The effects of transcranial direct current stimulation on speech production in individuals with acquired apraxia of speech

by

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Abstract

Background. Transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique, has been used as an adjunct to speech and language therapy to facilitate neuroplasticity in individuals with language impairments due to stroke. The extent to which these therapeutic results extend to motor speech disorders, particularly acquired apraxia of speech (AOS), is limited. AOS is a motor speech disorder that results in difficulties planning and sequencing the motor patterns required for speech production. Treatment for AOS typically involves using speech motor learning and/or phoneme placement strategies, and while these interventions have been shown to generalize to phoneme and word accuracy, the required dosage is intense and results between patients are highly variable. The present study seeks to assess the potential efficacy of anodal tDCS (A-tDCS) over the primary motor cortex coupled with training to improve both precision and consistency of speech production, as measured by percentage of phonemes correct (PPC) on tasks of increasing speech motor complexity.

Methods. A modified repeated measures single case study design was conducted across two participants, one receiving A-tDCS and a control receiving sham-tDCS (S-tDCS). Differences in speech accuracy, as measured by change in percentage of phonemes correct (PPC) within sessions, between conditions pre- and post-stimulation were examined using descriptive analyses and visual representations. Data was collected across four weekly sessions.

Results. The main findings included: 1) A-tDCS over the motor cortex resulted in a moderate intervention effect for motorically complex speech tasks over the S-tDCS condition, 2) A-tDCS resulted in an unanticipated positive effect for simple tasks during the first session over the S-tDCS condition, potentially reflecting an added improvement in linguistic as well as motor speech ability, and 3) effectiveness of A-tDCS was highly variable and appeared to diminish across sessions, while the S-tDCS condition showed greater consistency.

Conclusion. Bihemispheric stimulation of tDCS to the motor cortex has potential to simultaneously improve both chronic speech and language deficits during behavioural interventions, due to the spreading effect and lack of focal specificity inherent in neuromodulation. Future research is needed on the dose-response of tDCS and individual factors that may influence outcomes.

Preface

This thesis is an original work by Sarah Ehr. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board, Project Name: *The effects of transcranial direct current stimulation + training on reading and speech performance in individuals with apraxia of speech*; Pro00078460; 11 January 2018.

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Introduction and Literature Review

Apraxia of speech (AOS) is a complex communication disorder, which has historically challenged the field of speech language pathology both in terms of diagnosis and intervention. Presently, consensus is that acquired AOS is a neurologically based speech disorder which results in impairments in planning and sequencing the motor commands required for the production of speech, distinct from the deficits in musculature or language which define dysarthria and aphasia, respectively (Duffy, 2013). The purpose of the following review of the literature is to: (1) describe the distinguishing features of AOS, (2) explain the challenge of differential diagnosis between acquired AOS and aphasia, (3) discuss current best practices for treatment of AOS and outcome measures used to evaluate efficacy, and (4) explore the potential for use of tDCS as an adjunct to these treatments to facilitate rehabilitation.

Acquired Apraxia of Speech

Despite being described in the literature for over one hundred years, AOS was not identified as its own distinct disorder until Dr. Frederic Darley and his colleagues at the Mayo Clinic developed the term 'apraxia of speech' in the 1960s (Ogar, Slama, Dronkers, Amici, & Gorno-Tempini, 2005). Similar to its counterparts limb apraxia and nonverbal oral apraxia, AOS results in poorly sequenced movements which result in an inability to accurately produce the intended target (Galluzzi, Bureca, Guariglia, & Romani, 2015). The errors are evident in both the timing and spatial accuracy of movements, creating abnormalities most salient in articulation and prosody. Clinical characteristics of AOS include groping for the target articulatory position, a slow rate of speech with prolonged segment and intersegment durations, distorted phonemes, increasing errors with increasing utterance complexity, and a tendency to equalize stress over syllables and/or words. (Ballard et al., 2014; Bislick, McNeil, Spencer, Yorkston, & Kendall, 2017; Duffy, 2013; Marangolo et al., 2011). Deficits in AOS can range in severity from being mild enough that the individual only experiences occasional phonemic errors in complex contexts, to being so severe that speech is no longer a functional method of communication (Marangolo et al., 2011). Recently, the Directions into Velocities of Articulators (DIVA) model of speech production has been used to investigate the potential underlying impairment(s) that may result in AOS. Within this context, AOS is presently conceptualized as resulting from impairments in the feedforward system of motor control, and a subsequent over reliance on feedback-based corrections (Ballard, Tourville, & Robin, 2014; Maas, Mailend, & Guenther, 2015; Tourville & Guenther, 2011). The DIVA model's control systems directly correspond to hypothesized neuroanatomical regions, with the feedforward system consisting primarily of the left posterior inferior frontal gyrus (IFG) and ventral motor cortex, while the feedback system integrates additional somatosensory information from the somatosensory cortex and supramarginal gyrus, and additional auditory information from Heschl's gyrus and the posterior superior temporal gyrus (Tourville & Guenther, 2011).

Studies on areas of the brain implicated in AOS have been variable, and consensus has yet to be reached on which region (or regions) is the locus of the disorder. As the majority of individuals with AOS due to stroke have some degree of concomitant Broca's aphasia, the disorder has long been associated with lesions in BA 44/45, however, research has also been done examining the impact of injury to left premotor and supplementary motor areas, left anterior insula, left IFG, and the left basal ganglia (Ballard et al., 2014). While early research examining the anterior insula looked promising (Dronkers, 1996), attempts at replication have been unsuccessful (Moser, Basilakos, Fillmore, & Fridriksson, 2016; Trupe et al. 2013). Itabashi et al. (2016) hypothesized the insula findings were due to the frequency with which this region is compromised during middle cerebral artery (MCA) stroke, making lesion overlap highly probable, and independent of the presenting disorder. Graff-Radford et al. (2014) studied the neuroanatomy of individuals diagnosed with post-stroke pure AOS, or AOS without co-occurring aphasia or dysarthria, and their MRI analysis found maximal lesion overlap in the left premotor and motor cortices. These results are consistent with Josephs et al.'s (2006) findings in those with neurodegenerative disorders, which revealed that participants with primary progressive AOS had degeneration of the premotor and supplementary motor cortices, while those with the nonfluent variant of primary progressive aphasia showed degeneration of Broca's area. Studies comparing lesions of individuals with either pure AOS or AOS with aphasia determined injury to the left pre- and primary motor cortices to be the greatest predictor of AOS for both groups, however, there was much larger variability in implicated regions for those that had concomitant aphasia. In these cases, the inferior frontal gyrus (IFG) was frequently also implicated (Basilakos et al., 2015; Itabashi et al., 2016; Moser et al., 2016). Overall, these findings suggest the presence and severity of AOS can most likely be inferred from the extent of damage to the lateral premotor and motor cortices, and potentially the IFG when AOS co-occurs with aphasia.

Differential Diagnosis

Although AOS can result from any process that injures the implicated brain regions (i.e., trauma, neoplastic, or neurodegenerative conditions), vascular etiologies are the most common (Duffy, 2013). In addition to being the most common cause of AOS, MCA infarction frequently results in aphasia, and overlap between the two disorders is expected in the majority of cases of

AOS (Graff-Radford et al., 2014). The differential diagnosis of AOS from aphasia has proven to be problematic for researchers and clinicians alike, as the phonemic errors in AOS appear similar to those resulting from phonological paraphasias in most speech and language assessments (Galluzzi, Bureca, Guariglia, & Romani, 2015). Despite the perceptual resemblance among these disorders, the errors are the result of different mechanisms (i.e., linguistic for aphasia and motoric for AOS) and require distinct therapy approaches, making differential diagnosis crucial for planning interventions. Presently, the majority of clinicians make diagnoses by identifying and rating the severity of deviant features during speech tasks, and assessing AOS based on the presence of primary characteristics such as sound distortions, inconsistent errors, increasing errors with increasing complexity, and equal stress across syllables (Ballard et al., 2016; Haley, Cunningham, Eaton, & Jacks, 2018; Haley, Jacks, Richardson, & Wambaugh, 2017). Many researchers have questioned the validity and clinical utility of qualitative perceptual measures, and have sought to determine a quantitative verification method to use as a gold-standard for diagnosis (Ballard et al., 2016; Bislick et al., 2017; Galluzzi et al., 2015; Haley et al., 2018; Haley et al., 2017; Ziegler, 2017). In his critical review of characteristics used to differentially diagnose AOS, Ziegler (2017) argued properties of errors on individual phonemes, such as the complexity of typical acquisition, do not reflect the nature of the motor impairments. As such, phonological approaches are insufficient to capture the deficits in articulatory planning. His conclusions are consistent with the findings of Ballard et al. (2016), Bislick et al. (2017), and Haley et al. (2017; 2018), where they determined phonemic distortions and inconsistencies to be higher for individuals with AOS than those with aphasia but existing on a continuum, with significant overlap between the two groups. In Ballard and colleagues' (2016) predictive model, they found the greatest diagnostic sensitivity and specificity when examining frequency of errors in words of increasing length and a decrease in contrastive stress, as measured by vowel duration in multisyllabic words. Their work was corroborated by Basilakos et al. (2017) in their analysis of the diagnostic potential of various objective acoustic measures of speech production, including the Pairwise Variability Index (a measure of vowel duration in multisyllabic words), voice onset time variability, and proportion of distortion errors. Although work is still needed in this area, the evidence base currently suggests the presence and severity of AOS is best diagnosed by considering articulatory distortions and inconsistencies within the context of the required speech motor complexity, and dysprosodic speech with reduced stress and intonation.

Treatment of Apraxia of Speech

Literature on interventions to treat AOS is sparse, particularly in comparison to the numerous studies attempting to describe the nature and distinguishing features of the disorder. However, there are recognized behavioural interventions that are efficacious for treating the speech features associated with AOS, both in the acute and chronic stages (Duffy 2013; Mauszycki, Wright, Dingus, & Wambaugh, 2016). Duffy (2013) categorizes interventions for AOS into speaker-oriented approaches, with the goal of improved speech, and communication-oriented approaches, where compensatory strategies are used to facilitate listener comprehension independent of speech intelligibility. Communication-oriented approaches include use of augmentative and alternative communication (AAC) and/or using physical gestures to supplement speech or vocalizations. Speaker-oriented approaches are further categorized into articulatory-kinematic, rate-rhythm, and other techniques and approaches, and will be the focus of the remaining review (Duffy, 2013).

In their recent systematic review of interventions for AOS, Ballard and colleagues (2015) suggested there is strong evidence to support treatment effects associated with both articulatory-kinematic and rate-rhythm approaches. Articulatory-kinematic techniques focus on training the motor programming of articulatory movements and positions using a response-contingent multimodal cueing hierarchy and repeated productions, in an attempt to establish the correct motor pathway (Ballard et al., 2015; Duffy, 2013). Cues used in articulatory-kinematic hierarchies capitalize on the tendency for those with AOS to have greater success when they are provided with a model, as it eases the demands on their own motor programming capacity (Marangolo et al., 2011). The theory behind the articulatory-kinematic approach is based on principles of motor learning, and as such requires intensive treatment with many repetitions in order to build speech motor commands towards automaticity (Duffy, 2013; Wambaugh & Mauzycki, 2010). Sound production treatment (SPT) is a well-studied articulatory-kinematic intervention with established effect sizes, and a systematic review of ten investigations suggest it be used as a benchmark for other or supplementary treatment approaches (Bailey, Eatchel, & Wambaugh, 2015; Wambaugh & Mauzycki, 2010; Wambaugh et al., 2017). Comparatively fewer studies have been done on rate-rhythm approaches, however, the results are promising. When individuals with AOS are taught to slow their rate of speech and use a rehearsed rhythm and stress pattern, it has been shown to reduce both the prosodic abnormalities and phonetic errors frequently seen in this population, as intonation is known to facilitate articulation (Ballard et al., 2015; Duffy, 2013). These techniques also require an intensity similar to that of articulatory-kinematic approaches to be effective, and therefore, with either approach, clients with AOS are required to attend sessions multiple times a week and/or engage in intensive at home practice to achieve the necessary number of practice trials on a few carefully chosen targets in order to see improvements.

The various intervention approaches described are not mutually exclusive, and can be combined and augmented with additional supports to facilitate improvements. Recent advances in technology, including visual biofeedback (VBFB) and self-administered computer therapy, have the potential to supplement the traditional approaches and promote faster acquisition of motor skills (Basilakos, 2018; Mauszycki et al., 2016). Mauszycki and colleagues (2016) examined the effects of using electropalatography (EPG), a mechanism of VBFB using a pseudopalate that detects lingual contact, in conjunction with articulatory-kinematic therapy on the accuracy of speech sounds in individuals with chronic AOS. They found significant effects for all four participants on the majority of targeted phonemes, with generalization to untreated phrases. While promising, it remains to be seen whether the expense of creating the individualized equipment required for EPG is beneficial over and above traditional approaches.

Self-administered computer therapy could prove to be a more cost-effective supplement to traditional behavioural interventions, as it has the potential to increase the intensity of speech-language rehabilitation by providing more practice trials either outside of direct therapy or after discharge (Basilakos, 2018; Varley et al., 2016). In a randomized control trial, Varley et al. (2016) demonstrated a positive relationship between time spent on a treatment program and accuracy on naming and repetition tasks, although participants' gains were restricted to targeted items. The extent to which effective behavioural interventions, such as SPT, can be delivered or supplemented via self-administered computer programs, remains to be seen. An important challenge arises in this context, whereby clients who are unable to receive appropriate and individualized fading of cues and feedback, may run the risk of practicing faulty motor programs or developing an over reliance on cues. Duffy (2013) suggested that clinicians should be particularly cautious in their target stimuli selection and the cues that promote accurate articulatory responses, to try and mitigate the complications that could potentially arise in the context of self-administered therapy.

Potential for Transcranial Direct Current Stimulation

Non-invasive neurostimulation techniques, such as transcranial direct current stimulation (tDCS), could prove to be an economical solution for the current issues in treating individuals with post-stroke AOS. When paired with traditional behavioural therapy techniques for both aphasia and limb apraxia, tDCS has been shown to facilitate significantly greater improvements when compared to sham-stimulation or therapy alone (Baker, Rorden, & Fridriksson, 2010; Bolognini et al., 2015; Deroche, Nguyen, & Gracco, 2017; Fiori et al., 2011; Galletta, Conner, Vogel-Eyny, & Marangolo, 2016; Giustolisi, Vergallito, Cecchetto, Varoli, & Romero Lauro, 2018; Marangolo et al., 2011; Marangolo et al., 2013; Wang, Wu, Chen, Yuan, & Zhang, 2013). In a neuroimaging study, Saur and Hartwigsen (2012) demonstrated that long term recovery after stroke is primarily the result of two mechanisms: an initial functional takeover from the contralateral hemisphere, often followed by a subsequent restoration of activation to the perilesional areas of the injured region. Since hemispheres exhibit an inhibitory effect on one another, the over activation of the contralateral area(s) decreases neural activity in the injured hemisphere, therefore reducing the amount of neoplastic recovery that takes place (de Aguiar, Paolazzi, & Miceli, 2015; Murase, Duque, Mazzocchio, & Cohen, 2004; Saur & Hartwigsen, 2012). It is theorized that neuromodulation delivered via tDCS can help to facilitate neural rebalancing, which is the underlying mechanism of positive behavioural outcomes during rehabilitative therapy in the subacute and chronic stages of stroke recovery (Darkow, Martin, Würtz, Flöel, & Meinzer, 2017; Murase et al., 2004).

Bikson et al. (2016) define tDCS as "a technique in which the dose is a waveform of single sustained direct current, with the exception of one ramp-up and one ramp-down period, applied to the head using at least one cephalic electrode" (p. 642). Each tDCS device contains at least one anodal and one cathodal electrode, which function to increase and decrease cortical excitability, respectively. A weak current is delivered to the scalp via the anodal electrode, which then exits through the cathodal electrode after passing through the intermediary brain regions (Bikson et al., 2016; Lefaucheur et al., 2017). As the current flows through the brain, it alters the membrane potential of the neurons, which in turn alters the thresholds required for neuronal firing through depolarization or hyperpolarization, depending on the direction of the flow of current through the axon (Lefaucheur et al., 2017; Nitsche et al., 2008; Nitsche et al., 2003; Stagg & Nitsche, 2011). Unlike other neurostimulation techniques (e.g., transcranial magnetic stimulation), tDCS does not cause action potentials but instead facilitates/inhibits them by inducing changes in membrane potentiation, and subsequently, neural plasticity and long term potentiation (LTP; Giordano et al., 2017). Various stimulation parameters have been investigated to determine the most efficacious methods for eliciting LTP, conventionally adhering to 1-2mA for 10-30 minutes with no consistent standards for frequency, intervals, and electrode placement (de Aguiar et al., 2015; Giordano et al., 2017). Nitsche and Paulus (2000; 2001) demonstrated in a pair of studies that stimulation for several seconds was enough to induce excitability changes, whereas, longer sessions of several minutes were required for LTP. Monte-Silva et al.'s (2013) study examined repeated doses, and found LTP was maintained for longer periods after each subsequent session of anodal stimulation. In addition to duration and frequency of stimulation, a parameter impacting the efficacy of tDCS is current density (C/cm^2), with greater current densities resulting in stronger online and aftereffects of tDCS (Nitsche et al., 2008). Although increasing stimulation parameters can facilitate results, knowledge of the upper safety limits has yet to be tested and risks for adverse side effects, such as skin irritation, are increased with stronger doses beyond standard protocol (Bikson et al., 2016; de Aguiar et al., 2015; Nitsche et al., 2008). For this reason, conventional parameters in which no evidence of irreparable harm have been found in either healthy or clinical populations are adhered to in human studies (Bikson et al., 2016; Nitsche et al., 2008). Safety reviews of tDCS advise researchers and clinicians to take precautions when administering tDCS to children, the elderly, and those with lesions (i.e., individuals recovering from stroke), as it has yet to be determined how differences in the neuroanatomy of these individuals could impact the flow of current. In addition, those with contraindications to electrical stimulation should not receive tDCS (e.g., epilepsy, migraines) to reduce the risk of any serious adverse reactions (Bikson et al., 2016; Nitsche et al., 2008).

Substantive research has been done on the use of tDCS to enhance language and/or motor outcomes in participants receiving behavioural therapy after stroke, both in acute and chronic phases (Galletta et al., 2016; Marangolo, 2017; Kang, Summers, Cauraugh, & Kang, 2016). In a systematic review of 25 articles examining the use of tDCS in aphasia rehabilitation, Galletta et al. (2016) reported significant gains in the tDCS condition for all studies, although the inclusion of a sham-stimulation control group for comparison was limited. Outcome measures ranged from lexical retrieval during confrontation naming to conversational discourse, and similar effects were seen across studies independent of the chosen behavioural approach. An examination of Lefaucheur's (2016) database of published tDCS clinical trials provides complementary evidence in support of the effects of tDCS on language outcomes. Forty-nine studies examining tDCS in conjunction with treatment for both post-stroke aphasia and primary progressive aphasia (PPA) were included. Thirty-nine of these studies demonstrated greater effects of active tDCS when compared to a sham control group, even though stimulation parameters varied widely among the studies in the database. A critical review by ALHarbi, Armijo-Olivo, & Kim (2017) discussed the variability in tDCS and aphasia research, and how the inconsistencies in methodology combined with the variable nature of working with patients who have unique lesions and characteristics poses several challenges for analysis and interpretation of the evidence. The variability in outcomes has resulted in contradictory views expressed in the literature, with Elsner, Kugler, Pohl, & Mehrholz (2013) stating in their review of randomized control trials that no evidence exists as to the effectiveness of active tDCS relative to sham controls. A similar lack of consensus on using tDCS in combination with motor learning is also described by Kang et al. (2016) and Buch et al. (2017). Although they agree findings are generally supportive of using tDCS as a supplement to recovery of limb movement after stroke, they note that the inter- and intra-variability effects are not well understood, and as such, evidence-based individualized treatment cannot be administered at this time (Buch et al., 2017; Kang et al., 2016). While future research is required on the mechanisms and modulators of tDCS, a robust evidence base is emerging to inform its use both for aphasia and hemiparesis, with results quickly moving from the pre-efficacy to efficacy level (ALHarbi et al., 2017).

The extent to which the benefits of tDCS extend to motor speech disorders, particularly AOS, has yet to be determined. Marangolo et al. (2011; 2013) conducted two repeated measures studies examining the effects of tDCS in conjunction with language therapy in participants with concomitant AOS and nonfluent aphasia, and found significant improvements on all outcome measures when participants where in the active tDCS condition relative to the sham condition. In their first study, Marangolo et al. (2011) applied anodal-tDCS (A-tDCS) of 1mA to the lesioned IFG of three participants with chronic aphasia and apraxia: 1) for 20 minutes, 2) for 5 consecutive days during language treatment, and 3) with a 6-day washout interval. The outcome measures included response accuracy for single word naming, repetition, reading, and writing tasks. In the second study, Marangolo et al., (2013) expanded the sample size to eight participants with chronic AOS, and used bihemispheric anodal ipsilesional and cathodal contralesional stimulation of 2mA to the IFG for 20 minutes for 10 sessions with a 14-day washout interval. In addition to single word accuracy, they added accuracy of syllables and sentences, and response time as outcome measures. The authors report significant gains in all outcome measures for all participants, which is promising preliminary evidence for the use of tDCS in this population.

Summary

Presently, the evidence base on interventions for AOS has focused primarily on training motor sequences via the principles of motor learning and rate control, and while effects for current interventions are generally positive, they demand intensive treatment. TDCS is a potentially promising tool for the treatment of individuals with AOS, as it has been associated with improvements in both language and motor learning when combined with behavioural rehabilitation therapy for individuals with post-stroke aphasia and/or hemiparesis. Marangolo et al. (2011; 2013) is the only group to have investigated using tDCS in this population and their results were promising. However, no tasks were administered to differentiate linguistic errors resulting from phonological paraphasias vs. errors due to the apraxic impairment in motor planning. The distinction is critical, as the improvements seen in these experiments could be the result of the previously demonstrated effects of tDCS on aphasia, rather than AOS. As such, it remains unclear whether tDCS is a useful adjunct for treatment of motor speech disorders.

Purpose

Rationale

The present study seeks to assess the potential usefulness of A-tDCS as an adjunct tool with behavioural training to improve speech production in individuals with AOS by examining speech accuracy on tasks of increasing motor complexity. These speech tasks will differentiate between phonological paraphasias due to aphasia and phonemic errors due to AOS by comparing performance on tasks with low and high speech motor complexity. If the percentage of phonemes in error are similar at both levels of complexity the origin is likely linguistic, and if the number of errors significantly increases with motor complexity the origin is more likely to be in speech motor planning and/or programming. Additionally, if A-tDCS and training is faciliatory for improvements in AOS it is expected the improvements will be restricted to complex speech tasks.

Research Question

To what extent does A-tDCS over the primary motor cortex, in conjunction with behavioural training, improve speech accuracy in tasks of increasing motor complexity in adults with AOS?

Hypotheses

Based on the current literature, it is predicted that training plus A-tDCS over the primary motor cortex will lead to greater improvements in the precision of speech production, as measured by the percentage of accurate phonemes in contexts of increasing complexity (i.e., simple speech tasks of single phonemes to bisyllabic words, and more complex multisyllabic words), as compared to training and sham stimulation (S-tDCS). Additionally, it is hypothesized the improvements in the A-tDCS condition will be greatest in the most complex speech tasks (i.e., multisyllabic words).

Methods and Procedures

Participants

In order to examine the effects of anodal vs. sham stimulation on speech production in adults with AOS, two individuals (both male; ages 64 and 74) were recruited from Corbett Clinic at the University of Alberta. Inclusion criteria required participants to speak English as a first language and have previous right hand dominance in order to maximize the likelihood of motor speech localization in the site of stimulation. Those with a history of epilepsy and/or migraines were excluded so as not to confound results or increase the risks of participation. A screening procedure using speech tasks for assessing motor speech programming capacity (*Appendix A*) was administered at the first session in order to determine the presence and severity of AOS, as well as provide baseline data for interpretation (Duffy, 2013). Recordings were reviewed by an additional SLP with training and experience in AOS to determine presence and severity of AOS, based on Duffy's (2013) diagnostic criteria. Prior to participation, individuals provided their informed written consent.

Demographics of the two participants are listed in *Table 1*. Both subjects suffered from chronic communication difficulties due to a single CVA affecting the left hemisphere. Previous diagnoses by the clinicians at Corbett Clinic included Broca's aphasia concomitant with their AOS, and both presented with slow effortful speech, word-finding difficulties, phonemic errors, and articulatory groping consistent with their diagnoses.

Table 1. Demographics of the research participants.

Participants	Age	Sex	Aphasia Diagnosis	Time Post-onset	Concurrent therapy	Contraindications
Subject 1	64	M	Broca's	6 years	None	None
Subject 2	74	M	Broca's	10 years	None	None

Experimental Design

Post-hoc adjustments were made to the experimental design due to significant challenges recruiting participants that met the inclusion criteria. In the proposed investigation, a larger sample size (*N*=20) would have been divided into the two conditions and a 2 x 4 mixed ANOVA would have been run for the two independent variables: stimulation group (2 levels; between groups) and time (4 levels; within groups).

Since the final sample was considerably smaller than proposed (*N*=2), a modified repeated measures single case study across two participants was employed to interpret the results. Although a stable baseline across sessions was not established before introducing the intervention and it was not systematically removed and reintroduced from a single participant, the multiple time points recorded for each of the subjects allows for interpretation of results using descriptive analysis, and multiple converging measures including trend and percent non-overlapping data (PND) were used to add strength to the findings. Logan, Hickman, Harris & Heriza's (2008) checklist for evaluating the strength of single subject research designs (SSRD) was completed, and found the resulting study to be of moderate strength (*Appendix B*) based on their categories for levels of evidence.

Materials

Sessions were audio and video recorded onto an SD card using a Canon video camera, and transferred to a standard Dell laptop computer before being deleted from the card. This computer was also used to present the speech motor planning training tasks under stimulation (sentences with specific phonemes, *Appendix C*), with the sound level held constant at 60% of its maximum volume. The training task was presented via MATLAB software (The MathWorks, Inc., Natick, MA, USA) with a corresponding audio track to support production for individuals with concomitant language and/or reading disorders (i.e., aphasia and alexia, respectively). The same set of sentences were repeated for 30 minutes, however, the order of occurrence was randomized with each cycle. Assessment forms with the tasks for assessing motor speech programming capacity were used to score and record observations both pre-and post-stimulation (Duffy, 2013). A form outlining a detailed measurement protocol for electrode placement was followed to locate region FC5 on a 10/20 system (*Appendix D*). Nuprep Skin Prep Gel (Weaver and Company, Aurora, CO, USA) was applied to the area prior to attachment of the electrodes. A Chattanooga Iontophoresis tDCS device (Chattanooga Group, Hixon, TN, USA) was used to deliver 2mA of stimulation for 30 minutes via 5cm by 4cm sponge electrodes soaked in 7mL saline solution (0.9%; 36g/4L concentration).

Procedure

Participants attended four, two-hour sessions scheduled for the same time on four consecutive weeks. Before attending their first session, participants were randomly assigned to receive either A-tDCS or S-tDCS, and blinded to their stimulation condition. Subject 1 was assigned to the S-tDCS (control) condition, and Subject 2 was assigned to A-tDCS (experimental) condition.

Following the participants' completion of informed written consent forms, demographic and case history information was collected. The participants were then oriented to the experiment protocol. At each session, Duffy's (2013) tasks for assessing motor speech programming capacity were administered by the experimenter both pre- and post-stimulation. The assessment involves repeating increasingly complex speech tasks (i.e., single phonemes, words, and sentences), diadochokinetic tasks (e.g., repeating 'puhtuhkuh' rapidly), as well as rehearsed or automatic (e.g., counting) and conversational speech. Speech tasks required are summarized in *Table 2*.

Table 2. Level of complexity and number of stimuli in each of the speech tasks conducted during Duffy's (2013) tasks for assessing motor speech planning and programming capacity.

Speech Task	Level of Complexity	Number of Stimuli
Single Phonemes	Simple	15
Monosyllabic Words	Simple	15
Automatic Speech	Simple	2
Words of Increasing Length	Both	6 Simple, 4 Complex
Triple Repetitions	Complex	10
Sentences	Complex	3
Conversational Speech	Variable	1

The subject was seated closely to the experimenter and prompted to watch the experimenter's mouth to facilitate their own articulatory movements. Instructions stated that the participant should try their best to attempt a production, even if they felt they would be incorrect.

If the participant was not attending to the experimenter during a stimulus, the instructions were repeated and they were given a second attempt at the production. The experimenter made note of the responses as they occurred, and the recordings were later analyzed by both the examiner and a second experienced assessor to determine speech accuracy at differing levels of complexity.

Following the pre-stimulation tasks, Subject 2 (A-tDCS condition) received a 2mA current delivered through an active electrode over the primary speech motor cortex (region FC5 on a 10/20 system), and a reference electrode over the contralateral homologue region for 30 minutes. Subject 1 (S-tDCS condition) received the same current delivered for 30 seconds before the device is turned off to provide a perceptually similar experience to the A-tDCS (i.e., initial tingling). While under stimulation, both groups completed articulatory-kinematic exercises using sentences with specific phonemes presented with a corresponding audio track on MATLAB to practice oral motor movements during speech. Sixteen sentences were presented repeatedly in a randomized order, consistent with research that suggests individuals with AOS need many repetitions in order to facilitate improvements in motor planning and/or programming (Duffy, 2013). After the 30 minutes of training, electrodes were removed from the participants and the motor speech programming capacity tasks were administered again to measure speech accuracy and consistency (Duffy, 2013).

Data Analysis

Transcription

Audio and video recordings from each session were reviewed, and the phonemes and words from Duffy's (2013) tasks for assessing motor speech programming capacity were transcribed using the International Phonetic Alphabet (International Phonetic Association, 1999). When evaluating the effect of stimulation on single word repetitions, only the first production of the triple word repetitions was recorded in order to be consistent with the motor complexity of the single word repetition tasks. When an attempt was made at the target production, the number of correct phonemes was recorded and transformed into the percentage of phonemes correct (i.e., PPC). In the event the participant refused to make any attempt at the target production, the response was recorded as a refusal and excluded. If an attempt was made, but was partially unintelligible and/or abandoned by the participant, the number of phonemes the participant produced were included in the analysis. Only one trial of a stimulus was removed due to outright refusal, all others had at least an attempt at production. When the participant made self-corrections or had multiple attempts at producing the stimulus, their best attempt was recorded.

Descriptive Analyses

In order to compare speech motor planning and/or programming across conditions, separate descriptive analyses were conducted at each of the levels of motor complexity (i.e., single repetitions of simple words, single repetitions of complex words, and triple repetitions of complex words). Procedures for descriptive analysis for condition contrasts described by Chen, Hyppa-Martin, Reichle, & Symons (2016) were used to examine the visual representations of the findings. In order to determine if an intervention effect is present, they suggest four indicators be examined and evaluated: immediacy, variability, level, and trend.

Immediacy. Chen et al. (2016) suggest that in order to assess for immediacy, the first three data points should be compared between groups. Since each session involved two data points to track change pre- and post-stimulation, the first three differences in PPC within the first three sessions were compared to determine if immediacy was present in the data.

Variability. Difference in spread of the data around the mean of the A-tDCS and S-tDCS conditions was measured using the standard deviations of the differences in PPC between groups.

Level. Chen et al.'s (2016) third descriptive indicator requires analyzing the difference between the two means in order to determine the likelihood that an intervention effect was present. Mean PPC differences between participants were compared to assess for this indicator.

Trend. A line of best fit was extrapolated from the PPC data across all time points pre- and post-stimulation, and the slope of this line is used to assess the trend. If large differences are present between groups, it is compelling evidence for intervention effects.

Percentage Non-Overlapping Data (PND). A second approach to analysis of single-subject studies is recommended by Scruggs & Mastropieri (2001). By analyzing the percentage of data points during intervention that surpass those in the baseline measure, the presence and size of the intervention effect can be determined. Since we used a modified repeated measures single case study design, baseline was considered to be the pre-stimulation PPC of each session, and the PND was calculated on the percentage of data points in the post-stimulation trial that fell or maintained baseline level accuracy. As the control condition demonstrated typical results of practice effects, the maintenance was defined as the maximum difference within a session of the control group.

Effect Size. Petersen-Brown, Karich, & Symons (2012) use the first four criteria described above to determine the size of the intervention effect if one is present. At least two out of the four criteria must demonstrate a contrast in order for a small effect to be present, three out of four a moderate effect, and if all four demonstrate differences, a large intervention effect can be inferred. PND can also be used to interpret the effect size, with scores of 50-70% of non-overlapping data to reflect small intervention effects, 70-90% a moderate effect, and 90% or higher indicates a large effect (Scruggs & Mastropieri, 1998).

The Complex Speech Tasks

Single Repetitions.

Differences in PPC of single repetitions of the complex multisyllabic words were included in the first descriptive analysis, which reflected a modest challenge to the speech motor planner/programmer. In this speech task, the participant was presented with a complex multisyllabic word by the experimenter, and was asked to repeat it back immediately. As previously stated, for words that were repeated three times, only the first repetition was used to control for time between presentation of the stimulus and required production. Chen et al.'s (2016) descriptive analyses and Scruggs & Mastropieri's (1998) PND were used to determine if any differences were present between the two participants.

Triple Repetitions.

The speech task included repetition of a multisyllabic word three times after it was presented by the experimenter. This task taxes the speech motor planning and/or programming system more than single word production and demonstrates the variability in production characteristic of AOS. Both participants were able to complete the task at the greatest level of complexity. Exploratory analyses involved examining the immediacy, variability, level, trend, and PND to examine if differences exist between conditions at this level (Chen et al., 2016; Scruggs & Mastropieri, 2001).

The Simple Speech Tasks

The PPC of stimuli at the simple level of motor complexity (i.e., one repetition of single phonemes, monosyllabic, and bisyllabic word repetitions) were compared in order to confirm the hypothesis that 1) differences pre- and post-stimulation in PPC on simple speech tasks would be comparable between participants and 2) that the complex speech tasks would be different between the two participants over time. The four indicators used in descriptive analysis (i.e., immediacy, variability, level, and trend) were examined and the PND was calculated in order to determine if any unanticipated differences were present within and between the participants (Chen et al., 2016; Scruggs & Mastropieri, 2001).

Reliability

To ensure validity and reliability, transcriptions and frequency counts were verified by an independent assessor with experience in diagnosing and treating individuals with AOS. Sufficient interrater reliability was found, as after reviewing all of the video recordings and transcripts 100% consensus was achieved with respect to accuracy of the transcripts. If minimum acceptable agreement had not been reached, points of variability would have been examined by both raters and adjusted accordingly.

In order to assess intrarater reliability, ten percent of the data from each session was randomly selection to be reanalyzed by the same rater. Sufficient reliability was found within rater transcriptions, at 92.6% agreement.

Results

A total of 1119 stimuli ($N = 560$ for Subject 1; $N = 559$ for Subject 2) met inclusionary criteria for at least one form of visual analysis between the two conditions. One stimulus, the third repetition of the word 'statistics', was removed from Subject 2 during the first session post-stimulation due to refusal after two attempted productions.

In order to assess the likelihood the effects of intervention were due to improvements in speech motor planning and/or programming, comparisons between the percentage of correct phonemes on single repetitions at each level of complexity were examined ($N = 592$ simple sounds and words, and $N = 208$ complex words). Subsequent exploratory analyses of the triple repetitions of complex words was conducted in order to determine if further gains would be seen in increasing task complexity ($N = 479$).

Effect of Stimulation Condition on Complex Speech Tasks

Single repetitions.

A descriptive analysis was conducted in order to determine if differences exist in speech accuracy, as measured by PPC, between A-tDCS and S-tDCS conditions. Differences were found in all four indicators described by Chen et al. (2016), as well as in the PND.

Immediacy. *Table 3* displays the PPC data for both conditions within each of the four sessions, which also visually represented in *Figure 1*. Immediacy was present in the data, with the mean of the first three data points in the A-tDCS condition falling over two standard deviations above that of the S-tDCS condition ($M = 7.32$, $SD = 5.79$; $M = 0.00$, $SD = 2.46$, respectively).

Variability. Variability also differed, with the A-tDCS condition having considerably less consistency over trials than the S-tDCS condition (*SD* = 5.61; *SD* = 2.05, respectively). *Table 4* displays standard deviations of the two conditions for interpretation.

Level. Means are also reported in *Table 4*.The mean of the A-tDCS condition fell two standard deviations above the mean of the S-tDCS condition, indicating a difference in level between participants (*M* = 5.80, *M* = -0.21, respectively).

Trend. In *Figure 2*, the PPC of multisyllabic words was graphed across time points for the A-tDCS and S-tDCS conditions. Trends of the two participants differed markedly, with the A-tDCS condition displaying a slope of 2.12 and the S-tDCS condition a slope of -0.31.

PND. Two out of the four sessions in the A-tDCS condition resulted in greater improvement than the most extreme difference within sessions seen in the S-tDCS condition, resulting in a PND = 50%.

Effect Size. The results are indicative of a difference between the A-tDCS and S-tDCS intervention conditions, with evidence of a small to moderate intervention effect.

Table 3. PPC in single repetitions of multisyllabic words before and after stimulation within each session. PPC Difference reflects the change within a session, pre- and post-stimulation.

Condition	Session	Time	PPC	PPC Difference
Subject 1 (S-tDCS)	1	Pre-Stimulation	96.51 %	-1.19 %
		Post-Stimulation	95.32 %	
	2	Pre-Stimulation	98.38 %	-1.63 %
		Post-Stimulation	96.75 %	
	3	Pre-Stimulation	94.78 %	2.83 %
		Post-Stimulation	97.61 %	
	4	Pre-Stimulation	94.69 %	-0.85 %
		Post-Stimulation	93.84 %	
Subject 2 (A-tDCS)	1	Pre-Stimulation	76.04 %	8.98 %
		Post-Stimulation	85.02 %	
	2	Pre-Stimulation	79.01 %	12.09 %
		Post-Stimulation	91.10 %	
	3	Pre-Stimulation	91.75 %	0.88 %
		Post-Stimulation	92.63 %	
	4	Pre-Stimulation	90.41 %	1.26 %
		Post-Stimulation	91.67 %	

Table 4. Means and standard deviations of the differences in PPC within sessions pre- and post-stimulation on single repetitions of complex speech tasks.

Participant	Condition	Mean PPC Difference	SD of PPC Differences
Subject 1	S-tDCS	-0.21	2.05
Subject 2	A-tDCS	5.80	5.61

Figure 1. PPC Difference by session for the A-tDCS and S-tDCS conditions on single repetitions of complex words in the Duffy (2013) assessment.

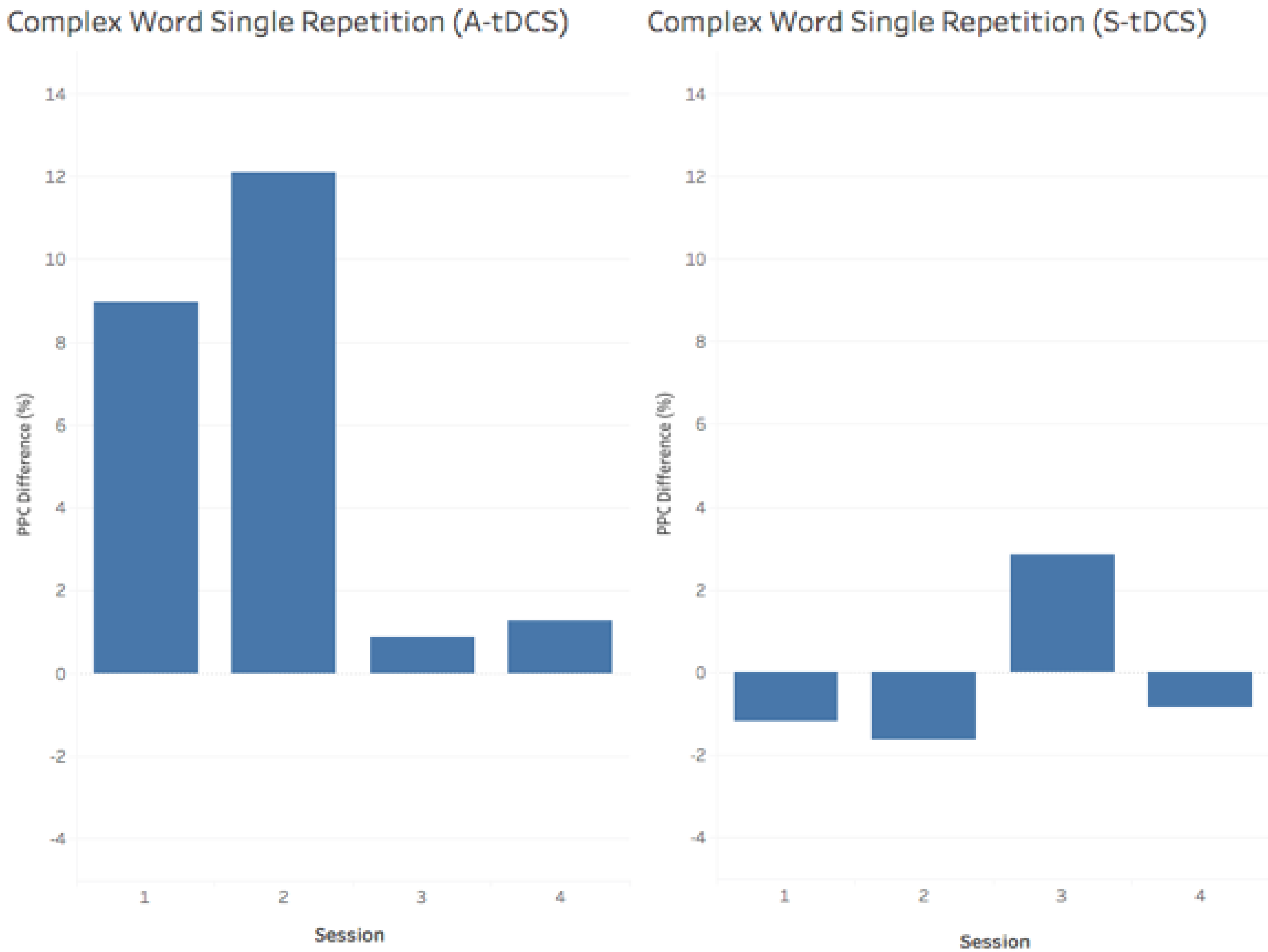
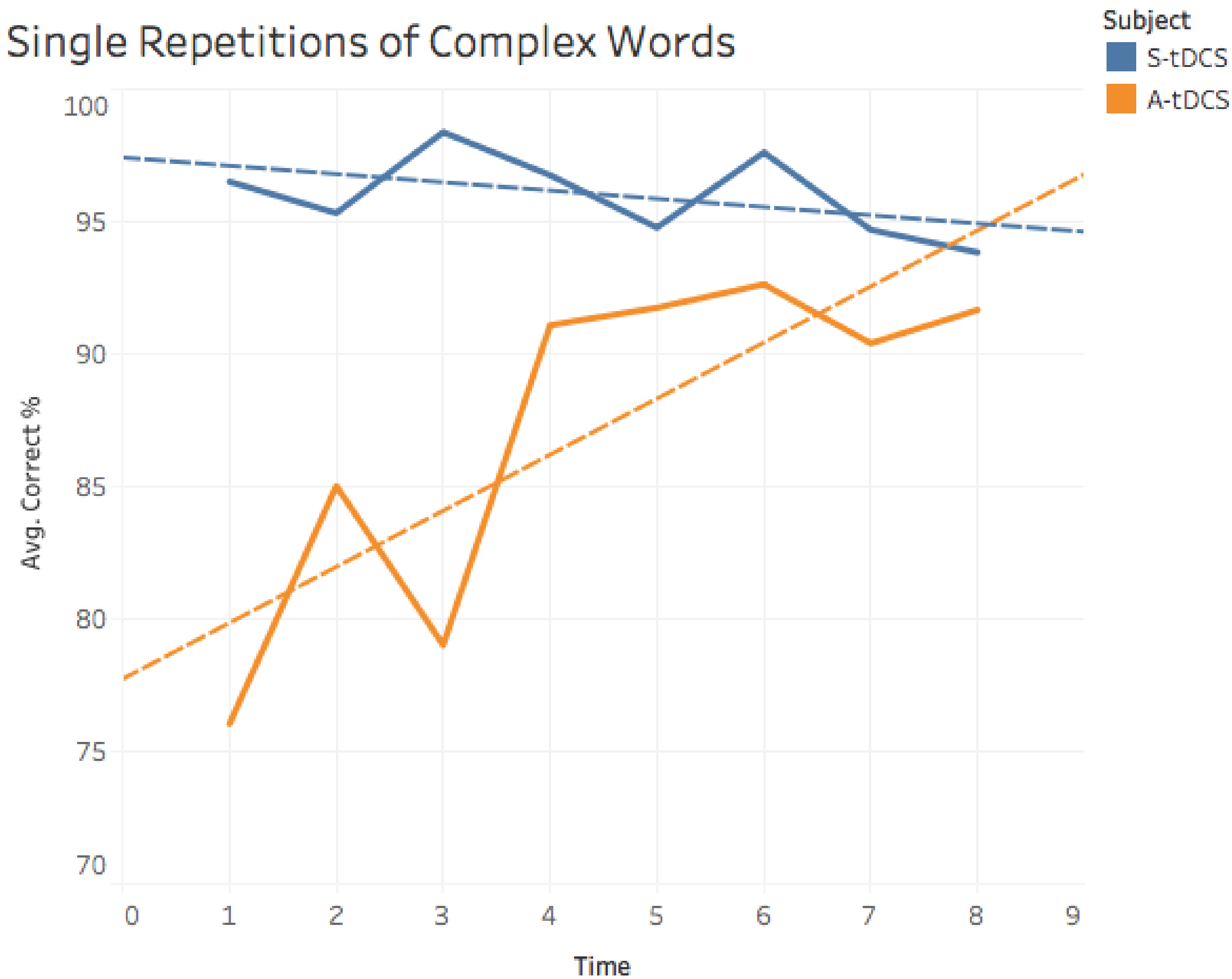


Figure 2. Average PPC in single repetitions of complex words for each of the eight time points across the four sessions. Time is reflected on the *x*-axis, with odd numbered time points representing the pre-stimulation results and even-numbered time points reflecting post-stimulation results.



Triple Repetitions.

The same procedure was used on the more complex triple repetitions of complex words in order to determine if increasing complexity resulted in a greater difference between the A-tDCS and S-tDCS participants. Once again, differences were found in all four indicators described by Chen et al. (2016), as well as a larger PND.

Immediacy. PPC and PPC Differences are presented in *Table 5*, and visually compared in *Figure 3.* Immediacy was present in the data, with the mean of the first three data points in the A-tDCS condition (*M* = 6.01, *SD* = 1.42) falling well over two standard deviations above that of the S-tDCS condition (*M* = 0.88, *SD* = 0.81).

Variability. Standard deviations of the differences in PPC pre- and post-stimulation for the simple speech tasks from each condition are presented in *Table 6.* The A-tDCS condition had considerably greater variability than the S-tDCS condition (*SD* = 3.02; *SD* = 0.66, respectively).

Level. *Table 6* also displays the mean differences in PPC of the tasks pre-and post-stimulation for both participants. Level differed between participants, with the mean of the A-tDCS condition falling over two standard deviations above the mean of the S-tDCS condition (*M* = 4.62, *M* = 0.93, respectively).

Trend. *Figure 4* displays the trend in PPC pre- and post-stimulation for both participants over the sessions, with a clear contrast between the slope of the A-tDCS condition at 1.56 and the slope of the S-tDCS condition at -0.04.

PND. Three out of the four sessions in the A-tDCS condition resulted in greater improvement than the most extreme difference within sessions seen in the S-tDCS condition, resulting in a PND = 75%.

Effect Size. The results are indicative of a difference between the A-tDCS and S-tDCS intervention conditions, with evidence of a moderate to large intervention effect.

Table 5. PPC in triple repetitions of multisyllabic words before and after stimulation within each session. PPC Difference reflects the change within a session, pre- and post-stimulation.

Condition	Session	Time	PPC	PPC Difference
Subject 1 (S-tDCS)	1	Pre-Stimulation	94.24 %	1.44 %
		Post-Stimulation	95.68 %	
	2	Pre-Stimulation	95.41 %	-0.04 %
		Post-Stimulation	95.37 %	
	3	Pre-Stimulation	95.27 %	1.25 %
		Post-Stimulation	96.52 %	
	4	Pre-Stimulation	93.68 %	1.08 %
		Post-Stimulation	94.76 %	
Subject 2 (A-tDCS)	1	Pre-Stimulation	77.68 %	5.78 %
		Post-Stimulation	83.46 %	
	2	Pre-Stimulation	85.87 %	4.72 %
		Post-Stimulation	90.59 %	
	3	Pre-Stimulation	87.94 %	7.54 %
		Post-Stimulation	95.48 %	
	4	Pre-Stimulation	89.78 %	0.45 %
		Post-Stimulation	90.23 %	

Table 6. Means and standard deviations of the differences in PPC within sessions pre- and post-stimulation on single repetitions of complex speech tasks.

Participant	Condition	Mean PPC Difference	SD of PPC Differences
Subject 1	S-tDCS	0.93	0.66
Subject 2	A-tDCS	4.62	3.02

Figure 3. PPC Difference by session for the A-tDCS and S-tDCS conditions on triple repetitions of complex words in the Duffy (2013) assessment.

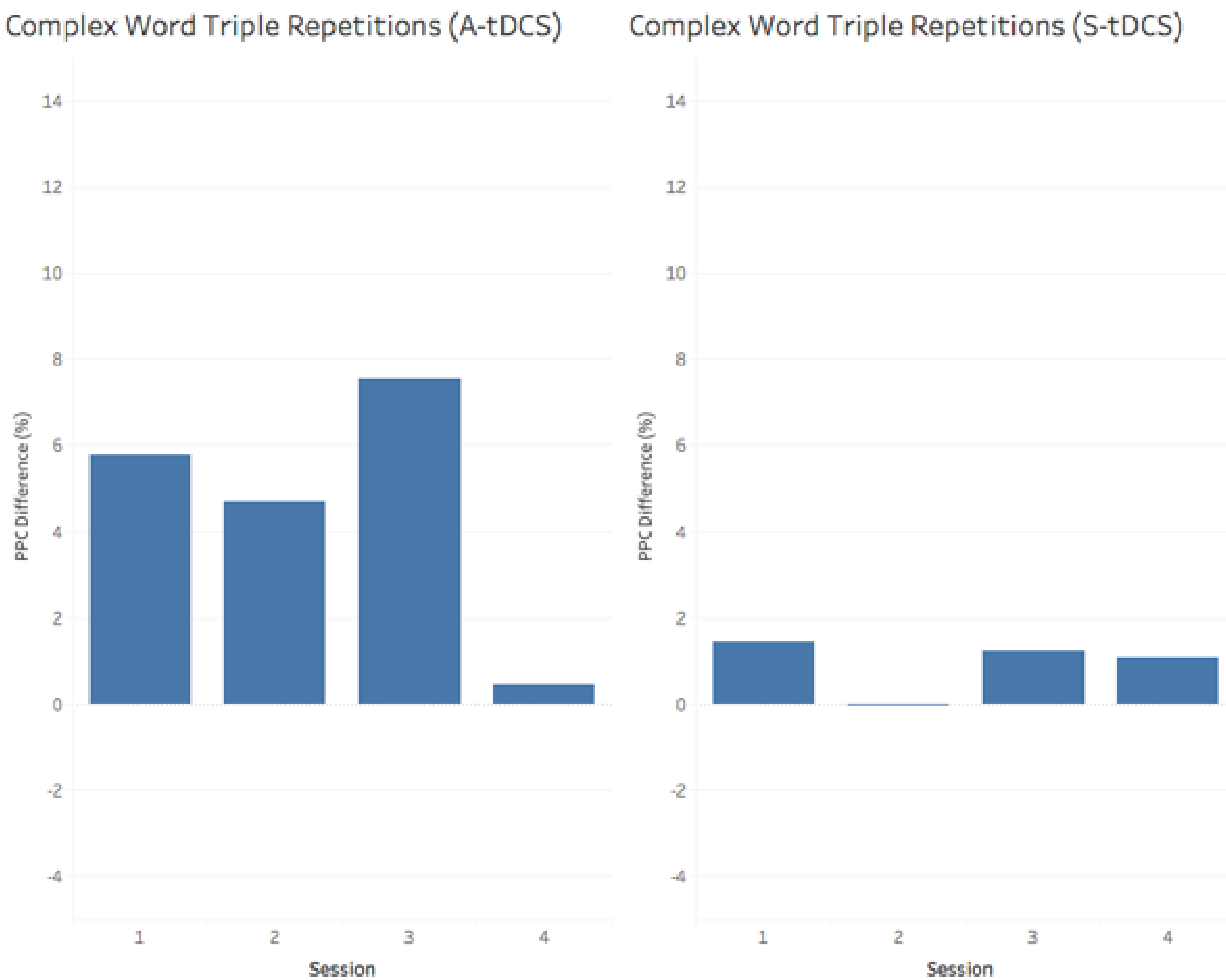
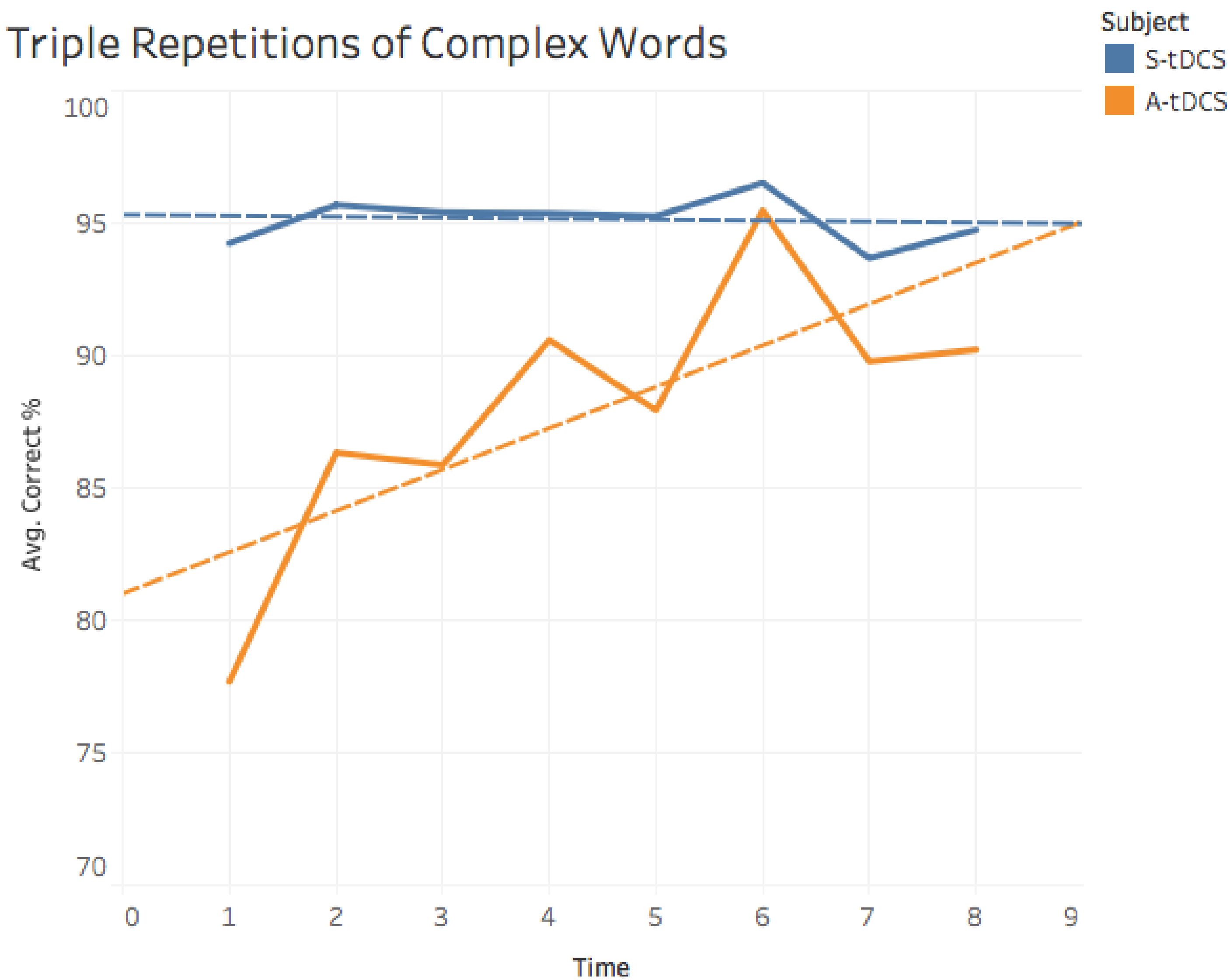


Figure 4. Average PPC in triple repetitions of complex words for each of the eight time points across the four sessions. Time is reflected on the *x*-axis, with odd numbered time points representing the pre-stimulation results and even-numbered time points reflecting post-stimulation results.



Effect of Stimulation Condition on Simple Speech Tasks

The motorically simple speech tasks were analyzed following the same procedure to demonstrate the hypothesis that no differences in phonological paraphasias would be present between groups. No differences were present in Chen et al.'s (2016) indicators, but were found in the PND.

Immediacy. In the analysis, the mean of the first three data points in the A-tDCS condition (*M* = 4.21, *SD* = 4.06) was within a standard deviation of the mean in the S-tDCS condition (*M* = 1.23, *SD* = 3.86), and therefore a difference in immediacy is not present between groups. The large standard deviations result in the considerable gains of A-tDCS in the first and second session to fall within normal variability, and therefore do not contribute enough to claim immediacy in the data. The first three data points from each condition are listed in *Table 7*, and visually represented in *Figure 5.*

Variability. Variability, as measured by standard deviations from the mean difference in PPC within sessions, did not differ between the two groups (S-tDCS condition *SD* = 3.17; A-tDCS condition *SD* = 3.45). Standard deviations are listed in *Table 8.*

Level. Differences between means, found in *Table 8*, were compared between the A-tDCS and S-tDCS stimulation conditions. Mean differences in the A-tDCS condition fell within the range of expected variability on simple speech tasks (*M* = 3.74), and therefore, while higher, were not in contrast from the mean of the S-tDCS condition (*M* = 1.37).

Trend. Graphs of PPC for each condition over time at each level of speech complexity, as seen in *Figure 6*, were compared to determine if significant differences exist in the slope of the data points. No difference existed between the participants in their improvement over the study on simple speech tasks, with the slope of the S-tDCS condition at 1.11 and the slope of the A-tDCS condition at 1.08.

PND. *Figure* 5 displays change in speech accuracy as measured by PPC of each participant at the simple level of speech complexity. Two out of the four sessions in the A-tDCS condition resulted in greater improvement than the most extreme difference within sessions seen in the S-tDCS condition, resulting in a PND of 50%.

Effect Size. These results suggest that overall there was minimal to no effect of stimulation on the motorically simple speech tasks, however, the unanticipated large difference between participants during the first session falls outside the range of expected variability.

Table 7. PPC in single repetitions of simple words before and after stimulation within each session. PPC Difference reflects the change within a session, pre- and post-stimulation.

Condition	Session	Time	PPC	PPC Difference
Subject 1 (S-tDCS)	1	Pre-Stimulation	92.25 %	-3.15 %
		Post-Stimulation	89.10 %	
	2	Pre-Stimulation	97.30 %	2.70 %
		Post-Stimulation	100.00 %	
	3	Pre-Stimulation	95.86 %	4.14 %
		Post-Stimulation	100.00 %	
	4	Pre-Stimulation	97.30 %	1.80 %
		Post-Stimulation	99.10 %	
Subject 2 (A-tDCS)	1	Pre-Stimulation	88.29 %	8.11 %
		Post-Stimulation	96.40 %	
	2	Pre-Stimulation	91.89 %	4.51 %
		Post-Stimulation	96.40 %	
	3	Pre-Stimulation	96.40 %	0.00 %
		Post-Stimulation	96.40 %	
	4	Pre-Stimulation	96.76 %	2.34 %
		Post-Stimulation	99.10 %	

Table 8. Means and standard deviations of the differences in PPC within sessions pre- and post-stimulation on single repetitions of simple speech tasks.

Participant	Condition	Mean PPC Difference	SD of PPC Differences
Subject 1	S-tDCS	1.37	3.17
Subject 2	A-tDCS	3.74	3.45

Figure 5. PPC Difference by session for the A-tDCS and S-tDCS conditions on single repetitions of simple sounds and words in the Duffy (2013) assessment.

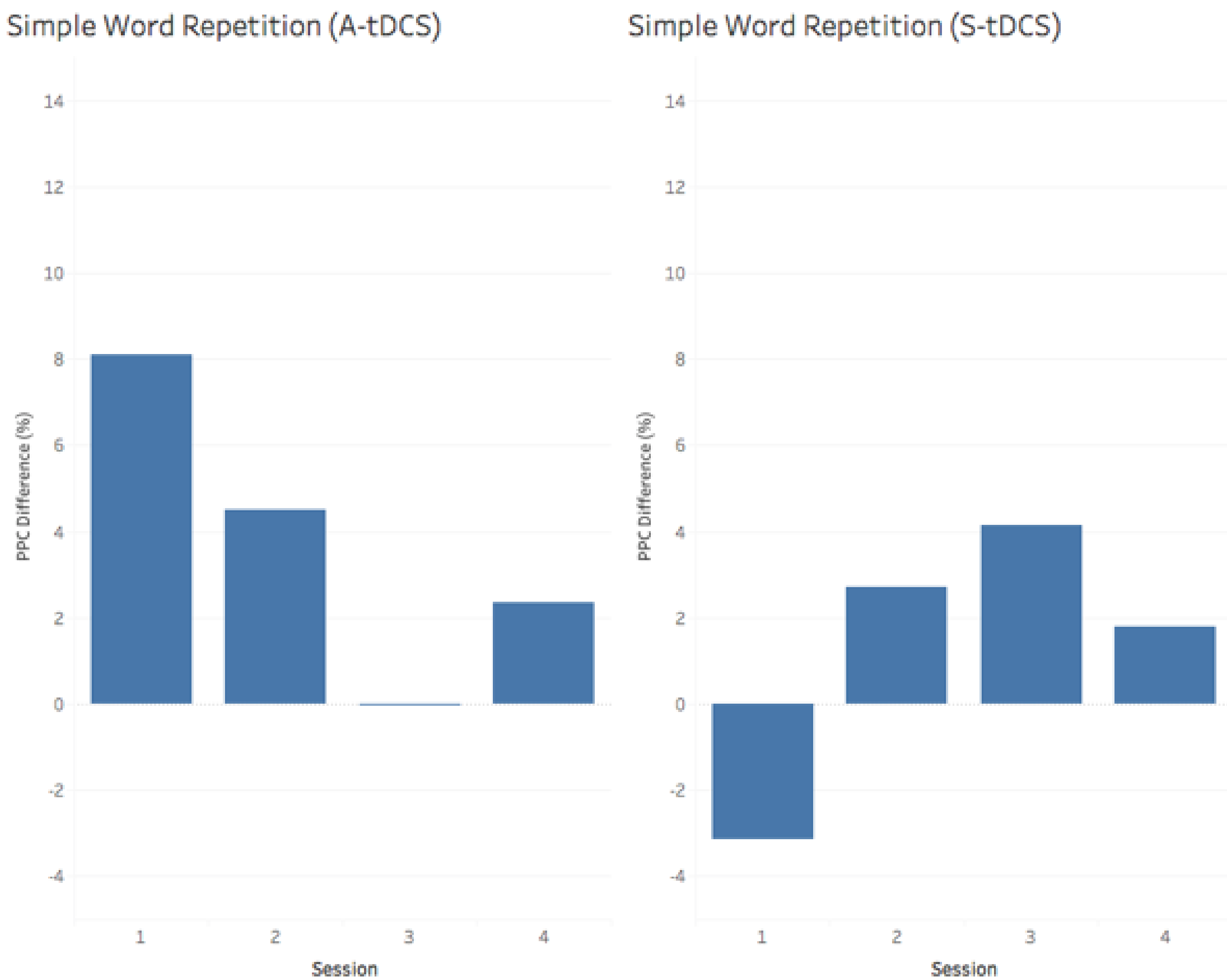
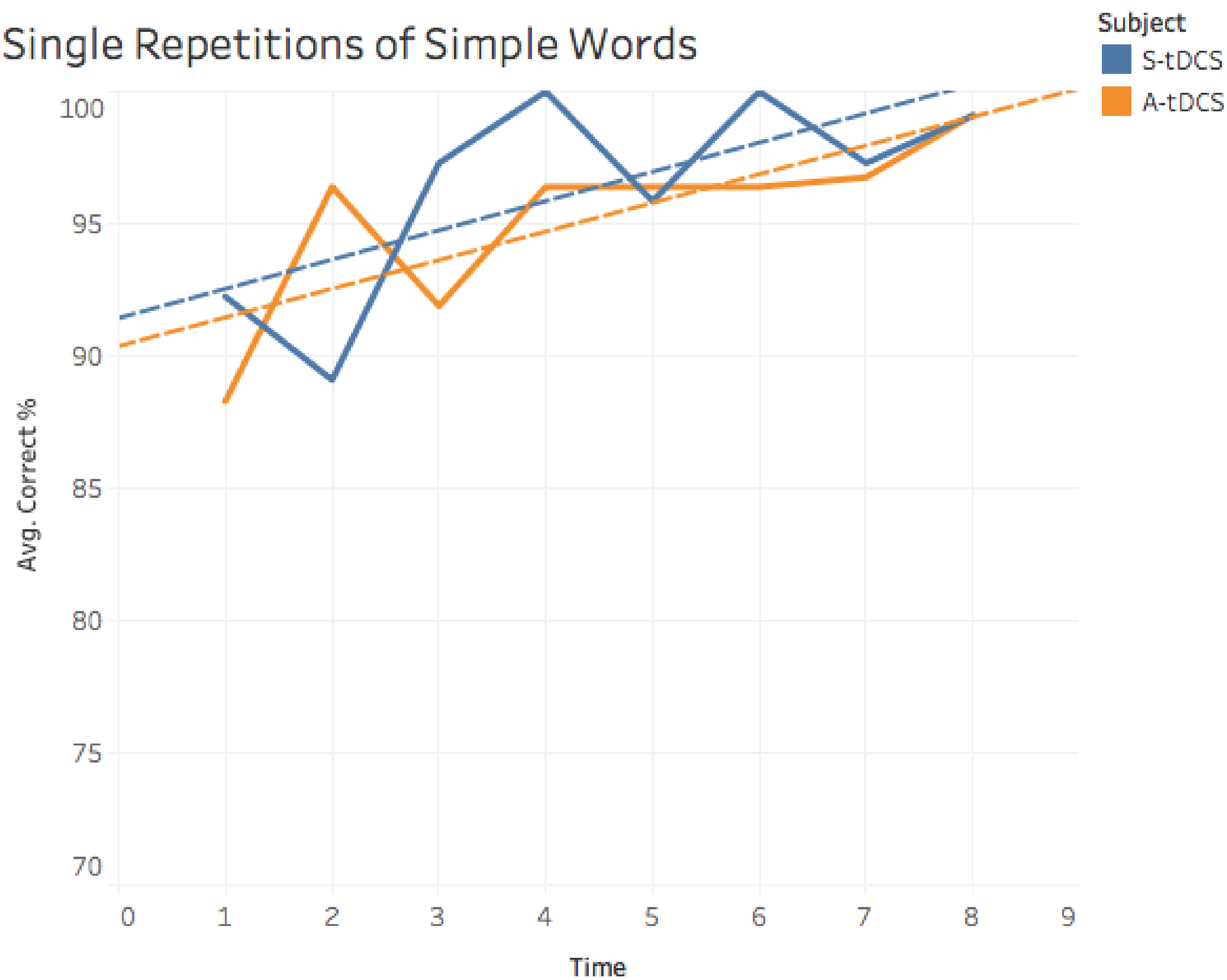


Figure 6. Average PPC in single repetitions of simple words for each of the eight time points across the four sessions. Time is reflected on the *x*-axis, with odd numbered time points representing the pre-stimulation results and even-numbered time points reflecting post-stimulation results.



Discussion

Rehabilitation after neurological injury is a long and laborious process, from the acute to the chronic stages. Since current interventions are time-consuming and have inconsistent success, using neurostimulation techniques such as tDCS to promote neuroplastic change could prove to be a highly useful treatment option in this population. The present study built on the existing work of tDCS and AOS done by Marangolo et al. (2011; 2013), with a greater emphasis on the benefits to motoric as opposed to linguistic outcome measures. Participants performed a series of speech tasks ranging in complexity from single phonemes to multisyllabic words (e.g., 'statistics') before and after receiving either A-tDCS or S-tDCS. The main findings were: 1) A-tDCS to the motor cortex resulted in a moderate intervention effect on the speech accuracy of productions of motorically complex speech tasks, as measured by PPC, when compared to the S-tDCS condition; 2) An unanticipated small intervention effect of the first session of A-tDCS was found on motorically simple speech tasks when compared to the control S-tDCS condition; 3) Differences in PPC were more variable in the A-tDCS condition, with the greatest improvement occurring in the first session and no difference in the final session.

Effect of Stimulation Condition on Complex Speech Tasks

In the complex speech tasks requiring enhanced motor speech planning and/or programming capacity, the increase in mean PPC in the A-tDCS condition corresponded to a moderate effect of intervention over the S-tDCS condition. Much of this improvement was due not only to a reduction in phonological errors after stimulation, but also decreased time spent searching for the correct oral position (i.e., articulatory groping), which reduced the amount of attempts that were abandoned before their completion. These findings are comparable to those of

Marangolo et al.'s (2013) study using similar stimulation parameters (i.e., 20 minutes of 2mA bihemispheric stimulation), where participants improved in both speed and accuracy on language measures only when they received the real stimulation. Unlike the findings of Marangolo et al. (2011; 2013), the results of the current investigation cannot solely be attributed to a rehabilitated capacity for phonological encoding. The gains made in PPC under true anodal stimulation were much greater for the motorically complex speech tasks, which reflects an improved ability to translate the encoded language into movement of the articulators. Evidence suggests increased difficulty with speech motor complexity is the one of the best diagnostic characteristics of AOS, and as such bringing the PPC closer to the level of simple speech tasks indicates increased capacity of the speech motor planner and/or programmer (Ballard et al., 2016; Basilakos et al., 2017).

The majority of the literature using tDCS as an adjunct to behavioural aphasia and hemiparesis interventions has focused on unilateral hemispheric anodal stimulation of the perilesional areas to improve language and motor control, respectively, which has variable success (Baker et al., 2010; Bolognini et al., 2015; Fiori et al., 2011). The results presented here provide further evidence to the emerging literature that interhemispheric inhibition from the intact hemisphere can be modulated by using bihemispheric stimulation (i.e., cathodal to the intact hemisphere and anodal to the lesioned hemisphere) in order to rebalance or normalize the distribution of brain function (Darkow et al., 2017; Marangolo et al., 2013; Murase et al., 2004). By not only stimulating the perilesional areas, but also inhibiting the contralateral region, it is likely the participant receiving A-tDCS was able to utilize remaining regions of his left cortex best suited to speech motor planning and/or programming, without the detrimental effects of interhemispheric inhibition. When only unilateral stimulation is used, the effects of inhibition have been reported to still be present (Murase et al., 2004).

Consensus on the most effective stimulation parameters has yet to be reached, and a large degree of variability exists in the research that has been conducted on tDCS thus far (Bikson et al., 2016; Nitsche et al., 2008). The present study used a dosage at the upper end of what has conventionally been researched on both healthy and clinical participants, and had effects comparable to other researchers using similar parameters (Lefaucheur et al., 2017; Marangolo et al., 2013; Monte-Silva et al., 2013) and no reported side effects. Taken together, these results and the lack of negative side effects inform future research into increasing the stimulation dosage, which has the potential to begin to resolve the methodological inconsistencies and variable results present in the tDCS literature to date (ALHarbi et al., 2017).

Effect of Stimulation Condition on Simple Speech Tasks

To our knowledge, this is the first study to attempt to elucidate the benefit of tDCS to motorically-based speech impairments (i.e., AOS) distinct from language impairments (i.e., aphasia). By using speech tasks that increase in their demand of motor speech planning and programming capacity, the degree of deficit from the linguistic and motor domains can be inferred, as phonological paraphasias will remain consistent across tasks while deficits due to AOS will increase as complexity increases (Duffy, 2013). It was hypothesized that A-tDCS to the motor cortex would result in improvements only in the complex speech tasks, and performance on simple speech tasks would remain constant. While our results are mostly consistent with this hypothesis, we did see an unanticipated marginal benefit of receiving true stimulation in the post-stimulation simple speech tasks during session number one. Two hypotheses are offered to explain these findings: 1) spreading of the neuromodulation benefited anatomically connected cortical regions responsible for phonological encoding; 2) personal factors of one or both participants, such as susceptibility to practice or fatigue effects, had an impact on their scores. Ultimately, future work that includes additional simple speech tasks, additional participants and withdrawal of treatment periods are needed to fully elucidate the nature of this effect.

While the effects found here are promising, much is still unknown about the specific mechanisms of tDCS, including how the current flows through the cortex while under stimulation. A large degree of variability exists in the neuroanatomy of different individuals, which impacts how the electrical current travels and if it stimulates the specific region responsible for the desired behavioural outcome. This is especially complicated in clinical populations in which an infarction is present. The missing cortical tissue does not allow current to flow in the manner that has been mapped in healthy populations, and as such the areas that receive modulation cannot confidently be determined (Bikson et al., 2016). In addition, for individuals in the chronic stages of recovery, like the participants in the present study, perilesional areas of the brain which are not usually responsible for certain functions take over what was previously controlled by lesioned areas. It is therefore difficult to determine which areas of the brain are responsible for which functions in individuals who have recovered considerably after their stroke. The uncertainty and lack of precision could result in untargeted regions receiving effects of neuromodulation, an effect described by Stagg et al. (2013) and Woods et al. (2016) as a spreading to neuroanatomically connected regions of the brain that are utilized during the online task. Since both language and motor skills are required for speech production, it is plausible the linguistic regions of the brain were inadvertently stimulated, which resulted in improvements in the participant's aphasia symptoms as well as those characteristic of AOS. The positive interaction of stimulation and treatment could have been widespread rather than isolated, which would be consistent with other studies of the effects of tDCS (Lefaucheur et al., 2017).

Alternatively, the results could be explained by individual differences in the effects of practice and/or fatigue which have consistently been established in research on repeated testing. Practice effects describe the tendency for subjects to improve their assessment performance with subsequent administrations, while fatigue refers to the loss of motivation over long periods of testing that leads to decreased accuracy and reaction times (Bartels, Wegrzyn, Wiedl, Ackermann, & Ehrenreich, 2010; Süss & Schmiedek, 2000). If the participant receiving A-tDCS, due to cognitive or personal factors, was more inclined to benefit from practice while the participant in the control condition was prone to cognitive fatigue, it could explain the divergent results from repeated testing. Although plausible, clinical observations made by the experimenter during sessions are in contradiction to this theory. Subject 1, in the S-tDCS condition, had strong personal protective factors that are known to lessen the effects of fatigue on cognitive measures, such as perseverance, a positive outlook, and a strong support system (MacIntosh et al., 2017). Subject 2, on the other hand, had lower tolerance for failure, tended to perseverate on his errors, and overall expressed a more negative outlook. These anecdotes lend strength to the first hypothesis, though the second is still worthy of consideration.

Potential Explanations of Diminishing Effects

As sessions progressed, the increased benefit of A-tDCS appeared to diminish. In the first three sessions of receiving A-tDCS, Subject 2's PPC in at least one of the complex speech tasks increased considerably, as seen in *Figure 1* and *Figure 3*. However, in the final session, no change was observed between his PPC in any task pre- and post-stimulation. Variability of the effectiveness of tDCS even within subjects is well documented in the literature, and two primary hypotheses are given to explain the appearance of this tendency in the present study: 1) variation in the state of mind, or brain state, at the time of testing, and 2) the transition from early forms of LTP (e-LTP) to the later more enduring form of LTP (l-LTP) (Giordano et al., 2017; Monte-Silva et al., 2013). Each of these is discussed in turn next.

In their discussion of pressing issues facing research into tDCS, Giordano et al. (2017) describe how converging evidence supports the hypothesis that effectiveness of tDCS is highly context dependent. As stated in the introduction, tDCS merely facilitates neural firing and is unable to cause action potentials on its own. Therefore, its effectiveness can be impacted by other factors which influence the excitability and/or inhibitory tendency of synapses, such as various individual traits that can be either consistent or fluctuating (e.g., hormonal levels, arousal, or brain state) (Giordano et al., 2017). Woods et al. (2016) explain the influence of this effect on experiments with consistent stimulation protocols, as in the majority of studies with suitable methodological rigor researchers are unable to adjust the stimulation protocols to suit variation in the internal states of the participants. Naïve subjects are particularly prone to increases in arousal due to the novelty of stimulation, and as such have enhanced variability in outcome measures (Woods et al., 2016). These findings are consistent with the performance of Subject 2, as he received the greatest effect of A-tDCS on his first session and displayed the lowest effect on a day when he exhibited reduced levels of arousal and motivation. While plausible, extensive research is needed in this area in order to determine the impact of various states of mind on responsiveness to tDCS, as well as to establish valid and reliable assessments that can be used to inform decisions on stimulation protocol in the future.

The reduced level of improvement in speech accuracy observed in Subject 2's final session could also be due to the natural dose-response (DR) curve of tDCS. Giordano et al. (2017) argue that non-invasive brain stimulation, including tDCS, follows a hormetic DR curve in which small doses are beneficial, with a tipping point in which the positive effects become null before transitioning into neural toxicity. Their position is consistent with the studies on LTP by Nitsche and Paulus (2000; 2001) and Monte-Silva et al. (2013), whereby multiple sessions of stimulation increased protein synthesis, the primary mechanism of l-LTP. While a single session of tDCS is enough to cause e-LTP through temporary modulation of glutaminergic receptors, the enduring change of l-LTP requires protein synthesis to more permanently alter the strength of the synapses, which is achieved through multiple sessions of tDCS (Monte-Silva et al., 2013). These findings and others on dosages of tDCS support the hormetic DR theory, as the beneficial neural changes have consistently been found to increase with subsequent sessions (Lefaucheur et al., 2017). However, it has yet to be determined at what point neurons have reached their full potential for l-LTP and further sessions of tDCS are no longer beneficial and may begin to be harmful (Bikson et al., 2016). It is possible that Subject 2's initial jump in results was due to the fast response of e-LTP, while subsequent sessions were indicative of the slower changes resulting from l-LTP, followed by the plateau of the hormetic DR curve indicating maximal results.

Conclusions

To conclude the findings of the present investigation, the data showed bihemispheric stimulation of tDCS to the motor cortex has potential to be used as a tool to improve both apraxic and aphasic symptoms during behavioural interventions. Due to the spreading effect and lack of focal specificity inherent in neuromodulation, tDCS appeared to be able to improve both motor speech and language outcomes simultaneously despite stimulation being applied exclusively to the motor cortex. Although consistently positive, the magnitude of effects of A-tDCS were variable over the four sessions, possibly reflecting fluctuations in individual factors that are hypothesized to excite or inhibit synaptic firing or the natural dose-response of neurostimulation.

Limitations

The final experimental methodology and choices in post-hoc analyses result in limitations in our explanatory power and ability to generalize to other individuals with similar presentations. The small sample size ($N = 2$) did not lend itself to the proposed statistical analysis of the data, nor was the data collected in a manner that met the methodological rigor of a true repeated measures single case study. Had the challenges recruiting participants been predicted, the study would have involved each client establishing a stable baseline before receiving stimulation, with a washout interval in between conditions. This would have controlled for the variability inherent between participants, especially in clinical populations, as each individual is being compared to their own results in the other condition. Most of the procedures used to analyze the data are best suited to comparisons of an experimental condition to baseline and/or a placebo condition, and as such had to be adapted to use to compare two individuals in different conditions. While they should be interpreted with caution, the multiple converging measures that were included provide strength to the findings and are consistent with previous literature. Finally, the study involved no follow-up or generalization measures, so it is unclear whether the benefits found in the participant who received true A-tDCS were maintained, or if the improvements would have transferred if new stimuli were presented.

Future Directions

Further research is needed in the areas of AOS and tDCS in order to determine the best use of tDCS to improve the outcomes of behavioural speech and language interventions. As this was only a pilot study with a small sample size, replication is necessary with larger groups in order to examine the statistical significance of results and begin to establish consistent, reliable effect sizes for comparison between studies. While the methodology lacked the rigor required to make broad generalizations, it provides compelling preliminary evidence to support continued research into stimulation of the primary motor cortex to improve the outcomes of traditional behavioural interventions for AOS. These future studies should also continue to examine differences in speech accuracy at different levels of motor complexity, in order to examine the specific benefits to the separate, distinct disorders of AOS and aphasia.

The findings presented in the current investigation have potential to inform stimulation parameters for future studies, as the dosage was on the high end of conventional without any negative effects observed. By conducting more experiments with higher stimulation parameters, researchers can provide evidence to refute or support the theory of the hormetic DR curve and establish the level at which participants are most likely to reach their maximum benefit. An interesting future study might examine DR of tDCS over four weekly sessions, followed by a washout period before administering another four weeks of stimulation. Researchers could then observe if improvements follow the hormetic DR curve consistently, or are more likely to reflect fluctuations more consistent with the brain state hypothesis.

The positive effects of tDCS to the motor cortex on language outcomes also provides further evidence for the spreading effect of modulation, and can aid in the ongoing discussion about the necessity of specificity of tDCS to the stimulation site. Future studies on using tDCS for cognitive rehabilitation could involve tasks in which multiple anatomically connected brain regions are used (e.g., working memory and language) and explore a wider variety of outcome measures in order to understand and quantify the effects of spreading neuromodulation. For individuals facing a variety of deficits after their injury, spreading effects of tDCS could prove to be highly clinically significant as they can receive benefits to multiple cognitive domains from a single session if the behavioural tasks are carefully planned to recruit the targeted areas.

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Appendix A

Tasks for Assessing Speech Planning and Programming Capacity (Apraxia of Speech)

I. "Repeat these sounds after me"

A. /i/ ______
B. /a/ ______
C. /u/ ______
D. /ei/ ______
E. /ai/ ______
F. /au/ ______
G. /m/ ______
H. /p/ ______
I. /t/ ______
J. /n/ ______
K. /k/ ______
L. /g/ ______
M. /s/ ______
N. /t/ ______
O. /"ch"/ ______

II. "Repeat these words after me"

. Mom ______
A. Bob ______
B. Peep ______
C. Bib ______
D. Tot ______
E. Deed ______
F. Kick ______
G. Gag ______
H. Fife ______
I. Sis ______
J. Zoos ______
K. Church ______
L. Shush ______
M. Lull ______
N. Roar ______

III. "Repeat these words"

. Cat ______
A. Catnip ______
B. Catapult ______
C. Catastrophe ______
D. Please ______
E. Pleasing ______
F. Pleasingly ______
G. Thick ______
H. Thicken ______
I. Thickening ______

IV. "Repeat these words three times"

. Animal ______
A. Snowman ______
B. Artillery ______
C. Stethoscope ______
D. Rhinoceros ______
E. Volcano ______
F. Harmonica ______
G. Specify ______
H. Statistics ______
I. Aluminum ______

V. "Repeat these sentences"

. We saw several wild animals.

______

My physician wrote out a prescription.

______

The municipal judge sentences the criminal.

______

"Repeat as fast and as steadily as possible"

A. "Puhpuhpuh" ______
B. "Tuhtuhtuh" ______
C. "Kuhkuhlkuh" ______
D. "Puhtuhkuhpuhtuhkuh" ______

VII. "Count from 1 to 10"

1 ______ 2 ______ 3 ______ 4 ______ 5 ______
6 ______ 7 ______ 8 ______ 9 ______ 10 ______

VIII. "Say the days of the week"

A. Sunday ______
B. Monday ______
C. Tuesday ______
D. Wednesday ______
E. Thursday ______
F. Friday ______
G. Saturday ______

IX. "Sing happy birthday/jingle bells"

How well is the tune carried? How adequate is articulation?

______

X. Description of conversational and narrative speech

______

XI. Description of reading aloud

______

Appendix B

The single subject research design (SSRD) checklist

	Item	Yes/No (1 point for each yes)
DESCRIPTION OF PARTICIPANTS AND SETTINGS	1. Was/were the participant(s) sufficiently well described to allow comparison with other studies or with the reader's own patient population?	No
INDEPENDENT VARIABLE	2. Were the independent variables operationally defined to allow replication?	Yes
	3. Were intervention conditions operationally defined to allow replication?	Yes
DEPENDENT VARIABLE	4. Were the dependent variables operationally defined as dependent measures?	Yes
	5. Was interrater or intra rater reliability of the dependent assessed before and during each phase of the study?	No
	6. Was the outcome assessor unaware of the phase of the study (intervention vs control) in which the participant was involved?	No
	7. Was stability of the data demonstrated in baseline, namely lack of variability or a trend opposite to the direction one would expect after application of the intervention?	No
DESIGN	8. Was the type of SSRD clearly and correctly stated, for example A–B, multiple baseline across subjects?	Yes
	9. Were there an adequate number of data points in each phase (minimum of five) for each participant?	Yes
	10. Were the effects of the intervention replicated across three or more subjects?	No
ANALYSIS	11. Did the authors conduct and report appropriate visual analysis, for example, level, trend, and variability?	Yes
	12. Did the graphs used for visual analysis follow standard conventions, for example *x*- and *y*-axes labeled clearly and logically, phases clearly labeled (A, B, etc.) and delineated with vertical lines, data paths separated between phases, Consistency of scales?	Yes
	13. Did the authors report tests of statistical analysis, for example celeration line approach, two-standard deviation band method, C-statistic, or other?	Yes
	14. Were all criteria met for the statistical analyses used?	No
Total **Strong (11-14), Moderate (7-10), Weak (<7)**		8/14 Moderate

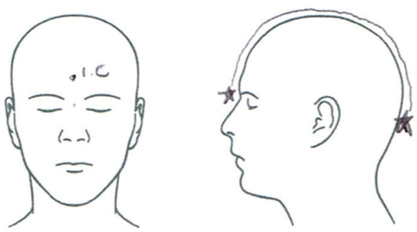
Appendix C

Online Stimuli - Sentences with Specific Phonemes

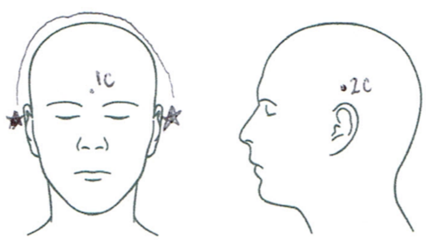
Target Phoneme	Sentence
/p/ and /b/	Popeye plays baseball
/p/ and /b/	Buy Bobby a puppy
/t/	Take Teddy to town
/d/	Do it for daddy
/k/	Kate eats the cake
/g/	Go get the wagon
/f/	Fred has five fish
/v/	Drive the van
/s/	I see the sun in the sky
/s/ and /z/	Suzy sees stars in the sky
/ʃ/	She went shopping
/ʧ/	I ride a choo choo train
/ʤ/	John told a joke to Jim
/r/	Run down the road. I have a red fire truck
/l/	Look at the lady
/s/ blends	Splash, sprinkle, streeet

Appendix D

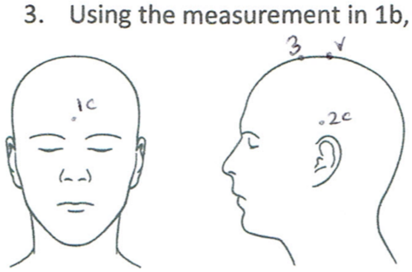
1. Measure from the nasion to the inion. Mark the halfway point on the scalp; this is the *vertex*.
    a. Make note of this measurement: ______cm
    b. 10% of this measurement: ______cm
    c. Using the measurement in 1.b, mark 10% superior to the nasion.



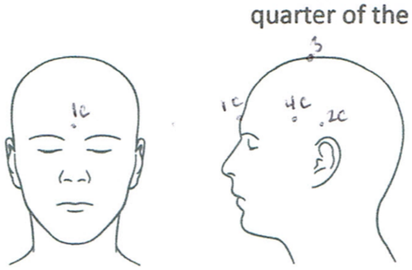
2. To ensure that you have the true center, measure from tragus to tragus and divide in half. Mark this point. This halfway point should line up with that measured in 1a.
    a. Make note of this measurement: ______cm
    b. 10% of this measurement: ______cm
    c. Using the measurement in 2.b, mark 10% superior to the left tragus.



3. Using the measurement in 1b, mark 10% anterior to the vertex



4. Measure the distance between point 1c and 2c.
    a. Make note of this measurement: ______cm
    b. 20% of this measurement: ______cm
    c. Using the measurement in 4b, mark 20% anterior to point 2c.
        i. Note, this measurement is 5% of the circumference of the head (20% of this quarter of the total circumference)



5. Measure the distance between point 3 and point 4c.
    a. Make note of this measurement: ______cm
    b. 25% of this measurement: ______cm
    c. Using the measurement in 5b, measure 25% superior to point 4c.
    d. With this point at the center, trace a 2''x 3'' rectangle. This is where the stimulation should be applied (FC5).