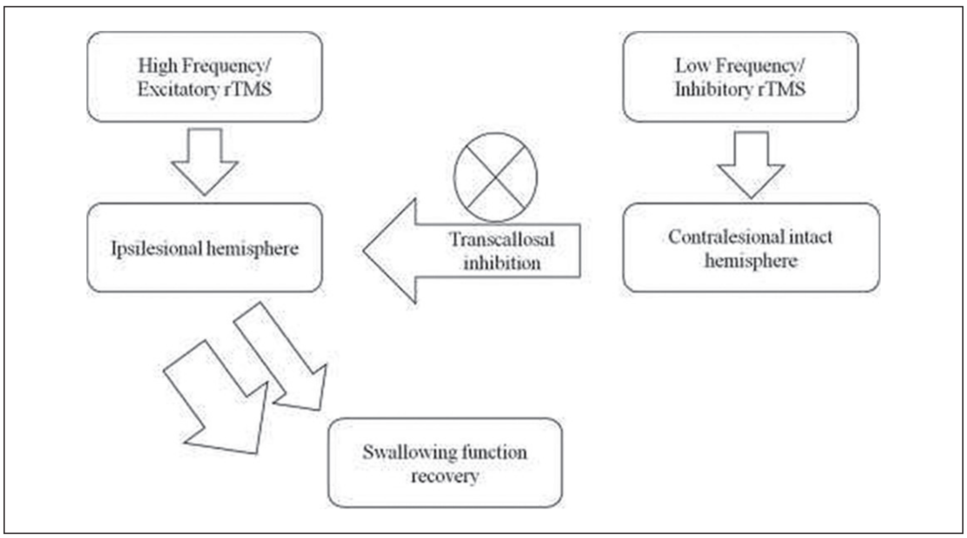

Figure 5. Bilateral excitatory-inhibitory rTMS and swallowing function recovery mechanism.

rTMS over exercise.[13] The positive effect in quality of life conferred by CI could also be explained by the theory that rTMS stimulus deployment to the prefrontal cortex during rTMS application would affect mood and motivation.[48]

Protocol 3: Bilateral excitatory rTMS

The combination of bilateral excitatory rTMS and CDT was superior to either CI (CDT and unilateral rTMS) or sham stimulation in providing more significant swallowing improvements.[12] Khedr et al.,[17] who used 3-Hz excitatory rTMS targeting both the ipsilateral and contralesional cerebral hemispheres, produced significantly greater improvements in swallowing function over time, as determined by the dysphagia degree. Because of the bilateral control of swallowing function, the remaining intact ipsilateral neurons and the contralateral intact hemisphere could eventually function again, complement each other, and overcome dysphagia. This natural process of reorganization could be hastened through excitatory bilateral rTMS.[17] Park et al.,[20] who used excitatory rTMS targeting the contralesional cerebral hemisphere, also found that CI significantly increased swallowing function over time, while CDT as a single therapy did not significantly increase swallowing function. However, the transcallosal inhibition process from the contralesional intact hemisphere to the ipsilesional damaged hemisphere could still exist and impede ipsilesional neuronal recovery (Figure 4).[21]

Protocol 4: Bilateral excitatory-inhibitory rTMS

Bilateral rTMS using excitatory stimulation to the ipsilesional hemisphere and inhibitory stimulation to the contralesional hemisphere seems to provide an optimal improvement in swallowing function through the mechanism of reorganization of the remaining intact neurons in the ipsilesional hemisphere and elimination of the transcallosal inhibition process (from the contralesional intact hemisphere to the ipsilesional damaged hemisphere) (Figure 5). This mechanism could be most appropriate for subacute unilateral hemispheric stroke dysphagia, wherein the effort of restoring swallowing function through speeding up the natural process of neuronal restoration could be maximized before stroke dysphagia could become chronic (i.e., past 6 months).[27–30]

Safety aspect

Only one study reported one complaint of dizziness and one complaint of nose bleeding.[13] There were no other complaints of adverse events from the rest of the patients in the included studies.

CONCLUSION

In conclusion, this scoping review provided an overview of the different available treatment protocols involving rTMS for post-stroke dysphagia. It seems that the combination of rTMS and CDT is safe and beneficial for swallowing function and quality of life among patients with subacute and chronic stroke. Bilateral rTMS could provide more significant improvements than unilateral rTMS. The combination of CDT and bilateral excitatory-inhibitory rTMS (compared to bilateral excitatory rTMS) may offer more optimal outcomes of swallowing function.

This study is novel because no prior study has reviewed the various rTMS utilization techniques in stroke dysphagia. Nonetheless, the study was limited by the following: lack of grey literature inclusion; relatively low number of studies analyzed; and the heterogeneity of the treatment protocols or methodologies of the included studies. In addition, the lack of risk of bias assessment was inherently a limitation of this scoping review. Proper systematic reviews with meta-analyses are recommended in the future when there are more studies with adequately homogeneous populations, interventions, and outcomes to arrive at meaningful and sound summaries.

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