TDCS OF THE CEREBELLUM: EFFECTS ON LANGUAGE ARTICULATION AND VERBAL FLUENCY

By

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ABSTRACT

Evidence from neuroimaging and cerebellar lesion studies indicate that the cerebellum plays a role in language articulation and verbal fluency. Previous studies have established that distinct areas of the cerebellum are differentially active during each of these tasks, with articulation engaging the anterior cerebellum and verbal fluency activating areas of the right posterolateral cerebellum. This study examined the effects of neuromodulation of the cerebellum on language articulation and semantic and phonemic verbal fluency. We used anodal transcranial direct current stimulation (tDCS) to apply 2 mA of current to two sites in the right cerebellum: the "motor" site (3 cm lateral to the inion) and the "cognitive" site (4 cm lateral to the inion and 1 cm down). Participants (17 females, 14 males; mean age 23.4 ± 6.3 years) completed articulation and fluency measures pre- and post- 20 min of motor (n=11), cognitive (n=10), or sham (n=10) tDCS. Subjects receiving tDCS to the motor site produced fewer syllables of "ba" in a 30 s period than the cognitive and sham tDCS groups. Subjects in the sham and motor groups showed a practice effect after tDCS on a semantic fluency task; however, tDCS over the cognitive site seemed to block this practice effect. Performance on the phonemic fluency task was not affected by anodal tDCS. The findings from this study support the idea that the cerebellum is involved in both motor and cognitive aspects of language, and that different regions of the cerebellum mediate performance on articulation and fluency tasks.

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INTRODUCTION

The Cerebellum

The cerebellum is a large structure located in the posterior fossa. In the medial-to-lateral direction, the cerebellum can be divided into three distinct areas: the vermis, the paravermis, and the two cortex-covered cerebellar hemispheres, which are connected by the midline vermis. The surface of the cerebellum is folded into long, transverse convolutions called 'folia', which are separated by parallel 'sulci'. Fissures and sulci separate the cerebellar surface into the anterior, posterior, and flocculonodular lobes (See Figure 1). The primary fissure separates the anterior and posterior lobes, while the posterolateral fissure separates the posterior and flocculonodular lobes. Each of these lobes is made up of lobules, with the anterior lobe including lobules I-V, the posterior lobe containing lobules VI-IX, and lobule X in the flocculonoodular lobe (Stoodley and Stein, 2011; Vlachos et al., 2007).

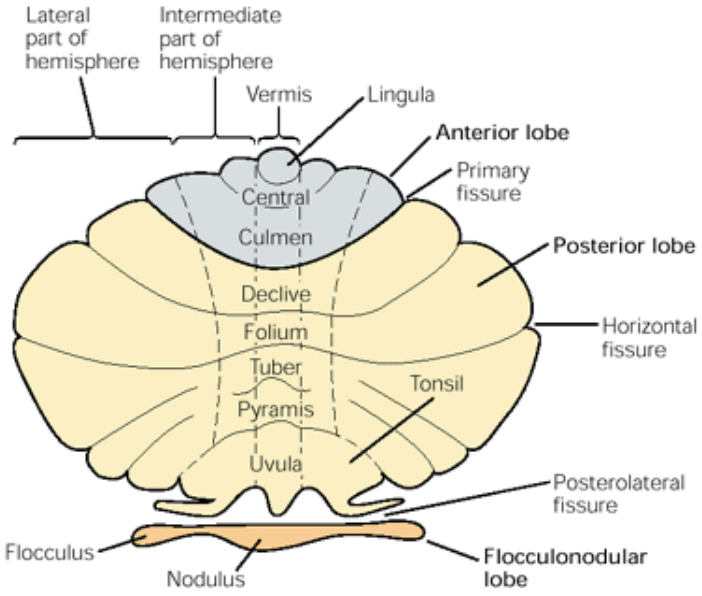


Figure 1. The Cerebellum is Composed of the Anterior, Posterior, and Flocculonodular Lobes (Ghez and Thach in Kandel et al., 2000).

The cerebellar lobes also have distinct functions. The anterior and parts of the posterior lobe form the spinocerebellum, a region which aids in the control of proximal muscle, posture,

and locomotion. The lateral parts of the cerebellar hemispheres, which are part of the posterior lobe, are collectively called the cerebrocerebellum. This structure receives signals from the cerebral cortex and aids in the initiation, coordination, and timing of movements and is also thought to play a role in cognition and affective state (Vlachos et al., 2007). The cerebellum has reciprocal connections with the cortex via a subcortical loop which includes the thalamic and pontine relays, and also makes reciprocal connections with the spinal cord. Most cerebrocerebellar connections are contralateral and spinocerebellar connections are primarily ipsilateral (Stoodley and Schmahmann, 2010).

The Cerebellum and Motor Function

The cerebellum is best known for its involvement in the coordination of smooth movements, maintenance of balance and posture, control of visually guided movements, and motor learning (Dow and Moruzzi, 1958; Holmes, 1939; Ito, 1984; Stein et al., 1986). Cerebellar damage causes a triad of symptoms, including ataxia, dysmetria, and intention tremor (Holmes, 1939).

It has been proposed that Purkinje cell modules located throughout the cerebellum carry out the basic processing operation in the cerebellar cortex, also known as the Universal Cerebellar Transform (Schmahmann, 2000, 2004). Similarly, Ito (1984) hypothesized that microcomplexes are formed in different regions of the cerebellar cortex and that each microcomplex processes its unique inputs in the same way. These hypotheses have been supported by studies that have shown that different regions of the cerebellum mediate different functions depending on their inputs and outputs (Schmahmann, 1996; Stoodley and Schmahmann, 2009). For instance, the vestibular regions of the cerebellum, the central vermis, and the flocculonodular areas mediate posture and balance. The paravermal regions control limb

movements, while the neocerebellum mediates complicated reaching and visually guided movements.

Multiple experimental (Chambers and Sprague, 1955a, 1955b; Snider and Eldred, 1951) and imaging studies (Grodd et al., 2001, 2005; Nitschke et al., 1996; Rijntjes et al., 1999) have established that the anterior lobe of the cerebellum has a primary representation of the body and that there is a secondary representation on lobule VIII. In addition, recent studies have suggested that there may be separate regions of the cerebellum for sensorimotor versus cognitive and affective functions (Stoodley and Schmahmann, 2009; Stoodley and Schmahmann, 2010).

The 'Cerebellar Transform' is the term used to describe the way that the cerebellum acts as a metasystem. Through this metasystem, the cerebellum adjusts the main sensorimotor, and possibly cognitive, pathways. For sensorimotor function, each cerebellar module acts to optimize each component of movement so it is best coordinated in relation to other movements in order to achieve a particular goal. This process is referred to as "automatic gain control", and by predicting the sensory consequences of an action in order to optimize it, each module is able to adjust the limits of the gain control. By generating a neural representation of the anticipated sensory outcomes of a specific movement being made, the cerebellum is able to determine whether the motor commands need to be altered in order for the goal to be reached (Stoodley and Stein, 2011).

When the cerebellum is damaged, a person does not lose the ability to move altogether. Instead, his movements are uncoordinated and jerky due to the cerebellum's failure to adjust the gain control. Eyeblink conditioning and visuo-motor adaptation studies have found that the ability to calibrate performance is impaired following cerebellar damage (Gerwig et al., 2005;

Straube et al., 2001; Yeo and Hesslow, 1998). This procedural learning is crucial for skill acquisition as well as for automaticity (Lang and Bastian, 2002; Nicolson and Fawcett, 1990).

The Cerebellum and Cognitive Function

The existence of cerebro-cerebellar channels (cortico-ponto-cerebellar and cerebello-thalamo-cortical loops) that link the cerebellum with motor cortices, association cortices, and paralimbic regions of the cerebral hemisphere has formed the anatomical basis for the possible role of the cerebellum in non-motor functions (Stoodley and Schmahmann, 2009; Stoodley and Schmahmann, 2010). Studies have found that a greater proportion of circuits link the cerebellum and the prefrontal cortex in humans compared to primates (Ramnani et al., 2006; Whiting & Barton, 2003), and preliminary results from diffusion tensor imaging suggests that the largest proportion of inputs to the cerebellum may be prefrontal instead of motor (Ramnani et al., 2006).

Cerebellar subdivisions based on connectivity with sensorimotor and association regions of the cerebral cortex have been revealed by studies of functional connectivity patterns (Buckner et al., 2011; Habas et al., 2009; O'Reilly et al., 2010). Similar to anatomical findings, activity in cerebellar lobules V, VI, and VIII has been found to be correlated with resting-state activity in sensorimotor cortices (Habas et al., 2009; Krienen & Buckner, 2009; O'Reilly et al., 2010) and reflect the primarily contralateral projections between the cerebellum and the cerebral cortex. These findings have been further supported by structural studies in humans that have found separate cerebro-cerebellar loops for lobule VII ("cognitive") and lobules V-VI ("sensorimotor") (Salmi et al., 2010). Taken together, these results suggest that the cerebellum is involved in sensorimotor and cognitive functions and that there are distinct regions of the cerebellum involved in each of these.

Patients with cerebellar lesions exhibit the Cerebellar Cognitive Affective Syndrome (CCAS; Schmahmann & Sherman, 1998), which is characterized by deficits in language, spatial processing, and working memory, in addition to affective symptoms such as emotional lability. An important discovery is that, depending on the location of the lesion, the CCAS can exist in the absence of the cerebellar motor syndrome. Anterior lobe damage is associated with the cerebellar motor syndrome (Schmahmann et al., 2009; Schoch et al., 2006), while posterior lobe damage can lead to the CCAS (Exner et al., 2004; Schmahmann & Sherman, 1998). These results suggest that motor dysfunction is not solely responsible for deficits on cognitive tasks.

The crossed cerebro-cerebellar connections also suggest that the lateralization of damage may affect the type of cognitive deficit observed. For instance, language problems are most commonly associated with right cerebellar lesions, while spatial deficits can result from left cerebellar damage (Riva & Giorgi, 2000; Scott et al., 2001). Damage to the midline vermis is associated with affective processing deficits (Levisohn et al., 2000; Riva & Giorgi, 2000; Tavano et al., 2007).

The Cerebellum: Speech and Language

Motor Control of Articulation

The dichotomy between motor and cognitive functions that is reflected in the anatomy of the cerebellum also suggests that the cerebellum could be involved in motor and cognitive aspects of language. Functional imaging studies have confirmed that separate areas of the cerebellum are activated during articulation and verb generation tasks. Specifically, articulation, reflecting the motor control of speech, activated bilateral areas in paravermal lobule VI. This medial part of lobule VI contains a map of the face, tongue, and articulatory muscles. In contrast, verb generation and inner speech tasks engaged lobules VII/Crus I in the right cerebellar hemisphere (See Figure 2; Frings et al., 2006).

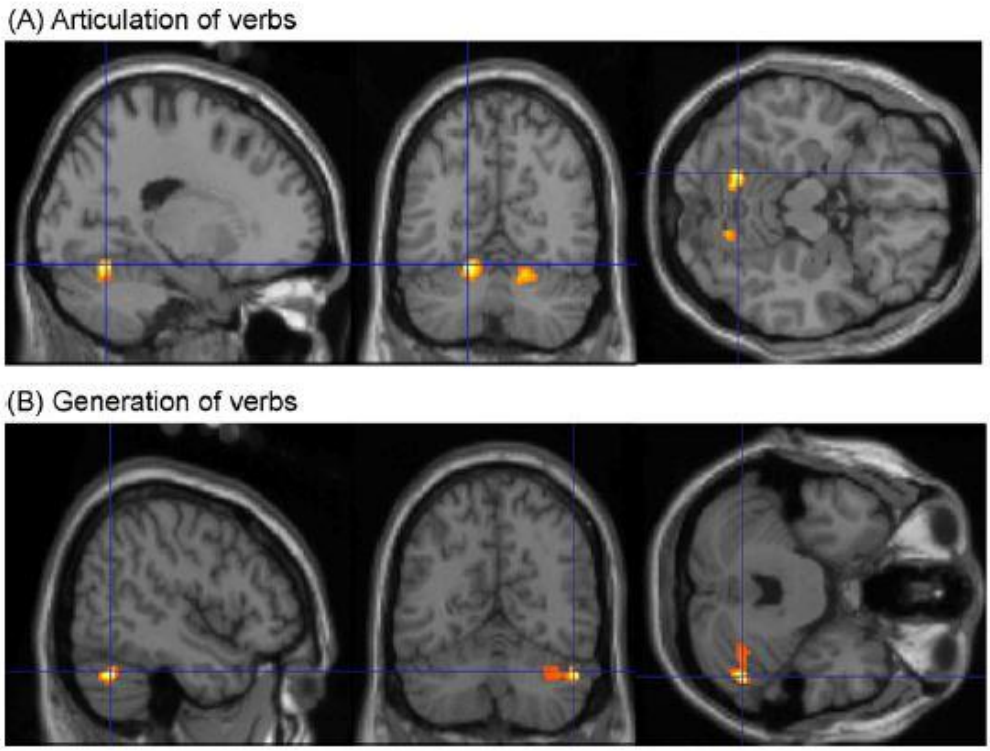


Figure 2. fMRI Shows that the Motor Aspects of Language (Articulation) Engage Medial Areas of Lobule VI. Verb Generation Tasks Show that the Right Lateral Lobule VII is Involved in Cognitive Aspects of Language (Frings et al., 2006).

Speech and Language Perception

Recent studies have suggested that the cerebellum contributes to speech perception and higher-order linguistic processing, including central-auditory operations, speech timing, phonological aspects of lexical access, and top-down mechanisms that help anticipate upcoming events. While the cerebellum might not be required for many aspects of comprehension and perception, it does make sense that it would be involved in tasks that are more cognitively demanding in regards to speed, acuity, memory load, and morphosyntactic processing (Hertrich and Ackermann in Mariën et al., Manuscript submitted for publication). Previous studies have documented the cerebellum's role in tasks that require very precise representation of temporal information, including motor sequence learning, rhythmic tapping, phoneme perception, and attentional anticipation (For a review, see Ivry and Spencer, 2004). It is thought that the

cerebellum contributes to speech and language perception through its involvement in the representation of phonological information of verbal utterances (Hertrich and Ackermann in Mariën et al., Manuscript submitted for publication). This prediction has been supported by studies showing that the processing of phonological distinctions that exclusively depend on timing relations, such as the duration of stop occlusions, is impaired in patients with cerebellar disorders (Ackermann et al., 1997; Ackermann et al., 1999). These types of studies examine the way that the perceived phonetic features of speech can depend on secondary cues, such as differences in voice onset time, or the time duration between a stop consonant burst and vowel onset, of voiced and unvoiced stop consonants (Ackermann et al., 1999). Further support for the cerebellum's role in aspects of speech timing has come from functional imaging studies that have found activation in areas of the cerebellum when healthy subjects are presented with similar stop consonant tasks (Mathiak et al., 2002).

Additional studies have suggested that the cerebellum also contributes to speech perception at an early stage of central-auditory processing (Petacchi et al., 2005; Sens et al., 2011). Specifically, the cerebellum is involved in mechanisms of perceptual switching and the segmentation of temporal sequences involved in auditory streaming (Kashino and Kondo, 2012). A study by Parsons et al. (2009) found that patients with cerebellar ataxia were impaired at pitch discrimination, despite having normal hearing. Furthermore, it has been suggested that disruptions in timing mechanisms and accompanying impaired temporal resolution of auditory processing following cerebellar dysfunction might contribute to the pathomechanisms of developmental dyslexia by disrupting the emergence of phonological awareness (Stoodley and Stein, 2011).

Speech Motor Planning

"Motor planning" is a term that encapsulates the process where relevant movement parameters are determined prior to the execution of a motor action. As discussed earlier, the cerebellum is involved in automatic gain control where it makes small adjustments based on sensory feedback received during motor movements. Models of speech production are based on a similar framework (Ziegler in Mariën et al., Manuscript submitted for publication). For instance, the DIVA model proposes a feedforward control subsystem that supplies motor plans for speaking, or the information required to execute speech movements. This model also suggests the existence of a feedback control subsystem that makes small corrections to bring the pre-planned movement closer to their predicted goals (Bohland et al., 2010; Perkell, 2012). The WEAVER++ model goes further to suggest that speech motor plans are comprised of articulation patterns on a syllabic level (Cholin et al., 2006; Roelofs, 2000).

Brain imaging techniques have been used to find support for the cerebellum's proposed role in speech motor planning. While functional imaging studies of speech motor control have shown that the cerebellum is a part of the minimal brain network of overt speaking (Ziegler in Mariën et al., Manuscript submitted for publication), the results have been unable to determine whether the cerebellum is involved in speech motor planning vs. execution due to the use of experimental paradigms that involve variation of stimulus length and complexity, which are both sensitive to the planning and execution aspects of speaking at the same time (Ziegler in Mariën et al., Manuscript submitted for publication).

Apraxia of speech is thought to be a clinical model of impaired speech motor planning (Ziegler, 2008). Most researchers agree that apraxia of speech is caused by lesions in the anterior peri- or sub-sylvian region of the left cerebral hemisphere (Dronkers, 1996; Ziegler, 2008). While cerebellar lesions do not cause apraxia of speech, they do cause ataxic dysarthria, a

disorder usually involving impairment in motor execution (Ackermann, 2008). Researchers have pointed to shared symptoms of these two disorders (e.g. slowness, scanning rhythm, irregularity of symptoms (Marien et al., 2001)), however, these similarities might be due to universal aspects of motor impairment or compensatory reactions rather than a shared pathomechanism (Ziegler in Mariën et al., Manuscript submitted for publication). Diadochokinetic tasks which challenge vocal tract motor functions (i.e. rapid repetition of /pa/, /ta/, or /ka/) have suggested some differences between apraxia of speech patients and those with cerebellar lesions. Patients with cerebellar lesions are excessively slow on these types of tasks as compared to normal speaking, which is not seen in patients with apraxia of speech (Ziegler in Mariën et al., Manuscript submitted for publication). These findings suggest that the cerebellum is involved in adaptive sensorimotor functions of the vocal tract while apraxia of speech impairs the capacity of planning the motor patterns for speaking (Ziegler and Wessel, 1996; Ziegler, 2002).

The Cerebellum and Verbal Working Memory

Verbal working memory is defined as the ability to temporarily store information that can be verbalized, such as letters, words, numbers, or nameable objects (Marvel and Desmond in Mariën et al., Manuscript submitted for publication). A phonological loop where speech-based information is stored and rehearsed was proposed to be a part of verbal working memory by Baddeley (2003). This phonological loop is comprised of two sub-components: a short-term passive storage process for speech-based and acoustic information and an active articulatory control process. Baddeley proposed that the active articulatory control process is further divided into two stages. In the first stage, verbal content that is presented visually is translated into a phonological representation that is put into phonological storage or aurally presented information that directly goes into storage. In the second stage, sub-vocal repetition helps maintain the

information in phonological storage (Marvel and Desmond in Mariën et al., Manuscript submitted for publication).

Clinical studies of patients with cerebellar damage have supported the theory that the cerebellum is involved in verbal working memory. For example, patients with cerebellar infarctions (Ben-Yehudah and Fiez, 2008; Leggio et al., 2011; Ravizza et al., 2006), spino-cerebellar ataxia (Cooper et al., 2012; Justus et al., 2005), and cerebellar tumors (Justus et al., 2005; Ravizza et al., 2006; Riva and Giorgi, 2000; Scott et al., 2001) have exhibited mild to moderate verbal working memory deficits compared to healthy, matched controls. Because of the diversity of cerebellar damage across patients in the studies and the variety of assessments used, it has been more difficult to determine how the cerebellum contributes to the sub-components of verbal working memory. Overall, researchers have concluded that the specific role of the cerebellum in verbal working memory is unclear (Marvel and Desmond in Mariën et al., Manuscript submitted for publication) and that the exact pattern of symptoms observed may depend on the region of the cerebellum and cerebro-cerebellar connections that are damaged (Desmond et al., 1997; Marvel and Desmond, 2010; Stoodley and Schmahmann, 2009). These inconclusive results have led some researchers to suggest more specialized functions for the cerebellum. For example, Ravizza et al. (2006) hypothesized that the cerebellum is involved in the first stage of articulatory control where verbal content is translated into a phonological representation via a memory trace. This trace can then be used by other brain regions that are directly involved in sub-vocal repetition (Marvel and Desmond in Mariën et al., Manuscript submitted for publication).

Neuroimaging studies in healthy subjects have lent support to Ravizza et al.'s (2006) hypothesis. To test verbal working memory, researchers commonly use the Sternberg task, or

variations on it, to measure phonological recoding, sub-vocal rehearsal, and phonological storage. The Sternberg task involves providing subjects with a set of letters to study and then asking them at a later point whether a test letter was included in the studied letter set (Sternberg, 1966). A study by Paulesu et al. (1993) compared subjects' performance on the Sternberg task with performance on a second task where subjects were asked whether a presented letter rhymed with the letter "B". By comparing the Sternberg task and the rhyming task, which did not include a delay phase and therefore, minimized phonological storage, Paulesu et al. were able to distinguish between the neural correlates underlying articulatory processes and phonological storage. The study found that phonological recoding and sub-vocal rehearsal activated motor areas in the brain, including Broca's area, the supplementary motor area, and the bilateral superior cerebellum. In contrast, phonological storage was associated with activation of the left supramarginal gyrus.

While the study by Paulesu et al. (1993) did not find cerebellar activation during phonological storage, the inferior cerebellum was not included in the field of view examined by the researchers. More recently, the inferior cerebellum has been implicated in non-motor aspects of verbal working memory, like phonological storage (Desmond et al., 1997). Desmond et al. compared cerebellar activity during a verbal working memory task for letters and a motoric rehearsal condition that did not involve working memory. The researchers found bilateral superior cerebellar activation during the working memory and motor tasks, but also right inferior cerebellar activity that was unique to the working memory task.

The differential activation of the cerebellum during verbal working memory tasks has been further explored in studies tracking the time course of activation (Chein and Fiez, 2001; Chen and Desmond, 2005). When information was perceived and recoded into a phonological

representation in the “encoding” phase of the Sternberg task, activation of motor-related cortical regions and bilateral superior cerebellum was observed. During the “delay” phase, where information is sub-vocally rehearsed and maintained in phonological storage, activity was seen in the right inferior cerebellum and left BA 40. These types of studies have suggested that lobes within the cerebellum differentially contribute to verbal working memory. The superior cerebellum is part of the cerebro-cerebellar motor circuit that recodes visually presented information into a phonological form, possibly creating a motor trace of the information (Marvel and Desmond in Mariën et al., Manuscript submitted for publication). Alternatively, the inferior cerebellum is part of the circuit that helps maintain information in the phonological store (Marvel and Desmond, 2010).

The Cerebellum and Verbal Fluency

The term "verbal fluency" is used to refer to the rate at which one produces words. This construct is commonly tested by word generation tasks, which measure one's ability to generate as many words as possible based on a predetermined word retrieval cue during a limited period of time. Semantic (e.g. category) and phonological (e.g. letter) fluency can be tested based on the word retrieval cue used (Molinari and Leggio in Mariën et al., Manuscript submitted for publication). These types of tasks have allowed researchers to assess the associative processes and strategies used in word searching (Abwender et al., 2001). Successful completion of a word generation task requires the ability to organize words into “clusters” that are either semantically related (words in the same category; eg. fish) or phonemically related (words starting with the same first two letters; eg.“ca”). Once an associative cluster is exhausted, a cluster shift to search for and identify new clusters is required (Arasanz et al., 2012).

Patients with cerebellar lesions frequently show impairments in verbal fluency tasks (Brandt et al., 2004; Leggio et al., 2000; Schmahmann and Sherman, 1998; Stoodley and Schmahmann, 2009). Furthermore, the results of previous studies suggest that cerebellar lesions more negatively impact the ability to generate words based on the phonemic rule than the semantic rule (Arasanz et al., 2012; Brandt et al., 2004; Leggio et al., 2000; Stoodley and Schmahmann, 2009). The selective impairment in clustering words phonologically has been cited as evidence that the cerebellum is specifically involved in phonemically related retrieval strategies (Leggio et al., 2000).

The properties of semantic and phonological retrieval cues and the way they are lexically represented may play a role in the differences seen in semantic and phonological fluency task performance (Rosser and Hodges, 1994; Troster et al., 1995). Semantic fluency tasks allow for the automatic activation of closely related semantic neighbors, which may be similar in physical or functional properties of the objects in the category (Rosser and Hodges, 1994). In contrast, phonological retrieval implements a less automatic process for word searching because it is based on the phonological level of word representation and not on meaning (Rosser and Hodges, 1994). Word retrieval strategies require sequencing abilities which allow one to compare previous and current stimuli by maintaining this information in working memory. When the word retrieval strategy is novel and not as automatic, such as in the case of phonemic cue retrieval, more cerebellar intervention is required to smooth and accelerate the sequence (Leggio et al., 2000). Less cerebellar activation is required when the word retrieval and matching strategies are not as cognitively demanding, such as in the case of semantic cue retrieval (Molinari and Leggio in Mariën et al., Manuscript submitted for publication).

This hypothesis has received additional support from studies showing that a decrease in word output and the number of category switches during the first 15 s of a phonemic fluency task can be observed in patients with right unilateral cerebellar lesions (Schweizer et al., 2010) and in healthy controls after receiving continuous theta burst stimulation over the right posterior/lateral cerebellar cortex (Arasanz et al., 2012). Previous studies have established that the first 15 s of a verbal fluency task are when word search and retrieval strategies are most flexible, and the most words and cluster switches are generated (Troyer et al., 1998). After the first 15 s of the task, the retrieval strategies are thought to lose flexibility, thus resulting in fewer words generated (Stuss and Alexander, 2007). Some researchers have suggested that the peak in word generation observed during the early phase of verbal fluency tasks reflects the involvement of neuronal networks that help optimize the speed of information processing (Stuss and Alexander, 2007).

The cerebellum's ability to facilitate smooth sequencing and fast processing of information is impaired following cerebellar damage, making performance on tasks that require nonautomatic strategies to become slower (Molinari and Leggio in Mariën et al., Manuscript submitted for publication). The primary function of the cerebellum has been theorized to be sequence processing, or comparing incoming patterns and outgoing responses (Braitenberg et al., 1997; Ivry, 1997), and this theory has received support from studies of the cerebellum's role in motor (Thach et al., 1992) and sensory (Bower, 1997; Restuccia et al., 2007) function. This model also fits with the hypothesis that the cerebellum is involved in "automatic gain control", through which it analyzes predicted sensory consequences to help adjust movements. The data from verbal fluency studies offer further support for these theories by showing that the cerebellum is involved in sequence processing in language (Molinari et al., 2008; Molinari and Leggio in Mariën et al., Manuscript submitted for publication). Instead of comparing predicted

sensory consequences to adjust motor movements, in verbal fluency tasks, the cerebellum has to compare previously generated words or clusters with those currently being generated.

Transcranial Direct Current Stimulation

Overview

The application of low-intensity transcranial direct current stimulation (tDCS) as a type of treatment for neurological and psychiatric pathologies is a rapidly expanding field of research (Angelakis & Liouta, 2011). tDCS is a non-invasive neurostimulation method that uses electrodes of different polarities, one over the site of interest and the other over a reference site, to deliver a low (1-2 mA) direct current. While there is not a consensus on the ideal size of the electrodes, most studies have used electrodes that are 25-35 cm^2, resulting in a current density of 0.03-0.08 mA/cm^2 when applying a current of 1-2 mA (Utz et al., 2010). In a 2007 study by Wagner et al., current density was found to be dependent on the size, polarity, and the position of the electrodes, as well as the current intensity and the properties of the tissue in the stimulated area.

The two electrodes used in tDCS studies are the anode and the cathode, with current flowing from the cathode to the anode (Nitsche et al., 2008). The flow of current between the two electrodes affects sodium and calcium channels, and therefore, exerts neuromodulatory effects, which alter the resting potential of the neuronal membrane (Nitsche et al., 2003; Nitsche et al., 2008). Anodal (positive) tDCS is frequently found to have excitatory effects, leading to membrane depolarization and an increase in neuronal firing rates. In contrast, studies have found that cathodal (negative) tDCS has inhibitory effects that lead to hyperpolarization of the neuronal membranes and a decrease in firing rate (Nitsche & Paulus, 2000; Utz et al., 2010). The effects of tDCS can be observed both during application and after stimulation has ended. Previous

studies have found that the aftereffects of tDCS depend on the stimulation duration and current intensity and may last up to 90 min in the human motor cortex (Nitsche and Paulus, 2001).

Safety and Tolerability of tDCS

tDCS has been used in over 400 published studies in a variety of populations, and no significant adverse side effects have been reported. A safety and tolerability study of 131 tDCS subjects by Kessler et al. (2012) found that the most common side effects reported were tingling (76%), itching (68%), burning (54%), and pain (25%). When asked to rate possible side effects on a 1-5 scale, overall symptom severity was low. Less than 2% of the responses reported a severity >3 on all questions except tingling (15%), itching (20%), burning (7%), pain (5%), and fatigue (3%). Kessler et al. also reported that none of the subjects asked to end the session early due to discomfort or withdrew from the experiment. These findings have been replicated in other studies, providing additional support that the side effects of tDCS are low risk and mild in intensity (Poreisz et al., 2007).

Effects of tDCS

There have been a growing number of studies conducted in the last 15 years that have allowed researchers to observe the effects of tDCS on multiple brain regions. Many early studies applied tDCS to the motor cortex as a way to investigate the physiological mechanisms that we now know to underlie tDCS as well as to observe how tDCS modulates motor function (Nitsche and Paulus, 2000; Utz, 2010). Several studies have found that anodal tDCS of M1 improves performance on motor tasks compared to sham (Boggio et al., 2006; Boggio et al., 2007; Fregni et al., 2005; Hummel et al., 2006) as well as improving motor learning (Reis et al., 2009).

In addition to the motor cortex, tDCS has been applied to other brain regions to determine how it can affect additional brain functions and behaviors. For instance, cathodal tDCS of the

visual cortex (V5) has been shown to impair visual motion discrimination while anodal tDCS improved it (Antal et al., 2004). Rogalewski et al. (2004) found that the application of cathodal tDCS to the somatosensory cortex (S1) disrupted tactile perception, while anodal and sham had no effect. Similarly, a study by Ragert et al. (2008) found that anodal stimulation of S1 led to improvements in spatial tactile acuity.

Other researchers have found that repeated anodal tDCS to the left dorsolateral prefrontal cortex (DLPFC) is associated with significant improvements in scores on the Beck Depression Inventory and Hamilton Depression Rating Scale (Fregni, Boggio et al., 2006), and that these improvements can last for up to 4 weeks (Boggio et al., 2008). While a consensus has not emerged, tDCS has also been shown to modulate pain perception and pain thresholds (Antal et al., 2008; Boggio et al., 2008; Fregni et al., 2006).

Effects of tDCS on Language

Several studies have examined whether tDCS can be used therapeutically to improve language-related skills. For instance, the application of anodal tDCS to locations in the temporal lobe has been linked to improvements in language learning (Flöel et al., 2008), verbal fluency (Cattaneo et al., 2011), picture naming (Sparing et al., 2008), proper name recall (Ross et al., 2010), and word reading efficiency in below average readers (Turkeltaub et al., 2011). While much of this research has focused on the way temporal lobe tDCS could be used to treat individuals with aphasia, researchers have only begun to consider the possible applications of tDCS to the cerebellum and its role in language.

tDCS Applied to the Cerebellum

As mentioned before, the cerebellum is known to be involved in the execution of smooth movements and motor control through its modulation of the primary motor cortex through

cerebello-thalamo-cortical connections. Normally, cerebellar inhibition of the motor cortex occurs when Purkinje cells are activated. A study in rats confirmed that anodal tDCS of the cerebellum decreased excitability of the motor cortex, supporting the idea that tDCS can modulate cerebellar neuronal activity (Oulad Ben Taib and Manto, 2013). The researchers proposed that anodal tDCS increases the inhibition exerted by Purkinje neurons over cerebellar nuclei, therefore, also inhibiting the normally facilitatory connections between the dentate nucleus and motor cortex. In another study, cathodal tDCS of the right cerebellar cortex resulted in a decrease of cerebello-brain inhibition while anodal tDCS increased it (Galea et al., 2009).

Researchers have also begun to study the effects of tDCS on the cognitive and learning functions of the cerebellum. In one study, cerebellar tDCS was found to impair a practice-dependent proficiency increase in verbal working memory (Ferrucci et al., 2008). This effect appeared to be specific to the cerebellum since tDCS of the DLPFC increased performance on the task. These findings were particularly significant since they suggest that tDCS of the cerebellum inhibited the "learning of learning" (Grimaldi et al., 2013). Jayaram et al. (2012) further examined the role of the cerebellum in learning by studying the effects of tDCS of the cerebellum on motor learning. This study found that anodal cerebellar tDCS applied during walking improved locomotor adaptation, while cathodal tDCS hindered it without affecting the rate of de-adaptation to the new locomotor pattern. Similarly, cerebellar tDCS has been found to enhance the acquisition process during adaptive motor learning (Galea, Vazquez et al., 2011).

The use of tDCS has provided researchers with a method for studying the cerebellum's role in cognitive functions, like verbal working memory, that is not complicated by factors such as medication side effects and concomitant damage in other brain regions. Cathodal tDCS applied to the right cerebellum in healthy subjects was found to decrease forward digit spans and

block the practice dependent increase in backward digit spans in a working memory task (Boehringer et al., 2013). In contrast, a study by Pope and Miall (2012) found that cathodal tDCS over the right cerebellum improved working memory performance compared to anodal and sham tDCS. Specifically, performance on arithmetic and verb generation tasks that required a high cognitive load was enhanced by cathodal tDCS. This result could suggest that the cerebellar cortex is able to enhance performance when cognitive tasks become difficult by releasing additional resources from prefrontal regions of cortex (Pope and Miall, 2012). The conflicting findings observed in cerebellar tDCS studies and the wide variety of tasks used make it difficult to predict how tDCS might affect performance on other tasks aimed at investigating the role of the cerebellum in cognitive functions.

Hypothesis and Purpose of the Current Study

While research has shown the cerebellum's involvement in cognitive and language tasks and that tDCS of the cerebral cortex can affect language performance, no study has investigated how tDCS of the cerebellum affects cognitive and language related skills. This study aims to examine the effects of anodal tDCS applied to the right cerebellum on language articulation and verbal fluency. Two electrode locations will be used: one in the "motor" position over the anterior lobe of the right cerebellum and one in the "cognitive" position over the posterolateral cerebellum. We predict that anodal tDCS applied to the "motor" site will affect language articulation, while not impacting verbal fluency. In contrast, we predict that anodal tDCS applied to the "cognitive" site will modulate performance on verbal fluency tasks while not affecting articulation.

METHODS

Participants

Participants were made up of a sample of 31 typically-developing, healthy individuals (10 for sham, 11 for tDCS of the motor region, and 10 for tDCS to the cognitive region) between the ages of 18 and 56 (Table 1). They were recruited through Georgetown University, and randomly assigned to one of the three groups. All participants provided written, informed consent to participate in the study and were compensated for their time at the rate of $25 per hour.

Table 1: Participant Demographics

	Motor (n = 11)	Cognitive (n = 10)	Sham (n = 10)
Gender	3 female, 8 male	7 female, 3 male	7 female, 3 male
Age (years ± SD)	24.64 ± 9.667	22.70 ± 2.214	22.80 ± 4.686
Education (years ± SD)	15.09 ± 1.136	15.50 ± 0.972	15.00 ± 1.563

Exclusion criteria included: left-handedness; non-native English-speakers; history of a neurological (including seizure), psychiatric, or developmental disorder; head trauma; metal in the head or implanted medical devices (e.g. pacemaker); pregnancy; current use of medications that could modulate the effects of tDCS (neuroleptic and antiepileptics, antidepressants, benzodiazepines, L-Dopa) (Hesse et al., 2007). Individuals with neurological disorders (including seizure) and psychiatric disorders were excluded based on the possibility that these disorders could impact brain organization (Appendix A). Subjects with metal in the head or implanted medical devices were excluded based on theoretical safety concerns that tissue damage could occur if conductive metals are implanted in the head or that medical devices could malfunction. To screen for these possibilities, the standard MRI screening form used by the Center for Functional and Molecular Imaging at Georgetown University was used (Appendix B),

which is the most thorough form available to identify possible metal in the body. Similarly, pregnant women were excluded because the safety of tDCS in pregnant women has not been fully studied. To ensure safety, all women of childbearing age completed a pregnancy test before receiving tDCS.

tDCS Sessions

Subjects participated in a 1 hour session where active or sham tDCS was administered using a NeuroConn DC-Stimulator (Jali Medical, Inc.) via two 5×5 cm saline-soaked pads. During the anodal tDCS sessions, 2 mA of current was applied for 20 minutes. This level of current applied for 20 min yields 30 min following the tDCS during which the subject could complete the experimental tasks while under the effects of tDCS (Galea et al., 2009). In the sham condition, the current was ramped up, delivered for 15 s, and then immediately ramped down. This allowed subjects to experience the initial tingling sensation associated with tDCS, which provides a good level of blinding between sessions, without receiving enough stimulation to modulate neuronal excitability (Nitsche et al., 2003).

tDCS Electrode Placement

The placement of the electrodes is important for spatial localization and direction of current flow. Previous studies have seen effects of cerebellar tDCS on the motor cortex (Galea et al., 2011; positioned 3 cm lateral to inion over right cerebellum) and on cognitive function without motor performance effects (Pope and Miall, 2012; right cerebellum, positioned 4 cm lateral to inion and 1 cm down). The placement was based on the International 10-20 system, which was developed in order to have consistent and easily replicated electrode placement (Oostenveld and Praamstra, 2001). The inion is one of the reference points on the skull and identified as the bony lump at the base of the back of the skull along the midline (Jasper, 1958).

In our experiment, we used two different electrode placements for anodal tDCS. In the first, we placed the electrode 4 cm lateral to the inion and 1 cm down while the reference electrode was placed on the deltoid ("cognitive" electrode placement). Using this electrode placement, based on the findings of Pope and Miall (2012), we expected to see effects on cognitive fluency tasks while not seeing effects on motor articulation. In the second, we placed the electrode 3 cm lateral to the inion, where we anticipated motor effects ("motor" electrode placement) without inducing changes in fluency. Because of the strong lateralization of language task activation in previous fMRI studies, tDCS was administered to the right cerebellum in both conditions (See Stoodley, 2012 for review).

Tasks

Subjects were asked to complete four tasks that they were familiarized with prior to starting data collection. Each participant completed the tasks before and after receiving real or sham tDCS for 20 minutes. The tasks included three phonemic fluency blocks (C, F, L/P, R, W) and one semantic fluency (animals/fruits) block, as well as articulation blocks. The order of the tasks was counterbalanced across participants.

Phonemic Fluency

To test phonemic fluency, we used the Controlled Oral Word Association Task (COWAT). As noted above, the letters C, F, L and P, R, W were used. These forms of the COWAT were chosen because there is a high correlation (r = .82, n = 54) between the two forms, which allowed us to test phonemic fluency before and after tDCS while avoiding practice effects that could skew the results (Benton et al., 1994). In addition, the same raw score to standard score conversion table could be used for each form. The order of the forms was counterbalanced across participants. During this task, subjects were orally prompted by the

experimenter to verbally generate as many words as they could think of that started with each of the letters during a 1 min period. Responses were recorded using a digital microphone. Incorrect responses included repetitions or different grammatical forms of previously produced words (Lezak et al., 2004). Previous studies of healthy subjects have found that scores on the Controlled Oral Word Association Task tend to increase with education and decrease with advancing age (Tombaugh et al., 1999). However, a study by Ruff et al. (1996) updated the norms for the CFL and PRW versions of the COWAT and provided an adjustment for gender and education level that can be applied to the normalized T-Scores.

Semantic Fluency

Subjects were orally prompted by the experimenter to produce as many words as possible during a 1 min block that fell into the category of animals or fruits. One of these categories was used during the pretest and the other was used following tDCS. The order of the semantic categories was counterbalanced across participants. Responses were recorded using a digital microphone. Incorrect responses included repetitions or different grammatical forms of previously produced words (Lezak et al., 2004). A study by Capitani et al. (1999) found that gender affects the mean number of words produced during semantic fluency tasks. Based on the findings from that study, we expected that males would produce 19.6 ± 5.9 words for animals and 14.6 ± 4.5 for fruits, and females would produce 19.0 ± 6.4 words for animals and 15.7 ± 4.8 for fruits.

Articulation and Motor Sequencing

In the articulation conditions, participants were asked to repeat "ba" or "pa ta ka" (sequenced articulation) for 30 s. Repetition of monosyllabic items requires successive opening and closing movements of the vocal tract and are widely recognized as a test of articulatory

performance (Ackermann and Hertrich, 2000). These two conditions served as motor controls for the cognitive conditions in the study to show that any deficits observed in the phonemic and semantic fluency tasks were not due to disruption of motor processes underlying articulation of speech. Alternatively, in the condition where tDCS was applied to the motor region of the cerebellum, comparing performance on these two tasks allowed us to observe the effects of tDCS on simple ("ba") and more complex ("pa ta ka") motor tasks.

A noise-reducing microphone (Sony USB noise-cancelling microphone) was used to record verbal responses during each task. In addition, the experimenter manually transcribed each participant's responses during the phonemic and semantic fluency tasks. The digital voice recordings were analyzed using Audacity (http://audacity.sourceforge.net/), which allowed us to determine the rate of speech in syllables per sec or units ("pa ta ka") per second. Following each session, the subject was asked to complete a questionnaire to monitor possible symptoms during and after tDCS (Appendix C). The questionnaire was a self-scored visual analog scale to rate side effects, such as tingling, itching, burning, attention, fatigue, and pain, from 1-10, with 1 indicating the most severe symptoms (ie. maximal pain) and 10 indicating the least severe symptoms (Galea et al., 2009).

Data Analysis

Phonemic Fluency

The digital voice recordings were used in order to measure the number of words each subject produced in the COWAT. When scoring the results, irregular plural forms (ex. people/person) of a word were counted separately, but regular plural forms of a word (ex. cat/cats) were only counted as one response. Similarly, variations on derivations (ex. run/runner)

were scored as separate responses while variations on inflectional morphology (ex. run/running) were only counted as one response.

Scores on the COWAT were converted to z-scores based on norms established by Ruff et al. (1996), which allowed for adjustments based on gender and education. A repeated measures ANOVA was also used to analyze the data. The pre-tDCS and post-tDCS measurements were used as the two time points and the groups were considered a between-subjects factor.

Semantic Fluency

The digital voice recordings were used in order to count the number of words each subject produced when asked to name as many animals or fruits as he could think of. An issue that arose when scoring the semantic fluency data was instances where subjects responded with a broad type of animal or fruit and also provided more specific examples within that type (ex. bird and robin; melon and cantaloupe). If the subject only provided the broader type without more specific subtypes, the broader type was counted as a response. When subjects provided a broader type and subtypes, we chose to not count the broader type as a response but did count all of the subtypes listed by the subject.

In our sample, subjects on average produced 9.067 more animals than fruits, which is out of line with the norms (an average of 5 word difference between animals and fruits). Because of this, we used the mean and standard deviation (SD) for pre-tDCS animals and fruits within our sample to convert all scores to z-scores. Because half of the subjects were naming fruits before tDCS and half after tDCS, the large difference in the average number of words produced for each category was a confounding variable when we attempted to use the change in score to calculate an ANOVA. Recalculating the raw scores as z-scores based on our sample norms eliminated this confound. A repeated measures ANOVA was used to analyze the data. The pre-tDCS and post-

tDCS measurements were used as the two time points and the groups were considered a between-subjects factor.

Articulation

The difference between the number of syllables (‘ba”) or the number of units (“pa ta ka”) produced over 30 s post- and pre-tDCS was calculated for each subject. A repeated measures ANOVA was also used to analyze the data. The pre- and post-tDCS measurements were used as the two time points and the three groups were the between-subjects factor.

Post-tDCS Questionnaire

An ANOVA was used to determine whether there were differences in the side effects experienced during and after tDCS by the subjects in the cognitive, motor, and sham groups. Separate ANOVAs were calculated for the 11 side effects rated by each subject during tDCS and for the 10 side effects rated by each subject after tDCS. Each of the side effects being rated was considered a dependent variable and the three groups were the between-subjects variable. The ANOVA was used to determine whether the mean rating for each side effect differed between the experimental groups. A repeated measures ANOVA was also used to analyze the data.

Power Analysis

A power analysis was conducted using G*Power (Version 3.1.7, Franz Faul, Germany). G*Power was used to calculate the effect size and actual power obtained in this study and to estimate the sample size that would be needed in a future study to achieve statistical significance.

RESULTS

Articulation Task

Outlier Analysis

The voice files for each subject were analyzed using Audacity to give the number of syllables ("ba") each subject produced in the 30 s blocks before and after tDCS. To identify any outliers that could potentially be skewing the data, the change in performance (Post-tDCS – Pre-tDCS) was calculated for each subject. SPSS was then used to identify subjects that had too large or too small of a change in performance on the task, and an outlier was defined by SPSS as a change in score that fell outside of 1.5 × Interquartile Range. There were five outliers identified when looking at the change in performance on the articulation task. Four of the outliers were subjects in the motor group and one was from the sham group (Table 2).

Table 2: Articulation Task Performance

	Pre-tDCS Syllables Produced in 30 s (Mean ± SD)	Post-tDCS Syllables Produced in 30 s (Mean ± SD)	Mean Difference ± SD (Post-tDCS – Pre-tDCS)
Motor (n = 7)	102.41 ± 38.10	94.00 ± 38.09	-8.40 ± 4.09
Cognitive (n = 10)	97.15 ± 34.85	98.47 ± 36.46	1.33 ± 10.32
Sham (n = 9)	108.34 ± 39.56	110.24 ± 44.45	1.90 ± 10.39

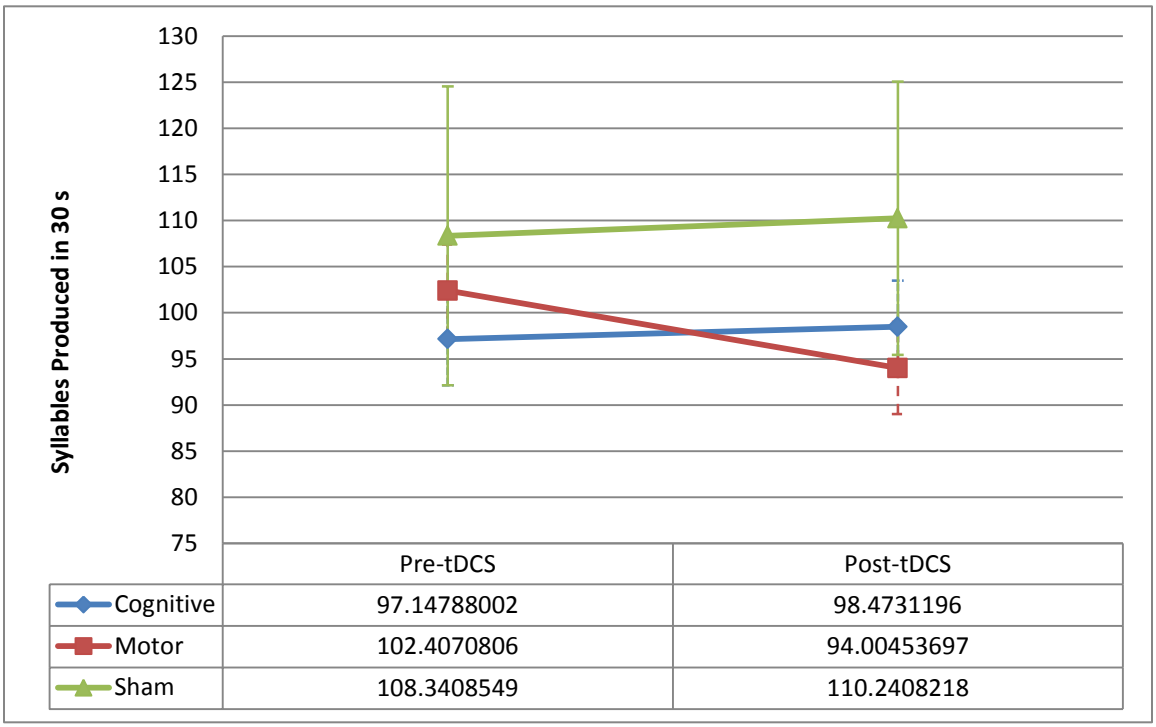
Repeated Measures ANOVA

Once the outliers were removed, a repeated measures ANOVA was used for analyzing the data. Doing this revealed that there was not a main effect for time of testing (pre-tDCS vs. post-tDCS; $F = 0.905$, $p = 0.351$) or group ($F = 0.234$, $p = 0.793$), but the interaction for time*group ($F = 3.067$, $p = 0.066$) approached statistical significance. This finding provides additional evidence that the change in performance on the articulation task varied depending on the type of tDCS received.

Visual Inspection of the Data

Given the small sample size used in this study, the study may be insufficiently powered to detect a statistically significant change in performance due to tDCS. Because of this, we opted to graph the mean scores on each of the pre-tDCS tasks and the post-tDCS tasks for the three groups. By doing this, it was possible to get a general idea of how performance on each task was altered by tDCS relative to the other groups. This method provided us with the clearest view of trends that might exist within the data.

While performance on the articulation task stayed relatively the same in the cognitive and sham groups, anodal tDCS applied to the "motor" area of the cerebellum was associated with a decrease in the number of syllables produced (Figure 3). This suggests that the impairment in articulation observed was due to the specific electrode site chosen in the motor group (3 cm lateral to the inion over the right cerebellum).



	Pre-tDCS	Post-tDCS
Cognitive	97.14788002	98.4731196
Motor	102.4070806	94.00453697
Sham	108.3408549	110.2408218

Figure 3. The Mean Number of Syllables ("ba") Produced during the Articulation Task in 30 s Blocks Pre-tDCS and Post-tDCS is Shown for the Cognitive, Motor, and Sham Groups. Error Bars Show the Standard Error.

Post-hoc Tests

Since the trend was so identifiable after graphing the data, and there was a statistical trend in the repeated measures ANOVA, we conducted an exploratory post-hoc Tukey test after the repeated measures ANOVA to determine the change in performance on the articulation task between each of the groups. The Tukey test showed that the largest difference in change in performance on the articulation task occurred between the motor and sham groups (mean difference = -11.085, $p = 0.848$). There was a much smaller difference seen between the motor and cognitive groups (mean difference = 0.3953, $p = 1.00$).

We also conducted exploratory, post-hoc T-tests to compare the change in performance (Post-tDCS – Pre-tDCS) between two groups at a time. Doing this allowed us to clearly see how motor tDCS affected performance on the articulation task relative to sham and cognitive tDCS. The post-hoc T-tests revealed that there was a significant change in performance between the motor vs. sham ($F = 6.06$, $p = 0.03$) and motor vs. cognitive groups ($F = 5.51$, $p = 0.03$) (Table 3).

Table 3: Post-hoc T-tests for the Articulation Task

	F	*p*
Motor vs. Cognitive	5.51	0.03
Motor vs. Sham	6.06	0.03
Cognitive vs. Sham	0.01	0.91

Sequenced Articulation Task

Outlier Analysis

The voice files for each subject were analyzed using Audacity to give the number of units (“pa ta ka”) each subject produced in the 30 s blocks before and after tDCS. SPSS was used to confirm that there were no outliers on the sequenced articulation task (Table 4).

Table 4: Sequenced Articulation Task Performance

	Pre-tDCS Units Produced in 30 s (Mean ± SD)	Post-tDCS Units Produced in 30 s (Mean ± SD)	Mean Difference ± SD (Post-tDCS – Pre-tDCS)
Motor (n = 11)	33.34 ± 10.93	36.53 ± 11.55	3.19 ± 5.77
Cognitive (n = 10)	35.12 ± 9.60	37.42 ± 10.80	2.30 ± 5.06
Sham (n = 10)	38.45 ± 11.37	42.94 ± 13.60	4.48 ± 4.89

Repeated Measures ANOVA

When a repeated measures ANOVA was conducted to compare performance on the sequenced articulation task before and after tDCS, the interaction between time*group ($F = 6.047$, $p = 0.435$) and the main effect for group ($F = 0.766$, $p = 0.475$) were not significant. However, the main effect for time was significant ($F = 12.283$, $p = 0.002$). The lack of a significant interaction between time*group shows that the type of tDCS received did not affect changes in performance on the sequenced articulation task.

Visual Inspection of the Data

Anodal tDCS did not seem to affect performance on the sequenced articulation task to the same degree as it did on the articulation task. Performance on the sequenced articulation task appeared to improve in all three groups, although there was a slightly larger degree of improvement observed in the sham group (Figure 4). Because the patterns were similar in all three groups, no post-hoc tests were conducted.

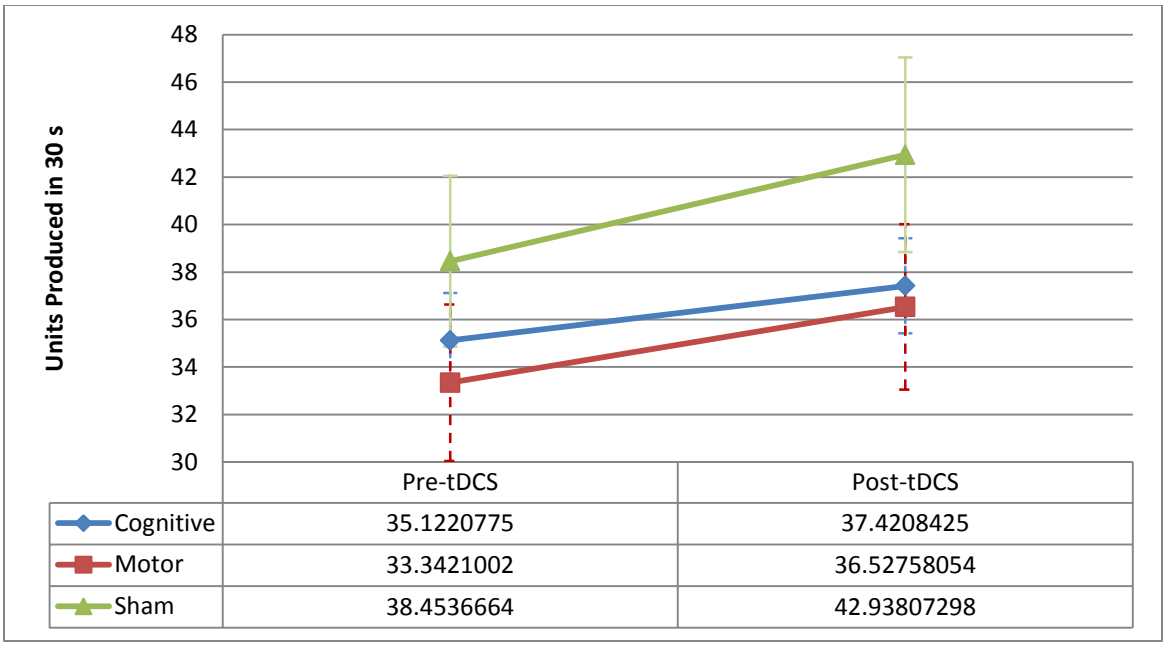


Figure 4. The Mean Number of Units ("pa ta ka") Produced during the Sequenced Articulation Task in the 30 s Blocks Pre-tDCS and Post-tDCS is Shown for the Cognitive, Motor, and Sham Groups. Error Bars Show the Standard Error.

Phonemic Fluency Task

Outlier Analysis

The raw scores on the phonemic fluency task were converted into z-scores based on norms established by Ruff et al. (1996), which allowed for adjustments based on gender and education. The change in performance (Post-tDCS – Pre-tDCS) was calculated for each subject and used to identify outliers. SPSS identified one outlier from the motor group that could potentially skew the results (Table 5).

Table 5: Phonemic Fluency Task Performance

	Pre-tDCS z-Score (Mean ± SD)	Post-tDCS z-Score (Mean ± SD)	Mean Difference ± SD (Post-tDCS – Pre-tDCS)
Motor (n = 10)	0.72 ± 1.13	1.02 ± 1.12	0.30 ± 0.55
Cognitive (n = 10)	0.45 ± 1.22	0.87 ± 1.28	0.41 ± 0.37
Sham (n = 10)	0.74 ± 1.11	1.09 ± 0.99	0.36 ± 0.82

Repeated Measures ANOVA

After removing the one outlier, a repeated measures ANOVA of performance on the phonemic fluency task was conducted. This statistical test revealed that the interaction between time*group ($F = 0.089$, $p = 0.915$) and the main effect for group ($F = 0.153$, $p = 0.859$) were not significant, while the main effect for time was significant ($F = 10.207$, $p = 0.004$).

Visual Inspection of the Data

Examination of the change in performance seen in the phonemic fluency task did not reveal any trends. On average, subjects in all three groups improved their performance, however, there was a discrepancy seen in the pre-tDCS performance measurement among the groups that carried over into the post-tDCS measurement (Figure 5). Subjects in the sham group performed better on the phonemic fluency task than the subjects in the other two groups, while subjects in the cognitive group had lower scores, on average, than subjects in the other groups. Since the task form (CFL or PRW) and order was counterbalanced across all of the groups, it is unlikely that this difference was due to an order effect. An ANOVA was used to determine whether this difference in pre-tDCS scores between the groups was statistically significant ($F = 0.19$, $p = 0.83$). Because the patterns were similar in all three groups, no post-hoc tests were conducted.

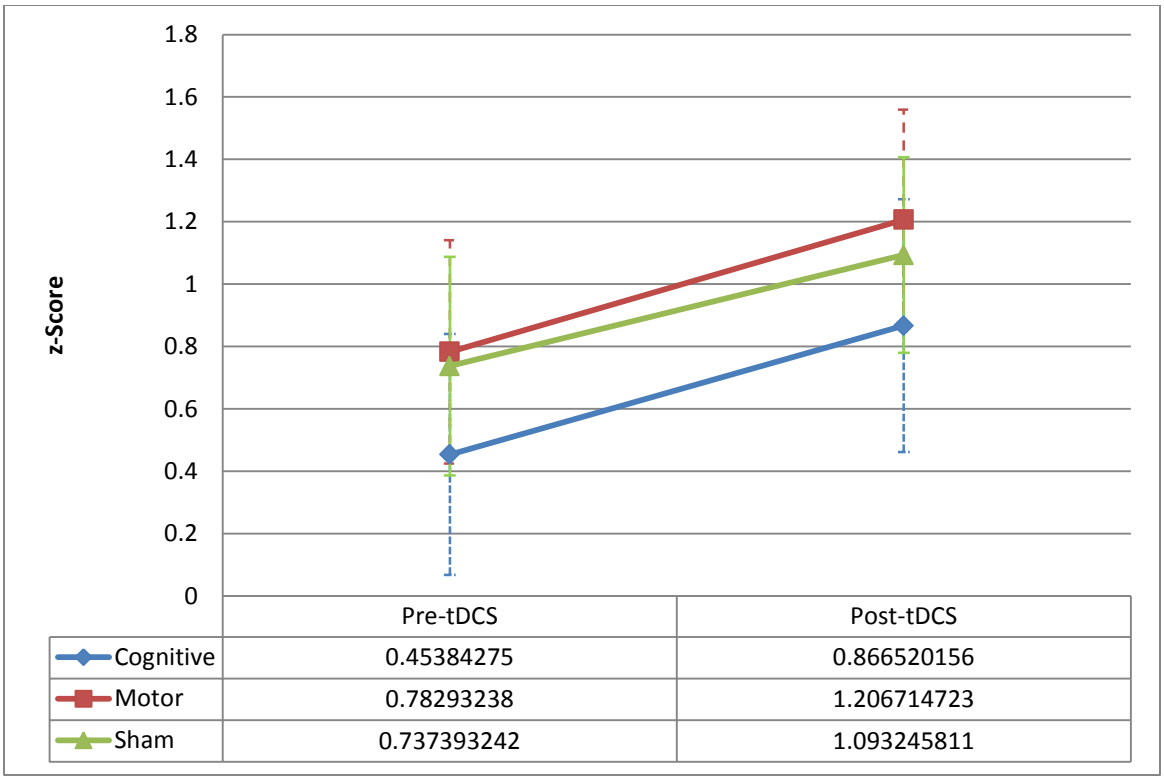


Figure 5. The Mean Z-score for Number of Words Generated during the Pre-tDCS and Post-tDCS Phonemic Fluency Tasks is Shown for the Cognitive, Motor, and Sham Groups. Error Bars Show the Standard Error.

Semantic Fluency

Outlier Analysis

The mean and SD for pre-tDCS performance on the animals (24.53 ± 4.27) and fruits (17.87 ± 5.11) versions of the semantic fluency task were used to calculate z-scores for the participants. There was incomplete data from one of the subjects in the motor group, and therefore, that subject was not included in the semantic fluency data analysis. The change in performance (Post-tDCS – Pre-tDCS) was calculated for each subject and SPSS was used to identify one outlier from the cognitive group who was removed from the analysis (Table 6).

Table 6: Semantic Fluency Task Performance

	Pre-tDCS z-Score (Mean ± SD)	Post-tDCS z-Score (Mean ± SD)	Mean Difference ± SD (Post-tDCS – Pre-tDCS)
Motor (n = 10)	-0.05 ± 1.14	1.00 ± 1.01	1.06 ± 1.24

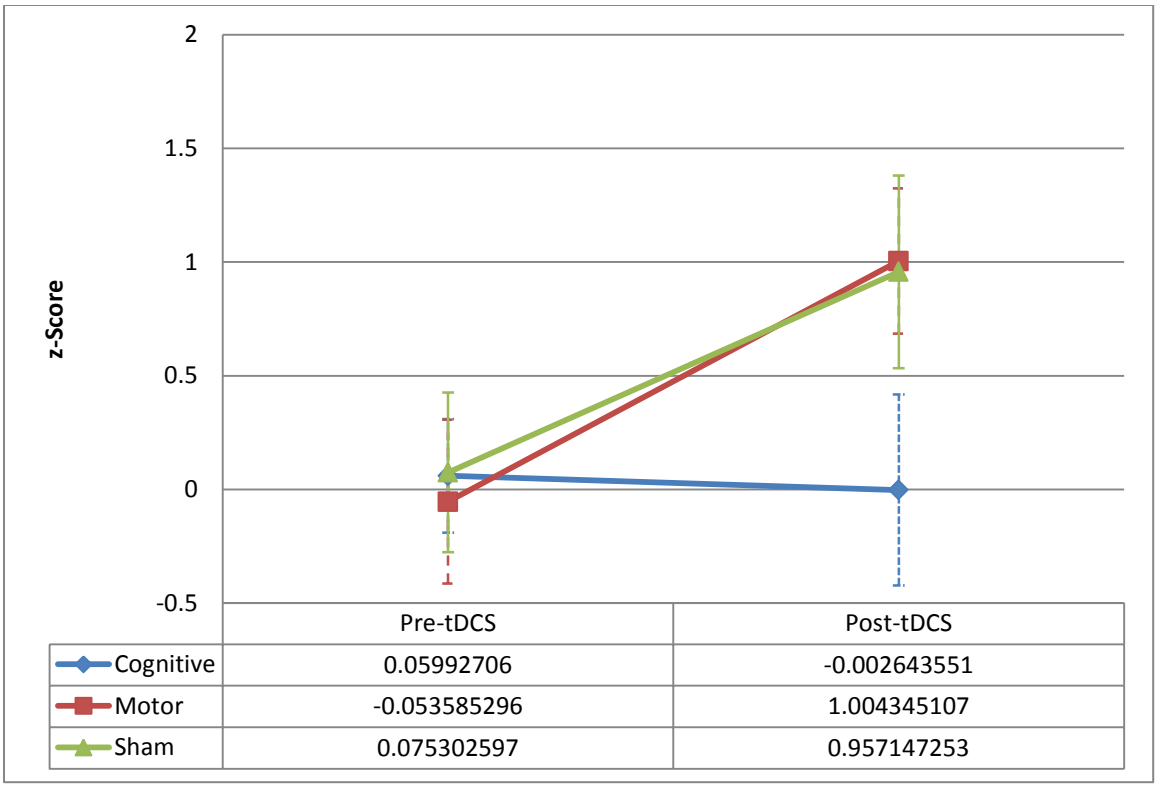
Cognitive (n = 9)	0.06 ± 0.75	-0.003 ± 1.26	-0.06 ± 0.72
Sham (n = 10)	0.08 ± 1.11	0.96 ± 1.34	0.88 ± 1.53

Repeated Measures ANOVA

A repeated measures ANOVA was used to analyze the semantic fluency data and revealed that there was a significant main effect for time ($F = 7.517$, $p = 0.011$) and a close to significant interaction between time*group ($F = 2.25$, $p = 0.126$). The results from the repeated measures ANOVA suggest that performance on the semantic fluency task was differentially affected depending on the type of tDCS received.

Visual Inspection of the Data

Visual inspection of the change in performance on the semantic fluency task did yield an interesting pattern. While subjects in all groups improved their performance to some degree, subjects in the motor and sham groups displayed a larger improvement that was not observed in the cognitive group (Figure 6). The results from the visual inspection of the data and the repeated measures ANOVA suggest that anodal tDCS applied to the "cognitive" location in the right cerebellum (4 cm lateral to the inion, 1 cm down) could inhibit practice effects on semantic fluency tasks. Even though the difference between groups was not statistically significant, the results do provide a direction that could be pursued in future research.



	Pre-tDCS	Post-tDCS
Cognitive	0.05992706	-0.002643551
Motor	-0.053585296	1.004345107
Sham	0.075302597	0.957147253

Figure 6. The Mean Z-score for the Number of Words Generated during the Pre-tDCS and Post-tDCS Semantic Fluency Tasks is Shown for the Cognitive, Motor, and Sham Groups. Error Bars Show the Standard Error.

Post-hoc Tests

Since a pattern could be clearly observed after graphing the semantic fluency data, we chose to conduct a post-hoc Tukey test after the repeated measures ANOVA to examine the relationship between the three groups. The post-hoc test showed that the cognitive group showed a slightly larger difference relative to the sham group (mean difference = -0.4876, $p = 0.503$) than it did to the motor group (mean difference = -0.4467, $p = 0.561$).

We also conducted exploratory, post-hoc T-tests to compare the change in performance (Post-tDCS – Pre-tDCS) between two groups at a time. Doing this allowed us to clearly see how cognitive tDCS affected performance on the semantic fluency task relative to sham and motor tDCS. The T-tests revealed that there was a significant difference in performance change between the cognitive and motor groups on the semantic fluency task ($F = 5.59$, $p = 0.03$). While

not statistically significant, the T-test for cognitive vs. sham groups still yielded a relatively low *p*-value (F = 2.84, $p = 0.11$), suggesting there was also a noticeable difference in the change in performance between those groups as well (Table 7).

Table 7: Post-hoc T-tests for the Semantic Fluency Task

	F	*p*
Cognitive vs. Motor	5.59	0.03
Cognitive vs. Sham	2.84	0.11
Motor vs. Sham	0.08	0.78

Post-tDCS Questionnaires

Subjects were asked to rate eleven possible side effects they may have experienced during tDCS and were given the opportunity to rate any other side effects that were not listed. Most subjects did not list any additional side effects they experienced, however, the few that were mentioned included heat (n = 2), mental cloudiness (n = 1), brief ringing in ears (n = 1), and slight dizziness or fatigue (n = 1). The mean rating and SD for each symptom for subjects within each group was calculated (Table 8). Overall, the rating of symptom severity was low, with the highest mean ratings for tingling (2.90 ± 2.16), itching (1.80 ± 2.29), and burning (1.54 ± 2.19) on the 10-point scale. When one-way ANOVAs were conducted for each side effect, there were not significant differences in the mean ratings given by the subjects in the motor, cognitive, and sham groups (Table 9). The lack of a significant difference between subjects in the three groups on their ratings of side effects experienced during tDCS suggests that active tDCS is not associated with long-lasting, negative side effects.

Table 8: Subject Ratings of Side Effects Experienced during tDCS

	Motor Group (n = 11)	Cognitive Group (n = 10)	Sham Group (n = 10)
Tingling	3.93 (2.34)	2.60 (1.91)	2.05 (1.90)
Itching	2.45 (2.51)	2.17 (2.82)	0.70 (0.72)
Burning	1.91 (1.45)	2.30 (3.32)	0.38 (0.64)
Pain	0.45 (0.90)	0.95 (0.99)	0.25 (0.33)
Fatigue	0.98 (1.83)	0.73 (1.72)	0.67 (1.20)
Nervousness	0.68 (0.90)	0.85 (0.97)	2.78 (3.64)
Headache	0.32 (0.45)	0.43 (0.73)	1.08 (1.60)
Difficulty Concentrating	0.84 (1.00)	0.68 (0.67)	1.78 (2.30)
Mood Change	0.18 (0.34)	0.23 (0.43)	0.80 (1.15)
Vision	0.66 (1.41)	0.20 (0.28)	0.85 (1.40)
Visual Sensation	0.43 (1.05)	0.20 (0.35)	0.55 (1.17)
Other	0.41 (0.94)	0.00 (0.00)	1.05 (1.89)

Table 9: Significance Testing for Side Effects Experienced during tDCS

	F	*P*
Tingling	2.31	0.12
Itching	1.83	0.18
Burning	2.36	0.11
Pain	2.03	0.15
Fatigue	0.11	0.90
Nervousness	2.84	0.08
Headache	1.62	0.22
Difficulty Concentrating	1.61	0.22

Mood Change	2.30	0.12
Vision	0.82	0.45
Visual Sensation	0.36	0.70
Other	1.91	0.17

Subjects were asked to rate ten possible side effects they may have experienced after tDCS and were given the opportunity to rate any other side effects that were not listed. The mean rating and SD for each symptom for subjects within each group was calculated (Table 10). Only one subject listed an additional side effect and said he felt a "dull headache between the eyes and groggy feeling". Overall, the rating of symptom severity was low, with the highest mean ratings for tingling (1.23 ± 1.78), itching (0.85 ± 1.30), and fatigue (0.79 ± 1.37) on the 10-point scale. When one-way ANOVAs were conducted for each side effect, there were not significant differences in the mean ratings given by the subjects in the motor, cognitive, and sham groups (Table 11). The lack of a significant difference between subjects in the three groups on their ratings of side effects experienced after tDCS reinforces the findings from other safety and tolerability studies, suggesting that there are not long-lasting side effects experienced after tDCS.

Table 10: Subject Ratings of Side Effects Experienced Post-tDCS

	Motor Group (n = 11)	Cognitive Group (n = 10)	Sham Group (n = 10)
Tingling	1.80 (2.29)	1.18 (1.68)	0.65 (1.09)
Itching	0.66 (0.95)	1.18 (1.91)	0.73 (0.91)
Burning	0.34 (0.48)	0.55 (0.96)	0.43 (0.69)
Pain	0.20 (0.37)	0.33 (0.44)	0.35 (0.66)
Fatigue	0.82 (1.40)	0.68 (1.47)	0.88 (1.38)

Nervousness	0.36 (0.47)	0.25 (0.42)	0.90 (1.64)
Headache	0.52 (0.84)	0.35 (0.47)	0.68 (1.03)
Difficulty Concentrating	0.55 (0.75)	0.20 (0.35)	0.85 (1.51)
Mood Change	0.23 (0.39)	0.25 (0.42)	0.77 (1.18)
Vision	0.66 (0.90)	0.28 (0.30)	0.75 (1.87)
Other	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)

Table 11: Significance Testing for Side Effects Experienced Post-tDCS

	F	*p*
Tingling	1.09	0.35
Itching	0.46	0.64
Burning	0.22	0.80
Pain	0.26	0.78
Fatigue	0.05	0.95
Nervousness	1.21	0.31
Headache	0.40	0.68
Difficulty Concentrating	1.09	0.35
Mood Change	1.74	0.19
Vision	0.44	0.65
Other	-	-

Power Analysis

As listed by G*Power, a small effect for the difference between two independent groups is estimated to be around d = 0.20, a medium effect is d= 0.50, and a large effect is d = 0.80. A power analysis was completed between each of the groups for all four task used in the study. We

chose to determine the effect size and power between two groups at a time to better understand how performance was affected by tDCS on each task. By doing this, we were able to gain a clearer understanding of how tDCS at each site affected performance without the third group skewing the overall effect size. The results of these analyses show that a large effect size was obtained in the articulation task between the motor vs. cognitive groups (d = 1.022) and the motor vs. sham groups (d = 1.073). A large effect size was also seen between the motor vs. cognitive groups on the semantic fluency task (d = 0.9655) while a high-medium effect size was seen between the cognitive vs. sham groups (d = 0.7344) (Table 12). Given the effect size and power achieved in this study, we were able to use G*Power to also estimate the sample size that would be required in a future study to achieve statistical significance (Table 12). These results supported the earlier findings that anodal tDCS at the motor site affected performance on the articulation task and tDCS at the cognitive site affected performance on the semantic fluency task relative to the other groups. The results from G*Power also suggest that it might be worth repeating this study with a larger sample to examine the effects of anodal tDCS on the articulation and semantic fluency tasks. However, the estimated sample sizes required to observe a significant difference in change in performance on the sequenced articulation and phonemic fluency tasks is likely too large to be feasible.

Table 12: Group-by-Group Power Analysis for Each Task

		Effect Size (d)	Power	Estimated Sample Size
Articulation	Motor vs. Cognitive	1.022	0.4923	54
	Motor vs. Sham	1.073	0.5089	48
	Cognitive vs. Sham	0.0566	0.0516	16270
Sequenced	Motor vs. Cognitive	0.1670	0.0652	1872
Articulation	Motor vs. Sham	0.2443	0.0829	876
	Cognitive vs. Sham	0.4386	0.1533	3820
Phonemic Fluency	Motor vs. Cognitive	0.2391	0.0799	912

	Motor vs. Sham	0.0882	0.0540	6680
	Cognitive vs. Sham	0.0806	0.0534	7996
Semantic Fluency	Motor vs. Cognitive	0.9655	0.5089	58
	Motor vs. Sham	0.1293	0.0586	3114
	Cognitive vs. Sham	0.7344	0.3261	100

Table 12. G*Power was used to calculate the effect size and power between each group on all tasks. G*Power was also used to estimate the sample size required to achieve statistical significance.

DISCUSSION

While the findings from this study were not statistically significant, the data did reveal trends that yield insight into the role of the cerebellum in language articulation and verbal fluency. The original hypothesis, that anodal tDCS applied to the "motor" location in the right cerebellum would have an effect on language articulation, was supported and reflected in the finding that performance on the articulation task declined in the motor group after tDCS had been applied. These results are in accordance with Galea et al.'s (2009) study which showed that anodal tDCS increased cerebellar inhibition of the motor cortex. If anodal tDCS also increased cerebellar inhibition of the motor cortex in the current study, this would provide an explanation for why performance on the articulation task was impaired in the motor group, while remaining consistent in the cognitive and sham groups.

Since patients with cerebellar lesions have been shown to have difficulty with sequenced articulation (Ziegler in Mariën et al., Manuscript submitted for publication), we expected that subjects in the motor group would show a change in performance on the sequenced articulation task as well. Why a similar result was not observed on the sequenced articulation task is not immediately clear. One possibility for why we failed to see an effect on the sequenced articulation task could be that we only stimulated the part of the cerebellum involved in simple articulation. In contrast to the study by Frings et al. (2006), where articulation was associated with relatively localized bilateral activity in paravermal lobule VI (See Figure 2), a study by Bohland and Guenther (2006) found that increased syllable complexity was associated with significantly greater activity in the right superior cerebellar cortex (Lobule VI) (Figure 7). It is possible that with the two electrode locations we used, we were not modulating activity in the

areas that have shown activation during sequenced articulation tasks, thus explaining why changes in performance were not observed.

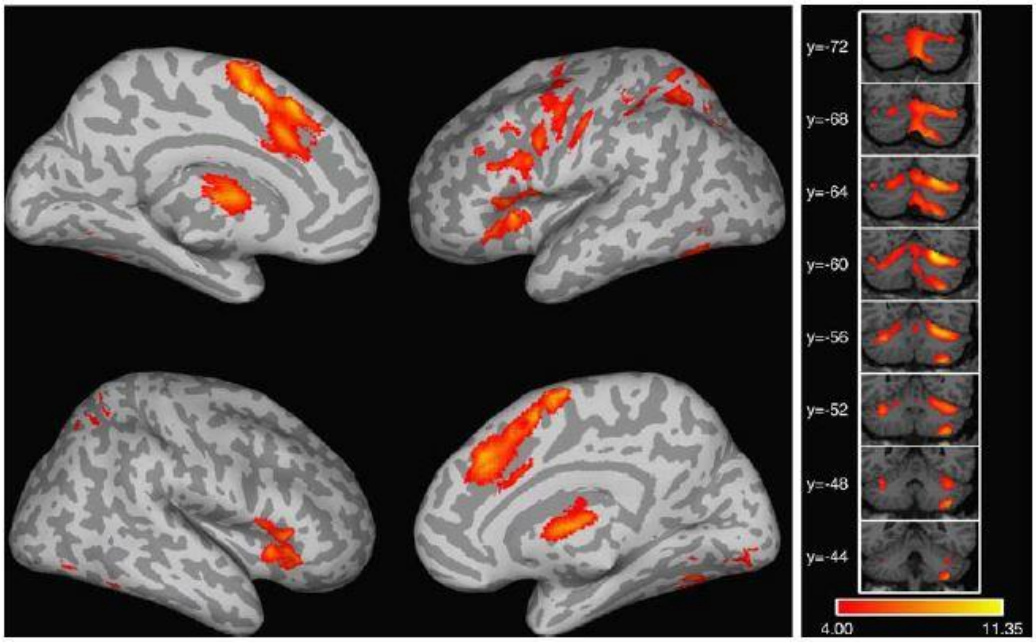


Figure 7. Areas in the Cerebellum Showing a Main Effect for Sequence Complexity. Sequenced Articulation was Associated with Greater Activity in the Right Superior Cerebellar Cortex (Lobule VI) (Bohland and Guenther, 2006).

The data from the verbal fluency tasks also revealed an interesting finding. Anodal tDCS applied to the "cognitive" location seemed to block the development of a practice effect on the semantic fluency task, while not impairing subjects in the motor and sham groups. This result was somewhat surprising, given previous research showing that cerebellar dysfunction is more closely associated with impairments on phonemic fluency tasks and not semantic fluency. However, the trend observed in this study does support the initial hypothesis that anodal tDCS applied to the "cognitive" site would have some effect on verbal fluency.

One possibility for why tDCS blocked a practice effect during the semantic fluency task but not the phonemic fluency task in the cognitive group could be that subjects had more opportunities to develop and refine strategies for successfully completing the phonemic word generation task. While subjects were only asked to name words for one semantic category before

tDCS and one after tDCS, they had three letters to generate words for before receiving tDCS, and three after. Presumably, the additional experience with the phonemic fluency task would allow subjects to identify word search and retrieval strategies that they were comfortable with. While anodal tDCS to the cognitive group blocked the development of a practice effect on the semantic fluency task, it is possible that having so much additional practice with the phonemic fluency task could have compensated for any deficit that the tDCS may have caused.

Taken together, the results of the articulation and semantic fluency tasks provide evidence that a functional topography exists in the cerebellum for motor and cognitive tasks. Functional imaging studies have previously shown that different areas in the cerebellum are active during motor and cognitive tasks (See Stoodley & Schmahmann 2009 for review), and our results suggest that these distinct areas can be targeted with tDCS by using different electrode placements. Since tDCS at the "motor" site was associated with impairments in articulation, it seems that the anterior region of the cerebellum is involved in the motoric aspects of speech, while tDCS applied to the posterolateral cerebellum ("cognitive" site) affected cognitive aspects of language.

Given the inconsistencies seen in previous studies, it was difficult to predict whether anodal tDCS would improve or impair performance on articulation and verbal fluency tasks. Anodal and cathodal tDCS of the cerebellum have been linked to impairments on verbal working memory tasks (Boehringer et al., 2013; Ferrucci et al., 2008), but cathodal tDCS has also been linked to improvements on arithmetic and verb generation tasks (Pope and Miall, 2012). The results from this study support earlier findings that anodal tDCS applied to the cerebellum negatively impacts performance.

While distinct changes in performance on the articulation and semantic fluency tasks were observed in the motor and cognitive tDCS groups, one issue that arose in this study was our inability to confirm whether tDCS was actually being applied to separate locations in the right cerebellum. Given the size of the electrodes used (5 × 5) and the small difference in location of the sites, it is possible that two distinct areas were not being stimulated in the motor and cognitive groups. Possible solutions for this problem that could be implemented in future studies would be to use smaller, high-density electrodes or to conduct tDCS and fMRI simultaneously. The latter option would provide the most assurance of stimulating the intended areas; however, the use of smaller electrodes would be an easier adjustment to make and would increase the likelihood that separate sites were being targeted.

The results from this study provide further evidence that the cerebellum is involved in both motor and cognitive aspects of language and that a functional topography exists within the cerebellum. While knowing this does not yield insight into the neural processes underlying these functions in the cerebellum, it provides the necessary groundwork for future studies that might be able to use more sensitive measures to better understand how the "universal cerebellar transform" is applied to both movement and cognition. Even though the results from this study were not statistically significant, the findings were significant in the sense that they identified trends that can be pursued in future research and highlighted methodological issues that could be corrected to improve the design of other tDCS studies. The role of the cerebellum in cognitive functions is complex and multifaceted, and these findings suggest that tDCS is a method that could be utilized to better understand this area of the brain.

APPENDIX A

SCREENING FORM

#2011-433 tDCS Studies of Language in Typical Adults

Participant Screening Form

We will need to ask you a few questions in order to determine whether you may be eligible for the research. These include questions about your education and medical history. First we would like to tell you a little about our research.

This research is being done to study transcranial Direct Current Stimulation, or tDCS, on healthy people to determine the brain-basis of language. TDCS is a technique by which small electric currents are applied to the scalp, which will allow investigation of the causal role of the brain area to which tDCS was applied in the behavioral task performed. This research is being done because understanding the specific organization of language functions in the brain may eventually lead to improved treatments for dyslexia and other language disorders. If you are eligible, the research will include no more than 6 visits for paper and pencil forms, behavioral tasks, and tDCS. No medications or invasive procedures are involved. TDCS requires you to sit while two salt-water soaked pads are placed on your head or shoulder and held in place with a strap. A small portable machine that is connected by thin wires to the pads passes a very small current. The current will be present for up to 20 minutes. Risks and side effects of the study that may occur include mild tingling, itching, redness, or pain in the skin under the pads. Fatigue is less likely to occur. Some participants will be asked to perform behavioral tasks with tDCS inside an fMRI scanner. An fMRI scanner is a large magnetic scanner that can be used to safely take pictures of the brain and other organs. These subjects will lie down in the scanner for the duration of the tDCS and associated behavioral testing.

You may feel uncomfortable answering questions about your education, medical, and psychiatric history. You do not have to answer any questions you do not wish to answer and you may stop at any time. Your participation in the screening is voluntary. A decision whether or not to participate in the screening will not affect your relationship with Georgetown University. You will not directly benefit from the screening.

If you do not qualify for the study, your answers during this screening will be destroyed.

If you qualify for an appointment, your answers will be kept with the research record if you decide to participate in the research project and sign the research informed consent form.

During this screening, we will collect information about you in this study. This information will include your name, birth date, and *information regarding your educational, medical and psychiatric history*. Your information is being used to be able to contact you if you are eligible and decide to participate in the research study. People at Georgetown University who are involved in the study or who need to make sure the study is being done correctly will see the information. These people will use your information for the purpose of the study.

We try to make sure that your answers to these questions are kept confidential but we cannot guarantee this.

Name/ID: _____ Date: _____

DOB: _____ Evaluator: _____

Sex (circle one): Male Female

tDCS Studies of Language in Typical Adults

Screening for Inclusion and Exclusion Criteria

Inclusion Criteria	**YES**	**NO**
Are you between the ages of 18 or older?	☐	☐
Are you right handed?	☐	☐
Have you completed high school?	☐	☐
Is English your native language? (or have spoken English since at least age 8)	☐	☐

Exclusion Criteria	**YES**	**NO**
Have you ever been diagnosed with a significant neurological disorder (including seizure, multiple sclerosis, epilepsy, cerebral palsy, encephalitis, stroke, dementia, etc.) or previous head injury causing a loss of consciousness?	☐	☐
Have you ever been diagnosed with hearing loss?	☐	☐
Do you have any metal in the head, excluding dental work?	☐	☐
Do you have any implanted medical devices (e.g. pacemakers)?	☐	☐
Do you have a history of any psychiatric disorders requiring treatment?	☐	☐
Do you take any anti-convulsant, antidepressant,		

sedative/hypnotics or anti-psychotic medication? ☐ ☐

(If female): Are you currently pregnant? ☐ ☐

(If fMRI experiment): Are you claustrophobic (bothered by or afraid of enclosed spaces)? ☐ ☐

Thank you for answering the screening questions.

[Indicate whether the person is eligible, requires additional screening at the lab, or is not eligible and explain why.]

Do you have any questions about the screening or the research? I am going to give you a couple of telephone numbers to call if you have any questions later. Do you have a pen? If you have questions about the research screening, you may call Dr. Turkeltaub at *(Office: 202-784-1764)* he will answer your questions.

If you have questions about your rights as a research participant, contact the Georgetown University IRB Office. Direct your questions to:

Institutional Review Board Telephone: (202) 687-1506

Address: Georgetown University Medical Center
3900 Reservoir Road, N.W.
SW104 Med-Dent
Washington, D.C. 20057

Thank you again for your time and your willingness to answer our questions.

_____
Name of Participant

_____
Signature of Participant

_____
Date

APPENDIX B

MRI SCREENING FORM

MAGNETIC RESONANCE (MR) PROCEDURE SCREENING FORM FOR PATIENTS

Date _____/_____/_____ Patient Number _____

Name _____ Age _____ Height _____ Weight _____
Last name First name Middle Initial

Date of Birth _____/_____/_____ Male ❒ Female ❒ Body Part to be Examined _____
month day year

Address _____ Telephone (home) (_____) _____-_____

City _____ Telephone (work) (_____) _____-_____

State _____ Zip Code _____

Reason for MRI and/or Symptoms _____

Emergency Contact _____ Telephone (_____) _____-_____

1. Have you had prior surgery or an operation (e.g., arthroscopy, endoscopy, etc.) of any kind? ❒ No ❒ Yes
   If yes, please indicate the date and type of surgery:
   Date _____/_____/_____ Type of surgery _____
   Date _____/_____/_____ Type of surgery _____
2. Have you had a prior diagnostic imaging study or examination (MRI, CT, Ultrasound, X-ray, etc.)? ❒No ❒ Yes
   If yes, please list:

	Body part	Date	Facility
MRI	_____	_____/_____/_____	_____
CT/CAT Scan	_____	_____/_____/_____	_____
X-Ray	_____	_____/_____/_____	_____
Ultrasound	_____	_____/_____/_____	_____
Nuclear Medicine	_____	_____/_____/_____	_____
Other_____	_____	_____/_____/_____	_____

3. Have you experienced any problem related to a previous MRI examination or MR procedure? ❒ No ❒ Yes
   If yes, please describe: _____
4. Have you had an injury to the eye involving a metallic object or fragment (e.g., metallic slivers, shavings, foreign body, etc.)? ❒ No ❒ Yes
   If yes, please describe: _____
5. Have you ever been injured by a metallic object or foreign body (e.g., BB, bullet, shrapnel, etc.)? ❒ No ❒ Yes
   If yes, please describe: _____
6. Are you currently taking or have you recently taken any medication or drug? ❒ No ❒ Yes
   If yes, please list:_____
7. Are you allergic to any medication? ❒ No ❒ Yes
   If yes, please list:_____
8. Do you have a history of asthma, allergic reaction, respiratory disease, or reaction to a contrast medium or dye used for an MRI, CT, or X-ray examination? ❒ No ❒ Yes
9. Do you have anemia or any disease(s) that affects your blood, a history of renal (kidney) disease, or seizures? ❒ No ❒ Yes
   If yes, please describe: _____

For female patients:

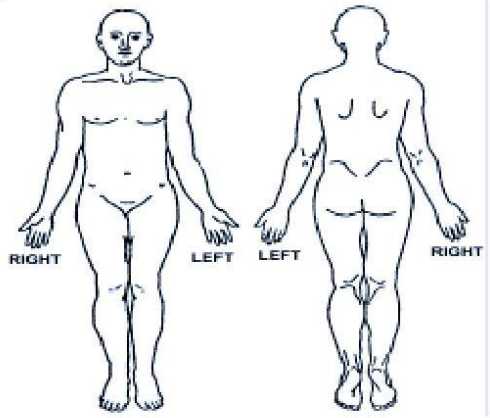
10. Date of last menstrual period:_____/_____/_____ Post menopausal? ❒ No ❒ Yes
11. Are you pregnant or experiencing a late menstrual period? ❒ No ❒ Yes
12. Are you taking oral contraceptives or receiving hormonal treatment? ❒ No ❒ Yes
13. Are you taking any type of fertility medication or having fertility treatments? ❒ No ❒ Yes
    If yes, please describe: _____
14. Are you currently breastfeeding? ❒ No ❒ Yes

WARNING: Certain implants, devices, or objects may be hazardous to you and/or may interfere with the MR procedure (i.e., MRI, MR angiography, functional MRI, MR spectroscopy). **Do not enter** the MR system room or MR environment if you have any question or concern regarding an implant, device, or object. Consult the MRI Technologist or Radiologist BEFORE entering the MR system room. **The MR system magnet is ALWAYS on.**

Please indicate if you have any of the following:

❒ Yes ❒ No Aneurysm clip(s)
❒ Yes ❒ No Cardiac pacemaker
❒ Yes ❒ No Implanted cardioverter defibrillator (ICD)
❒ Yes ❒ No Electronic implant or device
❒ Yes ❒ No Magnetically-activated implant or device
❒ Yes ❒ No Neurostimulation system
❒ Yes ❒ No Spinal cord stimulator
❒ Yes ❒ No Internal electrodes or wires
❒ Yes ❒ No Bone growth/bone fusion stimulator
❒ Yes ❒ No Cochlear, otologic, or other ear implant
❒ Yes ❒ No Insulin or other infusion pump
❒ Yes ❒ No Implanted drug infusion device
❒ Yes ❒ No Any type of prosthesis (eye, penile, etc.)
❒ Yes ❒ No Heart valve prosthesis
❒ Yes ❒ No Eyelid spring or wire
❒ Yes ❒ No Artificial or prosthetic limb
❒ Yes ❒ No Metallic stent, filter, or coil
❒ Yes ❒ No Shunt (spinal or intraventricular)
❒ Yes ❒ No Vascular access port and/or catheter
❒ Yes ❒ No Radiation seeds or implants
❒ Yes ❒ No Swan-Ganz or thermodilution catheter
❒ Yes ❒ No Medication patch (Nicotine, Nitroglycerine)
❒ Yes ❒ No Any metallic fragment or foreign body
❒ Yes ❒ No Wire mesh implant
❒ Yes ❒ No Tissue expander (e.g., breast)
❒ Yes ❒ No Surgical staples, clips, or metallic sutures
❒ Yes ❒ No Joint replacement (hip, knee, etc.)
❒ Yes ❒ No Bone/joint pin, screw, nail, wire, plate, etc.
❒ Yes ❒ No IUD, diaphragm, or pessary
❒ Yes ❒ No Dentures or partial plates
❒ Yes ❒ No Tattoo or permanent makeup
❒ Yes ❒ No Body piercing jewelry
❒ Yes ❒ No Hearing aid
(Remove before entering MR system room)
❒ Yes ❒ No Other implant _____
❒ Yes ❒ No Breathing problem or motion disorder
❒ Yes ❒ No Claustrophobia

Please mark on the figure(s) below the location of any implant or metal inside of or on your body.



IMPORTANT INSTRUCTIONS

Before entering the MR environment or MR system room, you must remove <u>all</u> metallic objects including hearing aids, dentures, partial plates, keys, beeper, cell phone, eyeglasses, hair pins, barrettes, jewelry, body piercing jewelry, watch, safety pins, paperclips, money clip, credit cards, bank cards, magnetic strip cards, coins, pens, pocket knife, nail clipper, tools, clothing with metal fasteners, & clothing with metallic threads.

Please consult the MRI Technologist or Radiologist if you have any question or concern BEFORE you enter the MR system room.

NOTE: You may be advised or required to wear earplugs or other hearing protection during the MR procedure to prevent possible problems or hazards related to acoustic noise.

I attest that the above information is correct to the best of my knowledge. I read and understand the contents of this form and had the opportunity to ask questions regarding the information on this form and regarding the MR procedure that I am about to undergo.

Signature of Person Completing Form: _____ Date _____/_____/_____
Signature

Form Completed By: ❒ Patient ❒ Relative ❒ Nurse _____ _____
Print name Relationship to patient

Form Information Reviewed By: _____ _____
Print name Signature

❒ MRI Technologist ❒ Nurse ❒ Radiologist ❒ Other_____

APPENDIX C

POST TDCS SYMPTOMS QUESTIONNAIRE

TRANSCRANIAL DIRECT CURRENT STIMULATION

Post-Study Questionnaire

Subject ID _____Testing Date_____

Study_____Lead Investigator_____

Please mark the exact middle of these lines

_____

_____

_____

_____

To what extent did you experience these symptoms *DURING* tDCS:

Tingling:

_____

0 10

not at all greatest imaginable

Where:

Itching Sensation:

_____

0 10

not at all greatest imaginable

Where:

Burning Sensation:

_____

0 10

not at all greatest imaginable

Where:

Pain:

_____

0 10

not at all greatest imaginable

Where:

Fatigue:

_____

0 10

not at all greatest imaginable

1

Nervousness:

0 — 10
not at all — greatest imaginable

Headache:

0 — 10
not at all — greatest imaginable

Difficulty Concentrating:

0 — 10
not at all — greatest imaginable

Mood change:

0 — 10
not at all — greatest imaginable

Change in your vision/visual perception:

0 — 10
not at all — greatest imaginable

Visual sensation (seeing lights for example) associated with the start or end of stimulation:

0 — 10
not at all — greatest imaginable

Other effects – Please describe:

1.

0 — 10
not at all — greatest imaginable

2.

0 — 10
not at all — greatest imaginable

To what extent did you experience these symptoms *AFTER* tDCS:

Tingling:

0 — 10
not at all — greatest imaginable

Itching Sensation:

0 — 10
not at all — greatest imaginable

Burning Sensation:

0 — 10
not at all — greatest imaginable

Pain:

0 — 10
not at all — greatest imaginable

Fatigue:

0 — 10
not at all — greatest imaginable

Nervousness:

0 — 10
not at all — greatest imaginable

Headache:

0 — 10
not at all — greatest imaginable

Difficulty Concentrating:

0 — 10
not at all — greatest imaginable

Mood change:

0 — 10
not at all — greatest imaginable

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