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'Non-invasive brain stimulation for the treatment of neurogenic dysarthria: A systematic review'.

Review Paper

Pasquale Balzan[a]; Catherine Tattersall[a]; Rebecca Palmer[b]

[a] Division of Human Communication Sciences, Health Sciences School, University of Sheffield, 362 Mushroom Lane, Sheffield S10 2TS, United Kingdom

[b] School of Health and Related Research, University of Sheffield; 30 Regent Street, Sheffield City Centre, Sheffield S1 4DA, United Kingdom

Corresponding author e-mail: pbalzan1@sheffield.ac.uk

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Abstract

Background: Although non-invasive central and peripheral stimulation are accruing support as promising treatments in different neurological conditions, their effects on dysarthria have not been systematically investigated. The purpose of this review was to examine the evidence-base of non-invasive stimulation for treating dysarthria, identify which stimulation parameters have the most potential for treatment and determine safety risks.

Method: A systematic review with meta-analysis, when possible, was carried out using the Guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses. Publications indexed in MEDLINE, PsychINFO, EMBASE CINHAL the Linguistics and Language Behavioral Abstracts, Web of Science, Cochrane Register of Control Trials and two trial registries were searched in December 2018 and updated in June 2021 using keywords related to brain and electrical stimulation, dysarthria and research design. Trials with randomised, cross-over or quasi-experimental designs, involving a control group and investigating treatment of neurogenic dysarthria with non-invasive stimulation were included. Methodological quality was determined using the Cochrane's Risk of Bias-2 tool.

Findings: In total, 6186 studies were identified, of which ten studies (six RCTs and four cross-over studies) fulfilled the inclusion criteria. All ten trials focused on brain stimulation (6 rTMS; 3 tDCS; and 1 rtACS). 268 adult participants, comprising Parkinson's disease, stroke and neurodegenerative cerebellar ataxia populations, were included. Adjunct speech-language therapy was delivered in two trials. Most trials reported one or more positive effects of stimulation on dysarthria-related abilities, however, given the overall high risk of bias and heterogeneity in participant, trial and outcome measurement characteristics, no conclusions can be drawn. Post-treatment size effects for two stroke trials demonstrated no statistically significant differences between active and sham stimulation across three dysarthria outcomes.

Conclusion: Evidence for use of NIBS in the treatment of dysarthria remains inconclusive. Research trials that provide reliable and replicable findings are required.

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Introduction

Dysarthria is an umbrella term for a group of motor speech disorders arising from neuromuscular disorders that cause disruptions in respiration, phonation, resonance, articulation and prosody [1]. Frequent causes of acquired dysarthria include cerebrovascular accident (CVA), traumatic brain injury, Parkinson's disease (PD), motor neuron disease and multiple sclerosis. Estimates of the incidence of dysarthria after the first ever ischemic CVA range between 25% and 42% [2]. Similarly, the presence of the disorder in traumatic brain injury and PD is approximately 30% and 50% to 90% respectively [3-5]. The limited literature on dysarthria treatment coupled with its high incidence and the potential to cause chronic and radical changes in daily living warrant the development of novel treatment methods to promote and facilitate rehabilitation outcomes.

Neurostimulation involves the voluntary modulation of neural circuits of particular anatomical regions, both centrally and peripherally, using invasive and non-invasive stimulation methods [6]. Non-invasive brain (central) stimulation (NIBS) targets the excitability of brain regions via the delivery of constant direct currents through electrodes or induction of electrical currents via Faraday's law and can provide several beneficial outcomes at a neuroprotective and rehabilitative level, such as, improving functions of non-affected cortical structures and modulating cortical excitability [7,8]. On the contrary, peripheral electrical stimulation, mainly neuromuscular electrical stimulation (NMES), involves the application of electrical signals through surface electrodes to induce contractions of targeted muscles [9, 10].

Although the therapeutic effectiveness of non-invasive stimulation across diverse trialsal diseases still needs to be fully elucidated by large-scale high-quality randomised controlled trials (RCTs), numerous studies suggest that NIBS, such as, transcranial magnetic

stimulation (TMS) and transcranial direct current stimulation (tDCS), hold therapeutic potential and can treat symptoms associated with neurological conditions, such as PD, tinnitus, epilepsy, aphasia and upper limb functions following CVA [11-13]. A recent systematic review has evidenced that TMS in the CVA population can improve motor functions without major adverse effects [14]. Several studies have demonstrated variable motor gains in the acute, sub-acute and chronic stages of CVA utilising both activating and inhibiting rTMS procedures with and without traditional therapy [15-17]. For instance, findings by Avenanti et al suggest that coupling physical therapy with inhibitory rTMS can modulate motor excitability and promote use-dependent plasticity to treat mild motor impairment [15]. Regarding NMES, a systematic review by Hankey et al found that when compared to no treatment, significant improvements were noted on several aspects of motor functioning after stroke following NMES treatment [18].

In keeping with the wider neurorehabilitation literature, mounting interest in the use of non-invasive stimulation to treat communication and swallowing disorders secondary to several neurological conditions has been observed [19, 20]. Accrued interest has been primarily observed in the fields of aphasia and dysphagia, with dysarthria and apraxia receiving less attention. Understanding the benefits of central and peripheral non-invasive stimulation across different dysarthria subtypes and clinical populations is the first stage to establishing whether these methods hold potential to improve treatment and care for individuals with the condition. The only relevant recently published systematic review by Mitchell et al reviewed treatment for dysarthria more broadly but focused only on non-progressive diseases [21].

As Duffy argues, the same medical aetiology can give rise to different types of dysarthria and hence, a myriad of speech disturbances [1]. For instance, a single hemispheric or brainstem CVA can result in spastic, ataxic, flaccid, hyperkinetic or mixed dysarthria. Similarly, heterogeneity of dysarthria types is also observed in other medical conditions, such

as, neurodegenerative diseases, traumas and tumours. As a result, broadening systematic searches to include all aetiologies for which dysarthria can result is essential to effectively capture all studies that have been carried out in the field and to indicate areas for further research.

The primary aim of this review was to examine the current evidence base of non-invasive central and peripheral stimulation for improving speech-related functions in persons with dysarthria and to determine the effects of an intervention, when possible. This review also aimed to describe the non-invasive stimulation parameters that have been used in the treatment of dysarthria, identify which stimulation characteristics have the most potential for treatment effect and determine potential adverse effects which may arise during or post-stimulation.

Methods

The PRISMA guidelines were followed for the completion of the review [22]. The protocol for this systematic review was submitted and published on PROSPERO under registration number CRD42019119830. Ethics committee approval was not required for this study as it used anonymised data and no primary data collection was carried out.

Literature Search

The following databases were searched twice in December 2018 and June 2021: MEDLINE, PsychINFO, EMBASE CINHAL the Linguistics and Language Behavioral Abstracts, Web of Science and the Cochrane Register of Control Trials (e.g. of search terms available in Appendix S1). Searches on the WHO ICTRP and ClinicalTrials.govtrial registries, and reference lists of studies included in the review were also carried out. No language or publication period restrictions were applied.

Eligibility Criteria for Including Studies

Titles, abstracts and full-text studies were assessed for eligibility based on the following inclusion criteria: (1) included children or adults with developmental or acquired dysarthria; (2) dysarthria was neurogenic in origin; (3) employed randomised control, cross-over or quasi-experimental designs; (4) intervention involved non-invasive stimulation therapies with or without traditional therapy approaches; (6) included a control intervention group and (7) outcome measures evaluated dysarthria on an impairment, activity and participation domain of the International Classification of Functioning, Disability and Health (ICF) [23].

Data Screening and Analysis

One author (PB) carried out the searches and collated all results in EndNote™. Duplicate records were then removed, and the abstracts of all remaining studies were screened against the inclusion criteria. For quality control purposes and to ensure that the inclusion criteria were applied consistently, another author (CT) blindly reviewed 15% of the total number of retrieved abstracts. An arithmetic sequence

Full text articles were then retrieved for abstracts meeting inclusion. Studies published in languages other than English were translated by a native speaker of the source language. Authors PB and CT screened the full text reports independently and author RP resolved disagreements between PB and CT. Relevant data from included studies were extracted using an assessment form developed at protocol stage (see Appendix S2).

A narrative synthesis using thematic analysis was used to analyse, integrate, and summarise the findings of all included studies. For comparable studies that included sufficient information to estimate effect size, a meta-analysis was carried out. Meta-analysis was carried out with the meta-package of R software (v4.0). Given the low statistical heterogeneity and small sample size, a fixed-effect model framework using the Inverse variance-weighted average method was used. We compared post-treatment values of active vs. sham activation,

thus preserving randomisation. Pooled mean difference (MD) along with their 95% Confidence Intervals (95% CIs) were derived and the standardized mean difference (SMD) was used to compare different outcomes. When multiple parameters from the same outcome and same study were analysed (e.g., for the AMR outcome in CVA), the sample size of each comparison was divided by the number of comparisons to avoid double counting of patients. Heterogeneity was assessed visually by means of forest plots and with the I-square statistic (with a prespecified 40% criterion for flagging high heterogeneity). Ideally, difference in changes from pre-to-post treatment between active and sham groups should have been analysed, however, suitable data was lacking. Papers did not report SDs or 95% Cis for the changes and p-values were not utilisable because they were related to non-parametric tests.

Methodological Quality

The risk of bias in RCTs and cross-over trials was assessed using the Cochrane's Risk of Bias-2 tool (ROB-2) [24]. The guidelines presented in the Cochrane Handbook for Systematic Reviews of Interventions were utilised for each of the five domains of bias: randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome and selection of the reported result [25]. Each of the domains, including the overall risk of bias, was judged as 'low', 'high', or 'unclear' risk of bias by authors PB and RP independently. Any discrepancies were discussed, and a rating agreement was achieved.

Results

A total of 6186 abstracts were retrieved from the two searches carried out in December 2018 and June 2021 respectively. An additional three records were forwarded by authors who were contacted for a full-text paper. 1481 duplicate records were removed. 4648 records were then excluded following abstract screening as they did not meet the inclusion criteria.

Comparisons of screening procedures by PB and CT for 705 abstracts (15% of total) evidenced an inter-rater agreement of 98%.

The remaining 57 records consisted of 33 full-text articles and 24 conference proceedings or abstracts. Out of the 24 conference proceedings, 10 records were categorised as studies awaiting classification as not enough information was available to make decisions about inclusion (see Appendix S3), the rest were excluded. Two full-text articles written in German [26, 27] and another written in Korean [28] were reviewed and translated by a proficient German and Korean speakers. Twenty-three of the 33 full-text records were excluded as they did not meet the inclusion criteria. The ten remaining records met the eligibility criteria and were included in this systematic review (Fig. 1).

Included Studies

A total of ten studies, six RCTs and four cross-over trials, were included in this review (Table 1). Trials were written in English (n = 9) and Korean (n = 1). All studies evaluated the effects of NIBS in improving dysarthria as a primary or secondary outcome measure. Six trials investigated the treatment of dysarthria using repetitive transcranial magnetic stimulation (rTMS), three trials using transcranial direct current stimulation (tDCS) and one study using repetitive transorbital alternating current stimulation (rtACS). None of the included studies evaluated the use of non-invasive peripheral stimulation (e.g. NMES) for treating dysarthria. Adjunct speech-language therapy (SALT) was administered in only two studies.

Participant Characteristics

A total of 268 adult participants were included in the ten trials: 98 participants in one study of rtACS, 118 participants in the rTMS studies and 52 participants were included in the three tDCS studies. Sample sizes of all the ten included trials ranged from 10 to 98 participants.

The underlying neurogenic condition giving rise to dysarthria varied across the included studies. Studies included participants with either subacute or chronic CVA (*n = 3),* PD (*n* = 5) neurodegenerative cerebellar ataxia (NCA; *n* = 2). Dysarthria subtype and severity was only specified in four studies: mild and mild-to-moderate hypokinetic dysarthria [29, 30, 31, 34].

Dysarthria Outcome Measures

All trials evaluated the effects of NIBS on dysarthria at an impairment level. In three papers, dysarthria outcomes formed part of a core disease-associated outcome measure: the National Institute of Health-Stroke Scale (NIHSS) and the International Cooperative Ataxia Rating Scale (ICARS). The other seven studies used several perceptual and acoustic measurements, such as, alternative and sequential motion rates, fundamental frequency and maximum phonation time to rate dysarthria. Only one study included outcomes at an activity level of the ICF [23], the Voice Related Quality of Life (V-RQOL) [29].

Non-Invasive Stimulation: Methodological Characteristics

rTMS

rTMS studies delivered stimulation five times a week for a total of 10 sessions (*n* = 3), five stimulation sessions in two weeks (*n* = 1), two stimulation sessions with a one-day interval in between (*n* = 1) and one session of rTMS stimulation (*n* = 1). Studies employed sham stimulation (*n* = 4), a control stimulation site (*n* = 1), and an active stimulation site (*n* = 1) as comparators.

Considerable differences in rTMS administration were reported between trials (Table 2). The location of brain stimulation varied considerably across the six studies, with several trials delivering stimulation to more than one site. The left dorsolateral prefrontal cortex (DLPFC; *n* = 2), the primary orofacial sensorimotor area (SM1; *n* = 1), the motor hand area

contralateral to the more impaired upper limb (n = 1), the left hemisphere hotspots for the evoked motor potential of the orbicularis oris muscles (n = 1), the right posterior superior temporal gyrus (STG; n = 2), the orofacial primary motor area (OFM1; n = 1) and the vertex (n = 1) were stimulated.

Studies delivered high-frequency rTMS (n = 3), low-frequency rTMS (n = 2) or both (n = 1). The number of rTMS pulses delivered in each session varied between 1500 pulses to 3,000 pulses per session across trials. Discrepancies between studies were also noted for the number and duration of trains and the train interval phases, with several studies not reporting any of these stimulation characteristics.

tDCS

Trials delivered anodal stimulation on the scalp over the cerebellum area and cathodal stimulation over the spinal lumbar enlargement (n = 2) or anodal stimulation on the primary motor cortex by finding hotspots obtained from motor evoked potential of the orbicularis oris muscle and the cathode attached on the contralateral side (n = 1) (Table 3). All three studies delivered a current intensity of 2 mA. tDCS stimulation was delivered for 20 (n = 2) or 30 (n = 1) minutes. In all trials, stimulation was administered five times a week for a total of 10 sessions. Sham stimulation involving an identical electrode setup was used as a comparator in all trials.

rtACS

The only trial employing rtACS delivered stimulation for 30 to 40 minutes daily for twelve consecutive days. Bipolar square pulses of 5 to 20 msec phase with a current intensity ranging from 200 and 400 μA were delivered as train of pulses (2 – 9 trains) via electrodes positioned on the eyelids. Separate inter-pulse intervals ranging from 23 to 190ms were set to

both eyes. This trial included two comparators, conventional drug therapy and combined drug therapy with rtACS.

Effects of Stimulation Modality on Dysarthria Outcome Measures

rTMS

Statistically significant improvements were reported in five out of six studies (Table 4). Significant improvements in all dysarthria outcomes were observed after 10 sessions of rTMS on the left hotspots for motor evoked potentials (MEPs) of the orbicularis oris and SALT [37]. Participants in the sham stimulation group who only received SALT also showed significant improvements in four out of the six outcome measures (three alternative motion rate measures and maximum phonation time). Between-group comparisons only showed one significant difference in sequential motion rate in favour of the active stimulation group [37].

One session of 1 Hz rTMS over the STG led to significant improvements in relative standard deviation of the second formant, an acoustic parameter describing jaw and tongue movements, and total pause time [34]. No other significant improvements were noted. Regarding the other stimulation parameters, except for a significant improvement in the range of the first formant following 10 Hz STG stimulation, no statistically significant changes were noted following stimulation over the vertex and the OFM1. 10 sessions of 1 Hz stimulation over the STG led to significant improvements in the phonetics score of the 3F Test – Dysarthric Profile (3FT) immediately post the 10 sessions and further improved at 6 and 10-week follow-up assessments [31]. In the sham group of this trial, the 3FT phonetics scores also significantly improved post the 10 sessions, nevertheless, scores remained stable during the follow up assessments.

10 Hz rTMS administered over the left primary orofacial sensorimotor area (SM1) gave rise to significant improvements in harmonic-to-noise ratio (additive noise in the voice signal), net speech rate, vowel space area (articulatory working space formed by corner vowels) and jitter (frequency instability) decrease [30]. These objective findings were not corroborated in the perceptual speech assessment. In contrast, no changes were noted following 10 Hz rTMS over the left DLPFC. Similarly, no statistically significant differences in dysarthria outcomes between real 10 Hz rTMS over the motor hand area contralateral to impaired upper limb and sham stimulation were observed after two stimulation sessions [26]. Another included trial found that 15 Hz rTMS of the left DLPFC only gave rise to statistical improvements on the V-RQOL measure, a patient-reported voice questionnaire [35]. No effect of rTMS stimulation was noted on impairment-based speech-related measures.

tDCS

Two tDCS studies in neurodegenerative cerebellar ataxia found no significant differences between real and sham tDCS across treatment stimulations on the dysarthria subsection of the ICARS (Table 5) [28, 29]. In the other tDCS study involving persons with CVA [28], real tDCS and SALT gave rise to statistically significant improvements in speech-related function. Significant improvements in maximum phonation time and sequential motion rates were also noted in the sham stimulation group receiving only SALT. Differences between groups after treatment only showed a significant increase in alternating motion rates-/pa/ for the tDCS group and SALT group. No other significant differences were found between stimulation groups.

rtACS

The only study that delivered rtACS reported a significant effect of stimulation on the dysarthria sub-section of the NIHSS in both the rtACS and combined rtACS and drug treatment

groups [36]. No significant changes were found in the group receiving drug therapy only (control). NIHSS comparisons between groups post-intervention were not carried out for the dysarthria sub-section.

Effects of active stimulation across comparable outcome measures and clinical populations

Table 5 illustrates the effects of active stimulation for comparable speech-related outcome measures in CVA and PD populations. The four PD studies that evaluated fundamental frequency as an outcome measure found no influence of active treatment. On the contrary, for the speech rate and rhythmicity outcome, two PD studies found a significant improvement post-stimulation. Due to missing data in the published papers and lack of response from trial authors, estimation of size effects could not be completed.

Size effects were estimated for two CVA trials [28, 37] using mean differences for maximum phonation time (MPT) and sequential motion rates (SMR), and standard mean differences (SMD) for the alternating motion rates (AMR) outcome (Fig. 3). Between-group post-treatment (T1) analysis was completed. Active vs. sham stimulation at T1 had no overall significant effect on any of three dysarthria outcomes (Fig. 3a. MPT: MD 0.0836, 95% CI -2.8714 to 3.0385, z = 0.06, p = 0.96; Fig. 3b. AMR: SMD 0.0183, 95% CI -0.7072 to 0.7437, z = 0.05, p = 0.96; Fig 3c. SMR: MD 0.4842, 95% CI - 1.5717 to 2.5402, z = 0.46, p = 0.64).

Adverse Stimulation Effects

rTMS and tDCS stimulation were well-tolerated in eight out of the ten included studies [29-35, 36]. In these studies, severe adverse effects, such as seizures or headaches were not reported and most studies only mention mild side effects or no side effects at all. No details

about the presence or absence of any adverse effects during non-invasive stimulation were reported in the two remaining studies [28, 36].

Quality of Included Studies

Two studies were rated at a low overall risk of bias on the ROB-2 [31, 32]. Another study was judged at some concerns of bias [33] while the remaining seven studies were all judged to be at a high overall risk of bias (Fig. 2).

Discussion

Given the high variability in participant and trial characteristics, such as, clinical groups (CVA, PD and NCA), stimulation techniques (rTMS, tDCS and rtACS) and parameters, study duration and outcome measures, the small sample sizes and the low methodological quality of most included studies, comparisons between trials within and across stimulation methods are restricted. Six studies comprising two clinical populations, CVA and PD found that NIBS, as standalone treatment or coupled with traditional therapy, may give rise to specific short-term improvements in several impairment-based speech functions. In addition, one study found that the positive effects of stimulation can persists and improve further in the consequent weeks following stimulation. Nevertheless, despite this preliminary indication of potential effect, most trials that found positive NIBS effects do not offer any convincing or replicatory evidence of improved dysarthria symptomology and hence, do not allow us to draw any conclusions. No benefit of using tDCS in neurodegenerative cerebellar ataxia was observed.

Whilst the debate is still in its early stages, motor training coupled with NIBS is often deemed to generate significant and better outcomes when compared to stand-alone NIBS [38]. Despite this preliminary support for a combined approach, most trials included in this review administered stand-alone NIBS and only two studies delivered NIBS in combination with

SALT. The latter two CVA trials evidenced significant improvements across most dysarthria outcome measures [28, 37]. However, as demonstrated by between-group post-treatment size-effects, the gains observed following NIBS and SALT were similar to the improvements noted by the control groups receiving stand-alone SALT. Since these findings are limited to two small-scale studies lacking rigorous methodological quality, we are unable to draw any conclusions about whether NIBS coupled with dysarthria therapy has the potential to magnify or consolidate the benefits associated with therapy by making the brain more receptive [39-41].

The limited comparability in dysarthria outcome measures, which further complicates the interpretation of the present results, sheds light on the lack of consistency in dysarthria assessment practices employed globally [42, 43]. Moreover, several outcome measures used to quantify dysarthria, such as the ICARS and NIHSS, are global inventories of neurological deficits and hence are drastically limited in the ability to identify characteristic features of dysarthria and to monitor improvements following intervention, and have poor reliability [44, 45].

The high heterogeneity in NIBS stimulation parameters was not unexpected. Since the neurophysiological underpinnings of how NIBS alters brain mechanisms are not well-identified and the optimal parameters for stimulation are still to be elucidated [46], substantial variability in stimulation characteristics were observed. Besides, justifications for the NIBS parameters used in the trials were not adequately and consistently presented in included trials. The findings do not permit any comparisons about the clinical effectiveness of different stimulation parameters or protocols to modulate speech mechanisms and functions, nor allow for the identification of optimal stimulation conditions for any of the clinical populations.

Variations in the cortical sites chosen for stimulation, even within the same clinical population, were also noted. Whilst our understanding of the clinicoanatomical basis of the dysarthrias is mostly based on the seminal work of Darley et al [47, 48], recent contributions on the neural basis of dysarthria may shed light on cortical localisations which may be targeted during stimulation. For instance, lesions to the superior anterior vermal and paravermal regions have been frequently implicated in ataxic dysarthria [49, 50]. Besides, since the same neurological condition, for instance CVA, may give rise to different dysarthrias (e.g. spastic, flaccid and mixed) comprising a wide array of speech disturbances [51], we propose that trials investigating NIBS in dysarthria should comprehensively describe, quantify and give clinical weighting to the differential diagnosis of the speech disorder. Undeniably, more systematic approaches in the manipulation of NIBS trial variables are necessary to increase our understanding of how different stimulation sites and parameters may facilitate dysarthria rehabilitation.

Regarding safety of NIBS, the trials reporting safety affects did not report any detrimental health risks or severe adverse events for participants with dysarthria. These findings corroborate previous NIBS research suggesting that stimulation is relatively safe if standard administration protocols and guidelines are followed [13,52]. Nevertheless, further large-scale research is required to determine the ideal safety parameters to be utilised with different dysarthria populations and to measure the influence of the less established NIBS techniques, such as ACS, on participant tolerability and safety.

The database searches did not identify any trials investigating the use of peripheral electrical stimulation, such as, NMES in treating dysarthria. When compared to other motor processes, such as limb movements, speech only uses around one fifth of maximum mechanical force capacity of speech-related muscles and is frequently viewed as intricately more complex

as apart from motor functions, it also encompasses phonological processes [53, 54]. These findings may have hindered researchers from investigating the use of NMES to treat dysarthria and to focus more on its applicability to treat other conditions, such as, dysphagia [55].

Notwithstanding all controversies, it may still be pertinent to investigate the applicability of NMES to treat dysarthria. Since the speech disorder predominantly causes muscular and neuromuscular disturbances [1], NMES may directly target the muscle and muscles groups implicated in dysarthria. If NMES parameters, such as, frequency, duration, duty cycle and ramp time, are adjusted to target different craniofacial muscle fibre types associated with speech and non-speech oral movements [44, 56, 57], then NMES may be hypothetically applicable to treat speech abnormalities associated with different subtypes of dysarthria.

Limitations

This review is subject to several limitations. Firstly, only experimental and quasi-experimental designs were included in this review. Inclusion of case series and reports could have augmented our understanding of the effects of non-invasive stimulation on dysarthria. Secondly, study selection and data extraction were only completed in full by one reviewer. Thirdly, even if 15 percent of the full list of retrieved records was screened independently by a second reviewer, screening of all records by two reviewers may have yielded fewer errors. Lastly, meta-analysis could only be carried out for two CVA studies involving similar clinical groups and clinical outcomes. Despite our efforts to contact authors for missing data, particularly for the fundamental frequency, and speech rate and rhythmicity outcomes, most attempts were unsuccessful.

Conclusion

Although non-invasive stimulation is a powerful tool that can be used to treat neurological and psychiatric disease symptoms, this review confirms that to-date there is inconclusive evidence supporting the use of non-invasive stimulation to treat dysarthria-related speech deviations. It was also not possible to identify sets of stimulation parameters nor optimal stimulation strategies that yielded more positive results in participants. These conclusions are drawn on five main factors: (1) limited number of included studies; (2) small sample size; (3) poor methodological quality of trials; (4) discrepant findings within and between studies; and (5) heterogeneity in participant characteristics and outcome measures.

The findings present substantial future research opportunities. High quality studies aimed at identifying which peripheral and cortical regions, and stimulation settings are optimal for treating speech impairment secondary to dysarthria is necessary. There is also a need to investigate whether a combined stimulation and traditional dysarthria therapy approach is better than stand-alone stimulation and whether non-invasive stimulation can provide better results when compared to stand-alone traditional therapy.

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Table and Figure Captions

Table 1. *Summary of Trial Characteristics.*

Table 2. *rTMS (repetitive transcranial magnetic stimulation): stimulation parameters of included trials.*

Table 3 *tDCS (transcranial direct current stimulation): stimulation parameters of included trials*

Table 4. *rTMS (repetitive transcranial magnetic stimulation) trials: findings*

Table 5. *tDCS (transcranial direct current stimulation) trials: findings*

Table 6. *The effects of stimulation on comparable impairment-based dysarthria measures in PD and CVA populations*

Figure 1. *Prisma Flow Diagram*

Figure 2. *ROB-2 (Risk of Bias-2) Summary: Authors' ratings for each domain of the included studies*

Figure 3. *Forest plots of active vs. sham post-stimulation effects on dysarthria outcomes in CVA*