

## Critical Review:

### Do Non-Invasive Brain Stimulation Techniques Improve Swallowing Function Post-Stroke?

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This critical review examines the recent literature regarding the use of non-invasive brain stimulation techniques (NIBS) on improving swallowing function post stroke. The main techniques under review are transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS). The studies evaluated include two double blind randomized control studies, one single blind randomized control study, and one double blind randomized control pilot study. Overall, research findings suggest that non-invasive brain stimulation techniques are feasible, patient tolerable, and effective at mediating the effects of post-stroke dysphagia when applied to the motor cortex on both the ipsilateral and contralateral hemisphere, post stroke. Clinical implications and future use and recommendations are discussed.

#### ***Introduction:***

Dysphagia refers to a swallowing disorder that can occur at any stage of the swallowing process (ASHA, 2013). The leading cause of dysphagia in the elderly population is due to stroke (Castell, 1995), and can result in airway obstruction, pulmonary problems, malnutrition and dehydration, weight loss, and death due to aspiration pneumonia (Ashford, Logemann, & McCullough, 2013). Given that dysphagia can affect as many as 50% of patients post stroke, and dispute regarding the use of traditional swallowing techniques to support swallowing improvement in the elderly “frail” population (Mistry, 2012) (Shaker, 2011), a more effective treatment method is required. According to a Mayo Clinic Study, more than 60% of patients residing in long-term care facilities present with some form of dysphagia (Shaker MD, 2011). Traditional swallowing techniques often lead to fatigue, and many treatment techniques cannot be implemented do to the issue of patient exhaustion. Recent research into the use of non-invasive brain stimulation techniques (both rTMS and tDCS) for aphasia has shown promising results (Doeltgen et al. 2012). These techniques have recently been extended to the treatment of dysphagia revealing similar positive outcomes as demonstrated by evidence based swallowing outcome measures (Verin, 2008) (Jefferson, 2009) (Shigematsu MD, 2013)

(Khedr, Abo-Elftoh, 2009) (Park, 2012). rTMS and tDCS have proven effective in facilitating the motor movement responsible for swallowing, potentially reducing the morbidity due to pulmonary aspiration and malnutrition. Therefore, given its low cost, effectiveness, non-invasive and non-strenuous nature, these finding could potentially lead to rTMS and tDCS becoming the preferred standard of care for treating dysphagia.

#### ***Objectives:***

The primary objective of this critical review is to evaluate the recent literature regarding the effectiveness of non-invasive brain stimulation techniques on post stroke dysphagia, evaluate the clinical implications, and provide recommendations for future research and clinical application.

#### ***Methods:***

##### *Search Strategy:*

A number of computerized databases were searched including PubMed, Scholars Portal, CINAHL, MEDLINE, PsychINFO, and EMedicine using the following terms:

(Non-Invasive brain stimulation) OR  
(tDCS) OR (rTMS) AND (Dysphagia)  
OR/AND (Stroke)

### Selection Criteria:

The articles selected for inclusion in this critical review were limited to those who administered either tDCS or rTMS on post-stroke patients with a randomized control group. There were no limits placed on the patient demographics, or the outcome measures used by the researchers.

### Data Collection:

The search results that included all relevant search criteria yielded a pool of 4 articles, of which (2) double blind randomized control studies, (1) single blind randomized control study, and (1) single blind randomized pilot study were chosen for this review.

### **Results:**

#### Double blind randomized control study:

A double blind randomized control study is considered the gold standard in medical research when investigating the effects of an intervention. (Center for Evidence Based Medicine, 2012). In this design, the patient and the researcher are both unaware of whether participants are in the treatment or control group.

A study conducted by Park, et al. (2013) used a double blind randomized control design to study the effects of high frequency rTMS over the contralesional hemisphere in post stroke dysphagia. Eighteen patients presenting with unilateral hemispheric stroke oropharyngeal dysphagia lasting more than one month were included in the study. Swallowing measures were obtained for all participants using videofluoroscopic dysphagia scale (VDS) and the penetration aspiration scale (PAS) before rTMS treatment and two weeks post treatment.

Appropriate group comparisons were performed with a Mann-Whitney U-test, and the chi-squared test was used to test unbalancing between groups. To compare the outcome scores, a Wilcoxon signed rank test was performed to compare PAS and VDS scores before and after treatment of each group. Significance level was set at  $P < 0.05$ .

The baseline scores of VDS of the treatment group were  $33.6 \pm 12.1$ , and  $3.41 \pm 2.32$  for PAS. Two weeks after treatment, scores were reduced to  $25.3 \pm 9.8$ , and  $1.93 \pm 1.52$

respectively. There were no changes observed in the control group. Following treatment, aspiration and pharyngeal residue were reduced by 33.4%.

Results indicate that 5Hz rTMS on the contralesional pharyngeal cortex can increase the speed of recovery during the chronic stage of dysphagia. The treatment produced significant changes in swallowing outcomes, and significantly reduced the instance of aspiration and pharyngeal residue in post stroke patients.

The evidence presented is valuable due to the appropriateness of study design and statistical analysis performed on the data. However, there are a number of factors that limit the strength of evidence. The researchers chose patients 1 month post-stroke to eliminate spontaneous recovery; However, Groher, M.E. (1997) suggests that most patients spontaneously recover/improve from dysphagia anywhere between a few days to months. And so, one cannot conclude that one month post-stroke is a sufficient timeline to rule out natural recovery. While the Park et al. did apply appropriate statistical analysis for nonparametric variables, the small sample size (18), does present a limitation for generalizing results.

Shigematsu, et al. (2013) conducted a double blind randomized control study to explore whether the application of transcranial direct current stimulation (tDCS) to the cortical motor and sensory pharyngeal area, can improve swallowing function post-stroke when paired with traditional swallowing maneuvers. A total of 20 patients presenting with chronic severe dysphagia lasting at least 1 month post-stroke participated in the study.

Swallowing function was evaluated at baseline, immediately following treatment, and one month upon cessation of treatment, by blinded speech pathologists using the DOSS, videofluoroscopy (VF) and videoendoscopy (VE) during trial swallows. Patients were also evaluated for residue on the Penetration Aspiration Scale.

Participants were randomly assigned to either the tDCS treatment group or a sham tDCS control group and randomly assigned to different researchers who were blinded to patient background and group assignment. Electrodes

were placed over the ipsilesional hemisphere of both groups using the 10-20 EEG electrode system. The treatment group received direct stimulation once a day for 20 minutes using a 1-mA current. The control group received a sham tDCS.

To assess the effects of tDCS on swallowing function, a speech-language pathologist, blinded to subject allocation, assessed all DOSS scores obtained at baseline, pre-treatment, and post-treatment. Improvements in both groups were compared using the Mann-Whitney *U* test. This revealed statistically significant higher DOSS scores immediately following tDCS for the treatment group, but not for controls. Both groups showed high DOSS scores one month post treatment.

The researchers conclude that tDCS in combination with traditional swallowing techniques can increase and sustain swallowing function for at least 1 month post treatment.

The level of evidence provided by this study is quite high. The researchers have attempted to control for participant variables by limiting the inclusion criteria, and placed restraints on the time since stroke, to ensure that they were adequately testing tDCS treatment in the post-acute stage. This timeline was also chosen in an attempt to eliminate spontaneous/natural recovery. The stimulation sites were adequately mapped using a well-established system, and implemented evidence based swallowing therapy techniques in conjunction with tDCS.

Despite numerous strengths, this study also demonstrates some limitations. While the researchers did obtain post-acute stroke patients for their study, there was a wide variance in post stroke timeline. The inclusion criteria were only set at 1 month post-stroke, with no maxim post-stroke timeline implemented. Given that spontaneous recovery can happen anywhere from a few days to a few months (Groher, 2007), this may account for some of the observed outcomes. The small sample size (20) used for this study is another limitation in the generalizability of results.

#### Single blind randomized control study:

Single blind randomized control studies are often used in medical research. It is an

experimental comparison study in which the participants are randomly placed into a treatment group or a control/sham group. This type of study is best for examining the effect of an intervention and the randomization of participants facilitates the statistical analysis (Center for Evidence Based Medicine, 2012).

A study conducted by Khedr, et al. (2009), used a randomized control study design to look at the effects of rTMS on post-stroke dysphagia. Khedr et al. examined the effects of rTMS on dysphagia in the 5<sup>th</sup>-10<sup>th</sup> day post stroke in 26 adults (mean age 57.3 years). Participants were evenly randomized to a treatment group (rTMS) or control/sham group.

The treatment group received 5 daily 10-minute sessions of rTMS targeting the ipsilateral esophageal motor cortex, and the control group received rTMS stimulation, but at a 90 degree angle from the affected area.

Dysphagia was scored prior to treatment using the Dysphagia Outcome Severity Scale (DOSS), and the degree of dysphagia (DD) scale, and again mid and post treatment.

The cortex was mapped out using the 10-20 system to ensure the motor and premotor cortices were covered. The magnetoelectric stimulation was then placed on the ipsilesional hemisphere, and rTMS was applied for 10min/day, over a period of 5 consecutive days.

Clinical ratings from the DOSS, and DD, were made by a blinded assessor, whereas the values for esophageal MEPs, resting motor thresholds, as well as the rTMS sessions were performed by a non-blinded assessor. Follow-up was conducted on the fifth session and again 30 and 60 days post treatment.

An appropriate t-test showed no difference in dysphagia severity between groups at baseline. Appropriate repeated measures ANOVAs revealed improved swallowing function for the treatment group over controls immediately following treatment and at two months follow-up.

Results indicate that 5 daily sessions of rTMS placed over the esophageal motor cortex post-stroke can produce significant changes in swallowing outcomes immediately following treatment and these changes were maintained for at least two months upon cessation of treatment.

Khedr, et al. (2009) were comprehensive in detailing of inclusion criteria, outcome measures, treatment and sham conditions, and analysis procedures. Variance between participants was well controlled.

The researchers effectively gathered baseline data, with well-established and proven methods of measurement. The stimulation sites were adequately mapped using the international 10-20 system, which is well-established and universally accepted.

The evidence presented is of high quality due to the appropriateness of study design and statistical analysis performed on the data. The results suggest that rTMS placed over the ipsilateral esophageal motor cortex in the acute stage post stroke does in fact improve swallowing function.

#### *Single blind randomized pilot studies:*

Pilot studies are comparative randomized trials that are designed to provide preliminary evidence on the clinical efficacy of a treatment (Center for Evidence Based Medicine, 2012). They are commonly used to address the feasibility of a treatment, the recruitment of participants, and are considered the best way to assess the feasibility of a large, expensive full-scale study. Doing a pilot study prior to a full scale main study can enhance the likelihood of success of the main study (Thabane, et al., 2010)

Kumar et al. (2011) conducted a pilot study to assess whether tDCS applied to the unaffected hemisphere in combination with swallowing maneuvers would facilitate swallowing recovery in acute-stroke patients. Fourteen patients 24-168 hours post-stroke, with dysphagia secondary to unilateral hemispheric stroke, and a DOSS score of  $\leq 5$  were required for inclusion in the study. Lesion site was identified using diffusion weighted imaging sequences on each patient's MRI. Each patient was randomly assigned to the tDCS or sham group, and blind to their group allocation. During stimulation electrodes were placed using the 10-20 EEG electrode system over contralesional hemisphere and expected to create maximal current density over the sensorimotor cortex and premotor regions which are believed

to be responsible for the reorganization of swallow post-dysphagic stroke.

Swallowing function was evaluated by blinded speech pathologists using the DOSS and NIHSS immediately before stimulation, and the DOSS only following the fifth session. The tDCS of a 2 mA current was applied over 5 consecutive days in conjunction with swallowing maneuvers to activate both the motor and sensory cortex.

The effect of treatment vs. sham was analyzed using a multivariate linear regression model using the DOSS score as the outcome variable after adjusting for lesion volume, NIHSS score at baseline, time to stimulation, and age. After controlling for the above mentioned variables, Kumar et al. (2011) concluded that patients who received tDCS gained a total of 2.6 points in DOSS score, compared to the sham group who gained 1.25 points, with a P-value of 0.019. A total of 6/7 individuals in the treatment group gained at least 2 points on the DOSS, compared with 3/7 in the sham group (P = 0.0107). Therefore, Kumar et al. (2011) concluded that because brainstem swallowing centers have bilateral innervation, enhanced cortical sensory and motor input from the contralesional hemisphere may be beneficial for swallowing recovery.

The level of evidence provided by this pilot study is quite high. The researchers have attempted to control for confounding variables by limiting the inclusion criteria and using a multivariate linear regression model to control for participant variables and randomization of participants was used to control for predictors of dysphagia recovery. Stimulation sites were mapped out using a well-established and universally accepted placement system. Swallowing therapy techniques used in conjunction with tDCS were also well established evidence based swallowing therapy techniques. However, given this was a pilot study there are inherent limitations, mainly sample size. Kumar et al. (2011) attempted to control for predictors of dysphagia recovery such as NIHSS, lesion volume, and age, the randomization of such a small sample size may have failed to correct for these variables. This also affects the generalizations that can be made from this study. Furthermore, the researchers

only assessed each patients DOSS score after 5 days, using this as their outcome measure. It would have been beneficial to follow these patients into the post-acute or chronic stage to see if the swallowing improvements were maintained over time. That being said, these are inherent limitations of all pilot studies and are mainly meant to gain insight into the clinical efficacy of a treatment, and assess the feasibility of a large scale study.

This pilot study does speak to the tolerability of using tDCS in conjunction with swallowing manoeuvres with early (sub-acute) stroke patients, as well as the efficacy of tDCS when applied to the contralesional hemisphere, and the feasibility of participant recruitment. Given the success of this pilot study, a full scale research study should investigate the efficacy of tDCS with swallowing therapy and explore the frequency of stimulation, timing of intervention, and whether the effects of treatment are maintained over time.

#### ***Discussion:***

Overall, evidence from these studies provide sufficient indication that by altering the motor cortex excitability through the use of non-invasive brain stimulation techniques (NIBS), swallow function post stroke can be improved. However, there are several inherent limitations that should be addressed before NIBS therapy is used as a standard treatment for dysphagia.

#### ***Future research considerations:***

Further research should focus on consolidation of current evidence to develop the best standard of care for the use of NIBS therapy on individuals with post-stroke dysphagia. A strong focus on patient characteristics, and a larger sample size should be implemented to confirm the efficacy and generalization of NIBS treatment. To strengthen the level of evidence, future research of rTMS and tDCS on post-stroke dysphagia, should consider the following recommendations:

- a) In future, research should focus studies on understanding the clinical/patient factors that affect the outcome of NIBS therapy; some of which include patient age, stroke

type, stroke severity, and duration of stroke before treatment.

- b) The stimulus type, duration, intensity and pairing of traditional swallowing therapy should be explored in depth, to determine what paradigm would yield the best possible outcome. Further research should also look into pairing NIBS with other empirically tested neurorehabilitation techniques, and whether this promotes greater success.
- c) Researchers should focus on increasing the sample size to allow for more sound generalizations, and increase the confidence of clinical application.
- d) To assess the maintenance of NIBS treatment, future studies should continue outcome measures for at least 6 months post-stroke to ensure patients are out of the spontaneous recovery timeframe.

#### ***Clinical Implications:***

Given that the use of NIBS therapy for treating post stroke dysphagia is a rather new undertaking, the studies reviewed demonstrate promising results for future clinical use. While this review did not uncover the most effective way of using NIBS therapy, its low cost, non-invasive nature, and tolerability even in the acute stage of dysphagia are great motivators to continue research in this area. Each study has used NIBS in a slightly different manner, and given the diverse nature of cerebral vascular accidents, there will likely never be a uniform way of administering this therapy. While the evidence thus far have suggested that both types of NIBS therapy do in fact improve swallowing function, while simultaneously decreasing the likelihood of aspiration and pharyngeal residue, there is still a great deal of experimental research that needs to be done in this area before NIBS should be used as a standard treatment for dysphagia secondary to stroke.

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