The Effects of tDCS on Speech Motor Control in Younger and Older Adults

Ву

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Abstract

<u>Purpose</u>. The present study focused on modulating features of speech motor control using transcranial direct current stimulation (tDCS). Recent studies have shown that tDCS modulates cortical activity within the brain, leading to changes in both cognitive and motor performance. More specific to the present study, tDCS has been shown to reduce vocal reaction times and increase speaking accuracy in healthy individuals (Fiori, Cipollari, Caltagirone, & Marangolo, 2014). The present study was designed to examine whether there is a differential effect on speech motor control performance (i.e., producing tongue twisters) following tDCS in younger versus older healthy adults. Method. Two groups of healthy individuals participated in the study. The first included younger adults (N = 30; range 18-43) and the second included older adults (N = 30; range 54-77). Each participant was asked to read a series of tongue twisters before and after one of three different stimulation conditions, with target stimulation over the left precentral gyrus: offline anodal tDCS (13 min, 1 mA); offline cathodal tDCS (13 min, 1 mA), and a sham condition. Accuracy, vocal reaction time, and rate of speech were measured. Results. The results showed no significant effects for stimulation type, or any significant interactions between age and stimulation type. There was a significant effect of age on rate of speech, showing that the older adults spoke, on average, slower than their younger counterparts. There was a significant effect of time (i.e., pre- and post-stimulation) on reaction time, showing that both younger and older adults (regardless of stimulation condition) displayed faster reaction times post-stimulation; this was believed to have been a practice effect. Finally, there was a statistical trend showing that individuals tended to become less accurate post stimulation, possibly due to fatigue or other non-stimulation conditions.

<u>Discussion</u>. Given the complicated nature of tDCS, there are multiple reasons as to why no significant effects of stimulation were elicited. It is possible that this study did not feature optimal stimulation parameters, in which the factors of current density, electrode position, stimulation duration, and neural resting state need to be addressed. However, other factors such as the variation of results of tDCS on different groups, should be considered as well. Finally, the fact that older adults spoke at a slower rate than younger adults was consistent with previous speech literature.

Preface

The research involved in this thesis is part of a larger research collaboration led by professors Carol Boliek and Jacqueline Cummine at the University of Alberta. The overall design of the study, as well as the acquisition of equipment, was completed by professors Carol Boliek and Jacqueline Cummine. I was responsible for assisting in the recruitment and running of the older adults in the study. The data analysis, as well as the following paper were completed by myself, with guidance provided from professors Carol Boliek and Jacqueline Cummine. No part of this thesis has been previously published.

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Introduction

Transcranial direct current stimulation (tDCS) is a relatively new approach to studying human behaviour that has already shown potential to improve performance across a wide variety of motor and language tasks in both younger (Kadosh, 2013; Price, McAdams, Grossman, & Hamilton, 2015) and older adults (Summers, Kang, & Cauraugh, 2015). However, the effects of tDCS on speech motor control are not well understood, especially as applied to older adults. The relationships between aging and brain functions associated with cognition (Seidler et al., 2010) and motor activities have been investigated (Summers et al., 2015) but the relationships, particularly with motor performance, remain unclear (Seidler et al., 2010). The purpose of the current study was to investigate the effects of tDCS on speech motor control in a normal aging population.

Age-Related Changes in Motor and Cognitive Function

Under typical aging conditions, speech and language processing remain largely intact (Glisky, 2007). However, some age differences have been observed such as slower processing times and a slower rate of oral reading by older adults (Ryan, 1972), which may be due to slower cognitive processing (Torre & Barlow, 2009). The literature also indicates that there are a series of motor performance declines associated with aging, for example, reduced abilities to coordinate movements as evidenced by decreased accuracy and slowed speed of movement (Ketcham, Seidler, Gemmert, & Stelmach, 2002; Salthouse & Somberg, 1982; Seidler-Dobrin, Alberts, & Stelmach, 2002). In recent years, the maintenance of cognitive and motor performance throughout the aging process has become a primary topic of interest in the neuroplasticity research literature (Summers et al., 2015). Non-invasive neurostimulation approaches have been used to diminish the effects of aging on function (Kar & Wright, 2014). Specifically, tDCS has generated interest as a potential non-invasive neurostimulation approach for improving cognitive, memory, language, and motor function.

Motor decline. In humans, aging is associated with physiological and neuromotor declines. These declines start, or accelerate, between the ages of 50 to 60 years (Booth, Weeden, & Tseng, 1994); by 80 years of age, nearly half of one's motor units, muscle fibers, muscle mass, and muscle strength have been lost (Booth et al., 1994; Larsson, Grimby, & Karlsson, 1979; Rogers & Evans, 1993). There also are a series of neurochemical changes associated with aging that are linked to motor function (Mattay et al., 2002). These include a proposed reduction in glutamate uptake capacity (Segovia, Porras, Del Arco, & Mora, 2001). A reduction in this neurotransmitter is linked to declines in motor behaviour and motor learning (Morrison & Baxter, 2012; Segovia et al., 2001). Declines in motor coordination (Seidler-Dobrin et al., 2002) are important for speech production, given the complexity of the speech system. More specifically, speech is a multifaceted motor skill that requires the coordination of the respiratory, laryngeal, and supralaryngeal subsystems by using approximately 100 muscles and 200 coordinative movements (Neef, Anwander, & Friederici, 2015). Declines in the speed and accuracy of movement (Ketcham et al., 2002; Salthouse & Somberg, 1982) are potentially contributing factors to changes in speech in older typically-aging adults that are reflected in the use of slower speech and reading rates (Torre & Barlow, 2009). Compounded with the declines noted in motor function are declines in non-motoric factors, including slowed cognitive processing (Torre & Barlow, 2009).

Cognitive decline. As Glisky (2007) notes, there is an overall association of decline and aging. Most relevant to this study is cognitive processing speed. Processing speed can be broken into smaller subcategories. Of importance to this work is linguistic processing (e.g., tasks that involve concepts such as letter reading, lexical decision, word naming, picture naming, and reading rate). Verhaegen (2014) notes that processing speed for older individuals has been estimated to be between 1.2 and 1.5 times slower than for younger adults. Worth noting, however, is that this estimate is based largely on verbal tasks. Verbal tasks involve the processing of language stimuli in the context of involve making judgements about lexicality or semantics (Verhaeghen, 2014). The task involved in the present study (i.e., the reading of a tongue twister) does not require the participants to necessarily evaluate words at a language level (i.e., a lexical decision task), but requires complex speech motor control. Thus, the present study will help to expand our understanding of the effects of neurostimulation on a heavily weighted motor speech task in older adults, which remains relatively unexplored. A complete review of the literature on age-related changes in cognition is beyond the scope of the present study (for review papers see Verhaeghen & Cerella, 2002; Park & Reuter-Lorenz, 2009).

Neuroanatomical decline. In terms of neurophysiology, aging is linked to decreases in both grey and white matter volume (for a review see Seidler et al., 2010). The cognitive and motor effects of these physical changes are still not well understood, but it is possible to link these changes to declines seen in aging adults (Seidler et al., 2010). For example, grey matter volume has been shown to be positively correlated to increased performance on motor tasks (Kennedy & Raz, 2005; Rosano et al., 2008). In terms of white matter integrity and motor performance, Sullivan et al., (2010) found a positive correlation between white matter integrity and motor performance on a knurled pin rolling between thumb and index finger task. White matter fibre tract integrity is another aspect linked to cognitive and motor decline in aging. Aging is associated with significant white matter deterioration, which is likely to impair the conduction of neural signals across the brain (Davis, Dennis, Buchler, et al., 2009). Furthermore, there is recent evidence to support that the cognitive decline accompanied with aging is linked to alterations in synaptic connectivity (Morrison & Baxter, 2012; Pakkenberg et al., 2003). Part of this change in synaptic activity is a decline in the uptake capacity for glutamate, the neurotransmitter present in most of the excitatory synapses which appears to be involved in functions such as motor behavior and cognition (Morrison & Baxter, 2012; Segovia et al., 2001). These changes are particularly evident in the prefrontal cortex where older adults exhibit higher activation of this region than younger adults (Davis, Dennis, Daselaar, Fleck, & Cabeza, 2009). Also worth considering is the hypothesis that the diminishing number of dendritic spines of the dorsolateral prefrontal cortex plays a part in the cognitive decline of older primates (Dumitriu et al., 2010; Peters, Sethares, & Luebke, 2008). Thus, the capacity of cognitive performance and plasticity mechanisms may be altered during healthy aging (Fertonani, Brambilla, Cotelli, & Miniussi, 2014). However, by mitigating or delaying these declines there comes the opportunity to increase functioning in older adults. Given this trend of decline in cognitive and motor function, it is understandable that research has targeted potential ways to impede or reverse the normal effects of aging on the brain.

Transcranial direct current stimulation (tDCS)

Basic principles. The use of tDCS to mitigate the effects of aging-related decline has seen rapid increases in recent years (Price et al., 2015). TDCS typically involves the application

of a weak polarizing direct current (e.g., 1-2mA) to the scalp (Been, Ngo, Miller, & Fitzgerald, 2007). There are several types of stimulation: anodal, cathodal and sham. One of the most discussed points in the literature in relation to tDCS is its underlying effect on neural excitability. A multitude of studies shows a general trend in which applying anodal tDCS to a brain region leads to increased neural excitability in that region, whereas cathodal stimulation leads to decreased neural excitability (Kadosh, 2013). Notably, the modification of neural excitability induced by tDCS has been shown to influence a variety of cognitive (Kadosh, 2013) and motor functions (Summers et al., 2015).

Online vs. offline stimulation. TDCS simulation protocols can be subdivided into two categories: online and offline. Online stimulation entails that the task completed is done simultaneously with the stimulation, whereas, offline stimulation refers to when the task is done before or after stimulation (Kadosh, 2013). Behavioural changes observed in these different protocols are believed to be brought about by differing underlying neural mechanisms. For example, during online stimulation, the application of the stimulation to the brain shifts the resting membrane potential of superficial interneurons (i.e., neurons nearest to the skull that interact with other neurons) resulting in changes to neuronal excitability (Summers et al., 2015). In contrast, in offline stimulation there is a shift from the initial membrane potential to a longer-term modification of synaptic plasticity, in which differing underlying neurophysiological mechanisms are active when compared to online stimulation (Summers et al., 2015). In anodal stimulation, the induction of offline effects is believed to be dependent on membrane depolarization; however, with cathodal stimulation, it is difficult to know what degree the membrane polarization changes play in inducing offline effects (Stagg &

Nitsche, 2011). What does appear to play a role in both offline anodal and cathodal tDCS is the modulation of glutamatergic (NMDA and AMPA) receptors, in processes akin to long-term potentiation (LTP) and long-term depression (LTD) (Stagg & Nitsche, 2011). The offline effects of tDCS also implicate the inhibitory neurotransmitter GABA (Nitsche et al., 2005; Stagg et al., 2009). There is evidence supporting that the excitatory effects of offline anodal tDCS are mediated, at least in part, by a reduction in GABAergic inhibition (Kim, Stephenson, Morris, & Jackson, 2014; Stagg et al., 2009). Reductions in GABA concentration as a result of anodal tDCS, have been shown to correlate with motor learning and motor memory processes (Kim et al., 2014). Furthermore, Summers et al., (2015) point out that a reduced capacity to modulate GABA mediated inhibitory process in older adults has been associated with age-related decline in cognitive and motor function (Gleichmann, Chow, & Mattson, 2011; Levin, Fujiyama, Boisgontier, Swinnen, & Summers, 2014). Thus, there is the potential to use tDCS to target deficient inhibitory activity in older individuals (Heise et al., 2014). It is worth noting however, that there is divergence in the literature regarding the physiological basis of cathodal tDCS. Stagg et al., (2009) found that cathodal tDCS led to significant decreases in both glutamate and GABA relative to sham stimulation; however, Kim et al., (2014) found that there were no significant changes in either glutamate or GABA after cathodal tDCS.

TDCS and healthy aging. There is currently a limited amount of research investigating the effects of offline tDCS in a healthy aging population, particularly in regards to the effects tDCS can have on expressive language tasks. However, there is initial evidence that tDCS can benefit older adults. In a meta-analysis related to tDCS and transcranial magnetic stimulation (TMS), Hsu et al., (2015) found that offline anodal designs produced greater benefits than

online designs for healthy adults, which is in contrast to Fertonani et al. (Fertonani et al., 2014). Furthermore, there is evidence that tDCS can lead to more prominent effects in older adults when compared to younger adults. One study found such results when testing skilled right hand motor function in younger and older adults following anodal stimulation over the left primary cortex (Hummel et al., 2010). In this task, a single session of anodal tDCS over the primary motor cortex of older healthy adults led to significant improvement in performance of skilled motor tasks, relative to sham stimulation (Hummel et al., 2010). However, there is no clear indication that tDCS effects are larger in older adults than in younger adults given that this differential performance between older and younger groups is not a consistent finding (Perceval, Flöel, & Meinzer, 2016). Another inconsistent finding, but still worth mentioning, is that in several studies investigating tDCS, anodal tDCS restored impaired performance of older adults to the level of functioning of the sham condition in younger adults (Perceval et al., 2016). Thus, it may be that there are some cases in which older adults benefit more from tDCS than their younger counterparts, and can even restore functioning to what a younger individual can do, but the mechanisms behind these differences need to be further investigated.

Another apparent gap in the literature revolves around the effects that offline cathodal tDCS has in older adults; for instance, cathodal stimulation was not discussed in the Hsu et al., (2015) meta-analysis. However, while not specifically discussing older adults, Stagg and Nitsche (2011) noted that no consistent effect of cathodal tDCS on motor tasks has been observed. Possible reasons for this may be because behavioral measures are relatively insensitive to small changes induced by tDCS or that the LTP-like synaptic modulation that occurs during learning is of sufficiently greater strength to be able to overcome the effects of cathodal tDCS hyperpolarization (Stagg & Nitsche, 2011).

Task Effects. Another aspect related to tDCS are task effects. There is evidence indicating that tDCS may be modulated by the type of task that is performed. In a recent metaanalysis focusing on anodal stimulation in older adults, it was found that the benefit from tDCS was larger for motor tasks than cognitive tasks (Summers et al., 2015). It is worth mentioning that the current study, which involves the oral production of a tongue twister, can be viewed more as a motor speech task, as opposed to a cognitive-language task. This can be said as the tongue-twister task does not require individuals to interact with their semantic networks to provide appropriate responses, as one would have to do in a language-based word-finding task. Rather, tongue twisters are thought to place increased demands on phonological processes (Keller, Carpenter, & Just, 2003), and it has been proposed that they are likely to challenge motor speech mechanisms as well (Lisman & Sadagopan, 2013). Furthermore, there has already been work done investigating speech motor planning and execution via the use of tongue twisters (Postma, Kolk, & Povel, 1990). In the present study, the dorsolateral prefrontal cortex is stimulated. This is an ideal location for tDCS when investigating a motor task involving complex speech articulation. Multiple studies investigating the effects of tDCS to the primary motor cortex have resulted in significant effects on both motor and cognitive performance (Kadosh, 2013; Charlotte J Stagg & Nitsche, 2011). Most relevant to this study is the work completed by Fiori et al. (2014). Their study indicated that with online stimulation, speech motor performance was improved as seen by an increase in accuracy of a tongue twister replication task. Worth noting is that that study involved the use of online, not offline

stimulation. There is still uncertainty in the literature regarding the effects that offline stimulation may play in modifying motor tasks of complex speech articulation.

Summary

Normal aging is accompanied by decreases in both cognitive and motor functions. TDCS is a relatively new technique that has the potential to improve human performance in a wide variety of tasks in both younger and older adults, but its known effects on complex speech are limited — particularly in relation to older adults. The goal of this study is to provide new information with respect to age-related changes associated with the production of complex speech coupled with offline tDCS. There currently exists a gap in the literature about what effects offline tDCS has on a complex motor speech task for young and older adults. The overall purpose of the current study is to assess the impact of tDCS on tasks requiring complex speech motor output (i.e., tongue twisters) in healthy, older, (and younger) adults.

Study Aims

This study aimed to explore whether tDCS over FC5 (the precentral gyrus) had a differential effect on speech motor control (vocal reaction time, accuracy, and speech rate) as a function of age. It is proposed that both younger and older adults would experience a transient increase in performance following the anodal stimulation condition. For cathodal stimulation, no change in performance was expected, which would be in line with previous literature using cathodal tDCS to study motor tasks (Stagg & Nitsche, 2011). Finally, no significant change in performance following the sham condition was expected.

Research Question 1: Does tDCS over FC5 (the precentral gyrus) have a differential effect on speech motor control as a function of age?

Hypothesis 1.1: Following anodal tDCS, it was expected that both younger and older adults would experience a transient increase in performance.

Hypothesis 1.2: Following cathodal tDCS, it was expected that both younger and older adults would experience no significant change in performance.

Hypothesis 1.3: Following the sham condition, it was expected that both younger and older adults would experience no significant change in performance.

Hypothesis 1.4: In the post-anodal condition, it was expected that performance of older adults would approximate pre-stimulation conditions of the younger adults.

Hypothesis 1.5: In the cathodal condition, it was expected that there would be significant performance differences in pre- and post-conditions between younger and older adults.

Hypothesis 1.6: In both the pre- and post-sham condition, it was expected that there would be significant performance differences between the younger and older adults.

Methods

Participants

Two groups of adults (i.e., younger and older) were recruited for this study. The younger group consisted of 30 participants (age range: 18-43; mean age = 26.97 ± 6.04 yrs; sex = 8 men). The older group consisted 30 participants (age range: 54-77; mean age = 66.37 ± 6.83 yrs; sex = 7 men). Participants were required to be right handed, and native speakers of English. Exclusion

criteria consisted of: a history of stroke, epilepsy, migraines, speech and/or language impairment, reading disorders, and attention deficit disorders. All participants reported normal or corrected-to-normal vision.

Partway through the recruitment and testing of the older adults, it was decided to add in a hearing and cognitive assessment. This was not used as exclusion criteria, but rather as an additional descriptive of the participants. All the younger adults, and 7 of the older adults, had already completed the study when this change was implemented. Thus, 23 of the 30 older adults completed these assessments. The cognitive assessment used was an adaptation of the Mini Mental Status Exam (MMSE). A typical failing score on the MMSE is obtained when a participant answers fewer than 24/30 points correctly. Our version of the MMSE only used 29 points. The removed question asked participants which county they were in; this was deemed an unfair question as the location of the study, the University of Alberta, is not commonly known as being part of a specific county or comparable district. No participant scored less than 24. The average score was 28.39; the standard deviation was 1.01; the range was 26-29. The hearing testing used a portable audiometer and hearing was tested at 40 dB HL at 1,000 Hz, 2,000 Hz, and 4,000 HZ for left and right ears. Three tones were presented to each ear at each frequency. The details of the hearing screen are presented in Table 1. While some participants did not respond to certain conditions, they were still able to functionally interact with the examiners, with no overt signs of being hard of hearing.

Table 1. Hearing Testing Results

	People	Responded	Did not respond	Did not	Did not
	Tested	appropriately at all conditions (i.e., heard at least 2/3	to 1 condition (i.e., did not hear	respond to 2	respond to multiple
		tones presented to each ear at each frequency)	2/3 tones in one ear at a specific frequency)	conditions	conditions, but used hearing aids during the study
Number of people	23	15	1	4	3

Materials

The thirty tongue twisters used in the study were adapted from literature on speech production (Bressmann & Irish, 2014; Dell, Burger, & Svec, 1997; Schwartz, Saffran, Bloch, & Dell, 1994; Sobkowiak, 1990), from an interest article (Plunkett, 2013), and from a collection of online tongue twisters ("Twister," 2015). Each tongue twister combined four words that were syntactically possible in English (e.g., "Santa's short suit shrunk"). Certain tongue twisters retrieved from the sources were modified to meet these criteria. Tongue twisters were sorted into two sets based on speech sounds to create tongue twister sets that were roughly equivalent in degree of difficulty (e.g., given two tongue twisters each involving the sounds "sh" and "s", one would be placed in each set). A complete list of tongue twisters used is presented in Appendix A.

Procedure

The study used a mixed within and between subjects experimental design. Younger and older adults (N = 30 per group) were recruited. Ten participants from each age group were randomly assigned to either the anodal tDCS, cathodal tDCS, or sham tDCS condition. Participants were blind to their assigned condition. Upon arrival, participants of the study completed an informed consent document, followed by a demographics questionnaire to clarify that they met the inclusion criteria and that no health conditions were present that would exclude them from participating.

Experimental Task

During the tongue twister task, a set of 15 tongue twisters was presented visually on a computer screen to each participant. Prior to the beginning of each set, there were two practice tongue twisters to familiarize the participants with the task. Tongue twisters were presented one at a time using *Eprime* software. The order in which the tongue twisters appeared was randomized. Each participant was instructed to read the tongue twister aloud as quickly and as accurately as possible. Participants' responses were digitally recorded. Participants completed one set of tongue twisters prior to stimulation, and then the secondary set of tongue twisters following offline stimulation. The tongue twister set that was presented first was randomized.

Stimulation

Following the completion of the first set of tongue twisters, participants were prepared for tDCS stimulation. Skin preparation of the scalp and the right shoulder involved cleaning with a light abrasion to reduce skin impedance. A pair of sponge electrodes (5 cm x 4 cm), soaked in a saline solution [0.9 % (36 g/4 L) concentration], was used to deliver stimulation. Current density was calculated as 0.04 mA/cm². Using the International 10/10 System the active electrode was placed over the FC5 position. The reference electrode was secured on the right shoulder. In both the anodal and cathodal conditions, 1 mA of current was applied for 13 minutes. In the sham condition, stimulation was initially delivered to the scalp, but the current was ramped up to 1 mA and ramped down over a period of 30 seconds in order to make the sham condition perceptually identical to anodal and cathodal conditions. This was repeated at the end of the sham stimulation period. During stimulation, participants were seated in front of a computer and asked to type in numbers that appeared on screen. There is evidence that the tasks completed during offline stimulation may benefit or interfere with performance completed on the following task (Gill, Shah-basak, & Hamilton, 2015; Horvath, Carter, & Forte, 2014) Thus, to reduce extraneous variables, it becomes important to both control and report what participants do during stimulation. The number task was chosen for the present study as it was deemed to be unrelated to the speech-motor task that was completed following stimulation. Thus, it was believed that it would not act as a priming condition for the following tongue twister task. Immediately following stimulation, participants were asked to repeat the equivalent alternative set of the pre-stimulation task. Stimuli were block randomized so that half of the participants received Set 1 at pre-stimulation and half received set 2 at prestimulation.

Data Analysis

The three dependent variables analyzed were accuracy of speech, rate of speech (measured in syllables per second), and vocal reaction time (measured in ms).

Reaction time. Vocal reaction time was obtained via the *Eprime* software, which recorded the time difference between when each tongue twister was presented, and when the participant made an audible response. Vocal reaction times that were unreasonable (i.e., < 200 ms) were not included for analysis. Analysis of the features of each elicited tongue twister was done using TF32 acoustic software.

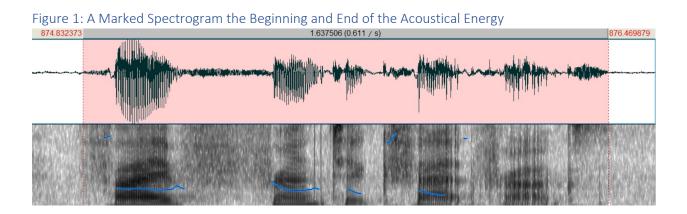
Accuracy. Pre- and post-stimulation accuracy percentages were calculated for each participant. Accuracy was determined as the percentage of words produced correctly in each block of tongue twisters. Given there were 15 tongue twisters in each block, and that each tongue twister had 4 words, the percentage was based on a total of 60 words for both pre- and post-measurements. For a word to be considered correct, it had to:

- Not contain any speech sounds with inaccurate place or manner features.
- 2) Not contain any added speech sounds.
- 3) Not contain any speech sound corrections.
- 4) Not contain any sound or word repetitions.
- 5) Have been attempted to be produced.

Tongue twisters with hesitations, pauses, or prolonged sounds were counted as correct. Tongue twisters were counted as incorrect if any of the errors were perceived. Worth noting is that there were several instances when participants lost their composure completing the tongue twister task, due to excess laughing or unintended distractions or noise, and as a result, did not attempt specific tongue twisters. In instances such as these, when a tongue twister was not attempted at all, the data was not considered. In total, 8 tongue twisters (of a potential 1,800)

were not considered due to these reasons. The range of tongue twisters not considered per participant was 0-2.

Speech rate. Only correctly produced tongue twisters were used to calculate speech rate. The amount of variation in rate that accompanied errors made was deemed to be a confounding variable. As a result, an average of 11.07 (of a potential 15) tongue twisters were used in determining speech rate for pre- and post-measurements; The standard deviation was 2.39 tongue twisters; and the range was 2-15 tongue twisters. Speech rate was measured in syllables per second using PRAAT software. Tongue twisters were marked at the beginning and end of each utterance, based on the corresponding spectrogram of each (Figure 1). The beginning of each tongue twister was marked where speech sound energy appeared on the spectrogram, and the ending of each tongue twister was identified by the cessation of speech sound energy. The time from the beginning and end of these markings was then divided by the number of syllables in the utterance to obtain a syllable per second value for each tongue twister.



Analysis

A 2X3X2 mixed ANOVA was completed using SPSS software for each dependent variable. The independent variables included age (young and old), stimulation type (anodal, cathodal, and sham), and time (pre- and post-stimulation). The first two factors were between subjects, and the last was a within-subject factor.

Results

A summary of each of the dependent variables as a function of stimulation group, prevs. post-stimulation and age group can be found in Table 2.

 Table 2. Mean (M) and Standard Deviation (SD) for each Dependent Variable

tDCS	Accuracy (% of words	Speech Rate (Syllables per		Reaction Times	
	correct)		second)		(milliseconds)	
	Pre	Post	Pre	Post	Pre	Post
Young Anodal	88.25	88.94	3.19	3.13	741.40	699.01
M	8.169	8.491	0.465	0.486	117.342	107.942
SD						
Old Anodal	88.61	86.33	2.89	2.84	719.32	696.42
M	9.623	8.644	0.408	.398	134.846	151.328
SD						
Young	87.75	87.81	3.56	3.60	660.51	608.72
Cathodal	6.396	6.748	0.561	0.455	81.236	76.903
M						
SD						
Old Cathodal	90.44	87.00	3.00	3.00	712.76	671.53
M	5.544	9.113	0.261	0.366	107.388	106.652
SD						
Young Sham	90.50	89.75	3.71	3.61	679.60	662.62
M	6.325	7.115	0.468	0.434	112.703	87.210
SD						
Old Sham	88.50	83.69	2.99	2.95	811.65	717.09
M	8.835	13.739	0.358	0.413	174.807	143.360
SD						

Accuracy. No significant effects or interactions were found. The effect of time was not significant, but was trending toward statistical significance [F(1, 54) = 3.640; p = .062]. This effect appeared to occur simply due to fatigue, particularly in the older adults (Figure 2A), as scores across nearly all conditions experienced a decline post-stimulation. Analysis showed no significant interaction of *Time X Stimulation Type X Age* [F(2,54) = .029; p = .971] (see Figure 2A and B) and no significant interaction of *Time X Stimulation Type* [F(2,54) = .391; p = .678].

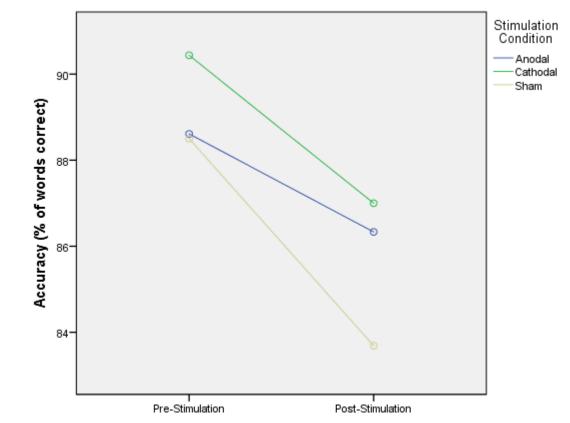


Figure 2A: Mean Accuracy of Older Adults Pre- and Post-Stimulation

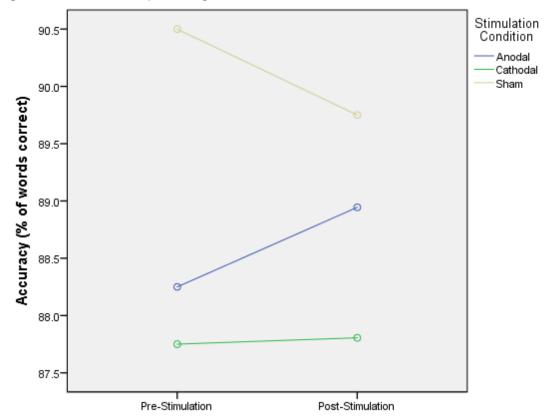


Figure 2B: Mean Accuracy of Younger Adults Pre- and Post-Stimulation

Speech rate. Only tongue twisters without errors were analyzed for rate. The only statistically significant main effect was for Age [F(1,50) = 20.464; p = <.001] where younger adults (Mean = 3.4685 syllables/second SD = .507 syllables/second) were speaking, on average, faster than the older adults (Mean = 2.9555 syllables/second SD = .3533 syllables/second) (See Figure 4). No significant interactions were found (all p's > 0.05). There was no significant interaction between *Time X Stimulation Type X Age* [F(2, 54) = .125; p = .883] (see Figures 3A and B). Neither did we see a significant interaction for *Time X Stimulation Type* [F(2, 54) = .477; p = .623].

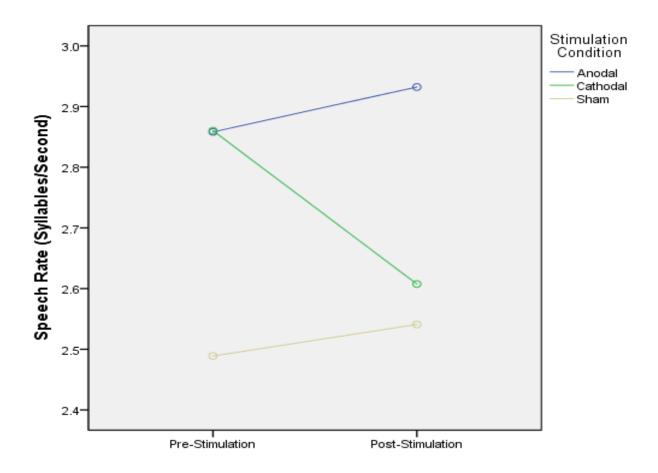


Figure 3A: Mean Speech Rate of Older Adults Pre- and Post-Stimulation

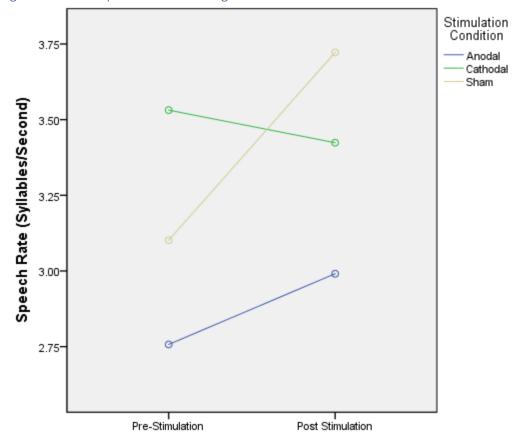
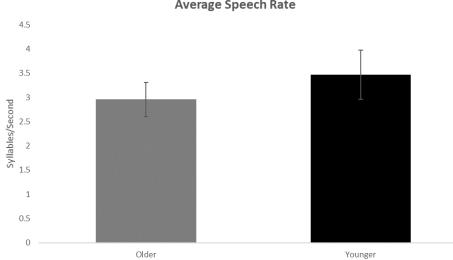


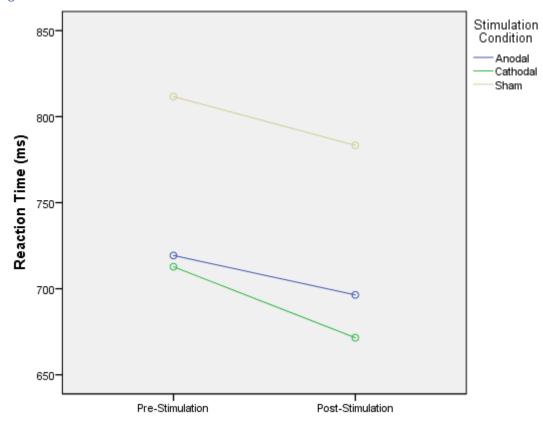
Figure 3B: Mean Speech Rate of Younger Adults Pre- and Post-Stimulation





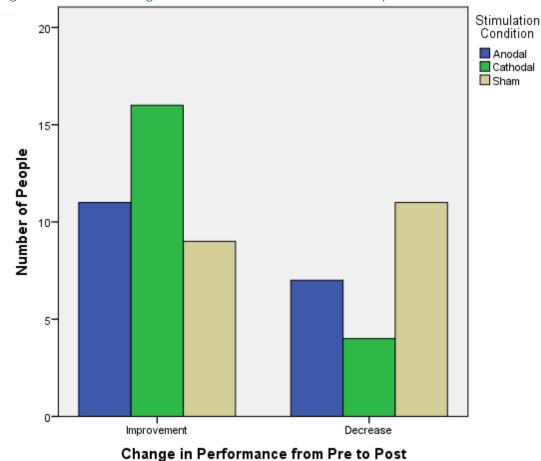
Average Speech Rate

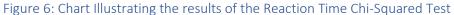
Reaction Time. Due to technical difficulties, two of the sixty participant's reaction times were not captured, and thus were not included in the analysis. The only statistically significant main effect was time [F(1,52) = 10.183; p = .002]. On average, scores in both the younger and older groups, across all stimulation conditions, improved in post-stimulation, likely due to a practice effect. This was likely the result of the participants becoming more familiar with how each tongue twister was introduced. No significant interactions were found. Analysis showed no significant interaction of *Time X Stimulation Type* [F(2,52) = .432; p = .652]. Neither did analysis show a significant interaction of *Time X Stimulation Type X Age* [F(2,52) = .180; p = .836].





Non-parametric tests. As a secondary method of analyzing the results, eighteen Chisquared tests were completed. Six were done for each dependent variable (i.e., accuracy, reaction time, and rate). Performance for these tests was binary, meaning that any change from the pre- and post-conditions was considered as either an improvement or worsening, regardless of size. No significant differences emerged because of these tests. However, there was one trend worth mentioning: a Chi-squared test comparing reaction time performance across age groups based on stimulation condition. The test indicated that reaction times trended towards improvement X^2 (2, N = 60) = 5.213, p = .074. Additionally, with cathodal stimulation, participants trended towards improvement more so than in the anodal or sham conditions. This is perhaps indicative of a different effect that cathodal stimulation is having, and may warrant additional research to discover if cathodal stimulation consistently improves reaction time in speaking tasks. However, if followed up, attention must be paid to how significant these changes are. In the present study, cathodal stimulation did trend towards improvement, but these improvements were not of significance to elicit a noticeable effect in an ANOVA looking at the interaction of *Time X Stimulation Type* [F(2,52) = .432; p = .652].





Discussion

The purpose of this study was to determine if age played a modulatory factor on the results of tDCS. The results of this study showed no significant effects of tDCS stimulation regardless of age or stimulation condition (anodal, cathodal, or sham). Without any significant findings in either age group, it is impossible to look at differences between them. Thus, the study's research question remains unanswered. However, these findings are still valuable to the field of tDCS research. No effects related to anodal tDCS were discovered. There are several reasons as to why this might be, most notable are three adjustable parameters which play a large role in tDCS outcomes: current density, electrode position, and stimulation duration

(Horvath et al., 2014). These factors, as well as several others, will be discussed in the following section. Given that no effects were discovered with anodal stimulation, it becomes difficult to make any meaningful interpretation from the cathodal stimulation. No significant results were discovered with Cathodal tDCS, but it is difficult to say whether this was due to suboptimal parameter settings, a lack of power in the study, or because cathodal tDCS truly did not bring about any significant changes.

Current Intensity and Density

In the present study, the current intensity (i.e., the ampere value) was 1 mA, which has been a standard intensity used for anodal tDCS (Cuypers et al., 2013). However, recent research has shown that increasing stimulation intensity might be of value, as the efficacy of stimulation appears to be modulated by intensity (Cuypers et al., 2013). Most relevant to the current study is the study that showed tDCS effects on a tongue twister recitation in healthy adults at 2 mA during an online task (Fiori et al., 2014). However, there is conflicting evidence with regards to intensity, as other evidence reveals inconclusive results that increasing intensity leads to improvements in cognitive performance following tDCS stimulation (Teo, Hoy, Daskalakis, Fitzgerald, & Mcclintock, 2011). Thus, increasing intensity may lead to improved effects, but there is no guarantee.

Related to intensity is current density (mA/cm²). A recent meta-analysis of tDCS in healthy participants found that the administration of higher current density resulted in higher accuracy percentages on cognitive tasks, and that it would be advisable for future studies to evaluate the effects of tDCS at higher doses (Dedoncker, Brunoni, & Baeken, 2016). Thus, increasing current density by either increasing the ampere value, or decreasing the area of the electrode sponge, could be repeated in future work related to speech production in healthy adults with the hopes of improving results.

Electrode Position

In the present study, the active electrode was placed over FC5, a region often referred to as Broca's area. The reference electrode was secured on the right shoulder. Multiple studies have shown improvements related to language function when active stimulation is applied to Broca's area. These include improvements to semantic fluency (i.e., rapid naming of categorical items), speech production, and object naming (Cattaneo, Pisoni, & Papagno, 2011; Fertonani, Rosini, Cotelli, Maria, & Miniussi, 2010; Fiori et al., 2014; Holland et al., 2011; Meinzer, Lindenberg, Antonenko, Flaisch, & Floel, 2013). The optimal montage for both active and reference electrodes, however, is more difficult to ascertain, as there are variations of placement locations for the reference electrode (e.g., on the contralateral side of the brain, or on an extra-encephalic location). The active electrode in the current study is approximately in the same position as the one used by Fiori et al. (2014), although they used the International 10-20 system for EEG placement, and placed the electrode on F5, in addition to placing the reference electrode over the contralateral frontopolar cortex. While this placement position may have induced differing results with the current study, it is impossible to be certain, given the other variables at play (e.g., current density and duration).

Stimulation Duration

The present study incorporated 13 minutes of active stimulation based on evidence that this duration, in conjunction with 1 mA anodal tDCS over the motor cortex, significantly increased motor cortex excitability up to 90 minutes following stimulation (Kadosh, 2013; Nitsche & Paulus, 2001). There does not exist an optimal time frame for stimulation delivery within the tDCS literature, as seen from the various time lengths used in different studies. For example, one recent meta-analysis found duration time frames ranging between 6 to 37.5 minutes (Summers et al., 2015). Thus, while different stimulation durations may impact the results of tDCS, it is still not possible to pick a time duration that guarantees optimal results. Indeed, the field of tDCS would benefit from future studies exploring the duration of stimulation and its effects.

Mental State during Stimulation

One aspect of tDCS often overlooked is motor and cognitive interference (Horvath et al., 2014). There exists evidence that motor and/or cognitive tasks undertaken during or after stimulation interfere and even negate the effects of stimulation (Horvath et al., 2014). Antal et al. (2007) had participants complete a cognitive task (i.e., a questionnaire based on geography, history, math, and language) during stimulation. They reported that this task abolished the effects of both anodal and cathodal stimulation on motor evoked potential amplitude modulation (i.e. over the first dorsal interosseous muscle). Quartarone et al. (2004) had participants complete motor imagery tasks following stimulation. This task appeared to abolish the effects of anodal stimulation, yet prolong the effects of cathodal stimulation. Other studies also have reported interference effects from either cognitive or motor tasks during or following stimulation [see (Antal et al., 2007; Miyaguchi, Onishi, Kojima, & Sugawara, 2013;

Thirugnanasambandam, Sparing, Dafotakis, & Meister, 2011)]. Conversely, there is evidence that certain tasks undertaken during stimulation can greaten the effects of tDCS. Gill et al. (2015) reported that incorporating a task which featured a higher cognitive load during stimulation led to participants performing both faster and more accurately on an offline cognitive task. In the present study, participants were asked to type in numbers that appeared on screen during the stimulation. It is possible that this task interfered with (or benefitted) the stimulation, but it is difficult to know with certainty. What is clear, is that descriptions of tasks completed during stimulation should be clearly indicated in future studies. By ensuring that participants engage in similar tasks during stimulation, future studies can better control their results, and data may be gathered regarding optimizing stimulation conditions.

Variability between Subjects

Worth addressing is the issue of inter-subject variability. There exists evidence that tDCS does not always lead to consistent results even when two groups receive the same treatment type. For example, Fricke et al. (2011) measured MEPs of two groups who underwent identical stimulation and found significant differences between the two. Other studies have found similar differences between groups undergoing identical stimulation [see (Nitsche, Grundey, et al., 2004; Nitsche, Liebetanz, et al., 2004)]. Given that tDCS can have inconsistent results, it becomes important to characterize the potential individual variability inherent in the samples being examined. This information will allow for the identification of potential patterns of responders and/or non-responders to emerge in the literature. It also allows for researchers to advocate for the continuation, or halting of, continued tDCS-related endeavours. See Appendix B for a series of graphs showing how individuals responded to specific types of stimulation.

These graphs are included to add transparency to the study, and so that future researchers, if interested, may better identify inter-subject variability patterns.

Working memory versus speech motor control

Perhaps the piece of literature most relevant to the present study was the 2014 work by Fiori et al. In that paper, Fiori et al. had their participants complete a series of tongue twisters. The tongue twisters were presented auditorily, and the participants were asked to repeat them after each one was presented. In the present study, the tongue twisters were presented on a computer screen, and participants were asked to read them, with no delay between when participants saw the stimulus, and when they began to produce it. The differences that emerge because of this change of procedure warrant a brief discussion. There is evidence that verbal material is kept in a working memory store via an articulatory loop, and it has been shown that Broca's area supports this rehearsal process (Rogalsky, 2008). It is possible that the behavioral measure of speech used in Fiori et al.'s study was reflective of a change in working memory ability, caused by tDCS over Broca's area. This change in working memory may have led to the improved and decreased performance in the anodal and cathodal stimulation groups, respectively. In the present study, on the other hand, there were minimal demands placed on working memory, as participants simply needed to read the tongue twisters that were presented on screen – they did not need to remember them for any length of time. Thus, overall, there is no reason to believe that working memory plays a significant role in the present study. Rather, given the limited demands placed on working memory, it can be argued that the task is more indicative of motor speech performance. There are few publications related to the effects of tDCS in speech motor control, especially with regards to the performance of healthy

adults. Thus, in healthy adults, it is possible that tDCS over Broca's area may not modify motor speech performance to the same degree as it does working memory performance.

Conclusion

This study did not answer the question as to whether age modulates the effects of tDCS stimulation on healthy adults. However, it can still be used as a guiding point for future, related, endeavours. This paper discusses multiple ways to improve the results related to anodal stimulation when working with speech tasks. These suggestions are based on previous research, but given the complex and often unpredictable nature of tDCS, they are not guaranteed methods to improve results, but rather guiding points for future research. Given its complicated features and results, tDCS certainly has its shortcomings. However, as Horvath et al. (2014) note, rather than seeing these issues as a detriment to the field, we should use them to guide upcoming projects. Future research must continue to test varying parameters of stimulation to optimize the associated results. For this reason, studies which do not show significant effects remain relevant; these studies, including the present, provide evidence for specific parameters which do not attain results, thus narrowing the field for determining parameters that can.

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Appendix A: Tongue Twister List

Set 1	Set 2
Brief Beastly Beach Breezes	Brad's burned bran buns
Fine Fresh Free Fish	Chef's sooty shoe soles
Gloria's Greek green gloves	Chop shops stock chops
Kick six sticks quick	Five frantic fat frogs
Luke's ducks like lakes	Flea-free fruit flies
Luther's moose's loosest tooth	Kate takes Tate's cake
Plastic potted pansy plants	Larry's really rarely leery
Santa's short suit shrunk	Proper copper coffee pot
Shops seldom sell shellfish	Richard's wretched ratchet wrench
Swizzle scissors sizzle thistles	Simon's minimum cinnamon synonym
Three short sword sheathes	Six thick thistle sticks
Trish's ritzy Irish wristwatches	This sister's sixth zither
Willy's real rear wheel	Which Swiss witch switched
Witch wished which wish	Whistle softer thistle sifter

Appendix B: Charts and Graphs of Individual Data

Chart of All Accuracy Data (Accuracy as % of words produced correctly)						
Younger Adult – Anodal Stim		Older Adult – Anodal Stim				
Participant	Accuracy	Accuracy	Participant	Accuracy	Accuracy	
#	Pre	Post	#	Pre	Post	
4	73	69	41	88	83	
6	95	93	42	90	83	
7	83	80	45	98	83	
13	93	93	48	95	93	
19	80	95	54	90	90	
26	95	85	56	86	90	
28	95	93	67	100	95	
32	98	93	72	95	98	
33	85	93	73	75	83	
34	88	98	74	70	68	
Younger Adu	Younger Adult – Cathodal Stim			Cathodal Stir	n	
Participant	Accuracy	Accuracy	Participant	Accuracy	Accuracy	
#	Pre	Post	#	Pre	Post	
2	83	85	50	90	90	
5	93	93	51	100	85	
11	85	98	52	90	88	
16	88	81	53	90	70	
18	93	93	58	97	100	
21	80	80	62	85	88	
23	78	83	63	90	75	
27	90	83	66	90	95	
31	98	88	69	80	85	
35	93	98	71	93	95	
-	Younger Adult – Sham Stim			Older Adult – Sham Stim		
Participant	Accuracy	Accuracy	Participant	Accuracy	Accuracy	
#	Pre	Post	#	Pre	Post	
1	95	90	43	83	78	
8	93	93	44	75	53	
9	93	95	46	90	90	
17	95	93	47	90	85	
20	85	85	49	98	97	
22	93	88	55	95	88	
24	78	73	57	93	90	
25	88	90	61	95	98	
29	88	98	68	73	70	
30	100	95	70	95	90	

Chart of All Accuracy Data (Accuracy as % of words produced correctly)

Younger Adult – Anodal Stim		Older Adult – Anodal Stim			
Participant		Participant			
#	Rate Pre	Rate Post	#	Rate Pre	Rate Post
4	2.54	2.35	41	2.49	2.54
6	4.06	3.09	42	2.66	2.52
7	2.63	2.52	45	2.65	2.65
13	3.76	3.66	48	3.1	3.08
19	3.19	2.9	54	3.92	3.75
26	3.03	3.01	56	2.91	2.97
28	3.43	3.81	67	2.94	2.9
32	3.17	3.53	72	2.54	2.38
33	3.12	3.49	73	2.94	2.61
34	2.99	2.92	74	2.8	3.02
Younger Adu	ılt – Cathodal	Stim	Older Adult -	- Cathodal Stir	n
Participant			Participant		
#	Rate Pre	Rate Post	#	Rate Pre	Rate Post
2	3.04	3.1	50	3.05	2.89
5	4.03	4.13	51	2.78	2.8
11	3.83	3.91	52	3.49	3.3
16	3.55	3.88	53	3.41	3.78
18	4.78	4.24	58	2.72	2.53
21	3.43	3.87	62	2.99	2.85
23	2.83	2.94	63	2.89	2.88
27	3.16	3.32	66	3.04	3
31	3.35	3.23	69	2.87	2.9
35	3.61	3.42	71	2.78	3.05
-	ılt – Sham Stir	n	Older Adult – Sham Stim		
Participant	_		Participant	_	
#	Rate Pre	Rate Post	#	Rate Pre	Rate Post
1	2.55	2.89	43	2.56	2.91
8	3.51	3.65	44	2.7	2.19
9	3.86	3.77	46	3.3	2.67
17	3.69	4.33	47	3.01	2.7
20	4.34	3.95	49	2.76	3.05
22	4.06	3.38	55	3.07	3.17
24	3.65	3.33	57	2.7	2.98
25	3.83	4.09	61	3.79	3.74
29	3.77	3.23	68	3.08	3.27
30	3.87	3.51	70	2.94	2.77

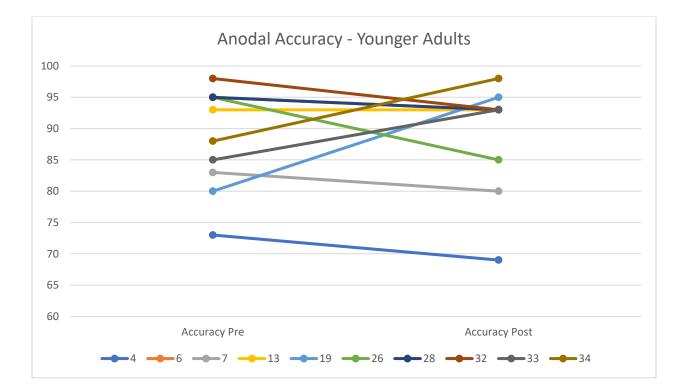
Chart of All Rate Data (Rate in Syllables/Second)

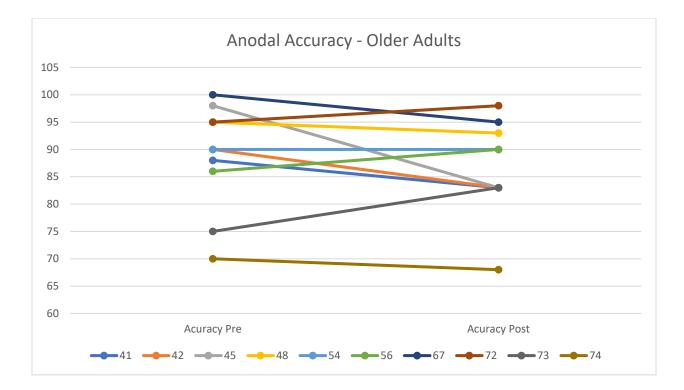
Younger Adult – Anodal Stim		Older Adult – Anodal Stim			
Participant	Reaction	Reaction	Participant	Reaction	Reaction
#	Time Pre	Time Post	#	Time Pre	Time Post
4		1171	41	597	496
6	820	713	42	673	651
7	919	893	45	650	532
13	575	550	48	761	768
19	555		54	636	613
26	834	768	56	662	698
28	654	662	67	547	560
32	621	624	72	936	918
33	753	622	73	794	837
34	756	759	74	938	889
Younger Adu	Younger Adult – Cathodal Stim		Older Adult –	Cathodal Stir	n
Participant	Reaction	Reaction	Participant	Reaction	Reaction
#	Time Pre	Time Post	#	Time Pre	Time Post
2	738	709	50	656	586
5	539	527	51	625	538
11	649	561	52	642	626
16	684	614	53	687	846
18	703	612	58	796	754
21	594	598	62	592	555
23	662	718	63	950	755
27	770	698	66	747	716
31	537	517	69	652	758
35	729	533	71	779	581
Younger Adu	Younger Adult – Sham Stim		Older Adult – Sham Stim		
Participant	Reaction	Reaction	Participant	Reaction	Reaction
#	Time Pre	Time Post	#	Time Pre	Time Post
1	694	789	43	748	797
8	610	607	44	1092	852
9	636	676	46	722	795
17	769	729	47	1075	980
20	661	582	49	631	502
22	686	590	55	581	594
24	950	806	57	695	715
25	558	560	61	876	899
29	656	665	68	915	978
30	576	618	70	782	720

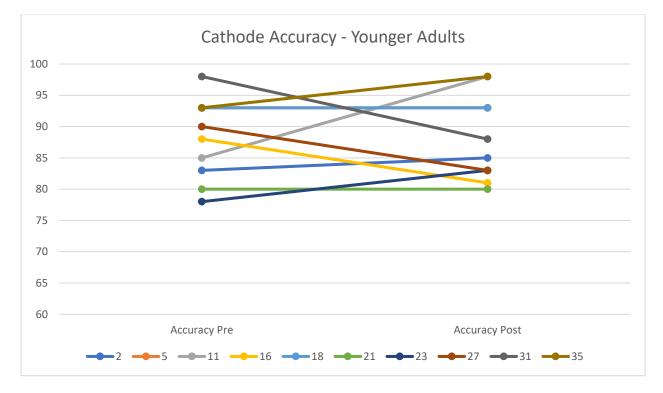
Chart of All Reaction Time Data (Reaction Time in ms)

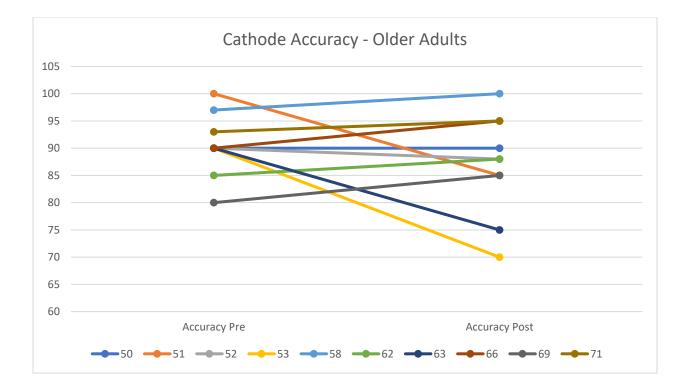
The following graphs show the changes from Pre- to Post-Stimulation for individual participants. Each Line represents an individual participant. The numbers associated with each participant show how they were coded into the study.

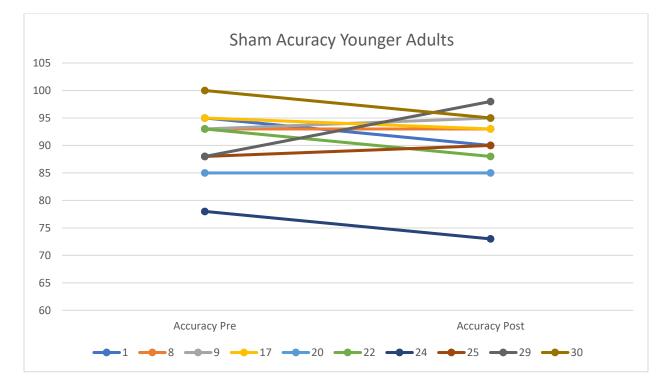
Accuracy Graphs:

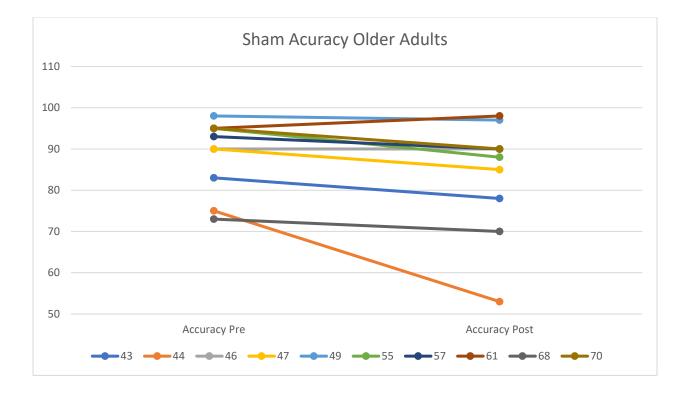




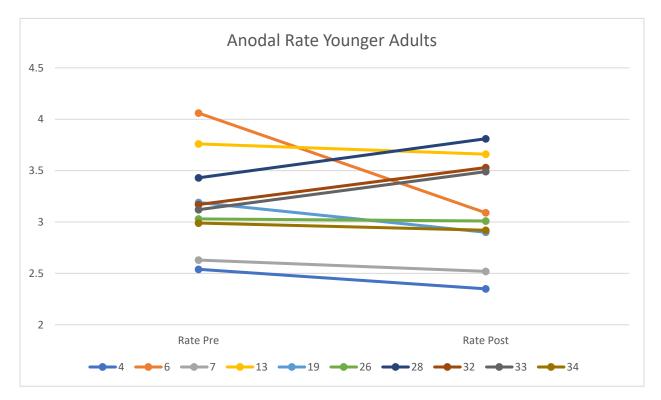


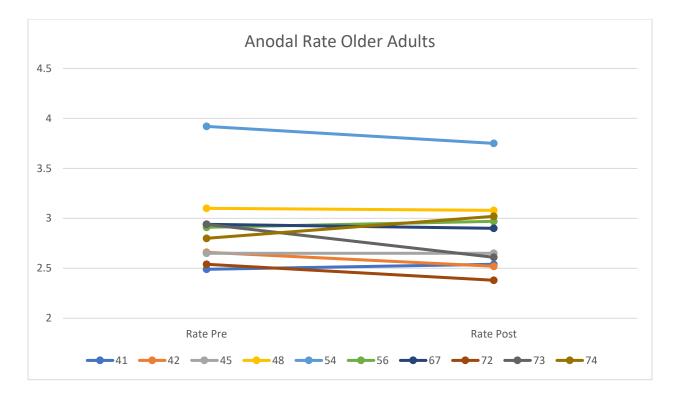


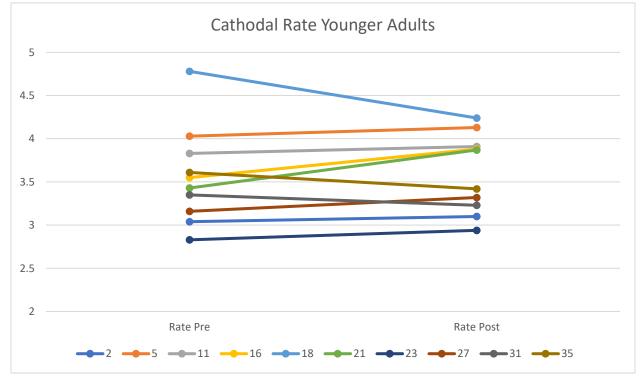


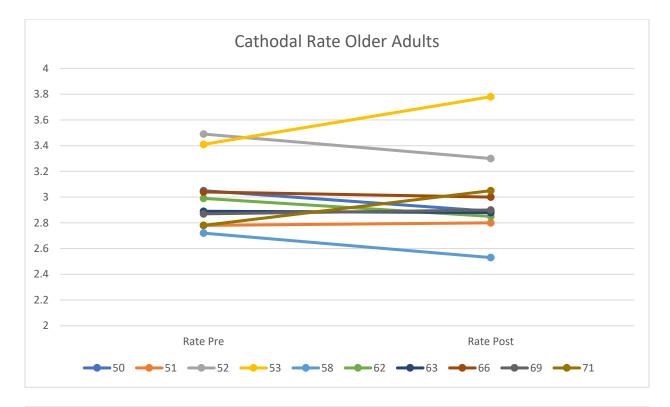


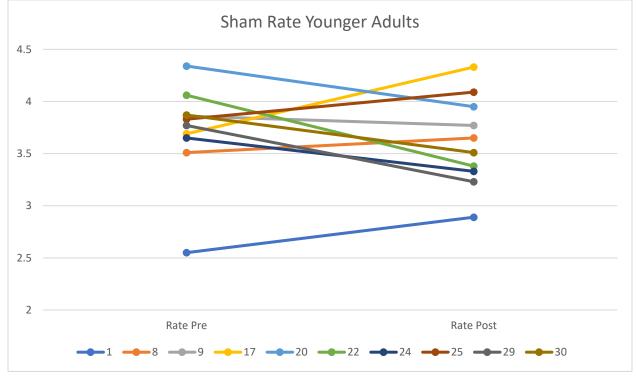
Rate Graphs:

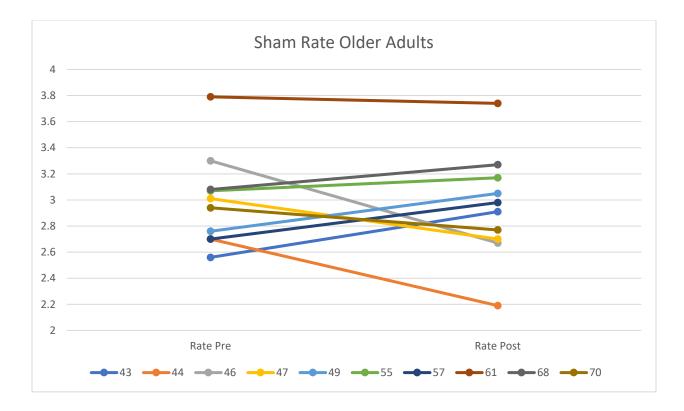












Reaction Time Graphs:

