Spinal tDCS is superior to both M1 and cerebellar tDCS in supporting balance ability. A randomized, placebo-controlled trial

Jitka Veldema (jitka.veldema@uni-bielefeld.de)  
Bielefeld University

Teni Steingräber  
Bielefeld University

Leon Grönheim  
Paderborn University

Jana Wienecke  
Bielefeld University

Rieke Regel  
Bielefeld University

Thomas Schack  
Bielefeld University

Christoph Schütz  
Bielefeld University

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Abstract

Objectives

Existing applications of non-invasive brain stimulation in the modulation of balance ability are focused on the primary motor cortex (M1). It is conceivable that other brain and spinal cord areas may be comparable or more promising targets in this regard. This study compares transcranial direct current stimulation (tDCS) over (i) the M1, (ii) the cerebellum and (iii) the spinal cord in the modulation of balance ability.

Methods

Forty-two sports students were randomized in this placebo-controlled study. Twenty minutes of anodal 1.5 mA tDCS over (i) the M1, (ii) the cerebellum, and (iii) the spinal cord, as well as (iv) sham tDCS were applied to each subject. The Y Balance Test, Single Leg Landing Test, and Single Leg Squat Test were performed prior to and after each intervention.

Results

The Y Balance Test showed significant improvement after real stimulation of each region compared to sham stimulation. While spinal tDCS supported the balance ability of both legs, M1 and cerebellar tDCS supported right leg stand only. No significant differences were found on the Single Leg Landing Test and the Single Leg Squat Test.

Conclusions

Our data indicate that the spinal cord is a highly promising target for the application of non-invasive brain stimulation in supporting balance control. Future research could compare the effects of different spinal cord stimulation protocols on healthy people and examine the potential of this approach in neurorehabilitation.

1. Introduction

Non-invasive brain stimulation (NIBS) methods are powerful tools modulating neural processing and can be successfully used for research and therapies. Motor abilities and performance are very common objectives of transcranial direct current stimulation (tDCS) and repetitive magnetic stimulation (rTMS) studies. Existing research focuses primarily on hand motor functions/abilities, while other motor skills have been insufficiently investigated. Our study investigates the potential of tDCS in the modulation of balance and postural control.
1.1. TDCS in the modulation of neural networks and motor abilities

TDCS consists of the application of a low-intensity direct current that flows between two (or more) electrodes. A simplified theory distinguishes between anodal tDCS (with anode placed over the region of interest and cathode over another cranial or extracranial region) and cathodal tDCS (with reverse electrode positioning). Anodal tDCS should induce depolarization of neurons, increase corticospinal excitability, and improve behavioural abilities. In contrast, cathodal stimulation should lead to a hyperpolarization of neurons, decrease corticospinal excitability, and worsen behavioural performance [1, 2, 3]. However, the real data show a large variability outside of this theoretical scope. A range of studies have shown that both anodal and cathodal tDCS may support human motor performance [4, 5, 6]. Similarly, both anodal and cathodal tDCS may induce an increase as well as a decrease in corticospinal excitability [7].

A key factor that determines the tDCS-induced effects is electrode positioning. A current systematic review indicates that tDCS applied over different regions modulates different aspects of walking in healthy people. While application over the primary motor cortex (M1) and cerebellum improved speed, synchronization, and variability during simple walking, dorsolateral prefrontal cortex (DLPFC) stimulation improved gait parameters under dual-task conditions [4]. However, another systematic review points to the fact that diverse interactions exist between tDCS specifications (M1/cerebellum, unilateral/bilateral/central, single/multiple sessions) and motor task interactions (uni-/bi-manual, greater/less difficulty) [8]. This makes it difficult to draw clear conclusions. In addition, the reference electrode positioning may significantly impact the tDCS-induced effects. A simulation study (based on a numerical body model) compared six different cathode positions (right temporal lobe, right supraorbital region, right deltoid, left deltoid, under the chin, right buccinator muscle) during anodal tDCS over the left M1 [9]. The results indicate that extracephalic electrodes may be more effective in modulation of the spinal cord and similar or low effective in modulation of the brainstem, than cephalic electrodes [9]. Our study will extent the knowledge in this area. The modulatory effects of three different tDCS electrode placements will be directly compared in a placebo-controlled design.

1.2. TDCS in the modulation of balance and postural control

Balance and postural control are complex sensorimotor functions controlled by integrated brain and spinal networks [10, 11, 12]. Their neural background is still not fully understood. A recent systematic review with a meta-analysis emphasized the key role of the brainstem, cerebellum, basal ganglia, thalamus, and several cortical regions based on (functional) magnetic resonance imaging ((f)MRI) and positron emission tomography PET data [10]. Similarly, another systematic review indicated the key role of the cerebellum and brainstem, followed by the basal ganglia, thalamus, hippocampus, inferior parietal cortex, and frontal lobe regions, using MRI investigations [11]. Additionally, the spinal cord seems to play a crucial role in balance and postural control, as indicated by electrophysiological studies [12]. It has been
repeatedly demonstrated that balance training leads (in addition to an improved balance ability), to spinal adaptations in the form of a suppressed Hofmann reflex (H-reflex) [12].

Although the available data indicate that several cortical and subcortical brain regions, the cerebellum, and the spinal cord are crucially involved during motor control [10, 11, 12], the present applications of NIBS focus strongly on M1 [13, 14, 15]. The evidence for the remaining central and peripheral nervous system is insufficient, similar to studies that directly compare the effectiveness of NIBS over different areas [13, 14, 15]. Therefore, the question arises whether other regions may be comparable or even more promising for NIBS applications. Our study will investigate and compare the effectiveness of tDCS over M1, cerebellum and spinal cord.

2. Methods

2.1. Study design

This is a randomized, placebo-controlled crossover study. Three single sessions of real tDCS (over (i) M1, (ii) cerebellum and (iii) spinal cord) and one session of sham tDCS were applied to each participant in a randomized order (PC-generated) with a washout period of at least 48 h in between. Balance ability was evaluated immediately before and after each intervention. The study was conducted according to the standards established by the Declaration of Helsinki and approved by the Ethics Committee of Bielefeld University (2022-043). A previous study registration was not performed.

2.2. Participants

The inclusion criteria were as follow: (1) age between 18 and 25 years, (2) no contraindications for tDCS (checked by safety screening questionnaire [16]), and (3) no relevant neurological, psychiatric, or orthopedic disorders. All subjects provided their written informed consent prior to participation. A G*power analysis (effect size = 0.25, α error probability p < 0.05, Power = 0.95) revealed that a sample size of at least 40 participants is needed to detect statistically significant effects using ANOVA with four interventions and two timepoints.

2.3. Intervention

Each subject completed four separate 20 minute interventional sessions: (1) 1.5 mA tDCS over M1, (2) 1.5 mA tDCS over cerebellum, (3) 1.5 mA tDCS over spinal cord, and (4) sham tDCS (stimulator turned off after 5 seconds) over M1. A DC-stimulator PLUS (NeuroConn Gmbh, Ilmenau, Germany) and two saline-soaked sponge electrodes (5cm x 7cm) were used. For M1 stimulation, the anode was placed over the CZ, and the cathode was placed over the right supraorbital area (Fp2). For cerebellar stimulation, the anode was placed over the O2, and the cathode was placed over the right buccinator muscle. For spinal stimulation, the anode was placed over the spinal cord at the Th8 level, and the cathode was placed over L2. A simulation study has indicated that this electrode placement is superior (in comparison to deltoid, umbilicus, and iliac crest cathode placements) regarding the electric field generated in lumbar and sacral
spinal segments [17]. The international 10/20 EEG system [18] and palpation method [19, 37] were used to determine electrode positioning during M1, cerebellar and spinal tDCS.

2.4. Assessments

Three different assessments (Y Balance Test, the Single Leg Landing Test and the Single Leg Squat Balance Test) were used to evaluate balance ability.

The Y Balance Test was performed using a test kit (FMS, Chatham, USA). The maximal reach of the free lower leg in the (a) anterior, (b) posterolateral, and (c) posteromedial directions was determined during a one leg stance on the opposite leg [21]. A better balance ability was associated with a greater reach distance. Five trials were performed for each leg and direction. The mean value of the five trials was used for analysis.

During the Single Leg Landing Test, participants were instructed to perform a forward jump (50% of their body height), land on a single limb, and achieve a stable position as quickly as possible [22]. The centre of gravity (COG) in the anterior-posterior and medial-lateral directions and the time taken to regain balance were recorded using a force plate (AMTI, Watertown, USA). A smaller COG area and a faster time to stabilize indicated better balance. Five trials were performed for each leg. The mean value was used for the analysis.

During the Single Leg Squat Test, probands performed five consecutive single-leg squats (10% of their body height) [22]. The centre of gravity (COG) in the anterior-posterior and medial-lateral directions was recorded using the force plate described above. The smaller the COG area was, the better the balance. Two trials were performed for each leg. The mean values were used for the analysis.

2.5. Analysis

The SPSS software package, version 27 (International Business Machines Corporation Systems), was used to analyse the data collected during this study. The independent sample t-tests evaluated pre-interventional comparability. Repeated measure ANOVAs with the factors “intervention” and “time” compared the pre-post changes across interventions. Mauchly’s sphericity tests and Greenhouse-Geisser corrections were applied. Due to multiple comparisons, a p-value of ≤ 0.01 was considered statistically significant. The outliers (mean ± 3 SD) were excluded from the analysis.

3. Results

Overall, 42 participants were randomized (age 25.1 ± 3.2 years, 19 females, 23 males, 36 right-handed, 6 left-handed). All participants tolerated the interventions well without severe adverse events. Four participants reported less severe side effects, such as burning sensation and nausea (one participant after M1 stimulation) and metallic taste in the mouth (three participants after cerebellar stimulation). The pre-interventional data did not differ significantly across interventions. Table 1 summarizes the data on balance collected during the experiment.
The ANOVAs detected significant time*intervention interactions on the Y Balance Test but not on the Single Leg Landing Test and the Single Leg Squat Test. The effects were observed more frequently for the left leg than for the right leg. For the left leg, significant improvement of balance ability (in comparison to the sham tDCS) was detected after M1 (F_{1,40} = 8.999; p = 0.005), (F_{1,36} = 18.624; p < 0.001), cerebellar (F_{1,40} = 8.796; p = 0.005), (F_{1,36} = 16.291; p = < 0.001), and spinal (F_{1,39} = 13.55; p = < 0.001), (F_{1,34} = 8.799; p = 0.005) tDCS for the posterior lateral and posterior-medial directions, respectively. For the right leg, only spinal tDCS induced significantly greater effects than the sham tDCS for both the posterior-lateral (F_{1,39} = 11.53; p = 0.002) and posterior-medial (F_{1,39} = 7.943; p = 0.008) directions. No significant effects were observed for the anterior direction. The intervention-induced effects did not significantly differ across real tDCS interventions. Figures 1 and 2 illustrate the intervention-induced changes.

4. Discussion

The aim of this study is to investigate and compare the effects of 1.5 mA tDCS applied over the M1, cerebellum, and spinal cord on balance and postural control. The data show that (1) stimulation of each region significantly improved balance and postural control during the Y Balance Test but not during the Single Leg Landing Test and the Single Leg Squat Test, and (2) spinal stimulation improved the balance ability of both legs, while M1 and cerebellar stimulation improved right leg stand only. We will discuss our findings against the background of previous studies below.

4.1. Stimulated area specific modulation

Although several neuroimaging data indicate that several cortical and subcortical regions, the cerebellum, the brainstem and the spinal cord are crucially involved during balance and postural control [10, 11, 12], the majority of existing studies have applied tDCS over the M1[13, 14, 15]. The previous evidence for the remaining regions was insufficient. Direct comparisons of different regions regarding tDCS-induced effects on balance and postural control were almost non-existent [13, 14, 15]. Thus, our results provide an important contribution to this field. We have demonstrated that tDCS over the cerebellum is comparable to and that tDCS over the spinal cord is even more effective than tDCS over the M1 in supporting balance and postural control in young healthy adults. Accordingly, a review suggests that the core systems of the automatic process of postural control are mostly achieved by the brainstem and spinal cord, while the forebrain structures and cerebellum act on the brainstem–spinal cord systems so that cognitive processes of postural control can be achieved [23]. A model developed in the 1990s indicated that so-called central pattern generators (CPGs) could play a crucial role in gait and posture control [24, 25, 26]. CPGs are located in the lower thoracic and lumbar regions of the vertebrate spinal cord and drive rhythmic and stereotyped motor behaviour such as walking or swimming without input from higher brain areas [24, 25, 26]. It is assumed that spinal reflex networks are crucially involved in these self-organizing neural circuits [27, 28]. This finding is supported by studies that detected suppression of H-reflexes after balance training, in parallel to balance and postural control improvement [20, 12].
4.2. Leg-specific modulation

Our data show a greater improvement in balance ability for standing on the left leg than on the right leg. This is true for M1 and cerebral tDCS, but not for spinal tDCS. This can be caused by electrode positioning in relation to the sagittal body plane in our study. The electrodes were placed symmetrically during spinal tDCS (anode over Th8, cathode over L2). In contrast, a stronger right-hemispheric modulation was expected from M1 tDCS (anode over CZ, cathode over right supraorbital area) and cerebellar tDCS (anode over O2, cathode over right buccinator muscle). Indeed, the effects detected in our study are not consistent with the theory that the cerebral controls the contralateral hemi body and the cerebellum controls the ipsilateral hemi body [29, 30]. This theory (among others) is based on fMRI investigations that show that active movement of a single lower limb is associated with increased neural activation of the primary sensorimotor cortex, supplementary motor area, cingulate motor area, secondary somatosensory cortex and basal ganglia of the contralateral hemisphere but with increased neural activation within the ipsilateral anterior lobe of the cerebellum [29].

A growing number of studies have demonstrated hemispheric asymmetries of motor control [29, 31, 32]. FMRI data show that brain activation during a movement of the non-dominant limb is more bilateral than during the same movement performed with the dominant extremity [29]. A TMS study demonstrated that voluntary movement of a hand resulted in an increase in MEP amplitude in the non-task hand. This increase was more pronounced during left hand movements than during left hand tasks [32]. Accordingly, lesion studies indicate that the non-affected hemisphere can compensate for damage to the non-dominant hemisphere rather than for damage to the dominant hemisphere [31, 33]. Hand motor recovery after left hemispheric stroke is two to three times slower than that after a right hemispheric incident [31, 33]. Thus, one may assume that NIBS over the dominant hemisphere has the potential to modulate neural processing and/or motor control within the whole body, while the targeting of the non-dominant hemisphere modulates the non-dominant hemi body only. Unfortunately, there exists insufficient evidence in this regard. Existing NIBS research strongly focuses on the dominant hemisphere (and leg) and neglects the non-dominant hemisphere (and extremities). Future research should address this gap.

4.3. Balance task-specific modulation

Our data demonstrate that the choice of assessment significantly influences the effects. While numerous significant tDCS-induced improvements were found on the Y Balance Test, no effects were detected on the Single Leg Landing Test and the Single Leg Squat. Accordingly, numerous studies have shown little consistency in balance performance when using different assessments [34, 35]. Balance performance during (i) single leg landing, (ii) stance on unstable platform and (iii) forward falls correlated only weakly in young healthy people [35]. Similarly, performance during (i) bipedal stance, (ii) stance on unstable platform, and (iii) Functional Reach Test were not correlated in children aged 7–10 years [34]. It can be assumed that different mechanisms are responsible for balance control. An interesting perspective on this topic offers the Balance Evaluation Systems Test [36]. This test battery differentiates between six balance control systems (biomechanical constraints, stability limits/verticality, anticipatory postural
adjustments, postural responses, sensory orientation, stability in gait). This assessment was developed to identify the underlying cause for poor functional balance in several cohorts [36]. Participants with balance deficiencies in one category do not necessarily show deficits in other categories [36]. Collectively, the present data show that balance and postural control are complex neural processes, and their neural background has not been fully understood to date.

5. Strengths and limitations

This is the first placebo-controlled study that compared the effects of tDCS over different areas on balance ability in healthy participants. Our results provide additional insights into the neural background of balance and postural control and support the development of innovative therapy strategies in several cohorts. A weakness of our experiments is the limited number of participants as well as missing neuro-navigation to determinate the exact location of optimal tDCS application.

6. Conclusions

The study shows that anodal 1.5 mA tDCS over the spinal cord is superior to 1.5 mA tDCS over both the M1 and cerebellum in supporting balance ability in healthy young people. While spinal cord modulation supported balance in both legs, M1 and cerebellar stimulation improved only right leg balance. Future studies should compare the effects of different spinal cord tDCS protocols in healthy people. Furthermore, spinal cord tDCS should be more closely examined in the framework of rehabilitation.

Declarations

Compliance with ethical standards

Funding

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Conflicts of interest/Competing interests

The authors declare that there is no conflict of interest.

Ethics approval

The study was approved by the Ethics Committee of Bielefeld University (EC no. 2022-043). All participants gave their written informed consent.

Availability of data and material
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Author contribution statement**

JV, CS and TSc conceptualized and designed the study. TSt, LG, JW and RR performed the acquisition of the data. JV, CS and TSt analyzed and interpreted the data. JV wrote the first version of the manuscript. JV, CS, TSc, TSt, LG, JW and RR reviewed the final version of the manuscript.

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**References**


Tables

Table 1 is available in the Supplementary Files section.

Figures
Figure 1

Intervention-induced changes (means and SD) in the Y Balance Test in relation to baseline.

Notes: ** = P ≤ 0.01; *** = P ≤ 0.001; □ = sham; ■ = M1; □ = cerebellum; □ = spinal
Figure 2

Intervention-induced changes (means and SD) in Single Leg Squat Test and Single Leg Landing Test in relation to baseline.

Notes: □ = sham; ■ = M1; ■ = cerebellum; ■ = spinal

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Tab1.xlsx