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Modulation of Corticospinal Excitability Using Cathodal Transcranial Direct Current Stimulation to Improve Walking in Individuals with Chronic Post Stroke Hemiparesis

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MODULATION OF CORTICOSPINAL EXCITABILITY USING CATHODAL TRANSCRANIAL DIRECT CURRENT STIMULATION TO IMPROVE WALKING IN INDIVIDUALS WITH CHRONIC POST STROKE HEMIPARESIS

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ABSTRACT

Background and Purpose: Individuals who have experienced a pyramidal cerebrovascular accident (pCVA) often exhibit impairments to volitional control of corresponding motor tasks. Promising effects in motor response, post-application of transcranial direct current stimulation (tDCS), have been reported in studies on individuals with the ability to achieve independent gait for 20 minutes. These studies mainly examined the effects of combined tDCS with locomotor training on lower extremity function among higher functioning individuals post-stroke. The purpose of this study was to determine the effect of tDCS among individuals post-stroke who may not have independent ambulatory capabilities, focusing on motor response and less demanding outcomes. The results of this study will extend knowledge on tDCS effects among lower functioning individuals post-CVA.

Methods: Four individuals with chronic stroke (2.38 ± 0.63 years) randomly received either cathodal stimulation or a sham treatment to their non-lesioned hemisphere. Transcranial magnetic stimulation (TMS) was used in order identify the tibialis anterior hotspot in the motor cortex of their lesioned hemisphere such that we were able to assess and reassess the effects of tDCS at the same hotspot location. Fourteen days later, subjects attended a second session where they received the intervention that they did not receive in the first session (either sham or cathodal tDCS). Lower extremity (LE) function was evaluated by comparing pre and post intervention Timed Up and Go (TUG) scores, as well as Step Length, Stride Length, Stride Width, Stance Time, Swing Time, Gait Velocity, Ambulation Time, and Cadence. Motor response was evaluated by comparing pre and post intervention Motor Evoked Potential (MEP) values.

Results: There was a statistically significant change in the MEP value measured before and after cathodal tDCS compared to sham ($p = 0.037 < 0.05$). There was no statistically significant difference when comparing tDCS to sham interventions for: resting motor threshold maximum stimulator output (rMT MSO%), TUG, Step Length, Stride Length, Stride Width, Stance Time, Swing Time, Gait Velocity, Ambulation Time, and Cadence.

Discussion: For those who are living post-stroke, the application of cathodal tDCS may provide a relative increase in cortical excitability of the ipsilesional hemisphere. Future tDCS research should incorporate functional interventions to see if they can promote lasting effects.

ACKNOWLEDGEMENTS

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INTRODUCTION

Stroke is a brain lesion that often affects neuromuscular control, impairing the ability of the brain to generate and transmit motor signals from the motor cortex, through the corticospinal circuitry, to the intended muscles[16]. In a non-impaired nervous system, this particular descending group of nerves from the motor cortex carries the signals for voluntary movement of the peripheral muscles[12]. For those with a stroke lesion, the signals are disrupted, and voluntary motor control is impaired. One barrier to recovery stems from the imbalance of cortical excitability between the two brain hemispheres, with the lesioned hemisphere having decreased excitability compared to the non-lesioned hemisphere. This imbalance of cortical excitability is associated with functional impairments[14].

A key concept in the rehabilitation of brain injuries is neuroplasticity, which can be described as the brain's ability to adapt and create new neuronal connections in response to injury[14]. Progressively challenging a patient's fine and gross motor control of muscles on their affected side leverages these neuroplasticity principles. This type of training helps stimulate the brain to reorganize and improve neuronal connections, and thereby improve transmission of motor signals[6]. While these conventional treatments can provide improvements in motor control for patients post-stroke, there has been recent research examining the benefits of supplementing treatments with neuromodulation[5, 9,11].

Neuromodulation consists of either invasive or noninvasive stimulation of the nervous system through electrical or chemical approaches[23]. Modulating cortical excitability using non-invasive neuromodulation techniques has been associated with improved motor performance, such as walking, in neurologically impaired individuals[5]. Modulation of cortical excitability can be performed using either cathodal or anodal transcranial direct current stimulation (tDCS).

tDCS is a form non-invasive electrical stimulation in which low-intensity electrical stimulation is applied to a targeted area of the brain in order to elicit neuronal responses in the distal motor units of the corticospinal tract. Single pulse transcranial magnetic stimulation (TMS) is another form of noninvasive brain stimulation that can be used in conjunction with tDCS as a tool to excite the corticospinal tract and elicit a motor evoked potential (MEP) of a targeted muscle[24]. Using a device such as TMS compared to participant volitional contraction of the tibialis anterior muscle allows the researchers to apply a stimulus that is of proportionately equal intensity amongst all participants.

When applied to the contralesional hemisphere (the hemisphere that does not contain a lesion), cathodal tDCS has been shown to have an inhibitory effect on motor excitability and is best used on the contralesional hemisphere in order to decrease interhemispheric inhibition, resulting in a relative increase in excitability in the affected hemisphere[4, 9,11]. In contrast, anodal tDCS applied to the ipsilesional hemisphere (the hemisphere that contains the lesion) has been shown to have an excitatory effect on motor excitability[5]. Emerging research using anodal stimulation is suggestive that it is best utilized over the ipsilesional hemisphere in order to increase that hemisphere's ability to transmit motor signals from the cortex to the intended peripheral muscle by increasing cortical excitability[7, 9]. This modulation of excitability allows for a restoration of balance between the two hemispheres and has led to functional improvement[20, 26].

When applied individually, anodal and cathodal tDCS have been shown to change corticomotor excitability in resting subjects. The study by Fregni et al demonstrated an improvement in hand motor function after the application of cathodal tDCS (applied to the unaffected motor cortex) and anodal tDCS (applied to the affected motor cortex)[9]. This effect has been observed in studies examining both upper and lower extremities[18]. When paired with a

functional task such as walking on a treadmill, anodal and cathodal tDCS facilitates transient increases in lower extremity extensor force and fine motor control within a single session[6]. Functional outcomes and corticomotor excitability are greater when tDCS and functional training are used together compared to anodal or cathodal tDCS alone[11].

Previous studies examining tDCS combined with locomotor training have been limited to patients who could walk continuously for 20 minutes at a time, or without an assistive device, but these high functioning individuals are not representative of the entire stroke community[5]. Many individuals with chronic stroke are limited in activities such as ambulation due to muscle impairments, requiring greater energy expenditure in performance. Therefore, many of these patients don't have the endurance to ambulate for 20 minutes at a time. The purpose of our study was to test the effect of cathodal tDCS on lower functioning individuals, with a protocol requiring minimal walking, to determine the potential benefit to this population.

Aim 1: To determine the effects of cathodal tDCS over contralesional motor cortex on the corticospinal excitability of paretic tibialis anterior (TA).

Hypothesis 1: Cathodal tDCS over the contralesional motor cortex will result in increased excitability of ipsilesional cortex as measured by MEP of the paretic tibialis anterior muscle.

Aim 2: To examine the functional outcomes associated with inhibition of contralesional motor cortex using the Timed-Up and Go (TUG) test, and gait variables (stride length, stride width, stance time, swing time, velocity, ambulation time, and cadence).

Hypothesis 2: Cathodal tDCS over the contralesional motor cortex will improve functional outcomes in people post stroke, specifically TUG and gait variables during ambulation.

METHODS

Subjects

A sample of 14 individuals was calculated in order to have 95% power at an α value of 0.05 for a two-sided paired t-test. Inclusion criteria included diagnosis of a cortical and/or subcortical lesion and ability to perform a TUG test with or without us of an assistive device. Exclusion criteria included contraindications to TMS or tDCS (metallic implants, history of seizure, and use of medications known to alter central nervous system excitability), those confined to a wheelchair, and anyone under the age of 18 years[29]. The protocol was approved by UNLV's Institutional Review Board.

Instrumentation

A Magstim 200 stimulation (Magstim,UK) via a double cone coil was used to apply TMS. A stereotactic image guidance system (Brainsight, Rogue Research Ic) was used to guide the site of TMS application. tDCS was delivered through a constant current stimulator via an 8 cm^2 oblong saline-soaked sponge cathode placed over the non-lesioned primary motor cortex (M1) for the leg. A carbonized reference anode was placed on the forehead above the contralateral orbit. Surface electromyography (EMG) (Bagnoli, Delsys Inc., Natick, MA) was used to measure the muscle activity from the tibialis anterior and soleus muscles of the affected limb. The SIGNAL (Cambridge Electronic Design Limited, UK) computer program was used to collect numerical data after each TMS pulse was applied. The Zeno Mat (ProtoKinetics LLC, PA), a walkway gait analysis mat, in combination with its ProtoKinetics Movement Analysis Software (PKMAS), was used to assess gait function by measuring stride length, stride width, stance time, swing time, velocity, ambulation time, and cadence. The Fugl-Meyer Assessment

was performed once with each participant, which is an assessment tool used specifically for individuals post stroke to determine motor and sensory function, balance, joint range of motion, and joint pain[10]. The maximum score for the motor function portion of the LE Fugl-Meyer is 34, indicating no impairment in motor function. The Timed Up and Go test (TUG) was also administered in order to determine lower extremity functional mobility by having participants ambulate a self paced 3 meters before and after each treatment session[21]. Many individuals who have suffered from a stroke suffer from gait deficits that greatly reduce their ambulation speed, increasing their risk for falls and diminishing their safety. The TUG is a useful outcome measure to examine a participant's functional mobility in a community setting and will be useful in assessing if application of cathodal tDCS will improve participant ambulation and transfer speed[27].

Procedure

Participants came to the research lab where informed consent was obtained. Subjects then signed a screening form, which detailed the inclusion and exclusion criteria to the study. Data collection occurred on two separate days with at least 14 days between the two sessions. Sessions were scheduled for approximately the same time of day and we requested that participants followed similar routines on both days. On the first day of data collection, the participants performed two different tests: the lower extremity Fugl-Meyer, and the TUG performed on the Zenomat, where gait parameters will also be collected for time conservation. Although the TUG and the Zenomat assess different variables, the TUG will be performed on the Zenomat in order to maximize the number of variables that will be measured in a period of time, therefore decreasing the amount of time the participant spends with the research team, keeping in mind participant consideration and comfort.

Next, with the participant standing, the skin above the bellies of the tibialis anterior and soleus affected by the stroke was shaved, cleaned, and exfoliated with rubbing alcohol swabs. Shaved areas were limited to twice the size of the electrode. The EMG sensors were then placed on the prepared skin [Figures 1 & 3], and the ground electrode was placed over the lateral malleolus. If the participant was able to volitionally contract the tibialis anterior muscle, they were asked to perform an isometric contraction of the tibialis anterior, lifting the toes into one of the researcher's hand, and the researcher would palpate the muscle belly for electrode placement. For the soleus, the participant would perform a concentric contraction by standing on their toes, and the researcher would feel for the lateral gastrocnemius muscle head. Keeping the researcher's fingers just distal to the head, the participant would then bend their knee and point their toes into the floor, and the researcher would find the bulk of the belly just distal and lateral head of the gastrocnemius. The same researcher performed electrode placement each session.

If there was difficulty finding the subject's muscle bellies, the tibialis anterior was instead found by creating an imaginary line between the ipsilateral tibial tuberosity and the intermalleolar line (referred to as the anatomical landmark frame, or ALF), and then placing the electrode at 20% of the ALF, just distal to the tibial tuberosity. For the soleus, the ALF was created between the medial side of the Achilles tendon insertion and the head of the fibula. The electrode was placed just proximal of the insertion of the Achilles at about 30%. Pictures of the sensor locations were taken to ensure consistent placement across sessions.

The participant was then seated in a chair with the affected leg supported and strapped into a footplate to keep his or her foot in a neutral dorsiflexed position. One of the researchers placed a band around the participant's head that contained a marker that is detected by a camera system that detects 3D space. The Brainsight Neuronavigation System (Rogue Research Inc) was

used to determine the brain "hotspot" which is the region of the motor cortex that consistently elicits the largest MEP of the targeted tibialis anterior muscle when TMS is applied[23]. The Brainsight Neuronavigation System provides a human brain template, created from the average of 25 different brain MRI scans. In combination with the template, 3D markers [Figure 6] were placed near the participant's skull. A camera [Figure 4] was used to detect the markers in space in order to create a 3D model brain similar in size and shape to the subject's brain**.**

Figure 1.TA Figure 2. Side view Figure 3. Soleus

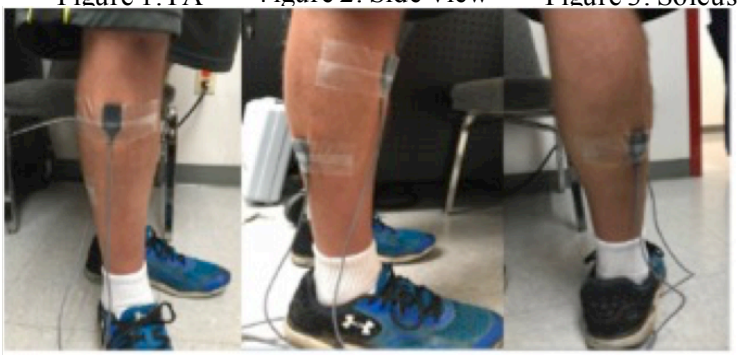
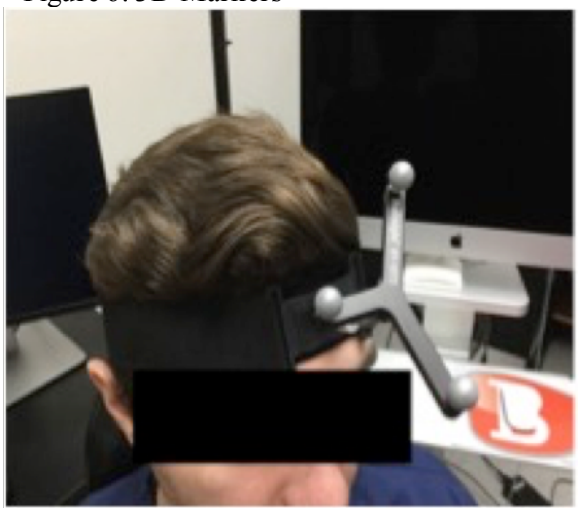


Figure 4. Camera Figure 5. Pointer

Figure 6. 3D Markers



A pointer [Figure 5] was used in combination with the camera to identify five key areas on the subject's skin: one over the nasion, one on the lateral portion of each orbit, and one antero-superior to the tragus of each ear. Then, a series of 30+ measurements were taken to establish accurate dimensions of the subject's skull circumference. These measurements record the most lateral, most superior, most anterior, and most posterior portions of the cranium to obtain an accurate representation of the subject's skull in 3D space that was reconstructed and used as our model on the Brainsight software.

After the model of the participant's brain was generated, the suprathreshold Machine Simulated Output (MSO) value of the affected tibialis anterior muscle was found. The suprathreshold is considered to be the minimum stimulus required to obtain a MEP with > 50 mV peak to peak amplitude over several attempts. The MSO is the output value indicated on the TMS device. This number can be adjusted up and down to identify the intensity required to confirm the suprathreshold. In order to find the suprathreshold MSO, the location of M1 was estimated by identifying a virtual line of connection from the superior aspect of the skull to the tragus of the ear on the side of the affected hemisphere. This area was confirmed by comparing

the Brainsight grid of the M1 to the target representing the TMS double coil. A series of TMS pulses at varying MSO values were given until the EMG reading on the SIGNAL software (Cambridge Electronic Design Limited, England) demonstrated consistent motor evoked potentials (MEPs) of the affected tibialis anterior and soleus greater than 0.05 mV within the M1.

Once the suprathreshold MSO was determined, an 8x4 grid constructed by Brainsight was placed over the affected motor cortex of the model on the software, indicating to the researchers the location of each spot for TMS stimulation on the actual brain. The grid was constructed of 32 different locations, and using the TMS coil, each spot was stimulated while the corresponding MEP amplitudes were recorded using SIGNAL. The coil contained a 3D marker that allowed the Brainsight camera to determine its location in comparison to the participant's brain, and this allowed for accurate stimulation of each spot in the grid. The hotspot was determined by the location that elicited the highest MEP amplitude at the given supramaximal stimulus level.

The hotspot was then used to determine the resting motor threshold (rMT) using the Parameter Estimation by Sequential Testing (PEST) procedure provided within the software TMS Motor Threshold Assessment Tool (TMS MTAT 2.0) [3]. This also involves using SIGNAL software to observe for an EMG reading greater than 0.05 mV. PEST generated the MSO of the rMT through the use of an algorithm, which refined the minimum TMS output percentage that was strong enough to elicit a reading greater than 0.05 mV.

Once the above steps were completed, a series of TMS pulses at varying MSOs were applied to the hotspot until the EMG reading on the SIGNAL software demonstrated consistent MEPs of the affected tibialis anterior that averaged 0.1 mV after ten pulses. In order to apply the

minimum number of pulses and maintain subject comfort, the MSO of the suprathreshold previously obtained was increased by increments of 2%, until the desired level was achieved.

Participants received either cathodal tDCS or sham treatment for 20 minutes and in the second session received the other, such that at the end of their second session they had experienced both sham and tDCS. The treatment that they received during the first session was determined randomly, and they received the other treatment during their second session. Only one of the researchers knew which treatment the patient received and that researcher was not involved in data collection. The remaining personnel involved were blinded to the intervention group.

tDCS strength was set at 0.06 mA/cm2. The electrical field was oriented with the stimulation electrode at the M1 leg area of the affected cortex and the reference electrode placed on the contralateral orbit[20]. The participant had his or her foot strapped with Velcro to a force plate set at 0˚ neutral dorsiflexion. With visual feedback, the participant activated the TA muscle at 20% maximal TA EMG activity at a consistent rate isometrically (2 second contraction, 2 second relax), set by a metronome at 30 Hz throughout the 20 minutes of tDCS application. After 20 minutes, the tDCS or sham treatment was removed and we assessed the post-test MEP values at 120% rMT.

The participant performed the TUG on the Zenomat as they did at the beginning of the session, starting with using PEST to determine the MSO of the rMT. However, for the second outcome measure regarding the MSO MEP, we utilized the same MSO that produced and average of 0.1 mV previously and stimulated the person's brain only ten times to find the new average of the ten readings. Then, the participant was disconnected from the EMGs and was required to perform a second TUG test on the Zenomat.

Data Analysis

IBM SPSS for Windows Version 24.0 was used to perform all statistical analyses. Descriptive statistics included mean and standard deviation of each variable were calculated based on time (pre/post intervention) and intervention type (cathodal tDCS/sham). A 2 x 2 repeated measures ANOVA was used to determine association between the intervention type, time, and the interaction between intervention type and time. Appropriate post-hoc analysis was then used to determine differences in pairwise comparisons. Statistical significance was defined as $P < 0.05$.

RESULTS

Four participants with chronic post-stroke hemiparesis completed the study. Participant characteristics are presented in Table 1.

For the MEP, there was no statistically significant interaction found for time and condition ($F(1,3)=0.810$, $p=0.43$). There was no statistically significant difference found for condition ($F(1, 3)=1.48$, $p=0.31$). There was a statistically significant difference found for time ($F(1, 3)=12.79$, $p=0.04$). Simple main effect analysis using paired samples T-Test showed that following cathodal stimulation, MEP amplitudes were higher (0.34mV±0.20) compared to before stimulation (0.24±0.12) ($p=0.02$). In contrast, following sham stimulation, MEP amplitude did not change (0.24±0.43) compared to before stimulation (0.25±0.16) ($p=0.74$).

For the rMT, TUG, Step Length, Stride Length, Stride Width, Stance Time, Swing Time, Gait Velocity, Ambulation Time, and Cadence, the 2 way ANOVA revealed no significant interaction between condition and time and there were no statistically significant differences found for condition or for time.

Table 1: Subject Demographics	
Age (yr)	63.50±6.75
Lesion Side (L|R)	4|0
Time Post Stroke (yr)	2.38±0.63
LE F-M Score	31.75±2.38

Table 2: Change in TMS and Gait Variables and Effect Significance of that Change based on Intervention Groups

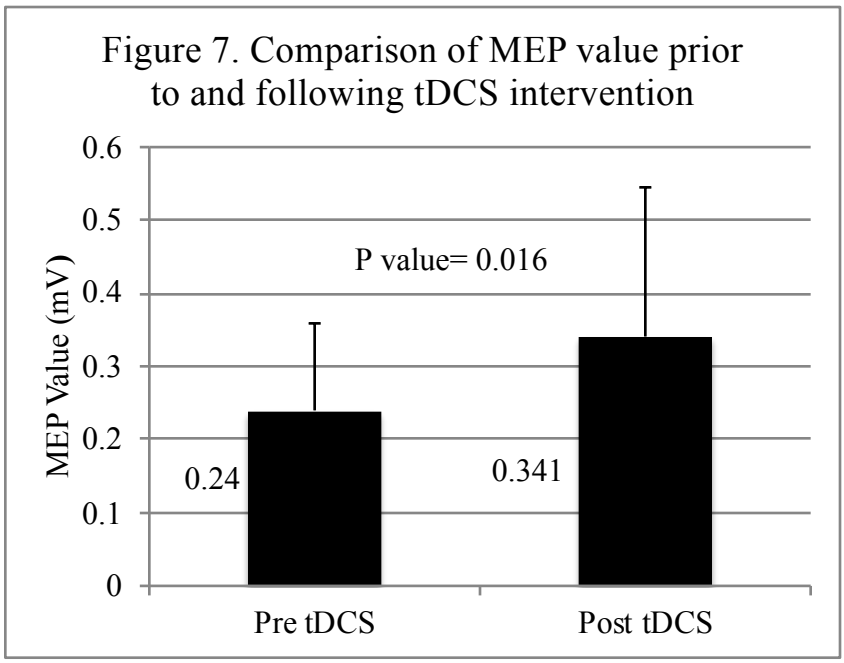
Variable Type	Variable	Intervention	Pre Intervention	Post Intervention	Difference	Effect	Effect Significance
TMS	rMT MSO%	tDCS	50.25±9.60	51.75±9.18	1.5	tDCS:	0.83
		Sham	51.00±10.10	49.75±9.71	-1.25	Time:	0.95
						Time x tDCS:	0.151
	MEP (mV)	tDCS	0.240±0.119	0.341±0.204	0.101	tDCS:	0.311
		Sham	0.254±0.163	0.241±0.430	-0.013	Time:	**0.037**
						Time x tDCS:	0.434
Gait Analysis	TUG (sec)	tDCS	10.93±1.77	10.85±1.65	-0.08	tDCS:	0.412
		Sham	12.26±3.42	11.33±2.05	-0.93	Time:	0.324
						Time x tDCS:	0.289
	Step Length (cm)	tDCS	50.65±4.82	52.74±3.97	2.09	tDCS:	0.328
		Sham	49.07±7.21	49.08±5.30	0.01	Time:	0.406
						Time x tDCS:	0.38
	Stride Length (cm)	tDCS	102.68±10.30	102.56±8.91	-0.12	tDCS:	0.437

	Sham	96.81±15.51	99.08±12.01	2.27	Time:	0.346
					Time x tDCS:	0.532
Stride Width (cm)	tDCS	12.13±4.60	12.97±3.07	0.84	tDCS:	0.879
	Sham	12.63±4.99	12.85±3.34	0.22	Time:	0.583
					Time x tDCS:	0.747
Stance Time (sec)	tDCS	0.864±0.097	0.854±0.066	0.01	tDCS:	0.648
	Sham	0.872±0.124	0.824±0.068	-0.048	Time:	0.374
					Time x tDCS:	0.528
Swing Time (sec)	tDCS	0.469±0.138	0.472±0.117	-0.042	tDCS:	0.734
	Sham	0.428±0.089	0.447±0.102	0.019	Time:	0.591
					Time x tDCS:	0.21
Gait Velocity (cm/sec)	tDCS	76.01±7.52	82.15±11.66	6.14	tDCS:	0.558
	Sham	75.18±19.59	77.04±13.03	1.86	Time:	0.261
					Time x tDCS:	0.634
Ambulation Time (sec)	tDCS	6.89±1.28	6.30±1.01	-0.59	tDCS:	0.278
	Sham	7.51±1.53	7.13±1.53	-0.38	Time:	0.1
					Time x tDCS:	0.755
Cadence (steps/min)	tDCS	90.35±13.16	97.13±11.45	6.78	tDCS:	0.979
	Sham	93.07±12.02	94.48±9.38	1.41	Time:	0.21
					Time x tDCS:	0.461

Table 3: MEP Change Pre and Post Intervention

	Pre-Intervention MEP (mV)	Post-Intervention MEP (mV)	P value
tDCS	0.240 ± 0.119	0.341 ± 0.204	0.016
Sham	0.254 ± 0.163	0.241 ± 0.430	0.735

*Using paired sample T test



DISCUSSION

We found that the MEP amplitude of the affected tibialis anterior muscle was significantly improved in those who received cathodal tDCS intervention, while there was no improvement for those who had the sham treatment. This indicates a relative increase in excitation of the corticospinal tract of the lesioned side due to inhibition of the contralesional hemisphere. The increased electrical conductivity to the affected tibialis anterior has positive

implications for future rehabilitation of an individual chronic post-stroke. Individuals with chronic stroke have passed the traditional "therapeutic window" in which neuroplasticity training is known to be most fruitful[14]. By inhibiting the contralesional hemisphere with cathodal tDCS there is an opportunity for the individual to perform rehabilitative interventions focused on increasing strength, endurance, and coordination in lower extremity musculature via changes in the corticospinal tract excitation[8]. This process allows the ipsilesional hemisphere to regain greater influence over the ipsilateral corticospinal tracts[4, 6]. This in turn can allow the ipsilesional hemisphere to become effectively stronger and more influential regarding the control of signals through the corticospinal tract due to increased communication from the affected motor region in the hemisphere to the tibialis anterior muscle and therefore increased rehabilitation potential[6, 11].

Although not statistically significant, there was a trend toward increased gait velocity in subjects that got tDCS treatment, although step length, stride length, stride width, and cadence did not seem to be affected. However, we cannot be sure if the application of cathodal tDCS is responsible for the trending increase in gait velocity, or if there was a learning effect from repeatedly performing the TUG. Despite, the TUG being a quick and simple test, reliable for quantifying change over time in older adult populations, a learning effect is still important to consider[21].

There are several possible explanations for why we did not find significant associations between our outcomes and tDCS application. One is that we were unable to recruit 14 participants, and in fact only recruited 4, leaving the study underpowered. It is likely that we were unable to detect actual effects given this small sample. Another reason may be due to testing cathodal versus anodal tDCS on the lower extremities. A majority of studies look at the

effect of cathodal tDCS on the upper extremities or focus more on the effects of anodal tDCS stimulation over the affected hemisphere. Jeffery et al. discussed how anodal stimulation has depolarizing effects, allowing for greater corticospinal tract conductivity, whereas cathodal tDCS has a hyperpolarizing affect. They noted that hyperpolarizing stimulation of the lower extremity compared to the upper extremity with equivalent currents had a minimal effect on the amplitude of measured MEPs recorded both at rest and during contraction of the tibialis anterior muscle[13]. This suggests that it is more difficult to suppress the excitability of the leg motor cortex compared to the hand motor cortex with cathodal tDCS due to fewer available inhibitory circuits compared to the hand motor cortex. Although we were not trying to suppress the excitability of the involved hemisphere, it is still possible that it makes suppressing the uninvolved hemisphere more difficult as well, making a large impact less possible and reducing the influence from the healthy cortex.

Although our goal was to recruit lower functioning patients, our participants were rather high functioning, even after having experienced a stroke. Several of our patients exercised regularly and were self-reported community ambulators. Our high functioning sample does not allow us to determine if step length, stride length, stride width, or cadence were improved by tDCS because they were not impaired to begin with. Chang et al tested anodal tDCS effects to see if application could not only increase cortical excitability but also lower limb motor function. They discovered that although there was some recovery of lower limb weakness with application of anodal tDCS, the amount of recovery was not enough to improve function in standing or gait[5]. However, they suggested that tDCS could be used as an adjuvant therapeutic modality to assist with improving lower limb motor function. We had similar results as Basanti et al, who performed a systematic review on the effects of anodal tDCS and motor function in healthy

individuals and those affected by stroke. Their review concluded that the evidence supports induced MEP with TMS and a tDCS intervention increases peak-to-peak MEP amplitude, indicating an increase in corticospinal tract excitation in both healthy and individuals affected by stroke. However, they did not see evidence for significant effects in motor function improvements for people with or without stroke[2]. Our study suggests that there may be a particular level of functional mobility deficits at which tDCS has its greatest impact on rehabilitation potential. Future studies should examine whether or not a specific level of functional mobility exists at which improvement with tDCS can be observed.

It is also important to note that another potential increase in MEP amplitude could have been due to performing isometric exercise during the session. EMG signals, and therefore MEP amplitudes, increase during sustained sub-maximal voluntary contraction, especially towards the end of a contraction[25]. Therefore, we can't determine if our participants increase in MEP was created solely by the application of tDCS, if their isometric dorsiflexion activity while receiving the tDCS, or a combination affected their MEP change.

Interestingly enough, many participants said they felt better the day after receiving treatment. Three of our subjects stated that they felt that they could walk better the next day and for a few days following their participation. We did not take measurements in the days following treatment so we cannot know the extent or reality of these reports. Additionally, there is high potential for placebo to account for the subjects' experience. It may be beneficial in future studies to collect data immediately after and then 24 hours after tDCS application. Another option for future studies would be to include patient reported outcomes. Chang et al. had measured the effects of anodal stimulation 24 hours post application and found that corticospinal excitation had indeed increased compared to sham. This resulted in statistically significant

increases in Fugl-Meyer scores as well as scores for the Lower Limb Motricity Index. They also discovered a trend for greater changes within the Functional Ambulatory Category with those who received anodal stimulation versus the sham[5]. Additionally, future work should consider the effects of tDCS on MEP with multiple applications as larger increases may be seen with more consistent application due to a cumulative effect[1].

Another implication for future research would be to examine the effects of cathodal tDCS on multiple lower extremity muscles. Our study only looked at the effects of cathodal tDCS on the tibialis anterior muscle, yet we looked at complete gait cycle outcomes. Other important muscles responsible for smooth gait, such as the quadriceps, gastrocnemius, and hamstrings, could be impacted by the use of tDCS[28]. Seeing that the MEP increased in the corticospinal tracts for tibialis anterior, it is likely that the corticospinal tracts of other lower extremity muscles were also positively affected. A study by Tanaka et al provides evidence that tDCS can be used to improve force produced by a paretic quadricep, therefore increasing the participant's ability to extend their knee[28]. Future research should consider therapeutic interventions to multiple muscles of the leg and other impairments, such as lack of hip extension or knee extension strength.

CONCLUSION

This study examined the effect of cathodal tDCS over the contralesional M1 area responsible for the tibialis anterior. Our subjects experienced a statistically significant increase in MEP when they received tDCS and no change when they received sham. However, there was no change in gait or TUG. Future studies should examine the effect of cathodal tDCS on individuals post-stroke with a variety of functional abilities, consider other muscles, and examine effects over 1-4 days.

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