Critical Review:

Is repetitive transcranial magnetic stimulation (rTMS) effective at reducing penetration and aspiration in stroke-induced dysphagia that persists beyond one month post-stroke?*

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This critical review examines the efficacy of repetitive transcranial magnetic stimulation (rTMS) in reducing penetration and aspiration in stroke-induced dysphagia that persists beyond one-month post-stroke. Five articles were included in this review. Study designs included 2 within-group studies and 3 randomized control trials. Overall, the results of this review provide suggestive evidence that rTMS is effective at reducing penetration and aspiration in individuals with dysphagia that persists beyond one-month post-stroke, given that more than one application of rTMS is provided. Recommendations for clinical practice and future research are discussed.

Introduction

An estimated 37 to 78% of adults experience dysphagia after a stroke (Martino, et al., 2005). Although many of these individuals recover their swallowing function, others experience dysphagia that is persistent with long-term consequences, such as an increased risk of malnutrition, dehydration and aspiration (Michou, Mistry, Jefferson, Tyrrell & Hamdy, 2014).

Increasing evidence suggests that repetitive transcranial magnetic stimulation (rTMS) can be an effective treatment to improve swallowing function in individuals with stroke-induced dysphagia. It has been suggested that rTMS can improve swallowing function in two ways: (a) increasing neural activity with high frequency stimulation or (b) decreasing neural activity with low frequency stimulation. Respectively, high frequency rTMS is thought to improve hemispheric reorganization in the unaffected hemisphere to improve swallowing function (Park, Oh, Lee, Yeo & Ryu, 2013). Alternatively, low frequency rTMS is thought to decrease transcallosal inhibition by reducing neural activity in the unaffected hemisphere and, as a result, increasing neural activity in the affected hemisphere (Verin & Leroi, 2009).

rTMS is a desirable treatment method for improving post-stroke dysphagia. First, rTMS is a low-risk, non-invasive intervention method that can be performed safely on adults at risk of aspiration (Cheng et al., 2014). Second, it is painless and requires little exertion from the client, which makes it suitable for a client who fatigues rapidly. Third, as a further benefit, rTMS does not require high functioning cognitive or language skills (Cheng et al., 2014), which suggests that rTMS is also suitable for individuals who experience post-stroke aphasia alongside their dysphagia.

It is important to look at the efficacy of rTMS at reducing penetration and aspiration in adults with dysphagia for more than one month post-stroke to reduce the influence of spontaneous recovery of swallowing function, which is greatest immediately post-stroke (Park et al., 2013).

Objectives

The primary objective of this review is to evaluate current literature regarding the efficacy of repetitive transcranial magnetic stimulation (rTMS) at reducing penetration and aspiration in stroke-induced dysphagia that persists beyond one month post-stroke. The secondary objective of this paper is to make suggestions regarding clinical implications and future research.

Methods

Search Strategy

A computer database search was conducted to find the articles included in this review. PubMed, CINAHL, Medline, Embase, and Scholars Portal were searched using the following key words:

> ((repetitive transcranial magnetic stimulation) OR (rTMS)) AND ((stroke) OR (cerebrovascular accident)) AND ((dysphagia) OR (deglutition disorder) OR (swallowing)).

Reference lists were also manually searched for articles that met inclusion criteria.

**This paper was created as a required assignment for the CSD9639 Evidence Based Practice for Clinicians course at Western. While it has been evaluated by course instructors for elements of accuracy and style, it has not undergone formal peer-review.*

Selection Criteria

Studies selected for inclusion were required to address the effectiveness of rTMS in stroke-induced dysphagia. Studies were limited to those that addressed penetration and aspiration, and included only participants a minimum of one month post-stroke. Research designs or measurements were not restricted.

Data Collection

The literature search generated 5 articles that met the selection criteria. Two within group studies and three randomized control studies were included.

Results

Within-Group Studies

Momosaki, Abo, and Kakua (2014) studied the effects of high-frequency bilateral rTMS when combined with an intensive swallowing program. The study included four adults aged 56 to 80 years who had been experiencing post-stroke dysphagia for 24 to 37 months. All participants received 10 sessions of rTMS over six consecutive days, followed by 20 minutes of swallowing rehabilitation exercises. The following evaluation methods were used before and after intervention: Modified Barium Swallow (MBS), Penetration-Aspiration Scale (PAS), laryngeal elevation delay time (LEDT), the Modified Mann Assessment of Swallowing Ability (MMASA) and the Repetitive Saliva-Swallowing Test (RSST). For the purposes of this review, results indicated that penetration and aspiration often diminished following ten treatment sessions of rTMS, as indicated by reduced scores on the penetration-aspiration scale for three out of four participants upon visual inspection.

Acknowledged limitations include the study design and heterogeneity of the participants. The study lacked a control group and blinding for all measures, which made it difficult to draw empirical conclusions about the efficacy of rTMS. Additionally, the small sample size limited knowledge about the generalizability of rTMS, and because a statistical analysis was not complete, the significance of the data is unclear. For the purpose of this review, one should also consider that study participants completed swallowing rehabilitation exercises in addition to rTMS therapy. As a result, it is difficult to determine the distinct role of rTMS in the participants' recovery. Despite these limitations, this study demonstrated some areas of strength. Momosaki et al. (2014) used numerous measures that were valid and reliable, and described their methods thoroughly to allow for easy replication. Participant eligibility was specified. Overall, the study by Momosaki et al. (2014) provided equivocal evidence that rTMS is effective at reducing penetration and aspiration in stroke-induced dysphagia that persists beyond one month post-stroke.

Verin & Leroi (2009) examined the efficacy and practicality of low-frequency rTMS on seven adults aged 46 to 76 with chronic, post-stroke dysphagia following a hemispheric or sub-hemispheric stroke. All participants received five 25-minute sessions of rTMS over five consecutive days. Evaluation methods included the dysphagia handicap index and videofluoroscopic swallowing studies prior to and three weeks post intervention. Of relevance to this review are the results indicating that penetration and aspiration scores statistically decreased for liquids following rTMS intervention ($p < .05$).

Verin and Leroi's (2009) study lacked a control group, which limited the strength of the evidence and made it difficult to draw empirical conclusions. Additionally, the statistical analysis was questionable. Given the small sample size, use of a repeated measures ANOVA may not have been appropriate. Instead, non-parametric tests might have been more suitable. The small sample size also limited generalizability. Strengths of the study included a thorough description of participant eligibility and the methods employed. Blinding was used in analysis of the videofluoroscopic swallowing studies, which strengthened the evidence. Overall, the study by Verin & Leroi (2009) provided suggestive evidence that rTMS is effective at reducing penetration and aspiration for liquids, but not pastes, in adults with chronic, post-stroke dysphagia.

Randomized Control Trials

Cheng, Chan, Wong, and Cheung (2014) examined the effectiveness of high frequency rTMS on 4 adults aged 67 to 76 years with chronic, stroke-induced dysphagia. Participants were randomly assigned to receive either 10 sessions of active rTMS or 10 sessions of sham stimulation ($n = 2$). Each session lasted thirty minutes and was conducted over two weeks. Post-study, sham participants also underwent 10 sessions of active stimulation, which created a crossover study. The following evaluation methods were used at baseline, 1 week post-intervention and 1 month post-intervention: the Iowa Oral Performance Instrument (IOPI), the Swallowing Activity and Participation Profile (SAPP) and a videofluoroscopic swallowing study (VFSS), which was used to calculate the Oropharyngeal Swallow Efficiency (OPSE) score. OPSE is a measurement of swallowing safety/efficiency, and included in the OPSE formula is a measurement of percent aspirated bolus (Mittal et al., 2003). Because authors reported changes in terms of OPSE scores, rather than penetration-aspiration scores or percent bolus aspirated, results should be interpreted

cautiously in terms of this review, as it is difficult to determine the role of reduced aspiration in the improved OPSE scores.

Acknowledged limitations included a small sample size, which restricted the ability to draw conclusions about the generalizability of rTMS, and the lack of a sham coil during sham rTMS. Instead of a sham coil, researchers unplugged the active coil, which did not act as an appropriate control as it lacked many features associated with an active rTMS coil (i.e. a clicking noise and some perception on the client's scalp). It should also be noted that the researchers were not blinded, which limited the strength of the evidence. Strengths of the study included randomization, and blinding of the participants of group assignments. Methods were described clearly with sufficient detail and measures were reliable. Participant eligibility was specified. Overall, the study by Cheng et al. (2014) provided equivocal evidence that rTMS is effective at reducing penetration and aspiration in stroke-induced dysphagia that persists beyond one month post-stroke, particularly given the lack of reported data about the role of penetration/aspiration in the improved OPSE score.

Michou, Mistry, Jefferson, Tyrrell, and Hamdy (2014) studied the effects of high frequency rTMS, pharyngeal electrical stimulation (PES) and paired associated stimulation (PAS) on 18 adults aged 31 to 83 years with dysphagia for a minimum of six weeks post-stroke. Evaluation methods included measurements of bolus transfer time and penetration-aspiration scores following videofluoroscopic swallowing studies, which were conducted at baseline, post active intervention, and post sham intervention. Relevant to this review are the six participants that received a single application of both real and sham rTMS. Results of the statistical analysis showed no statistically significant difference in penetration-aspiration scores between the real and sham applications of rTMS, which suggested that a single application of rTMS did not significantly improve penetration and aspiration.

Acknowledged limitations included participants with various dysphagia severities, which might have affected outcomes more favorably for certain individuals, and the "wash-out period" between active and sham rTMS applications, which implies that active rTMS sessions might have had carryover results in post-sham data analysis. Data relevant to this review also lacked a control group and no measures of inter or intra-rater reliability were reported, all of which limit the strength of the evidence. The small sample of individuals who received rTMS intervention also limited the ability to generalize the data. Despite these limitations, the study demonstrated several areas of strength. Michou et al. (2014) used both randomization and blinding. Statistical analysis was appropriate as the authors employed a pairwise comparison (Wilcoxon test) and non-parametric correlations, both of which were corrected with Holms' step-down technique, to determine the statistical significance of the penetration-aspiration scores. Overall, the study by Michou et al. (2014) provided suggestive data that rTMS is not effective at improving penetration and aspiration in persistent stroke-induced dysphagia when only one application of rTMS is provided.

Park, Oh, Lee, Yeo, and Ryu (2013) researched the effects of high-frequency rTMS on post-stroke dysphagia using a double-blind randomized control trial. The study included 18 adults aged 69 to 80 years with dysphagia for at least one month following a unilateral hemispheric stroke. Participants were randomly divided into two groups with the experimental group receiving active rTMS and the control group receiving sham rTMS. Ten sessions were conducted over two weeks, lasting approximately 10 minutes each. Both groups participated in a videofluoroscopic swallowing study at baseline, at the end of treatment, and two weeks post-treatment. Evaluation methods included the videofluoroscopic dysphagia scale (VDS) and the penetration-aspiration scale (PAS). Results of a Wilcoxon signed rank task indicated that penetration and aspiration significantly diminished in the group that received active rTMS intervention ($p < .05$). Notably, this significance was maintained two weeks post-intervention.

The authors acknowledged some limitations of their study, including that is difficult to determine the role of spontaneous recovery in participants who are as little as one-month post-stroke and that the study had a moderately small sample size, which made it difficult to generalize the information. Despite using randomization, the experimental and control groups presented significantly different at baseline VDS measures. Given that the control group had less severe dysphagia than the experimental group, it limited the strength of the data as the control group had a reduced opportunity for swallowing improvement. Inter- and intra-rater reliability were also not reported. The study, however, did demonstrate many strengths. The authors ensured that the study was double-blind and methods were described clearly and thoroughly for duplication. Randomization was employed and an appropriate control group was included. Participant eligibility was also specified. Overall, this study provided suggestive evidence that rTMS is effective at reducing penetration and aspiration in unilateral hemispheric stroke-induced dysphagia that persists beyond one month post stroke.

Discussion

Current literature provides suggestive evidence that rTMS is effective at reducing penetration and aspiration in stroke-induced dysphagia that persists beyond one month post-stroke when more than one application of rTMS is applied.

Despite optimistic findings across all studies with more than one application of rTMS, data must be interpreted cautiously as it is difficult to generalize the data given the small sample sizes. The strength of the evidence is also limited in certain studies given the lack blinding, randomization and/or a control group.

Furthermore, the articles were notably different in terms of the parameters used for rTMS application. Certain researchers employed low-frequency rTMS (Verin & Leroi, 2009) while others used high-frequency rTMS (Cheng et al., 2014; Michou et al., 2014; Park et al., 2013; Momosaki et al., 2014). Even within the high-frequency rTMS experiments, frequencies ranged between 3 and 5Hz. Studies also varied in terms of the number of rTMS applications, the number of applications per day, the intervals of pulses and the areas of stimulation. While Cheng et al. (2014) chose to stimulate the tongue motor cortex, other researchers chose to stimulate muscles of the pharynx (Park et al., 2013; Michou et al., 2014; Momosaki et al., 2014) or the mylohyoid muscle specifically (Verin & Leroi, 2009). Consequently, it is unclear what methods or frequencies are most appropriate or offer the best results.

Lastly, long-term outcomes of rTMS intervention on the reduction of penetration and aspiration in post-stroke dysphagia remain unclear. At most, results were measured at one-month post-rTMS (Cheng et al., 2014). Despite positive findings, the long-term effectiveness of rTMS intervention at reducing penetration and aspiration beyond one month post-intervention is unknown for this population.

Clinical Implications and Recommendations

Based on suggestive evidence from the studies reviewed, rTMS has the potential to reduce penetration and aspiration in adults experiencing post-stroke dysphagia more than one month post-stroke.

While rTMS does appear to be clinically effective, further research is warranted. Further research should continue the use of randomized control trials that provide stronger levels of evidence, while incorporating larger sample sizes to increase the confidence of clinical implementation. Possible directions of future research include an investigation of parameters that optimize swallowing outcomes, such as the optimal frequency of stimulation, site of stimulation, lesion site, impairment levels or time between stroke-onset and intervention. Further information should also be obtained about the long-term outcomes of rTMS on the reduction of penetration and aspiration in post-stroke dysphagia.

References

Cheng, I., Chan, K. M., Wong, C. S., & Cheung, R. (2014). Preliminary evidence of the effects of high-frequency repetitive transcranial magnetic stimulation (rTMS) on swallowing functions in post-stroke individuals with chronic dysphagia. *International Journal of Language & Communication Disorders, 00*(0), 1-8.

Martino, R., Foley, N., Bhogal, S., Diamant, N., Speechley, M., & Teasell, R. (2005). Dysphagia after stroke: Incidence, diagnosis, and pulmonary complications. *Stroke*, *36*, 2756-2763.

Michou, E., Mistry, S., Jefferson, S., Tyrrell, P., & Hamdy, S. (2014). Characterizing the mechanisms of central and peripheral forms of neurostimulation in chronic dysphagic stroke patients. *Brain Stimulation*, *7*, 66-73.

Mittal, B. B., Paulosji, B. R., Haraf, D. J., Pelzer, H. J., Argiris, A., Vokes, E. E., … Logemann, J. A. (2003). Swallowing dysfunction – preventative and rehabilitation strategies in patients with head-and-neck cancers treated with surgery, radiotherapy, and chemotherapy: A critical review. *International Journal of Radiation Oncology, Biology, Physics*, *57*(5), 1219-1230.

Momosaki, R., Abo, M., & Kakuda, W. (2014). Bilateral repetitive transcranial magnetic stimulation combined with intensive swallowing rehabilitation for chronic stroke dysphagia: A case series study. *Case Reports in Neurology*, *6*, 60-67.

Park, J. W., Oh, J. C., Lee, J. W., Yeo, J. S. & Ryu, K. H. (2013). The effect of 5Hz high-frequency rTMS over contralesional pharyngeal motor cortex in post-stroke oropharyngeal dysphagia: A randomized controlled study. *Neurogastroenterology & Motility*, *25*(4), 324-e250.

Verin, E., & Leroi, A. M. (2009). Poststroke dysphagia rehabilitation by repetitive transcranial magnetic

stimulation: A noncontrolled pilot study. *Dysphagia, 24*, 204-210.