Published in final edited form as:

Eur J Neurosci. 2014 April ; 39(8): 1343–1348. doi:10.1111/ejn.12492.

Transcranial direct current stimulation (tDCS) reduces the cost of performing a cognitive task on gait and postural control

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Abstract

This proof-of-concept, double-blind study is designed to determine the effects of transcranial direct current stimulation (tDCS) on the “cost” of performing a secondary cognitive task on gait and postural control in healthy young adults. Twenty adults aged 22±2yrs completed two separate double-blind visits in which gait and postural control were assessed immediately before and after a 20-minute session of either real or sham tDCS (1.5 mA) targeting the left dorsolateral prefrontal cortex. Gait speed and stride duration variability, along with standing postural sway speed and area, were recorded under normal conditions and while simultaneously performing a serial-subtraction cognitive task. Dual task cost was calculated as the percent change in each outcome from normal to dual task conditions. tDCS was well-tolerated by all subjects. Stimulation did not alter gait or postural control under normal conditions. As compared to sham stimulation, real tDCS led to increased gait speed ($p=0.006$), as well as decreased standing postural sway speed ($p=0.01$) and area ($p=0.01$), when performing serial-subtraction task. Real tDCS also diminished ($p<0.01$) the dual task cost on each of these outcomes. No effects of tDCS were observed for stride duration variability. A single session of tDCS targeting the left dorsolateral prefrontal cortex improved the ability to adapt one’s gait and postural control to a concurrent cognitive task and reduced the cost normally associated with such dual tasking. These results highlight the involvement of cortical brain networks in gait and posture control, and implicate the modulation of prefrontal cortical excitability as a potential therapeutic intervention.

Keywords

Standing; Walking; Balance; Noninvasive; Dual Task

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INTRODUCTION

The control of standing and walking is not autonomous as once believed, but instead depends upon a host of cognitive functions and underlying brain networks (Yogev-Seligmann *et al.*, 2008). Moreover, these essential human behaviors are most often performed in unison with concurrent cognitive tasks (Huxhold *et al.*, 2006). Considerable research indicates that as compared to normal conditions, cognitive “dual tasking” alters both gait (Dubost *et al.*, 2006) and postural control (Prado *et al.*, 2007). This “cost” of performing a cognitive task—which is often greater in aging (Lindenberger *et al.*, 2000; Rankin *et al.*, 2000) and disease (Teasdale *et al.*, 1993; Yardley *et al.*, 2001; Marsh & Geel, 2000; Hausdorff *et al.*, 2008) — suggests that these tasks interfere with one another as they call upon shared networks within the brain (Montero-Odasso *et al.*, 2012a). As such, strategies aimed at modulating neural activity within these networks may optimize the ability to dual task and maximize functional capacity within numerous populations.

Transcranial direct current stimulation (tDCS) is one noninvasive and safe strategy to modulate neural activity by sending low amplitude currents between two or more surface electrodes placed upon the scalp. Approximately 20 minutes of tDCS alters cortical excitability for up to 40 minutes (Ragert *et al.*, 2008). Although the mechanisms are not entirely clear, tDCS targeting the left dorsolateral prefrontal cortex (dlPFC) acutely improves a host of cognitive and motor functions during this period, including problem solving (Metuki *et al.*, 2012), decision making (Hecht *et al.*, 2010), working memory (Javadi & Walsh, 2011a; Javadi *et al.*, 2011b; Fregni *et al.*, 2005), selective attention (Gladwin *et al.*, 2012) and movement accuracy during reaching tasks (Reis & Fritsch, 2011), in healthy younger and/or older adults. Still, it is unknown if tDCS-induced modulation of neural activity within this region can enhance the ability to stand and walk while simultaneously performing a cognitive task.

The goal of this study was to determine the acute effects of facilitating neural activity within the left dlPFC on gait and postural control when walking and standing under normal and cognitive dual task conditions in healthy young adults. We hypothesized that as compared to sham (i.e., control) tDCS, a single 20min session of real tDCS would reduce the cost of performing a cognitive dual task on markers of gait and postural control. We tested this hypothesis by conducting a double-blind proof-of-concept study in a cohort of healthy young adults.

METHODS AND MATERIALS

Subjects

Twenty healthy young adults (10 men and 10 women, age=22±2 years, height =1.7±0.1 m, body mass=65±10 kg) were recruited and provided written informed consent conformed with The Code of Ethics of the World Medical Association (Declaration of Helsinki) as approved by the Institutional Review Board of Peking University First Hospital, Beijing. All subjects were right-handed as determined by the Edinburgh Handedness Inventory (Oldfield, 1971). Exclusion criteria included any acute medical condition requiring hospitalization

within the past six months, the use of centrally-acting medication, as well as any self-reported cardiovascular disease, neurological disease, musculoskeletal disorder, or any other condition that may influence physical function.

Experimental Protocol

All testing was performed at the Sport Science Research Center, Beijing Sport University. Subjects completed two separate study visits at the same time of day separated by one week (Fig 1). On each visit, gait and postural control were assessed immediately before and after either real or sham tDCS, as described in the following sections. The real and sham tDCS conditions were randomized and double-blinded; i.e., subjects and testers were not aware of the tDCS condition, and stimulation was administered by a research assistant uninvolved in any other assessment procedure. At the end of each study visit, subjects completed a short questionnaire (Brunoni *et al.*, 2011) surveying for potential adverse effects associated with tDCS.

tDCS Procedures

Noninvasive tDCS was delivered by study personnel uninvolved with any other study procedure. We used a battery-driven electrical stimulator (Chattanooga Ionto® Iontophoresis System) connected to a pair of saline-soaked 35 cm² synthetic surface sponge electrodes placed on the scalp. The anode was placed over the left dlPFC (i.e., the F3 region of the 10/20 EEG electrode placement system) and the cathode over the right supraorbital region (Boggio *et al.*, 2008). This montage is thought to induce a facilitation of activity within the left prefrontal cortex (under the anode) (Javadi *et al.*, 2011b; Fecteau *et al.*, 2007) and has been shown acutely enhance numerous cognitive functions. The real tDCS condition consisted of 20 minutes of continuous stimulation at target intensity of 1.5mA. This amount of stimulation is safe for healthy young adults (Herwig *et al.*, 2003) and has been shown to induce acute changes in cortical excitability (Nitsche & Paulus, 2000) and numerous cognitive functions (Gandiga *et al.*, 2006). At the beginning of each session, stimulation was increased manually from 0.1 to 1.5 mA in 0.1 mA increments. Subjects were instructed to notify study personnel if the stimulation became uncomfortable. In this instance, stimulation intensity was set to 0.1 mA below the highest intensity level reached. Current was automatically ramped down at the end of the session. For the sham condition, we followed an inactive stimulation protocol, as compared to an “off-target” active protocol, in order to minimize participant risk (Davis *et al.*, 2013). On this day, the same electrode montage and session duration were used; however, current was automatically ramped down 60 seconds after current was manually increased to target level by the technician. This is a reliable control as sensations arising from tDCS diminish considerably after the first minute of stimulation (Gandiga *et al.*, 2006).

Assessments of Gait and Postural Control

Within each of the four assessment periods (i.e., pre and post real and sham tDCS), the testing order of each domain (i.e., gait and postural control) was randomized. Within each domain, multiple trials were completed, also in random order, under different experimental conditions as described below.

Gait was assessed along a custom-built 50m indoor walkway instrumented with force sensors (resolution = 4 sensors/cm², sampling frequency = 100 Hz) to record foot pressure patterns. Two trials were completed under each of two different conditions: walking normally and walking while performing a cognitive task. The cognitive task consisted of verbalized, serial subtractions of three from a random 3-digit number between 400 and 500. Subjects were instructed to walk at their preferred speed before each trial. No instructions were given regarding task prioritization within dual task trials. In addition to stance phase plantar pressure distributions, the time taken to complete each trial and cognitive task responses were manually recorded and saved for offline analysis.

Postural control was assessed by measuring postural sway as subjects stood on a stationary force platform (Kistler Instrument Corp., Amherst, NY). Two 60sec trials were completed under three different experimental conditions: standing with eyes open, eyes closed, and eyes open with cognitive dual task; i.e., simultaneous performance of the same serial-subtraction task as described in the previous paragraph. Subjects were instructed to stand as still as possible prior to each trial. During each trial, postural control was measured by recording center-of-pressure (COP) fluctuations at a sampling frequency of 1000 Hz. Cognitive responses were also manually recorded during dual task trials.

Data Analysis

Primary study outcomes included measures related to gait and postural control, as well as the cost of performing a cognitive task on gait and postural control. Secondary outcomes included cognitive task performance within dual task trials. Within each assessment period (i.e., pre and post real and sham tDCS), outcome values were averaged across the two trials completed within each experimental condition (i.e., gait: normal and dual task; postural control: eyes open, eyes closed, dual task).

Gait outcomes included average gait speed and step duration variability. Gait speed (m/s) was calculated by dividing distance walked by the time taken to complete the trial. Stride duration variability (%) was determined by calculating the coefficient of variation about the average step duration (i.e., the time between consecutive heel-strikes) and multiplying by 100.

Postural control outcomes included average COP speed and area. COP time-series were first filtered using a 10 Hz low-pass filter to minimize potential effects of high frequency measurement noise. COP speed (cm/s) was computed by dividing total path length by trial duration. COP area (cm²) was determined by calculating the area of a confidence ellipse enclosing 95% of the center-of-pressure trajectory (Norris *et al.*, 2005).

The cost of performing the cognitive task on each gait and postural control outcome (i.e., dual task cost) was determined by calculating the percent change in each variable from normal to dual task conditions (Beauchet *et al.*, 2008; Ullmann G, *et al.*, 2011; Hausdorff *et al.*, 2008).

For each dual task trial, cognitive task performance was determined by calculating the error rate; in other words, the total number of mistakes divided by the total number of responses.

Statistical Analysis

Descriptive statistics were used to summarize group characteristics and all primary and secondary study outcomes. The effect of tDCS on each outcome was analyzed using 2×2 repeated-measures ANOVAs. Model effects included tDCS condition (real, sham), time (pre-, post-tDCS) and their interaction. Study outcomes obtained from each condition were analyzed with a separate model. Significance level was set to $p=0.05$ for all analyses. Tukey's post-hoc testing was completed on significant models in order to identify differences between variable means within each tDCS condition and time point combination.

RESULTS

Subject Characteristics

All 20 subjects completed all study procedures. Seven subjects received tDCS at the maximum intensity of 1.5 mA. The average intensity for the entire cohort was 1.1 ± 0.3 mA. Stimulation was well-tolerated by all subjects and was not associated with any self-reported adverse events.

The Effects of tDCS on Gait and Postural Control

The acute effects of tDCS on gait speed are presented in Fig 2 and 4. Neither real nor sham tDCS affected preferred gait speed under the normal walking condition. During the dual task condition, a trend ($F_{1,38}=3.5$, $p=0.08$) towards a significant interaction between tDCS condition (real, sham) and time (pre-tDCS, post-tDCS) was observed, such that gait speed appeared to be faster following real tDCS as compared to sham tDCS and both pre-tDCS assessments (Fig 2). A significant interaction ($F_{1,38}=9.2$, $p=0.006$) between tDCS condition and time was observed for the dual task cost on gait speed (Fig 4A). Post-hoc analyses revealed that within the real tDCS condition, performing the cognitive task reduced gait speed *less* in the post-tDCS state as compared to pre-tDCS, while sham tDCS had no effect on this outcome. tDCS did not have a significant effect on step duration variability in either walking condition, or the dual task cost on this variable.

The acute effects of tDCS on postural control are presented in Fig 3 and 4. Neither real nor sham tDCS affected COP speed or area when subjects stood quietly with eyes open or closed. Within the dual task condition, however, significant interactions were observed between tDCS condition and time for both COP speed ($F_{1,38}=7.3$, $p=0.01$) and area ($F_{1,38}=5.9$, $p=0.01$) (Fig 3). Post-hoc analyses revealed that within the real tDCS condition, COP speed was slower and COP area was smaller in the post-tDCS assessment as compared to pre-tDCS assessment. In contrast, neither outcome was affected by sham tDCS. Similar statistical interactions between tDCS condition and time were also observed for the dual task cost on both COP speed ($F_{1,38}=6.1$, $p=0.01$) and COP area ($F_{1,38}=6.8$, $p=0.008$) (Fig 4B and C). Whereas sham tDCS did not alter the dual task cost on either outcome as compared to pre-test, real tDCS significantly reduced the dual task cost on both outcomes.

The Acute Effects of tDCS on Cognitive Performance in Dual Task Trials

Serial-subtraction task performance during cognitive dual task trials was extremely high. When walking, the average number of given responses was 19.2 ± 4.8 and the average number of erroneous responses was 0.6 ± 0.3 , leading to an error rate of $3.5 \pm 2.0\%$. When standing, the number of given responses was 29.1 ± 6.8 (note that standing trials were longer than walking trials), the number of errors was 0.9 ± 0.4 , and the error rate was $3.0 \pm 2.4\%$. Response numbers, error numbers and error rates when standing or walking were unaffected by real or sham tDCS ($p=0.5-0.8$).

DISCUSSION

This proof-of-concept, double-blind, sham-controlled study in healthy young adults indicates that as compared to sham stimulation, a single session of real tDCS reduced the cost of dual tasking on multiple outcomes related to gait and postural control. While additional research is needed, these results provide strong preliminary evidence that modulation of dlPFC excitability may be one strategy to enhance the ability to stand and walk while simultaneously performing secondary cognitive tasks in healthy young adult populations.

The dlPFC is a primary brain region supporting executive function (Kane & Engle *et al.*, 2002), attention (Knight *et al.*, 1995) and the ability to perform more than one cognitive task at the same time (Szameitat *et al.*, 2002). Several recent structural and functional neuroimaging reports (Goble *et al.*, 2011; Harada *et al.*, 2009; Huppert *et al.*, 2012) indicate that the dlPFC is also involved in the control of standing and walking. Rosano (2008) reported that older adults with less gray matter within the bilateral dlPFC tend to walk with shorter steps and longer time spent with both feet on the ground. Holtzer *et al.* (2011) utilized functional near-infrared spectroscopy (fNIRS) to demonstrate that undisturbed walking induces bilateral prefrontal cortex activation in healthy younger and older adults. Interestingly, walking while performing a cognitive task (i.e., reciting alternating letters of the alphabet) further increased prefrontal cortex activation, yet this effect was mitigated within the older group. Our results extend this notion by demonstrating that even in healthy young adults, experimental manipulation of cortical excitability within the left dlPFC acutely improves outcomes related to gait and postural control under dual task conditions.

There are several potential neurological mechanisms that may have led to tDCS-induced improvement in the ability to adapt one's gait and posture to a cognitive stressor. To date, multiple theories have been developed to explain the costs associated with cognitive dual tasking (Yogev-Seligmann *et al.*, 2008). The capacity-sharing theory suggests that cognitive resources are limited in capacity and as a result, performing two tasks that require shared cognitive resources will diminish performance in at least one of the tasks (Tombu & Jolicoeur *et al.*, 2003). In the current study, performing the serial subtraction task disrupted gait and postural control, suggesting that these tasks require shared cognitive resources. As such, real tDCS may have reduced observed detrimental dual task costs by increasing the availability of cognitive resources and/or improving the allocation of available resources to one or both tasks (Leite *et al.*, 2011; Filmer *et al.*, 2013). On the other hand, the bottleneck theory of dual task control posits that if two tasks are processed by the same neural

networks, a “bottleneck” occurs such that processing of one task will be delayed until the network or processor is free from the other task (Ruthruff *et al.*, 2001). Within this framework, tDCS-related improvements may have stemmed from increased processing speed and shortened time delay between two tasks (Pashler, 1994; Redfern *et al.*, 2001). In the current study, all subjects performed the serial-subtraction task well and no tDCS-related changes in performance were observed (perhaps due to a ceiling effect). As more difficult cognitive tasks require more activation with the dlPFC (and other brain regions) (Szameitat *et al.*, 2002), future work should examine standing and walking during concurrent performance of several cognitive tasks that vary in difficulty. This method would enable further insight into the effects of tDCS on the interplay between cognitive and motor function during both single and dual task conditions. By choosing cognitive tasks that require rapid reaction to a presented stimulus (e.g., the n-back task), the effects of tDCS on both resource allocation and processing speed, together with their importance for gait and postural control, may also be explored.

We chose a tDCS montage to target the left dlPFC because considerable work indicates that a single session of tDCS administered with these parameters enhances cognitive task performance, and particularly within verbal tasks requiring attention and short-term memory (Metuki *et al.*, 2012; Hecht *et al.*, 2010; Javadi & Walsh 2011a; Javadi *et al.*, 2011b; Fregni *et al.*, 2005; Gladwin *et al.*, 2012; Filmer *et al.*, 2013). In the current study, it is unclear if the observed tDCS-related reduction in the cognitive task costs to gait and postural control arose from specific neuronal changes with the left dlPFC or from overall changes in brain excitability. The effects of active tDCS targeting one or more other brain regions are therefore worthy of investigation. For example, as facilitation of excitability within the right dlPFC has also been shown to improve cognitive performance, particularly in visual-based memory tasks (Rossi *et al.*, 2001; Gagnon *et al.*, 2010), the impact of stimulating particular brain regions may be dependent upon the type of cognitive dual task being performed. Furthermore, in the current study, we did not measure the extent to which tDCS modulated cortical activity within different brain regions. Future work utilizing single and paired-pulse transcranial magnetic stimulation techniques to link tDCS-induced changes in cortical neurophysiology with behavioral changes is thus needed to elucidate the mechanisms underlying tDCS-induced reduction of dual task costs. Finally, tDCS alters cortical excitability by sending electrical currents between relatively large electrodes placed upon the skin. The effects of tDCS on cortical excitability are therefore relatively diffuse and variable between subjects (Datta *et al.*, 2012). It is thus possible that tDCS-related behavioral changes stemmed from altered cortical excitability within other networks within the brain. To that end, application of neuro-navigation techniques (Datta *et al.*, 2012) may optimize individual effects of tDCS on cortical function and thus, its beneficial effect on standing and walking.

In conclusion, this study provides novel evidence in healthy young adults that modulation of cortical excitability improves the ability to stand and walk while performing a secondary cognitive task. Additional work is warranted to determine the extent to which observed laboratory-based performance improvements transfer to other environments (i.e., competitive sports). Moreover, as mounting evidence suggests that daily tDCS treatments

may result in persistent changes in both cognitive function (Dockery *et al.*, 2009) and sensorimotor performance (Zimerman *et al.*, 2012), repeated tDCS exposure may ultimately lead to long-term functional improvements. Finally, as biological aging and numerous age-related diseases appear to increase the role of cognition and underlying brain networks in the control of standing and walking (Manor & Lipsitz 2013; Manor *et al.*, 2010; Montero-Odasso *et al.*, 2012b), tDCS holds great potential as a therapeutic balance intervention and fall-prevention strategy for these more vulnerable populations.

Acknowledgments

We would like to thank Dr. Dapeng Bao and Dr. Yang Hu from the Sport Science Research Center at the Beijing Sport University for providing the experimental balance equipment utilized in this study.

Dr. Pascual-Leone serves on the scientific advisory boards for Nexstim, Neuronix, Starlab Neuroscience, Neuroelectronics, and Neosync; and is listed as an inventor on several issued and pending patents on the real-time integration of transcranial magnetic stimulation (TMS) with electroencephalography (EEG) and magnetic resonance imaging (MRI).

This study was supported by grants from the National Natural Science Foundation of China (grant number 11372013), the Sidney-Baer Foundation, and a KL2 Medical Research Investigator Training (MeRIT) award (1KL2RR025757-04) from Harvard Catalyst | The Harvard Clinical and Translational Science Center (UL1RR025758).

Study funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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<u>Pre-tDCS Assessments</u>		tDCS setup	<u>Real/Sham tDCS</u> (Visits separated by 1 week)	<u>Post-tDCS Assessments</u>	
Gait	Postural Control			Gait	Postural Control
5 min	10 min	10 min	20 min	5 min	10 min

Figure 1. Study Protocol

Subjects completed two study visits separated by one week. Each visit was completed at the same time of day. During each visit, gait and postural control were assessed immediately before and after either real or sham tDCS targeting the left dorsolateral prefrontal cortex. The order of tDCS condition was randomized, as was the testing order of gait and postural control within each assessment period.

Figure 2. The effects of noninvasive transcranial direct current stimulation (tDCS) on gait speed in healthy young adults

Gait speed was assessed immediately before and after both real and sham tDCS targeting the left dorsolateral prefrontal cortex. tDCS did not significantly alter gait speed in the normal walking condition. In the dual task condition, subjects appeared to walk faster following real tDCS only, but this trend did not reach significance ($p=0.08$). Error bars represent one standard deviation from the mean.

Figure 3. The effects of noninvasive transcranial direct current stimulation (tDCS) on postural control in healthy young adults

Postural control was assessed immediately before and after both real and sham tDCS targeting the left dorsolateral prefrontal cortex. tDCS did not alter postural control when subjects stood with eyes open or closed. As compared to sham stimulation, however, real tDCS resulted in a significant reduction in center-of-pressure (COP) area and speed when standing while performing a cognitive task (i.e., Dual Task). * indicates a significant interaction ($p < 0.05$) between tDCS condition (real, sham) and time (pre-tDCS, post-tDCS). Error bars represent one standard deviation from the mean.

Figure 4. The effects of noninvasive transcranial direct current stimulation (tDCS) on the cost of performing a cognitive dual task on gait and postural control

As compared to sham tDCS, real tDCS reduced the dual task cost (i.e., the percent change from normal to dual task conditions) on gait speed (A) and standing postural sway speed (B) and area (C). * indicates a significant interaction ($p < 0.05$) between tDCS condition (real, sham) and time (pre-tDCS, post-tDCS). Error bars represent one standard deviation from the mean.