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Transcranial direct current stimulation in post-stroke dysphagia: a systematic review of randomized controlled trials

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ABSTRACT

Introduction: The aim of this research was to systematically review all the randomized controlled trials that have evaluated the effect of transcranial direct current stimulation (tDCS) on post-stroke dysphagia.
Methods: Three electronic databases were searched for relevant articles that were uploaded from their inception to March 2015: PubMed, Cochrane Library (Cochrane Central Register of Controlled Trials), and Scopus. All data was that was related to the location of the cerebrovascular accident (CVA), the parameters of tDCS, post-stroke time to commencement of tDCS, the stimulated hemisphere, stimulation dose, any outcome measurements, and follow-up duration were extracted and assessed. Finally, a number of observations were generated through a qualitative synthesis of the extracted data.
Result: Three eligible randomized controlled trials were included in the systematic review. All three trials reported that, in comparison to a placebo, tDCS had a statistically significant effect on post-stroke dysphagia.
Discussion: The results of our systematic review suggest that tDCS may represent a promising novel treatment for post-stroke dysphagia. However, to date, little is known about the optimal parameters of tDCS for relieving post-stroke dysphagia. Further studies are warranted to refine this promising intervention by exploring the optimal parameters of tDCS.
Conclusion: Since brainstem swallowing centers have bilateral cortical innervations, measures that enhance cortical input and sensorimotor control of brainstem swallowing may facilitate recovery from dysphagia.

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Introduction

Dysphagia is a common consequence of damage to the nervous system. It can be caused by several conditions including traumatic brain injury (1,2), neurodegenerative conditions (3,4) or stroke (5,6). Stroke is a leading cause of dysphagia and more than 70 percent of stroke survivors experience dysphagia following a stroke as a result of a paralysis of the pharyngeal muscles. This condition can cause discomfort when swallowing and can result in difficulties with drinking, eating, and breathing (7). Dysphagia is often associated with several complications such as poor nutrition and hydration (8), choking, and aspiration pneumonia (9,10). Aspiration pneumonia increases both the

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mortality of the impacted patients and the likelihood that they will be hospitalized (11). In addition to resulting in potentially serious medical complications, dysphagia significantly impacts the quality of life of patients and caregivers (12-14). For this reason, early diagnosis and management of post-stroke dysphagia should be considered to represent a critical element in the clinical care provided to patients who are in the acute or subacute phase of stroke.

As a result of development in brain imaging and non-invasive brain stimulation techniques, researchers are increasingly recognizing the significant contribution that the primary motor cortex (M1) makes to swallowing function. For example, contralesional hemispheric reorganization is associated with the spontaneous recovery of the swallowing function following a stroke (15). Re-organization with increased pharyngeal representation in the non-dominant or weaker (unlesioned) hemisphere appears to be associated with the recovery of the swallowing function (16-18). Indeed, the swallowing motor network has been shown to be adaptable to both peripheral and cortical stimuli, and it exhibits remarkable plastic changes (19-21). Given the likely importance of primary motor networks in the control of swallowing, attention has turned to non-invasive brain stimulation (NBS) techniques as a means of painlessly modulating M1 excitability.

In recent years, several novel rehabilitation interventions, including noninvasive brain stimulation (NBS) with transcranial magnetic stimulation [TMS] (22,23) or transcranial direct current stimulation [tDCS] (24-26), have demonstrated promise in terms of their abilities to improve stroke-related disabilities such as motor dysfunction, aphasia, and dysphagia. Specifically, tDCS is a safe, portable, easy-to-use, and noninvasive brain stimulation technique that can be coupled with peripheral therapies (e.g., motor, language, swallowing) to potentially influence stroke recovery (26). Furthermore, tDCS has considerable advantages compared to other cortical neurostimulation-based treatments that have been trialed in the rehabilitation of dysphagia. Such advantages include portability, ease of use, low costs and a less invasive intervention that does not require pharyngeal intubation. These benefits make tDCS an attractive option for bedside delivery. In the current study, we aimed to systematically search existing literature related to the application of tDCS in stroke patients to identify and critically evaluate all the randomized controlled trials that have addressed the efficacy of tDCS in the recovery of post-stroke dysphagia.

Methods

The methodology outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement (PRISMA) was followed for the purposes of conducting this systematic review (www.prisma-statement.org).

Eligibility criteria

All randomized controlled trials evaluating the efficacy of tDCS as a neuromodulatory intervention to improve swallowing function in post-stroke dysphasia among patients with different types of strokes and stroke lesion sites were included. Meeting abstracts that were deemed to contain sufficient information were also taken into consideration.

Search strategy and study selection

Three electronic databases: PubMed, Cochrane Library (Cochrane Central Register of Controlled Trials), and Scopus were searched from their inception to March 2015 without language or any other limitations to identify studies that were potentially relevant to the research objectives of the current study. The following search criteria was employed: (stroke OR CVA OR cerebrovascular accident(AND (swallowing disorder OR dysphagia) AND (transcranial direct current stimulation OR tdcs OR transcranial electrical stimulation). Following the removal of duplicate results, the titles and abstracts of all remaining articles were screened. The full texts of all potentially eligible studies were then reviewed, and those that met the inclusion criteria were included in the analysis. The references of the included studies were also examined to ensure that all potentially relevant studies were included in the review. The entire study selection process was performed by two independent reviewers.

Data collection

The collected data was decoded using a predesigned data extraction sheet and the following information was extracted: the location of the cerebrovascular accident (CVA), the parameters of tDCS, post-stroke time to commencement of tDCS, the stimulated hemisphere, stimulation dose, any outcome measurements, and follow-up duration. Data extraction was performed by two independent reviewers, and any disagreement was discussed with a third reviewer until consensus was achieved. Finally, we reported the results by qualitative synthesis of the extracted data.

Results

Following the systematic search of the electronic data resources, 57 potentially relevant citations

were retrieved. After the removal of duplicate results and following a review of the titles and abstracts, four studies were considered for the full-text assessment. Following the review of the full texts, one study was excluded because it did not meet our inclusion criteria. Finally, three trials that all met the inclusion criteria were included in the systematic review. The PRISMA flowchart of the systematic review is shown in Figure 1.

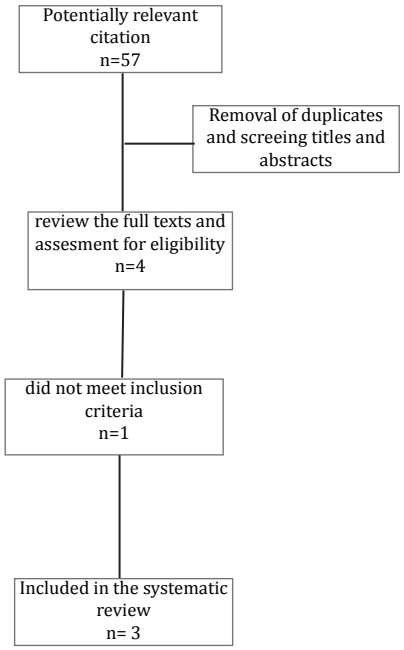

Figure 1. PRISMA flowchart

Study characteristics

All of the included controlled trials were published in peer-reviewed journals, and all evaluated the effect of anodal tDCS in comparison to a placebo in post-stroke dysphagia cases. One trial applied tDCS on the contra-lesional, lateral sensorimotor cortex (27), while the two other trials employed tDCS on the ipsi-lesional pharyngeal motor cortex (28,29). Table 1 presents an overview of the primary characteristics of each trail that was included in the current review.

Qualitative Data Synthesis

In the study by Kumar et al., 14 stroke patients within 1-7 days of unilateral hemispheric infarction (subacute) were randomized to receive anodal transcranial direct current stimulation (2 mA for 30 min) versus placebo stimulation to the unaffected hemisphere over five consecutive days with concurrent standardized swallowing maneuvers. The Dysphagia Outcome and Severity Scale (DOSS, scale range of 1-7) was assessed before and after treatment. tDCS, in conjunction with conventional swallowing exercises, improved clinically assessed swallowing function (27). An improvement in swallowing function was represented by a mean 2.6 point increase on the 7-point videofluoroscopy-based DOSS with six out of seven patients in the active group improving by at least two points. The placebo control group demonstrated a much smaller mean increase in DOSS score (1.25/7 points), with three out of seven patients improving by at least two points.

In the second trial (Yang et al.), 16 patients were randomized to either active anodal tDCS (n=9) or placebo treatment (n=7). The stimulation paradigm was 10 days of 1 mA anodal tDCS applied for 20 min over the ipsilesional hemisphere at the beginning of a 30 min conventional swallowing training session. The intervention group received anodal tDCS over the affected pharyngeal motor cortex and conventional swallowing training for

Table 1. Study characteristics of included trials.

Author Year Reference	CVA Location	Sample Size	Time Post-onset	tDCS Type	Stimulated Hemisphere	Stimulation Dose	Outcome
Kumar 2011 (27)	Unilateral hemispheric infarction	N = 14	24-168 hour	Anodal tDCS vs. sham	Contra-lesional, lateral sensorimotor cortex	2 mA for 30 min for 5 consecutive days	Improved DOSS scores
Yang 2012 (28)	Hemispheric lesion 8 right, 8 left	N = 16	Mean 25.2 days	Anodal tDCS vs. sham	Ipsi-lesional pharyngeal motor cortex	1 mA for 20 min for 10 days	Improved FDS score
Shigematsu 2013 (29)	13 supratentorial, 7 infratentorial 12 left, 8 right	N = 20	5-38 weeks (mean 12)	Anodal tDCS vs. sham	Ipsi-lesional pharyngeal motor cortex	1 mA over 20 min sessions for 10 days	Improved DOSS scores

CVA: Cerebrovascular accident; tDCS: transcranial direct current stimulation; DOSS:Dysphagia outcome and severity scale; FDS: Functional dysphagia scale.

the first 20 min of each session. The last 10 minutes of each session involved swallowing training alone. Treatment was comparable in the control group; however, the tDCS lasted only 30 seconds (28). The results of this study demonstrated an improvement in swallowing function as assessed by a videofluoroscopy-based assessment, the functional dysphagia scale (FDS), in both an active and placebo anodal tDCS group. There was no difference between groups immediately after the intervention period. However, the mean swallowing function scores improved significantly in the active tDCS group at the three-month post-intervention follow-up period. In two patients (one from each group), cerebral glucose metabolism was assessed using positron emission tomography. Immediately post-intervention, the patient that received active anodal tDCS showed increased metabolic activity in the postcentral gyrus of the unaffected hemisphere in comparison to the patient that received a placebo stimulation (28).

Finally, in the study by Shigematsu et al. (29), 20 chronic stroke patients (more than four weeks post-infarct) were randomized to either active anodal tDCS (n=10) or placebo treatment (n=10). The tDCS paradigm consisted of 20 min of anodal tDCS at 1 mA over ipsilesional pharyngeal motor cortex over a period of ten days. The intervention group received anodal tDCS over the affected pharyngeal motor cortex (with the cathode placed on the opposite hemisphere in the supraorbital region) and conventional swallowing therapy. Treatment was comparable between the tDCS group and the control group; however, the tDCS lasted only 40 seconds. DOSS was assessed pre and post intervention and at a 1-month follow-up point.

The average DOSS scores increased by 1.4/7 points immediately following the two-week intervention period and continued to increase to 2.8/7 points at the 1-month follow-up, with nine out of ten patients improving by at least two points at the 1-month follow-up stage. The patients that underwent the placebo stimulation improved to a lesser degree (0.5/7 and 1.2/7 points immediately and 1 month following intervention, respectively), with four out of ten patients improving by at least two points at the 1-month follow-up stage.

The results of these studies demonstrate that anodal tDCS paradigms applied over either the ipsilesional or contralesional hemisphere have the potential to improve swallowing function in patients with stroke after repeated tDCS sessions.

Discussion

To the best of our knowledge, this is the first systematic review that has evaluated the efficacy of tDCS in the treatment of stroke-related dysphagia. Three eligible randomized controlled trials were reviewed. The small number of available trials in this area and the fact that all of them have been conducted in the last four years indicates that evaluating the effect of tDCS on post-stroke dysphagia is a novel line of research in the medical literature. Nevertheless, the results of the current systematic review indicate that tDCS does have a beneficial effect on the recovery of swallowing function in post-stroke dysphagia. However, there is considerable heterogeneity among the reviewed trials in terms of the parameters of tDCS, post-stroke time to start stimulation, and the target site. That said, in general, the results provide preliminary evidence to support the role of tDCS in this regard. There is now a requirement to confirm these findings in larger and less heterogeneous trials.

The parameters of tDCS differed among the included trials in terms of either the intensity or site of stimulation (lesioned hemisphere (28,29) vs. contralesional hemisphere (27)). This highlights the heterogeneity of tDCS parameters employed in clinical studies to date and emphasizes the need to further explore the parameters of stimulation that optimally facilitate the recovery of swallowing function in a clinical population.

In terms of the site of stimulation, although a previous study established the basis of using anodal tDCS on unaffected hemispheres in dysphagic patients (30), activation of affected hemispheres can also be applicable. It is probable that the stimulation of affected hemispheres would increase the chance of stimulating over the infarct volume. However, since brainstem swallowing centers have bilateral innervations with little evidence for transcallosal inhibition (31), it could be hypothesized that stimulation of either hemisphere would produce an increase in pharyngeal excitability. Furthermore, stimulation of the uninvolved hemisphere is less likely to be affected by neuronal loss or tissue damage, and responses are more likely to be more uniform. Stimulating the non-lesioned hemisphere is also expected to be safer with respect to any potential seizure risk or tissue damage in the acute stroke phase.

The optimal dose for stimulating the pharyngeal motor cortex has not been established; a recent report suggests that doses higher than those used for stimulating the primary motor cortex are necessary to produce comparable responses from the swallowing cortex (32). Therefore, comparing the optimal sites of stimulation (affected or unaffected hemisphere) and optimal effective doses should be further addressed in future studies.

This review has some limitations. The main

limitation is the small number of trials that were included as well as their small sample sizes. Another limitation is the heterogeneity that can be observed between the trials in terms of the site of stimulation and tDCS parameters. This prevents the development of an accurate conclusion in this area.

Conclusion

On the basis of the results presented in our systematic review, tDCS could be considered to represent a promising novel treatment for post-stroke dysphagia. Further studies are warranted to refine this promising intervention by exploring the optimal parameters of tDCS in terms of stimulation intensity, frequency and duration, methods by which the beneficial and long-term effects of tDCS can be maximized, and to select patient populations that exhibit the optimal treatment effects in terms of lesion site, acuteness, age, or severity of dysphagia.

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Conflict of Interest

The authors declare no conflict of interest.

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