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Transcranial direct current stimulation in post stroke aphasia and primary progressive aphasia: Current knowledge and future clinical applications

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Abstract.
BACKGROUND: The application of transcranial direct current stimulation (tDCS) in chronic post stroke aphasia is documented in a substantial literature, and there is some new evidence that tDCS can augment favorable language outcomes in primary progressive aphasia. Anodal tDCS is most often applied to the left hemisphere language areas to increase cortical excitability (increase the threshold of activation) and cathodal tDCS is most often applied to the right hemisphere homotopic areas to inhibit over activation in contralesional right homologues of language areas. Outcomes usually are based on neuropsychological and language test performance, following a medical model which emphasizes impairment of function, rather than a model which emphasizes functional communication.
OBJECTIVE: In this paper, we review current literature of tDCS as it is being used as a research tool, and discuss future implementation of tDCS as an adjuvant treatment to behavioral speech-language pathology intervention.
METHODS: We review literature describing non-invasive brain stimulation, the mechanism of tDCS, and studies of tDCS in aphasia and neurodegenerative disorders. We discuss future clinical applications.
RESULTS/CONCLUSIONS: tDCS is a promising adjunct to traditional speech-language pathology intervention to address speech-language deficits after stroke and in the neurodegenerative disease, primary progressive aphasia. Limited data are available regarding how performance on these types of specific tasks translates to functional communication outcomes.

Keywords: Stroke, aphasia, primary progressive aphasia, transcranial direct current stimulation

1. Introduction

Communication through language is central to the human experience. Disorders of language, such as post stroke aphasia and primary progressive aphasia (PPA), impede interaction and hamper interpersonal connections and reintegration into family life, work, and school (Tippett, Hillis, & Tsapkini, 2015; Wise, 2003). In the setting of post stroke aphasia, some degree of language recovery over time is common, mostly occurring within the first few months after stroke; however, severe and debilitating language deficits frequently persist, and

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decline in cognitive/language abilities and overall function can occur in those who do not receive speech-language pathology intervention (Dhamoon et al., 2012; Iadecola, 2013). In the setting of PPA, there is insidious onset and gradual deterioration of language function over time with different linguistic features, patterns of atrophy, and underlying pathology characterizing each of the variants of this neurodegenerative disease (i.e., logopenic, nonfluent/agrammatic, semantic variants) (Gorno-Tempini et al., 2011; Josephs et al., 2008; Mesulam,1982).

Speech-language pathology intervention is the mainstay of treatment for individuals with aphasia and PPA. Clinicians strive to provide evidence-based interventions to improve language abilities after stroke and compensate for deficits, and perhaps improve or slow decline in language abilities in neurodegenerative disease, such as PPA. Therapy is beneficial for language recovery in stroke, especially in the first three months post stroke (Hillis, 2010; Lazar et al., 2010); however, gains in therapy are variable and progress may be slow, especially in the chronic stage for patients with large lesions in the left hemisphere (Bhogal et al., 2003; Brady, Kelly, Godwin, & Enderby, 2012). Similarly, although encouraging findings are reported regarding behavioral therapy in PPA (e.g., Meyer et al., 2013; Newhart et al., 2009; Rapp & Glucroft, 2009; Tsapkini & Hillis, 2013), evidence of maintenance of therapy gains is limited.

Non-invasive brain stimulation is a recent adjunct to behavioral speech-language pathology. This can take two forms: Transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). TMS is thought to modify cortical excitability by increasing or decreasing activity in targeted areas of the cortex by using a rapid time-varying magnetic field (Hallet, 2000; Walsh & Pascual-Leone, 2003). This involves discharging a current through a coil of copper wire that is held over the subject's scalp. The current pulse flowing through the coil generates a rapidly fluctuating magnetic field that penetrates the scalp and skull unimpeded, and induces a changing electrical field in the cerebral cortex below the coil. TMS has been employed to the right hemisphere to improve naming in individuals with chronic nonfluent aphasia. The mechanism proposed to explain this treatment effect is suppression of overactive right hemisphere homologues (e.g., Naeser et al., 2005, 2012).

Transcranial direct current stimulation (tDCS), the focus of this paper, is another method that has been proposed to boost behavioral language treatment in post stroke aphasia (Baker, Rorden, & Fridriksson, 2010; Fiori et al., 2011; Fridriksson, Richardson, Baker, & Rorden, 2011; Jung, Lim, Kang, Sohn, & Paik, 2011; Marangolo et al., 2014; You, Kim, Chun, Jung, & Park, 2011) and PPA (Cotelli et al., 2014; Tsapkini, Frangakis, Gomez, Davis, & Hillis, 2014. Although the precise mechanism of tDCS is still emerging (Weiss & Bikson, 2014), the prospect of augmenting the effectiveness of behavioral therapy is attractive to clinicians, patients, and their families and caregivers.

In the last 10 years, there has been an increased interest in using tDCS to modulate cognitive functions in healthy individuals as well as in individuals with various disorders. There are several reasons for this increased interest in tDCS research. One reason pertains to *safety considerations*: tDCS seems to have no significant adverse side effects, provided that stimulation parameters are kept within safety limits (see Nitsche et al., 2008; Poreisz, Boros, Antal, & Paulus, 2007). In a meta-analysis study, the most common adverse sensation was mild tingling and mild itching under the electrodes and infrequent headache, fatigue, and nausea (Poreisz et al., 2007). Furthermore, tDCS is not reported to provoke seizures and current tDCS protocols are not found to induce brain edema or changes in the blood brain barrier (Nitsche et al., 2004). A second benefit of tDCS pertains to *portability and cost*. The tDCS apparatus is more portable, less expensive, and easier to use than other technologies, like TMS. These features allow treatment to be delivered not only in clinical settings, but also in a patient's own home. Third, tDCS allows one to *easily conduct placebo (sham) stimulation-controlled studies*, because, with the exception of a slight itching and mild tingling sensation, participants rarely experience sensory phenomena related to the stimulation. A method to blind participants as to whether they are receiving real or sham tDCS in a research treatment protocols is turn the tDCS stimulator on for 30 seconds at the start of the sham condition to induce scalp sensations associated with stimulation, and then gradually decrease and turn off tDCS within the next 15 seconds (Gandiga, Hummel, & Cohen, 2006). Finally, tDCS is also *well suited to neurostimulation concurrent with behavioral speech-language pathology treatment*. For example, Broca's area (inferior frontal cortex) can be easily and comfortably targeted with tDCS along with behavioral treatment for naming. At the start of stimulation, most participants

perceive a slight itching sensation under the electrodes, which then quickly subsides in most cases. In contrast, TMS of the same region can inadvertently stimulate the trigeminal nerve, causing facial twitching or painful sensations, making participation in a behavioral therapy task difficult, if not impossible (e.g., Crinion, 2015; Holland & Crinion, 2012).

2. Mechanism of tDCS

tDCS is a safe, non-invasive, non-painful electrical stimulation of the brain which modulates cortical excitability by application of weak electrical currents. It is usually administered via saline-soaked surface sponge electrodes attached to the scalp and connected to a direct current stimulator with low intensities (Lang et al., 2005). The polarity of the tDCS electrode is widely thought to determine whether the effect on the underlying brain tissue is excitatory or inhibitory. The anode is generally thought to induce excitation (i.e., likelihood of neural firing), whereas the cathode induces inhibition. It should be noted that cathodal tDCS has variable effects on other functions such as cognition (e.g., Monte-Silva et al., 2013). Cathodal polarization is thought to decrease cortical excitability due to hyperpolarization of cortical neurons; whereas, anodal polarization increases cortical excitability due to subthreshold depolarization (Bindman, Lippold, & Redfearn, 1962; Creutzfeldt, Fromm, & Kapp, 1962; Gomez Palacio Schjetnan, Faraji, Metz, Tatsuno, & Luczak, 2013).

The brain mechanisms that induce the after-effects of tDCS are modulated by N-methyl-D-aspartate receptor (also known as the NMDA receptor), a glutamate-gated ion channel widely expressed in the central nervous system that plays key roles in excitatory synaptic transmission (Nitsche et al., 2003). Furthermore, animal and human studies indicated that tDCS influences long-term potentiation (LTP) and long-term depression (LTD)-like mechanisms which are critical for learning and memory (Liebetanz et al., 2002; Monte-Silva et al., 2013; Nitsche et al., 2003; Rioult-Pedotti, Friedman, & Donoghue, 2000). Nitsche and Paulus (2001) showed for the first time that weak tDCS is capable of inducing duration-dependent, long-lasting cerebral excitability elevations in humans. tDCS does not generate action potentials; moreover, it is site-specific, but not site-limited, meaning that it affects not only the targeted site, but related cortical areas as well.

3. tDCS in aphasia research

The positive effects of tDCS in language functions are identified in studies of healthy controls, individuals with aphasia, and in individuals with neurodegenerative disorders, such as PPA. In healthy individuals, excitatory anodal tDCS administered to left perisylvian brain areas can improve language processing (Flöel, Rösser, Michka, Knecht, & Breitenstein, 2008; Iyer et al., 2005; Sparing, Dafotakis, Meister, Thirugnanasambandam, & Fink, 2008) when compared to sham stimulation. In addition, a handful of studies utilized fMRI to elucidate the neural underpinnings of language improvement due to anodal tDCS in healthy individuals (Holland et al., 2011; Meinzer et al., 2012; 2014; Meinzer, Lindenberg, Antonenko, Flaisch, & Flöel, 2013). There is a burgeoning literature of tDCS studies in aphasia. Studies vary in their design as well as the regions that are targeted for tDCS. Several important variables need to be considered before implementing tDCS in treatment studies.

3.1. Stimulation area

The optimal target for tDCS is an important consideration for recovery and reorganization of function in post-stroke aphasia. Based on functional magnetic resonance imaging (fMRI) studies of aphasia language recovery, the most extensive recovery seems to occur by means of restitution of the residual language network in the left hemisphere (e.g., Fridriksson, Richardson, Fillmore, & Cai, 2012). In other studies, successful aphasia recovery is attributed to reliance on the intact right hemisphere (e.g., Norton, Zipse, Marchina, & Schlaug, 2009; Turkeltaub, Messing, Norise, & Hamilton, 2011). It is important to note, however, that a consensus on where favorable brain changes occur to support aphasia recovery does not exist at this time. Nevertheless, two themes have emerged with regard to where brain stimulation is targeted. These approaches are based on the model of interhemispheric inhibition, on the presumption that either facilitating activity in lesioned or perilesional areas or decreasing activity in inhibitory contralesional areas allows for improved language function.

3.2. Facilitating activity in the lesioned/ perilesional areas

Several authors advocate the interhemispheric inhibition model to facilitate the remaining left

perilesional cortex with excitatory stimulation in order improve language recovery. In these studies, the anode is placed on potentially relevant areas of the left hemisphere (e.g., perilesional region), whereas the cathode (reference electrode) is placed on the arm/shoulder, supraorbital area, or buccinator muscle. In two sham tDCS (S-tDCS) controlled trials, Fridriksson and colleagues administered anodal tDCS (A-tDCS) to perilesional brain regions along with a computerized anomia treatment for five days to chronic individuals with aphasia (typically more than one year post stroke) (Baker et al., 2010; Fridriksson et al., 2011). The placement of the anode over the left hemisphere (20 minutes, 1 mA) was determined individually, on the basis of fMRI images acquired during an overt picture-naming task. Naming accuracy for treated and untreated items was measured before treatment, after the fifth tDCS session, and one week after the end of tDCS treatment. Accuracy after treatment increased for treated and untreated items after A-tDCS, but not after S-tDCS. Improvement was maintained for at least one week (Baker et al., 2010) and up to three weeks (Frikdriksson et al., 2011) after the completion of the protocol. In a recent study, Vestito, Rosellini, Mantero, and Bandini (2014) investigated the long-term outcome of A-tDCS to the left frontal (perilesional) region. Three individuals with aphasia underwent A-tDCS, 20 minute duration, 1.5 mA and S-tDCS over the left frontal region, coupled with simultaneous naming training for ten sessions. They found a significant beneficial effect of A-tDCS (as compared to baseline and S-tDCS) in all the participants and the benefits persisted until the 16th week, when a decline in naming performance emerged. Up to the 21st week, the number of correct responses, though no longer statistically significant, remained above the baseline level. See Fig. 1 for an example of a perilesional electrode placement for an individual with a left frontal lesion.

3.3. *Downregulating activity in the right hemisphere*

In these studies, the cathode is placed on potentially relevant areas of the right hemisphere (e.g., homologues of Broca's or Wernicke's areas), whereas the anode (reference electrode) is placed on the arm/shoulder, supraorbital area, or buccinator muscle. For example, Jung et al. (2011) applied cathodal stimulation (1 mA for 20 min) to the right homologue of Broca's area in individuals with subacute and chronic aphasia. tDCS stimulation was combined

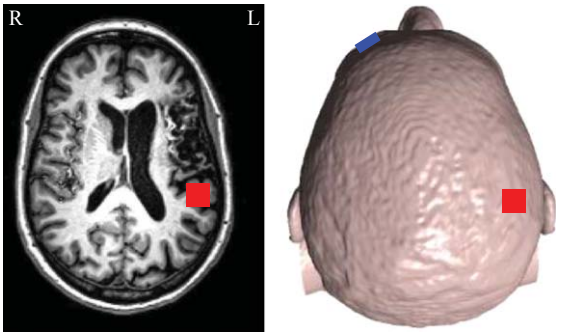

Fig. 1. Perilesional stimulation site for a participant with left frontal lesion. The structural MRI on the left shows the left frontal lesion and the approximate location of the electrode projected on the head model is shown on the right. Red square indicates anode electrode placement (left temporal cortex) and blue square indicates cathode electrode placement (right forehead).

with speech-language therapy for ten sessions and all participants showed a significant improvement in aphasia quotients based on the Korean version of the Western Aphasia Battery (Kim & Na, 2004). It should be noted that Jung et al. (2011) did not include a sham condition. In another study, Kang, Kim, Sohn, Cohen, and Paik (2011) used a double blind, counterbalanced sham-controlled, crossover study to study the effect of cathodal stimulation (2 mA for 20 min) to the right homologue of Broca's area with simultaneous word-retrieval training in individuals with chronic aphasia. Significantly improved picture naming was observed following the fifth tDCS treatment session, but no changes were observed after sham tDCS. More recently, some researchers utilized a bilateral tDCS electrode placement approach, with simultaneous anodal left hemisphere and cathodal right hemisphere stimulation over specific cortical regions. The rationale for implementing bilateral tDCS is based on the assumption that simultaneously facilitating the intact portion of the left hemisphere through anodal stimulation while at the same time downregulating activity of the contralesional hemisphere through cathodal stimulation should foster greatest recovery. For example, Marangolo and colleagues (Marangolo et al., 2013; 2014) found significant improvement in speech and language skills after simultaneous stimulation over the left and right Broca's areas (anode to the left Broca's area and cathode to the right Broca's area) along with behavioral treatment compared to sham stimulation. Similarly, Manenti et al. (2015) showed that after 20 sessions of bihemispheric stimulation on dorsolateral prefrontal cortex (DLPFC) (tDCS anodal was placed on the left DLPFC and tDCS cathodal was placed on the right DLPFC), an aphasic

individual achieved an improvement in treated and untreated verb naming compared to sham stimulation.

3.4. Stimulation electrode intensity and duration of tDCS stimulation

These are important variables that influence the outcome of tDCS studies on aphasia recovery. In most studies, two equal sized electrodes are used; each electrode has an area of 25 cm^2 (5 cm × 5 cm). In some studies, 35 cm^2 (5 cm × 7 cm; e.g., Marangolo et al., 2013, 2014) and 36 cm^2 (6 cm × 6 cm; e.g., Jung et al., 2011) electrodes are used. Given that tDCS studies typically employ large electrodes for stimulation, they offer limited spatial resolution. Further, it is also difficult to know precisely which region or regions of the brain are being affected. Computer modeling studies also suggest that the distribution of current in the brain associated with tDCS can be quite diffuse, and that regions of maximal stimulation can be unpredictable, varying with factors like reference electrode size and position (Bikson, Datta, & Elwassif, 2009). In addition, lesioned tissue may not respond in the same way as normal tissue with respect to the propagation of current. Fridriksson and colleagues reported that current sometimes becomes sequestered within lesioned tissue instead of traveling to perilesional areas. In chronic stages of stroke, when lesions can become gliotic and filled with cerebrospinal fluid, the current can be dispersed by the fluid, preventing maximal stimulation of targeted tissues (Datta, Baker, Bikson, & Fridriksson, 2011).

The intensity and duration of the stimulus are relatively uniform across studies. Most studies use a stimulation intensity of 1 mA (e.g., Baker et al., 2010; Fiori et al., 2011; Fridriksson et al., 2011; Jung et al., 2011), 1.5 mA (e.g., Vestito et al., 2014), or 2 mA (Kang et al., 2011; Marangolo et al., 2013, 2014; Monti et al., 2008; Shah-Basak et al., 2015). In almost all studies, tDCS is delivered for 20 minutes. Monti et al. (2008) applied A-tDCS for 10 minutes and reported that they did not find beneficial effects, suggesting that 20 minute intervals of A-tDCS is preferable to briefer durations of stimulation.

An alternative to conventional sponge-based tDCS is to use high definition tDCS. High definition tDCS (HD-tDCS) is a new non-invasive brain stimulation technique that improves current focality and field intensities at desired cortical targets using multiple gel-based electrodes, similar to those used in electroencephalography (EEG) (Datta et al., 2009; Dmochowski, Datta, Bikson, Su, & Parra, 2011). Preliminary studies confirm the safety and tolerability of HD-tDCS (Borckardt et al., 2012, Caparelli-Daquer et al., 2012; Minhas et al., 2010). However, several questions remain concerning the optimization of HD-tDCS dose, tolerability of receiving HD-tDCS for consecutive days, and how the HD-tDCS approach compares to traditional sponge-based electrodes in stroke rehabilitation outcome.

Richardson, Datta, Dmochowski, Parra, and Fridriksson (2015) compared conventional sponge-based tDCS (CS-tDCS) and HD-tDCS in post stroke aphasia in conjunction with behavioral treatment, using a randomized crossover trial. They showed that CS-tDCS and HD-tDCS are comparable in terms of implementation, acceptability, and treatment outcomes for eight individuals with chronic post-stroke aphasia. Naming accuracy and response time improved for both stimulation conditions. Change in accuracy of trained items was numerically higher (but not statistically significant) for HD-tDCS compared to CS-tDCS for most patients. These results are very encouraging and emphasize the need for larger randomized controlled trials.

3.5. Type of aphasia treatment

The type of behavioral treatment tasks used to couple with tDCS differ among studies. A majority of the studies focus on anomia (e.g., Baker et al., 2010; Fiori et al., 2011; Flöel et al., 2008; Fridriksson et al., 2011; Marangolo et al., 2013; Shah-Basak et al., 2015; Vestito et al., 2014). This is likely because naming impairment (anomia) is the most pervasive and reliable symptom for all types of aphasia. For example, Baker et al. (2010) and Fridriksson et al. (2011) used lexical semantic therapy–in particular a word-picture matching task–and showed improvement in naming accuracy immediately following completion of the study and at one week after study completion. Jung et al. (2011) used an individually tailored language treatment including Melodic Intonation Therapy (Albert, Sparks, & Helm, 1973), auditory comprehension training, and other treatment tasks paired with tDCS stimulation and found a significant improvement in aphasia quotient scores after the completion of treatment. Although tDCS is typically paired with a behavioral treatment task to treat aphasia, Monti et al. (2008) administered tDCS in isolation (without a behavioral task). They reported significant improvement in naming following stimulation alone. Most of the studies focus on very similar outcome measures, such as improvement on naming

accuracy (e.g., Baker et al., 2010; Vestito et al., 2014; Shah-Basak et al., 2015). To date, functional outcomes measures are not included in tDCS research, although this is a vital aspect of evidence-based aphasia therapy (Tippett, 2015).

3.6. Number of treatment sessions and follow up periods

In most studies, the number of therapy sessions is relatively low (i.e., one to five sessions). Only a few studies employ more than five sessions (e.g., Manenti et al., 2015; Shah-Basak et al., 2015; Vestito et al., 2014). In addition, studies to date focus on relatively short-term follow up periods. For example, Fridriksson et al. (2011) included a three-week follow up after the end of stimulation, while Shah-Basak et al. (2015) included an 8 weeks post stimulation follow up and Vestito et al. (2014) included a 21 week post stimulation follow up. The longest follow up reported to date is 44 weeks post stimulation (Manenti et al., 2015).

3.7. Time post onset

Most studies are conducted in the chronic phase after stroke. Only two studies have evaluated tDCS paired with language therapy in acute to sub-acute aphasic stroke patients (Jung et al., 2011; You et al., 2011) and only one of these (You et al., 2011) was sham-controlled. In the Jung et al. (2011) study, 37 (27 subacute) individuals with aphasia received speech therapy combined with cathodal tDCS to the right Broca's area and anodal to contralateral forehead (1 mA for 20 min). Individuals with less severe, fluent type of aphasia who received treatment before 30 days post onset made the greatest language improvements following ten days of therapy paired with tDCS. You and colleagues (You et al., 2011) evaluated 2 mA tDCS over superior temporal gyrus (STG) paired with language therapy in 21 individuals with global aphasia, comparing three groups of seven patients each who received: Cathodal right STG, anodal left STG, or sham tDCS. Greater gains in auditory comprehension were observed in patients who received cathodal tDCS (17%) compared to sham (10%) or anodal tDCS (10%). However, those who received cathodal tDCS were the least impaired on auditory comprehension at baseline, making it difficult to sort out the effects of tDCS. Furthermore, four of seven patients in the anodal tDCS group had lesions of the left STG, so it is not clear that they had structurally intact cortex beneath the left STG stimulating electrode, which may account for the negative results compared to sham. Thus, there is insufficient evidence to determine if tDCS augments speech-language pathology intervention in facilitating aphasia recovery at the acute or sub-acute stage post stroke. However, these two studies show that in a fairly large number of patients indicate that 1-2 mA tDCS is well tolerated and safe when delivered for ten days in combination with language therapy.

3.8. Individual variability in tDCS response

Although there is increased interest in tDCS research, very little attention is focused on inter-individual variability in response to tDCS and how this can impact the outcome of a study (see Li, Uehara, & Hanakawa, 2015; Wiethoff, Hamada, & Rothwell, 2014 for detailed reviews). This is especially important in aphasia research because of variability in lesion site, size, recovery mechanisms, and deficit severity levels (e.g., Torres, Drebing, & Hamilton, 2013). It is very unlikely that the same approach will be effective for every patient considering the complexity of language networks, the heterogeneity of lesion size/site, and individual variation in language processing. A recent study by Shah-Basak and colleagues (Shah-Basak et al., 2015) explored individual variability in patient response to different patterns of stimulation utilizing a two-phase study approach. In Phase 1, participants underwent anodal and cathodal tDCS of the left and right prefrontal areas, as well as a sham condition, in separate sessions. A preferred electrode montage was established for each participant by assessing transient improvement on a picture naming task. In Phase 2, participants were randomized to receive either real-tDCS or to receive sham stimulation for 10 days using the optimal electrode configuration that was identified in Phase 1. Results indicated that in Phase 1, despite considerable individual variability, the greatest average improvement was observed after left-cathodal stimulation. Seven out of 12 subjects responded optimally to at least one montage, demonstrated by transient improvement in picture naming. In Phase 2, aphasia severity improved at two weeks and two months following real tDCS, but not sham. Despite individual variability with respect to optimal tDCS approach, certain montages result in consistent, though transient, improvement in persons with chronic post-stroke aphasia.

This preliminary study supports the notion that *individualized* tDCS treatment may enhance aphasia recovery.

4. tDCS Studies in neurodegenerative disorders

Despite the plethora of reports on language recovery using tDCS after stroke, only a few studies have examined it in neurodegenerative diseases. tDCS is employed in neurodegenerative disease as a possible means to augment behavioral intervention effects and reduce the rate of decline in language and other cognitive skills. Unlike stroke-aphasia studies that focus on either facilitating the left hemisphere or inhibiting the right hemisphere, studies on neurodegenerative disease mostly focus on facilitating the left hemisphere function.

Four studies examined tDCS in Alzheimer's disease (AD) (Boggio et al., 2009; 2011; Ferucci et al., 2008), including one study in which tDCS was applied for five sessions and showed greater improvement with tDCS vs. sham on a visual recognition task, but without any task performed during either tDCS or sham conditions (Boggio et al., 2012). One study was performed on participants with frontotemporal dementia (FTD). This study included only one session of tDCS with no effect on verbal memory, although no task was practiced during tDCS (Huey et al., 2007). Three studies were performed in patients with PPA (Cotelli et al., 2014; Tsapkini, Frangakis, Gomez, Davis, & Hillis, 2014 Tsapkini et al., 2015). Using a sham-controlled tDCS trial, Cotelli et al. (2014) investigated the effect of anodal tDCS to the left dorsolateral prefrontal cortex paired with naming therapy in non-fluent/agrammatic variant of PPA for ten sessions in a between-subjects design ($n = 8$ in each treatment group). Significant improvement in naming was observed in both anodal and sham groups immediately following treatment and 12 weeks post treatment, but this effect was significantly greater in anodal tDCS than sham tDCS patients. Using a within-subject crossover design ($n = 6$), Tsapkini et al. (2014) investigated the effect of anodal tDCS to the left inferior frontal gyrus paired with a spelling intervention program for 15 sessions. Significant improvement in spelling was noted for trained items in both tDCS and sham conditions; however, consistent and significant improvement for untrained items was only found in the tDCS plus spelling intervention condition. Furthermore, the improvement lasted longer in the tDCS plus spelling intervention condition compared to sham plus spelling intervention condition. In a recent study on a larger cohort of PPA patients ($n = 19$) treated in a within-subject cross over design, Tsapkini et al. (2015) found that independent of modality (oral and written word production outcomes), tDCS combined with speech and language interventions was more beneficial than sham combined with speech and language interventions: Therapy gains were sustained longer (up to 2 months) and generalized to untrained items. Another study in AD showed improvement in naming one month after the completion of tDCS (Boggio et al., 2012). Long terms benefits of tDCS is not clearly identified in neurodegenerative disorders. Determining the duration of therapeutic effects is critical, especially in neural degeneration, because it enables more effective planning of whether and when treatment should be repeated. These recent studies offer promise that tDCS may be a tool that could potentially improve our interventions in neurodegenerative diseases. More studies are needed to replicate and establish these effects.

5. Future clinical applications

tDCS holds promise in the treatment of post stroke aphasia and primary progressive aphasia. The safety profile, low cost, ease of administration, and portability of tDCS contribute to its potential for future clinical application. However, many questions remain, ranging from practical concerns and clinician competency and training to questions about the mechanism of tDCS action, anodal vs. cathodal stimulation, electrode configuration, duration and timing of neuromodulation, and effects on neural networks.

Research suggests that tDCS would likely translate to clinical practice as an *adjunct* to behavioral therapy (Crinion, 2015; Monti et al., 2013), rather than a stand-alone intervention.

Based on previous research on language recovery, the greatest improvement from post stroke aphasia occurs within the first three months (Lazar et al., 2010). Therefore, it is reasonable that the effects of tDCS would be enhanced if cortical stimulation is delivered during this time period. Preliminary results from an ongoing, randomized, double-blind, sham controlled study on the effect of tDCS paired with naming treatment in subacute aphasia from the **S**troke **C**ognitive **O**utcome and **RE**covery (SCORE) lab show that the effects of language treatment can be

enhanced by tDCS stimulation during the first three months post stroke.

Speech-language pathologists, especially those in medical settings, have familiarity with relatively invasive techniques in evaluation and treatment, and therefore, are likely able to be able to employ neuromodulation in clinical settings. For example, fiberoptic endoscopic evaluation of swallowing (Leder & Murray, 2008), management of tracheoesophageal prostheses (Singer et al., 2013), and application of tracheostomy speaking valves (Pandian et al., 2014) are routine aspects of contemporary clinical care. Speech-language pathologists need to enter the clinical setting as competent entry-level professionals, with clinical and management skills appropriate for a clinical fellowship year with limited supervision. Knowledge of specialized clinical skills, such neurorehabilitative techniques, is typically acquired in the work settings during supervised practice and in continuing education. As with other specialized techniques, there will be a need for continuing education regarding tDCS to facilitate competent practice on a range of topics from neuromodulation, identification and demarcation of cortical targets, device use and operation, electrode positioning, etc.

Before incorporating tDCS into clinical practice, it is vital that this technique be thoroughly vetted. Prior experience with another stimulation technique serves as an illustrative example. Surface electrical stimulation was introduced as a treatment technique approximately two decades ago (Freed, Freed, Chatburn, & Christian, 2001) to treat dysphagia. This technique became widely accepted and practiced; investigators subsequently evaluated this intervention and found that electrodes, which are placed on and around the thyroid cartilage, pull the larynx downward, potentiating laryngeal penetration and aspiration, an undesirable outcome (Ludlow et al., 2007). Modification of the electrical stimulation approach was advanced, including use of electrical stimulation as a sensory technique (Gallas, Marie, Leroi, & Verin, 2010) or as a resistance exercise in selected patients (Ludlow et al., 2007). Similarly, Do-It-Yourself (DIY) brain stimulation is an increasingly active community who use tDCS in the home setting to treat disorders and enhance normal function. DIY brain stimulation is accomplished with tDCS devices which are available to the public and are not regulated as medical or investigational devices, or with devices which are constructed by DIYers (Wexler, 2015).

Further research is indicated to establish if neuromodulation combined with language therapy affects functional communication in ways which are meaningful to individual circumstances and needs, central to the concept of patient-centered care (Byng, Cairns, & Duchan, 2002; Ersser & Atkins, 2000). Also appropriate stimulation dosing and modification based on patient characteristics, such as stroke size, location, and chronicity, remain unexplored. Examination of the effects of tDCS on neural networks is needed. Our lab is currently using resting state fMRI to elucidate the neural mechanisms of stimulation-induced behavioral improvements in PPA. A better understanding of the therapeutic and neuromodulatory mechanisms of tDCS as an adjunct to language therapy in PPA may have an impact on the development of effective interventions for this neurodegenerative disease. The development of a therapy that could slow the rate of decline in language skills may also impact quality of life for individuals with PPA. Finally, larger randomized control trials focusing on individualized treatment target locations are needed. Future studies should evaluate the comparative effectiveness of tDCS on augmenting language therapy at different time points relative to stroke onset to identify optimal timing of tDCS to augment language therapy in aphasia recovery.

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Conflict of interest

The authors have no conflict of interest to report.

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