

Transcranial direct current stimulation 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 was 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 ± 2 years completed two separate double-blind visits in which gait and postural control were assessed immediately before and after a 20 min 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. The 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 with 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 the 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 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 postural control, and implicate the modulation of prefrontal cortical excitability as a potential therapeutic intervention.

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 with 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; Marsh & Geel, 2000; Yardley *et al.*, 2001; 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 optimise the ability to dual task and maximise 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 min of tDCS alters cortical excitability for up to 40 min (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 (Fregni *et al.*, 2005; Javadi & Walsh, 2011a; Javadi *et al.*, 2011b), selective attention (Gladwin *et al.*, 2012) and movement accuracy during reaching tasks (Reis & Fritsch, 2011), in healthy younger and/or older adults. However, 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.

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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 hypothesised that, as compared with sham (i.e. control) tDCS, a single 20 min 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.

Materials and methods

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 conforming 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 hospitalisation within the past 6 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 1 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 randomised 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.

Transcranial direct current stimulation 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 cm^2 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 electroencephalographic electrode placement system) and the cathode over the right supra-orbital region (Boggio *et al.*, 2008). This montage is thought to induce a facilitation of activity within the left prefrontal cortex

(under the anode) (Fecteau *et al.*, 2007; Javadi *et al.*, 2011) and has been shown to acutely enhance numerous cognitive functions. The real tDCS condition consisted of 20 min of continuous stimulation at a target intensity of 1.5 mA. 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 with an 'off-target' active protocol, in order to minimise participant risk (Davis *et al.*, 2013). On this day, the same electrode montage and session duration were used; however, the current was automatically ramped down at 60 s after the 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. before and after real and sham tDCS), the testing order of each domain (i.e. gait and postural control) was randomised. 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 50 m 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 verbalised, serial subtractions of three from a random three-digit number between 400 and 500. Subjects were instructed to walk at their preferred speed before each trial. No instructions were given regarding task prioritisation 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, USA). Two 60 s 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.

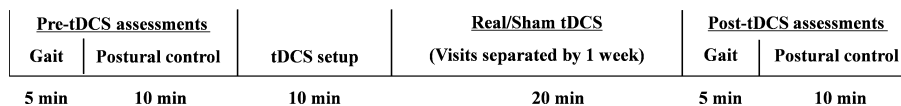


FIG. 1. Study protocol. Subjects completed two study visits separated by 1 week. Each visit was completed at the same time of day. During each visit, gait and postural control were assessed immediately before and after either real or sham tDCS targeting the left dlPFC. The order of tDCS condition was randomised, as was the testing order of gait and postural control within each assessment period.

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. before and after 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 the 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 minimise the potential effects of high-frequency measurement noise. The COP speed (cm/s) was computed by dividing the total path length by trial duration. The COP area (cm²) was determined by calculating the area of a confidence ellipse enclosing 95% of the COP 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; Hausdorff *et al.*, 2008; Ullmann & Williams, 2010).

For each dual task trial, cognitive task performance was determined by calculating the error rate, i.e. the total number of mistakes divided by the total number of responses.

Statistical analysis

Descriptive statistics were used to summarise the group characteristics and all primary and secondary study outcomes. The effect of tDCS on each outcome was analysed using 2×2 repeated-measures ANOVAs. Model effects included tDCS condition (real, sham), time (pre-tDCS, post-tDCS) and their interaction. Study outcomes obtained from each condition were analysed with a separate model. The 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 transcranial direct current stimulation on gait and postural control

The acute effects of tDCS on gait speed are presented in Figs 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 with 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 with pre-tDCS, whereas 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 Figs 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

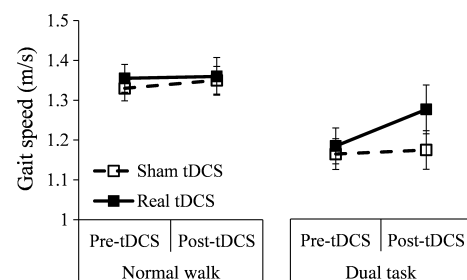


FIG. 2. The effects of noninvasive tDCS on gait speed in healthy young adults. Gait speed was assessed immediately before and after both real and sham tDCS targeting the left dIPFC. tDCS did not significantly alter gait speed in the normal walking condition. In the dual task condition, subjects appeared to walk faster following real tDCS only, but this trend did not reach significance ($P = 0.08$). Error bars represent 1 SD from the mean.

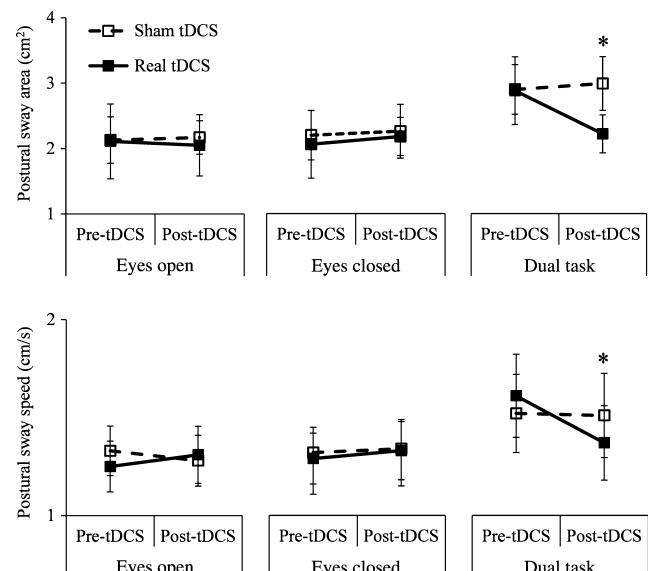


FIG. 3. The effects of noninvasive tDCS on postural control in healthy young adults. Postural control was assessed immediately before and after both real and sham tDCS targeting the left dIPFC. tDCS did not alter postural control when subjects stood with eyes open or closed. As compared with sham stimulation, however, real tDCS resulted in a significant reduction in COP area and speed when standing while performing a cognitive task (i.e. Dual Task). *Significant interaction ($P < 0.05$) between tDCS condition (real, sham) and time (pre-tDCS, post-tDCS). Error bars represent 1 SD from the mean.

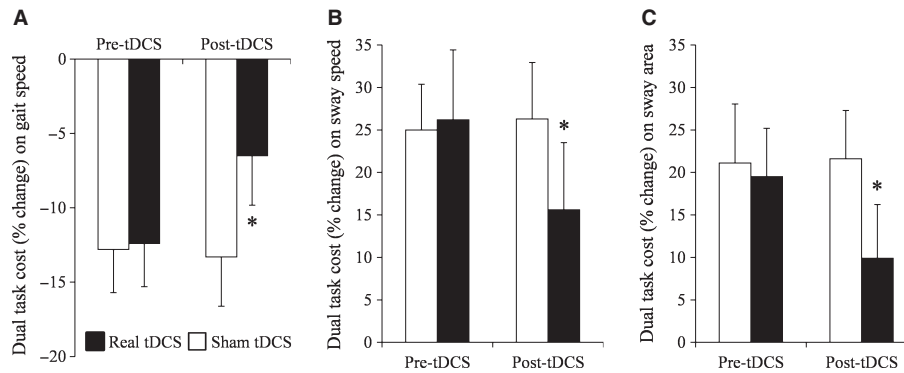


FIG. 4. The effects of noninvasive tDCS on the cost of performing a cognitive dual task on gait and postural control. As compared with sham tDCS, real tDCS reduced the dual task cost (i.e. the percent change from normal to dual task conditions) on gait speed (A) and standing postural sway speed (B) and area (C). *Significant interaction ($P < 0.05$) between tDCS condition (real, sham) and time (pre-tDCS, post-tDCS). Error bars represent 1 SD from the mean.

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 with the 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 with pre-test, real tDCS significantly reduced the dual task cost on both outcomes.

The acute effects of transcranial direct current stimulation on cognitive performance in dual task trials

The 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 $3.0 \pm 2.4\%$. The response numbers, error numbers and error rates when standing or walking were unaffected by real or sham tDCS ($P = 0.5\text{--}0.8$).

Discussion

This proof-of-concept, double-blind, sham-controlled study in healthy young adults indicates that, as compared with sham stimulation, a single session of real tDCS reduced the cost of dual tasking on multiple outcomes related to gait and postural control. Although additional research is needed, these results provide strong preliminary evidence that modulation of dIPFC 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 dIPFC is a primary brain region supporting executive function (Kane & Engle, 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 (Harada *et al.*, 2009; Goble *et al.*, 2011; Huppert *et al.*, 2012) indicate that the dIPFC is also involved in the control

of standing and walking. Rosano *et al.* (2008) reported that older adults with less gray matter within the bilateral dIPFC tend to walk with shorter steps and longer time spent with both feet on the ground. Holtzer *et al.* (2011) utilised functional near-infrared spectroscopy 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, but this effect was mitigated within the older group. Our results extend this notion by demonstrating that, even in healthy young adults, the experimental manipulation of cortical excitability within the left dIPFC acutely improves outcomes related to gait and postural control under dual task conditions.

There are several potential neurological mechanisms that may have led to the tDCS-induced improvement in the ability to adapt 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.*, 1999). 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 (Tomblu & Jolicoeur, 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). However, the bottleneck theory of dual task control posits that, if two tasks are processed by the same neural networks, a 'bottleneck' occurs such that the 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 dIPFC (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, particularly within verbal tasks requiring attention and short-term memory (Fregni *et al.*, 2005; Hecht *et al.*, 2010; Javadi & Walsh, 2011; Javadi *et al.*, 2011; Gladwin *et al.*, 2012; Metuki *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 the 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 utilising single and paired-pulse transcranial magnetic stimulation techniques to link the tDCS-induced changes in cortical neurophysiology with behavioral changes is thus needed to elucidate the mechanisms underlying the 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, the application of neuronavigation techniques (Datta *et al.*, 2012) may optimise the 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 the 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 *et al.*, 2010; Montero-Odasso *et al.*, 2012b; Manor & Lipsitz, 2013), tDCS holds great potential as a therapeutic balance intervention and fall-prevention strategy for these more vulnerable populations.

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Abbreviations

COP, center-of-pressure; dlPFC, dorsolateral prefrontal cortex; tDCS, transcranial direct current stimulation.

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