Received: 21 March 2022 | Revised: 10 June 2022 | Accepted: 30 June 2022

DOI: 10.1111/ejn.15756

SHORT COMMUNICATION

EJN European Journal of Neuroscience FENS WILEY

Transcranial direct current stimulation (tDCS) modulates motor execution in a limb reaching task

Thomas Zandonai[1,2] | **Matteo Bertucco**[3] | **Nadia Graziani**[3] |
Veronica Montani[3] | **Paola Cesari**[3]

[1]Department of Pharmacology, Paediatrics and Organic Chemistry, Miguel Hernández University of Elche Alicante, Spain

[2]Neuropharmacology on Pain and Functional Diversity (NED), Institute of Health and Biomedical Research of Alicante (ISABIAL Foundation), Alicante, Spain

[3]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

Correspondence
Thomas Zandonai, Department of Pharmacology, Pediatrics and Organic Chemistry, Miguel Hernández University of Elche, Crta. Nacional, N-332. s/n, 03550 Sant Joan, Alicante, Spain.
Email: tzandonai@umh.es

Edited by: Gregor Thut

Abstract

The majority of human activities show a trade-off between movement speed and accuracy. Here we tested 16 participants in a quick pointing action after 20 minutes (2 mA) of transcranial direct current stimulation (tDCS) delivered at the supplementary motor area in a single-blind crossover design study for testing the feedforward components in the control of action. tDCS stimuli were delivered in three randomized sessions of stimulations as anodal, cathodal and sham as a control. The task performed pre- and post-tDCS stimulation, was to point as fast and as precise as possible with the big toe to targets having different sizes (2 and 8 cm; Width) and positioned at different distances (20 and 60 cm; Distance). An optoelectronic motion capture system was used to collect the kinematics of movement. The result indicates that individuals after receiving anodal stimulation decreased their movement time and increased their movement speed, while the opposite happened after receiving a cathodal stimulation. The scarcity of studies in this area invites us to plan a research that aims at the trade-off especially in the clinical settings.

KEYWORDS
brain stimulation, lower limb, motor control, supplementary motor area

1 | INTRODUCTION

Transcranial direct current stimulation (tDCS) is a neuromodulatory technique that has been increasingly studied for its potential use as a clinical tool (Brunoni et al., 2012; Charvet et al., 2020). tDCS is considered a non-invasive intervention that induces changes in the excitability of the human cortex by delivering weak direct electrical currents through the scalp via two electrodes placed on the head. These changes depend on the current flow that can increase or decrease neuronal excitability. Indeed, the mechanisms are electrode-dependent and involve either: (a) membrane depolarization (anodal stimulation increases excitability); or (b) membrane hyperpolarization (decreased by cathodal stimulation; Filmer et al., 2014).

Despite the growing number of studies (Lucena et al., 2019), findings about tDCS effects on motor control

---

Abbreviations: D, distance; Hz, Hertz; M1, primary motor cortex; MT, movement time; SD, standard deviation; SMA, supplementary motor area; tDCS, transcranial direct current stimulation; TMS, transcranial magnetic stimulation; W, target.

Thomas Zandonai, Matteo Bertucco and Paola Cesari *equal contribution.*

are limited. While a recent meta-analysis (Baharlouei et al., 2020) indicated that anodal tDCS improves both static and dynamic balance in healthy participants, recently the attention on tDCS related more in studies that induce changes in the motor activity as a function of targeted brain areas (Morya et al., 2019). For instance, interest might be devoted in stimulating the premotor and the supplementary motor area (SMA) for studying action planning including gait movements (Jacobs et al., 2009). SMA is involved in movement preparation as supported by its activation before movement execution particularly for movements that are internally generated rather than triggered by sensory events (Jacobs et al., 2009). Because SMA plays a major role in pre-planning movements, in this study we are interested to reveal whether modulating its activity via tDCS can lead to polarity-specific changes resulting in functional effects related to the production of motor responses (Carlsen et al., 2015). So far, few studies have investigated the effects of tDCS on SMA. A study aimed to examine the role of the SMA in planning the movements required to complete reaction time, balance and pegboard tasks using anodal tDCS stimulation for 3 days. During administration of tDCS, participants performed a balance task significantly faster than controls (no tDCS administration). After tDCS, subjects significantly decreased their reaction time. Findings evidenced that the SMA is highly involved in planning and executing fine and gross motor skill tasks, and that tDCS is an effective modality for increasing SMA-related performance on these tasks (Hupfeld et al., 2017). Furthermore, Manji et al. (2018) investigated the effect of combined therapy body weight-supported treadmill training and tDCS on gait function recovery of stroke patients. Thirty stroke patients were recruited. The facilitative effects of tDCS on SMA possibly improved postural control during exercise, and efficacy rehabilitation training in gait after stroke (Manji et al., 2018).

As shown up to now, tDCS has been applied mainly for testing body posture and locomotion, interestingly fast and accurate movements were never considered. Indeed, action preparation is strongly involved when the task requires the speed–accuracy trade-off in action performance. For these movements, brain excitation and inhibition are fundamental in controlling limb acceleration and deceleration for then hitting the target. Already several studies sustain the dorsomedial parieto-frontal pathway involvement in visuomotor transformation for step-tracking movements performed to reach targets positioned in different directions and at different distances in space (Fabbri et al., 2012; Messier & Kalaska, 2000). Interestingly, movement direction and amplitude are processed differently with distinct timing and within different cortical areas. In particular, virtual disruption of the medial intraparietal area led to error in the initial direction of movements, while virtual disruption of the dorsal premotor cortex and SMA intervened in movement amplitude (Davare et al., 2015; Fabbri et al., 2012).

In behavioural studies the trade-off between action speed and precision is directly related with the amount of movement displacement and inversely related with the precision required defined by the target sizes (Bertucco et al., 2013; Bertucco & Cesari, 2010). For these movements, brain excitation and inhibition are fundamental in controlling limb acceleration and deceleration for correctly hitting the target.

Interestingly, Horvath and colleagues in a general review evidenced how the only reliable neurophysiological effect produced by tDCS, among many considered, was related to the motor-evoked potential amplitude measures, reinforcing the interest and the specificity in testing action performance (Horvath et al., 2015). Moreover, the authors underlined the presence of a huge percentage (almost 80%) of tDCS studies that lack the presence of an important control condition such as sham (Horvath et al., 2015). Consequently, the main aim of the study was to evaluate the effects of anodal and cathodal and sham tDCS applied on SMA before individuals perform fast and accurate lower leg movements.

The task was to point with the big toe to two targets having different sizes and positioned at two different distances. Accuracy was highly required, so that trials where targets were over or under shoot were not considered. In order to accomplish this complex task hitting correctly the target by applying high movement speed, a pre-programmed action is highly required (Bertucco & Cesari, 2010). Our main hypothesis was that after receiving anodal tDCS stimulation, participants will decrease their movement time (MT) while the opposite will happen after receiving a cathodal stimulation. We were expecting no effect after a sham stimulation. For movement speed, we were expecting an increase of movement speed after anodal stimulation, a decrease of movement speed under cathodal stimulation, and no change of movement speed after sham stimulation.

2 | EXPERIMENTAL PROCEDURES

2.1 | Participants

Sixteen participants (8 males, 8 females) with mean age: 24.1 ± 3.5 years with no sensory or motor dysfunctions were recruited among the students at the School of Sport and Exercise Science, at the University of Verona. Participants read and signed an informed consent form before participating in the experiments. The Ethics Committee of the Department Neuroscience, Biomedicine and Movement Sciences approved this single-blind crossover design study research. The ethical principles in the Declaration of

Helsinki were applied, and the protocol was executed in accordance with safety procedures for non-invasive brain stimulation (Fregni et al., 2015; Poreisz et al., 2007).

The exclusion criteria were the presence of sensory or motor dysfunctions, symptomatic cardiopathy and metabolic disorders such as obesity (body mass index > 30 kg m^{-2}). Another exclusion criterion was the presence of implanted metal devices (e.g. pacemakers, metal plates, wires).

2.2 | Apparatus

The experimental set-up was composed of an eight-infrared-emitting-cameras motion capture system (MX 13, VICON, Oxfordshire, UK) equipped with retro-reflective markers. The system sampling frequency was 250 Hz. Reflective markers were positioned on the following bony markers bilaterally: heel and big toe. Participants were positioned such that the lower limb movement was aligned with the *x*-directions of the local coordinate system.

A battery-powered DC stimulator (Newronika S.r.l, Milan, Italy) delivered through a saline-soaked pair of surface sponge electrodes (5 × 5 cm) was used for stimulation (Holgado et al., 2019).

2.3 | Procedures

Participants were enrolled in the experiment with three randomized ordered sessions (anodal vs. cathodal and sham as a control) each at least 48 h apart to ensure a complete wash-out of any residual tDCS effects.

In each of the three testing sessions, participants received either the anodal or cathodal or sham stimulation, following the randomization, for 20 min before starting the task. It has been shown that tDCS effects are greatest 10–25 min following stimulation (Kuo et al., 2013). They performed the task before (pre-) and after (post-) tDCS stimulation.

The task consisted of goal-directed pointing movement with the tip of the big toe of the dominant leg to a round target (width – diameter W) at a certain distance (D) that was marked on the floor. The targets were positioned in front of the participant on a notional line passing perpendicularly to the frontal plane through the middle of the feet position. The task was to execute a single discrete movement. The instruction to the participants was to perform the movement "as fast and as accurate as possible", precision was strongly requested such that they were asked to land with the big toe within the boundary of the target. After pointing to the target, participants were instructed to hold the final position for about 1.5 s. In all, two target distances (D: 20 and 60 cm) and two target widths (W: 2 and 8 cm) were used. Each trial started with the subject standing in the initial position with feet parallel at waist width (the internal distance of the feet was about 15–20 cm apart; Figure 1). The command was "when ready go", such that participants were free to initiate toe pointing at any moment in a self-paced manner. The distance (D) was measured from the initial position of the big toe marker of the

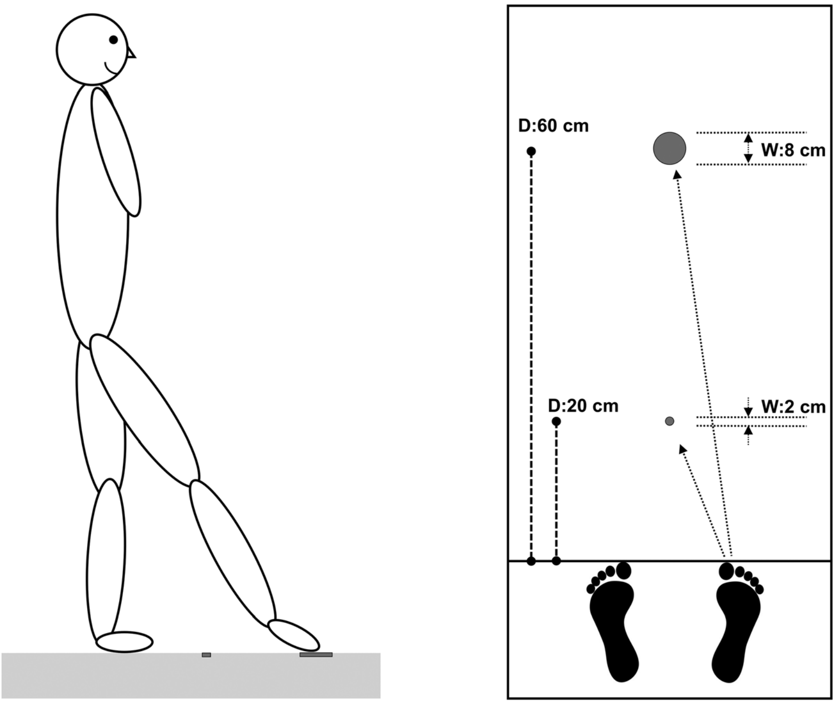

FIGURE 1 Schematic representation of the experimental procedure. The participants were asked to execute a single discrete pointing task with the lower limb toward to two different targets (width: 2 and 8 cm) and two different movement amplitudes (a: 20 and 60 cm) as fast and as accurate as possible. For ease of representation only two experimental conditions are depicted in the figure: D: 20 cm – W: 2 cm; D: 60 cm – W: 8 cm

pointing limb in the sagittal plane to the target centre. The conditions were presented in pseudo-random order, while the trials within a condition were blocked. The subjects performed four–five practice trials prior to each condition for correctly hitting the target and landing within the target boundary. Only one error (a trial that over- or undershot the target) was accepted per condition (maximum of 5% of error per condition over accepted trials). If an error occurred, the subject immediately repeated the trial. Each participant performed a total of 15 successful trials for each condition.

2.4 | tDCS procedure

Direct current stimulation was delivered via two scalp electrodes. The active electrode was saturated with sterile saline (0.9% NaCl) and positioned 1.8 cm anterior to Cz (measured based on the International 10–20 system for electroencephalography), which was determined by mapping the centroid of the SMA based on Talairach space onto standardized head coordinates (Jasper, 1958; Talairach & Tournoux, 1988). This site has been previously used for SMA stimulation using tDCS (Carlsen et al., 2015; Hayduk-Costa et al., 2013) and transcranial magnetic stimulation (TMS; Müri et al., 1994). The reference electrode was placed above the eyebrows in the centre of the forehead. Current was set at 2 mA and delivered for 20 min. Subjects were blinded for stimulation conditions. Indeed, for the sham, stimulation (control) was similar to the anodal and cathodal stimulation but the device was power on while ramping up to 2 mA then after 30 s turned off without the participant's awareness.

2.5 | Data analysis

Data analysis was performed using Matlab 9.6 software (MathWorks, Inc., United States) (Natick MTMI. MATLAB, 2018). The kinematic data were digitally low-pass filtered at 12 Hz using a fifth-order Butterworth filter. The peak of tangential speed (PV) was calculated from the speed profile in the anteroposterior direction (coordinate x) of the marker on the big toe of the pointing foot. The starting time of the movement (T_0) was defined as the instant when the tangential speed of the marker reached 5% before the PV during that particular trial. The end time of the movement (T_f) was defined as the time when the tangential speed of the marker reached 5% after the PV and remained below that threshold for at least 100 ms (Bertucco & Cesari, 2010; Duarte & Latash, 2007). The MT was defined as the time between T_0 and T_f. The marker on the big toe of the standing foot (the foot that did not move) was monitored to ensure that no motion had taken place. Movement amplitude was defined as the distance between the position of the big toe marker of the pointing foot in the anteroposterior direction at T_0 and T_f. Then the average speed of the movement was defined.

2.6 | Statistical analysis

We analysed the effects of the experimental manipulation onto two dependent measures, MT and speed, using mixed-effect multiple regression models. Mixed-effect multiple regression models offer several advantages over conventional regression such as they do not assume independence amongst observations, the ability to give unbiased results in the presence of missing data, the flexible specification of the covariance structure among repeated measures, the generalization for non-normal data and, finally, the greater power (Harrison et al., 2018). In particular, we were interested in taking into account the potential large interindividual variability of the effect of the stimulation. Therefore, the random structure of the models included by-subject random intercepts and by-subject random slopes for the type of stimulation. Two participants (S07 and S13) were excluded from the analysis because her/his performance was two standard deviations below the mean for the MT and movement amplitude (distance), respectively.

Each model included four fixed effects and their interaction: session (two levels: pre-stimulation, post-stimulation), type of stimulation (three levels: anodal, cathodal, sham), distance (two levels: 20 cm vs. 60 cm) and target width (two levels: 2 cm vs. 8 cm). The specifications of the models are as follows.

$$\mathsf{Modelling\ MT} < -\mathsf{lmer}(\mathsf{MT} \sim (\mathsf{stimulation} + \mathsf{session} + \mathsf{target} + \mathsf{distance})^4 + (\mathsf{stimulation}|\mathsf{subject}), \mathsf{data})$$

$$\mathsf{Modelling\ speed} < -\mathsf{lmer}(\mathsf{speed} \sim (\mathsf{stimulation} + \mathsf{session} + \mathsf{target} + \mathsf{distance})^4 + (\mathsf{stimulation}|\mathsf{subject}), \mathsf{data})$$

Observations with a standardized residual at a distance greater than 2.5 standard deviations from zero (Baayen et al., 2008) were removed (2.6% of the data for both the time and the speed). *P*-values were calculated using Satterthwaite approximations for degrees of freedom (Kuznetsova et al., 2017; Luke, 2017) corrected for multiple comparisons using the Benjamini–Hochberg procedure (Benjamini & Hochberg, 1995). Statistical analysis was performed using lme4 package (Bates et al., 2015), lmerTest package (Kuznetsova et al., 2017) and emmeans package (Lenth, 2021) in the R environment (R Core Team, 2020).

3 | RESULTS

All participants successfully performed the goal-directed pointing movement for the two distances (D) and the two targets (W). None of the participants reported discomfort during the stimulations. Participants scored less than 5% of errors for each task condition.

Considering the MT (Figure 2), the main effects of target width ($F_{1,4,859} = 1514.23$, $p < 0.001$) and distance ($F_{1,4,859} = 6446.24$, $p < 0.001$) were significant indicating, respectively, longer MT for small compared with large targets (M = 0.36, SD = 0.06 for 2 cm vs. M = 0.32, SD = 0.06 for 8 cm), and longer MT for longer compared with short distance (M = 0.30, SD = 0.04 for 20 cm vs. M = 0.38, SD = 0.05 for 60 cm). Importantly, the triple interaction: stimulation × session × distance was significant ($F_{2,4,859} = 8.19$, $p < 0.001$), indicating that, for the long distance (60 cm), the MT was shorter in the post-session compared with the pre-session for the anodal stimulation ($t_{4859} = 2.19$, $p = 0.03$), and MT was longer in the post-session compared with the pre-session for the cathodal stimulation ($t_{4859} = -3.49$, $p < 0.001$), while no difference between the pre- and post-sessions was present for the sham condition. There was a significant interaction stimulation × target ($F_{2,4,859} = 12.42$, $p < 0.001$), indicating that the difference (i.e. longer time) between the MT for the small target compared with the large target was slightly greater for the sham than the other two stimulations. No other significant effects were present.

Considering movement speed (Figure 3), the main effects of stimulation were significant ($F_{2,4,857} = 5.57$, $p = 0.03$), indicating that, overall, action was faster in both the anodal and cathodal stimulations compared with the sham (M = 124.89, SD = 57.97 vs. M = 124.41, SD = 58.68 vs. M = 119.32, SD = 55.70, respectively). The main effect of target width was significant ($F_{1,4,857} = 1718.83$, $p < 0.001$), indicating that action was faster for the large target compared with the small target (M = 130.96, SD = 55.01 for the 8 cm

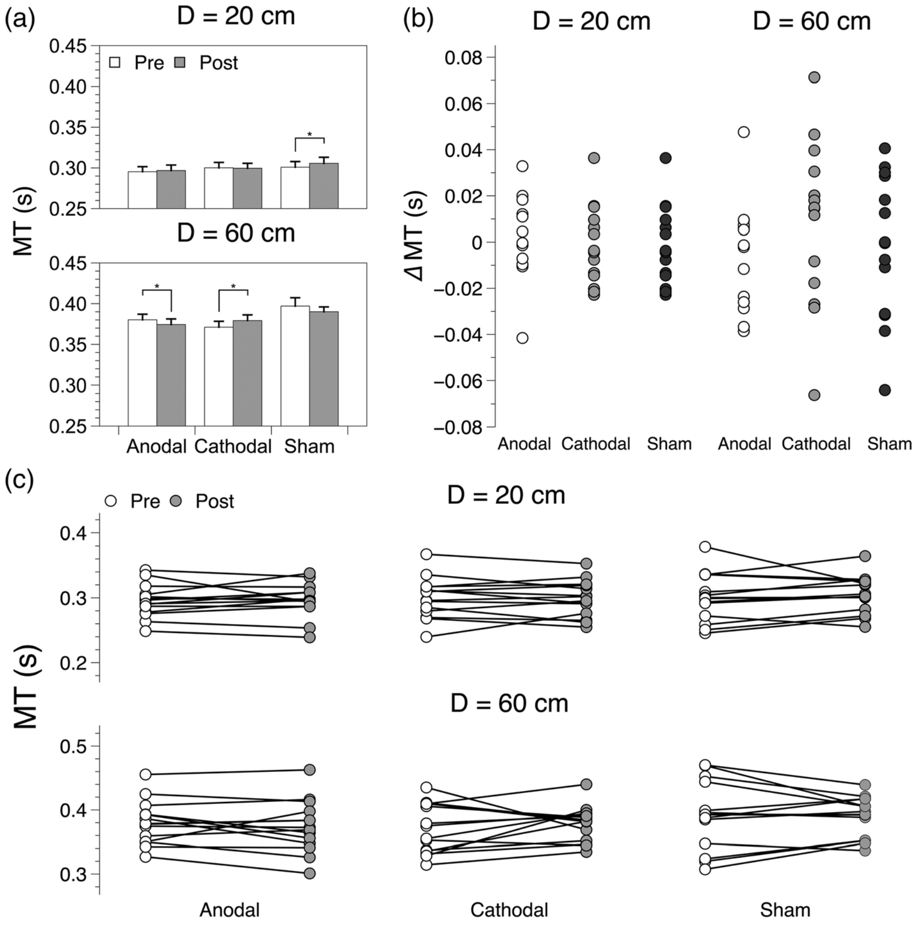

FIGURE 2 (a) Bar graph with mean and error bars of movement time (MT) on the transcranial direct current stimulation (tDCS) (anodal, cathodal and sham) for the two target distances (D = 20 cm, on the top; D = 60 cm, on the bottom). White bars: before the stimulations, pre; grey bars: after the stimulations, post. (b) Scatterplots of difference (Δ) between pre- and post-stimulations test (○ anodal, ● cathodal and ● sham). and (c) Stripcharts on the tDCS stimulations for the two target distances. White circles: before the stimulations, pre; grey circles: after the stimulations, post. Asterisk (*) indicates a statistical difference $P < 0.05$. Error bars represent standard error of the means (SEMs) adjusted to correctly reflect the variance in the within-subject design (Morey, 2008)

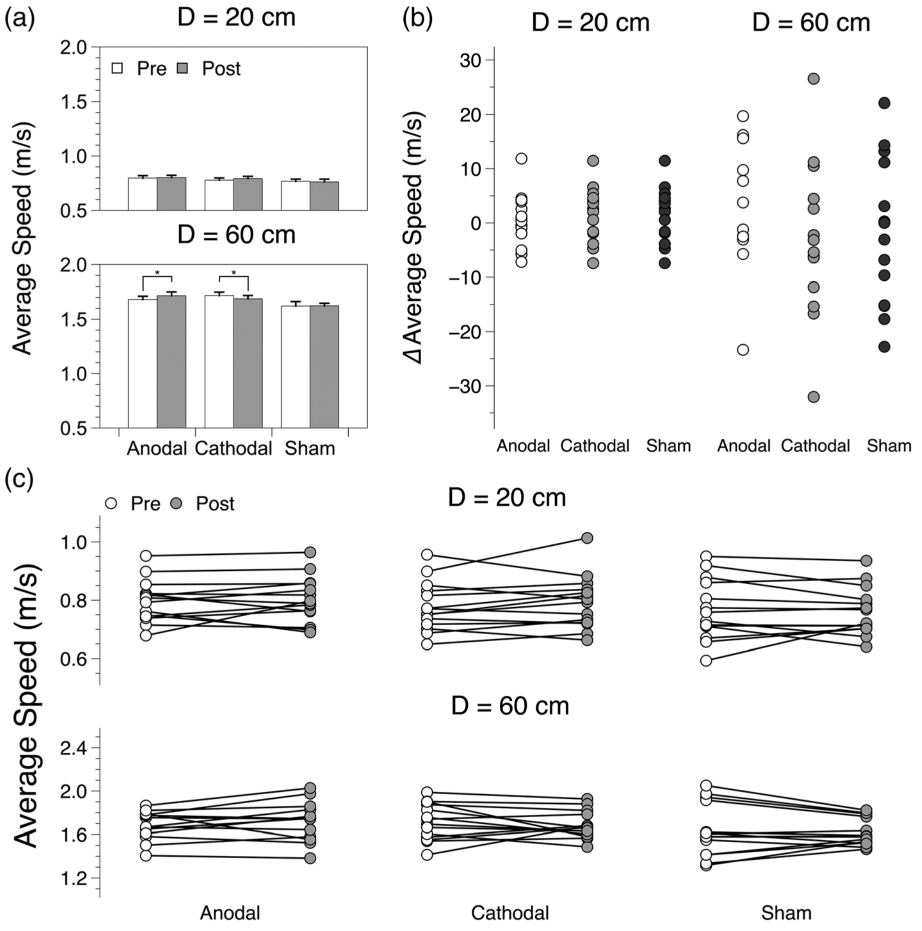

FIGURE 3 (a) Bar graph with mean and error bars of average speed on the transcranial direct current stimulation (tDCS) (anodal, cathodal and sham) for the two target distances (D = 20 cm, on the top; D = 60 cm, on the bottom). White bars: before the stimulations, pre; grey bars: after the stimulations, post. (b) Scatterplots of difference (Δ) between pre- and post-stimulations test (○ anodal, ● cathodal and ● sham). and (c) Stripcharts on the tDCS stimulations for the two target distances. White circles: before the stimulations, pre; grey circles: after the stimulations, post. Asterisk (*) indicates a statistical difference $P < 0.05$. Error bars represent standard error of the means (SEMs) adjusted to correctly reflect the variance in the within-subject design (Morey, 2008)

target vs. M = 114.78, SD = 51.66 for the 2 cm target). The main effect of distance was significant ($F_{1,4,858} = 51708.90$, $p < 0.001$), indicating that action was faster for the long distance compared with the short distance (M = 167.42, SD = 19.59 for the 60 cm distance vs. M = 78.33, SD = 12.81 for the 20 cm distance). The interaction between stimulation and distance was significant ($F_{2,4,858} = 18.60$, $p < 0.001$), indicating that, for the long distance, the speed for both the anodal and cathodal stimulations was higher compared with the sham stimulation. The interaction between the target and the distance was significant ($F_{1,4,857} = 71.58$, $p < 0.001$), indicating that the difference between the large and small targets (i.e. faster for the large) was greater for the long distance compared with the short distance. Crucially, the stimulation vs. session vs. distance was significant ($F_{1,4,857} = 5.96$, $p = 0.003$), indicating that, for the large target only, the speed was higher in the post-session compared with the pre-session for the anodal condition, it was slower for the cathodal condition, and there was no difference for the sham. Finally, quadruple interaction, session vs. stimulation vs. target vs. distance was significant ($F_{2,4,857} = 6.79$, $p = 0.001$), indicating that, for the small target during the short distance, the speed was lower in the post-session compared with the pre-session in the sham condition ($t_{4857} = 2.42$, $p = 0.02$); and for the large target in the long distance, the speed was higher in the post-session compared with the pre-session in the anodal condition ($t_{4857} = -3.94$, $p < 0.001$); and it was lower in the post-session compared with the pre-session in the cathodal condition ($t_{4857} = 1.94$, $p = 0.05$). No other significant effects were present.

4 | DISCUSSION

Transcranial direct current stimulation (tDCS) offers a non-invasive means by which to study the neural processes underlying general behaviours (Filmer et al., 2014). In this experimental study, for the first time we investigated how tDCS could induce effects in a classical relation between movement amplitude and accuracy in a lower limb quick pointing action. Our findings evidenced that tDCS application (2 mA for 20 min) changes the motor cortex plasticity by specifically modulating MT and speed when the SMA receives anodal and cathodal stimulation.

The protocol was similar to that of Bertucco and Cesari (2010) in that participants were fully aware and under control of the task difficulty: they were asked to concentrate to the target distance and target width, to consider the trade-off between speed and precision, and to initiate the action at their own will when ready to go. As such, individuals followed the expected performance guided by the speed accuracy trade-off constrains, showing increased movement amplitude with larger target width as the target distance and width increased (Bertucco & Cesari, 2010; Duarte & Latash, 2007). In our experimental condition, individuals are required to avoid target overshooting or undershooting in order to increase task difficulty and require a correct action pre-programming.

Our hypothesis was that the motor system may encode parameters related to action such as reaching distance and maximum speed. Both distance and speed should be determined before movement particularly when actions are required to be fast and precise, therefore, an increased connectivity during motor planning may suggest processing of information related specifically to reaching distance and speed (Yeom et al., 2020).

Our results confirmed that tDCS on SMA increase the brain excitability on speed only through anodal stimulation. This result sounds consistent as in tDCS literature when referring to activation it is often thought that it is mainly due to the anodal stimulation (Brunoni et al., 2012; Charvet et al., 2020; Filmer et al., 2014). Moreover, previous studies on healthy populations have shown improvements in RT following anodal tDCS applied over the SMA, and these changes were attributed to the upregulation of neural structures underlying motor response preparation and/or initiation (Carlsen et al., 2015; Hupfeld et al., 2017). Even more, in monkeys, firing rate in SMA was correlated with both movement direction and movement amplitude but in particular when considering movement amplitude, a higher firing rate has been found to correlate with a larger limb displacement (Fu et al., 1993, 1995). Fabbri and colleagues found in humans that frontal areas, including dorsal premotor cortex, ventral premotor cortex and SMA, modulate with movement amplitude (Fabbri et al., 2012). As such, individuals followed the expected performance guided by the speed accuracy trade-off constrains, showing increased movement amplitude with larger target width as the target distance and width increased (Bertucco & Cesari, 2010; Duarte & Latash, 2007). Indeed, in this study our findings evidenced an increase on speed only for long distance (60 cm). However, it is too early to reach firm conclusions about this. The majority of previous studies, where an increase of motor performance was evident, show an application of anodal tDCS over primary motor cortex (M1), and only a few studies have investigated whether anodal tDCS applied over the SMA (Sadler et al., 2021).

Regarding the cathodal effects, we confirmed our hypothesis. In fact, we have seen a decrease of movement speed (pre- vs. post-; Figure 2), confirming a previous study on SMA (Carlsen et al., 2015). Nevertheless, in this study, authors used a 1.0-mA intensity, while we applied 2.0 mA. Conversely, other authors showed that 20 min of 2.0 mA cathodal tDCS shifted cortical plasticity from diminution to facilitation (Batsikadze et al., 2013; Mosayebi Samani et al., 2019) or non-conclusive effects by cathodal stimulation (Wiethoff et al., 2014) evidencing the importance of the stimulation parameters (Jamil et al., 2017).

The present investigation has some limitations that need to be addressed. Firstly, our effect by tDCS to have a strong statistical power would have required a major sample than we recruited. Second, despite three randomized ordered sessions, it is possible that a learning effect would have manifested by participants. Finally, with reference to the position of the electrodes, the tDCS effects with respect to the stimulation area for the lower limb are different than for the upper limb, and different areas can be stimulated at the same time with less or more precision (Foerster et al., 2018; Patel & Madhavan, 2019; Quiles et al., 2022). In this first study where we investigated how tDCS could induce effects in a classical relation between movement amplitude and accuracy in a lower limb quick pointing action, we cannot rule out an effect on M1 due to a possible modulation induced by the position of our electrodes (Foerster et al., 2018; Patel & Madhavan, 2019; Quiles et al., 2022).

Here, we investigated how tDCS can modify a trade-off action in the lower limb. A comparison with the literature on healthy volunteers is not feasible as most of the studies have focused on stroke (Bai et al., 2022; Comino-Suárez et al., 2021), multi-limb coordination (Leenus et al., 2015) and Parkinson's disease (Lee et al., 2019). Therefore, our data must be taken with caution and confirmed by future studies, this anodal excitement would open up new scenarios in medical practices that involve brain stimulation.

In conclusion, to the best of our knowledge, this is the first detailed study of how tDCS – under our experimental conditions – effects modified the speed of movement in standing human subjects during a trade-off task. Its potential importance could be focus on gait parameters in the practice of posture and gait rehabilitation (e.g. clinical rehabilitation). To achieve this goal, future studies should investigate how the performance in such tasks is modified by tDCS intervention in individuals with posture and gait impairments.

ACKNOWLEDGEMENT

None.

CONFLICT OF INTEREST

None.

FUNDING INFORMATION

This research did not receive any specific grant from funding agencies in the public, commercial or not-for profit sectors.

AUTHOR CONTRIBUTIONS

Conceptualization, TZ, MB and PC; Data curation, TZ, MB, NG and PC; Formal analysis: TZ, MB, NG, VM and PC; Investigation, TZ, MB, NG, VM and PC; Methodology, TZ, MB, NG, VM and PC; Roles/Writing – original draft, TZ, MB. VM and PC; Writing – review & editing, TZ, MB, NG, VM and PC; Supervision, PC.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/ejn.15756.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in Figshare at https://doi.org/10.6084/m9.figshare.20039762.

ORCID

Thomas Zandonai https://orcid.org/0000-0002-7606-9675
Matteo Bertucco https://orcid.org/0000-0002-5653-6387
Veronica Montani https://orcid.org/0000-0002-4614-3002
Paola Cesari https://orcid.org/0000-0002-1705-6065

REFERENCES

Baayen, R. H., Davidson, D. J., & Bates, D. M. (2008). Mixed-effects modeling with crossed random effects for subjects and items. *Journal of Memory and Language*, *59*(4), 390–412. https://doi.org/10.1016/j.jml.2007.12.005

Baharlouei, H., Saba, M. A., Shaterzadeh Yazdi, M. J., & Jaberzadeh, S. (2020). The effect of transcranial direct current stimulation on balance in healthy young and older adults: A systematic review of the literature. *Neurophysiologie Clinique*, *50*(2), 119–131. https://doi.org/10.1016/j.neucli.2020.01.006

Bai, Z., Zhang, J., & Fong, K. N. K. (2022). Effects of transcranial magnetic stimulation in modulating cortical excitability in patients with stroke: A systematic review and meta-analysis. *Journal of Neuroengineering and Rehabilitation*, *19*(1), 1–18. https://doi.org/10.1186/s12984-022-00999-4

Bates, D., Mächler, M., Bolker, B. M., & Walker, S. C. (2015). Fitting linear mixed-effects models using lme4. *Journal of Statistical Software*, *67*(1), 1–48. https://doi.org/10.18637/jss.v067.i01

Batsikadze, G., Moliadze, V., Paulus, W., Kuo, M. F., & Nitsche, M. A. (2013). Partially non-linear stimulation intensity-dependent effects of direct current stimulation on motor cortex excitability in humans. *Journal of Physiology*, *591*(7), 1987–2000. https://doi.org/10.1113/jphysiol.2012.249730

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society: Series B: Methodological*, *57*(1), 289–300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

Bertucco, M., & Cesari, P. (2010). Does movement planning follow Fitts' law? Scaling anticipatory postural adjustments with movement speed and accuracy. *Neuroscience*, *171*(1), 205–213. https://doi.org/10.1016/j.neuroscience.2010.08.023

Bertucco, M., Cesari, P., & Latash, M. L. (2013). Fitts' law in early postural adjustments. *Neuroscience*, *231*, 61–69. https://doi.org/10.1016/j.neuroscience.2012.11.043

Brunoni, A. R., Nitsche, M. A., Bolognini, N., Bikson, M., Wagner, T., Merabet, L., Edwards, D. J., Valero-Cabre, A., Rotenberg, A., Pascual-Leone, A., Ferrucci, R., Priori, A., Boggio, P. S., Fregni, F., Paulo, S., Nitsche, M. A., & Bolognini, N. (2012). Clinical research with transcranial direct current stimulation (tDCS): Challenges and future directions. *Brain Stimulation*, *5*(3), 175–195. https://doi.org/10.1016/j.brs.2011.03.002.Clinical

Carlsen, A. N., Eagles, J. S., & MacKinnon, C. D. (2015). Transcranial direct current stimulation over the supplementary motor area modulates the preparatory activation level in the human motor system. *Behavioural Brain Research*, *279*, 68–75. https://doi.org/10.1016/j.bbr.2014.11.009

Charvet, L. E., Shaw, M. T., Bikson, M., Woods, A. J., & Knotkova, H. (2020). Supervised transcranial direct current stimulation (tDCS) at home: A guide for clinical research and practice. *Brain Stimulation*, *13*(3), 686–693. https://doi.org/10.1016/j.brs.2020.02.011

Comino-Suárez, N., Moreno, J. C., Gómez-Soriano, J., Megía-García, Á., Serrano-Muñoz, D., Taylor, J., Alcobendas-Maestro, M., Gil-Agudo, Á., del-Ama, A. J., & Avendaño-Coy, J. (2021). Transcranial direct current stimulation combined with robotic therapy for upper and lower limb function after stroke: A systematic review and meta-analysis of randomized control trials. *Journal of Neuroengineering and Rehabilitation*, *18*(1), 1–16. https://doi.org/10.1186/s12984-021-00941-0

Davare, M., Zénon, A., Desmurget, M., & Olivier, E. (2015). Dissociable contribution of the parietal and frontal cortex to coding movement direction and amplitude. *Frontiers in Human Neuroscience*, *9*, 241. https://doi.org/10.3389/fnhum.2015.00241

Duarte, M., & Latash, M. L. (2007). Effects of postural task requirements on the speed-accuracy trade-off. *Experimental Brain Research*, *180*(3), 457–467. https://doi.org/10.1007/s00221-007-0871-x

Fabbri, S., Caramazza, A., & Lingnau, A. (2012). Distributed sensitivity for movement amplitude in directionally tuned neuronal populations. *Journal of Neurophysiology*, *107*(7), 1845–1856. https://doi.org/10.1152/jn.00435.2011

Filmer, H. L., Dux, P. E., & Mattingley, J. B. (2014). Applications of transcranial direct current stimulation for understanding brain function. *Trends in Neurosciences*, *37*(12), 742–753. https://doi.org/10.1016/j.tins.2014.08.003

Foerster, Á. S., Rezaee, Z., Paulus, W., Nitsche, M. A., & Dutta, A. (2018). Effects of cathode location and the size of anode on anodal transcranial direct current stimulation over the leg motor area in healthy humans. *Frontiers in Neuroscience*, *12*, 1–12. https://doi.org/10.3389/fnins.2018.00443

Fregni, F., Nitsche, M. A., Loo, C. K., Brunoni, A. R., Marangolo, P., Leite, J., Carvalho, S., Bolognini, N., Caumo, W., Paik, N. J., Simis, M., Ueda, K., Ekhtiari, H., Luu, P., Tucker, D. M., Tyler, W. J., Brunelin, J., Datta, A., Juan, C. H., … Bikson, M. (2015). Regulatory considerations for the clinical and research use of transcranial direct current stimulation (tDCS): Review and recommendations from an expert panel. *Clinical Research and Regulatory Affairs*, *32*(1), 22–35. https://doi.org/10.3109/10601333.2015.980944

Fu, Q., Flament, D., Coltz, J., & Ebner, T. (1995). Temporal encoding of movement kinematics in the discharge of primate primary motor and premotor neurons. *Journal of Neurophysiology*, *73*(2), 836–854. https://doi.org/10.1152/jn.1995.73.2.836

Fu, Q., Suarez, I., & Ebner, T. (1993). Neuronal specification of direction and distance during reaching movements in the superior precentral premotor area and primary motor cortex of monkeys. *Journal of Neurophysiology*, *70*(5), 2097-2116 https://doi.org/10.1152/jn.1993.70.5.2097

Harrison, X. A., Donaldson, L., Correa-Cano, M. E., Evans, J., Fisher, D. N., Goodwin, C. E. D., Robinson, B. S., Hodgson, D. J., & Inger, R. (2018). A brief introduction to mixed effects modelling and multi-model inference in ecology. *PeerJ*, *2018*(5), 1–32. https://doi.org/10.7717/peerj.4794

Hayduk-Costa, G., Drummond, N. M., & Carlsen, A. N. (2013). Anodal tDCS over SMA decreases the probability of withholding an anticipated action. *Behavioural Brain Research*, *257*, 208–214. https://doi.org/10.1016/j.bbr.2013.09.030

Holgado, D., Zandonai, T., Ciria, L. F., Zabala, M., Hopker, J., & Sanabria, D. (2019). Transcranial direct current stimulation (tDCS) over the left prefrontal cortex does not affect time-trial self-paced cycling performance: Evidence from oscillatory brain activity and power output. *PLoS ONE*, *14*(2), e0210873. https://doi.org/10.1371/journal.pone.0210873

Horvath, J. C., Forte, J. D., & Carter, O. (2015). Evidence that transcranial direct current stimulation (tDCS) generates little-to-no reliable neurophysiologic effect beyond MEP amplitude modulation in healthy human subjects: A systematic review. *Neuropsychologia*, *66*, 213–236. https://doi.org/10.1016/j.neuropsychologia.2014.11.021

Hupfeld, K. E., Ketcham, C. J., & Schneider, H. D. (2017). Transcranial direct current stimulation (tDCS) to the supplementary motor area (SMA) influences performance on motor tasks. *Experimental Brain Research*, *235*(3), 851–859. https://doi.org/10.1007/s00221-016-4848-5

Jacobs, J. V., Lou, J. S., Kraakevik, J. A., & Horak, F. B. (2009). The supplementary motor area contributes to the timing of the anticipatory postural adjustment during step initiation in participants with and without Parkinson's disease. *Neuroscience*, *164*(2), 877–885. https://doi.org/10.1016/j.neuroscience.2009.08.002

Jamil, A., Batsikadze, G., Kuo, H. I., Labruna, L., Hasan, A., Paulus, W., & Nitsche, M. A. (2017). Systematic evaluation of the impact of stimulation intensity on neuroplastic after-effects induced by transcranial direct current stimulation. *Journal of Physiology*, *595*(4), 1273–1288. https://doi.org/10.1113/JP272738

Jasper, H. (1958). The ten-twenty electrode system of the international federation. *Electroencephalography and Clinical Neurophysiology*, *10*, 371–275. http://www.ljemail.org/reference/ReferencesPapers.aspx?ReferenceID=1205676

Kuo, H.-I., Bikson, M., Datta, A., Minhas, P., Paulus, W., Kuo, M.-F., & Nitsche, M. A. (2013). Comparing cortical plasticity induced by conventional and high-definition 4 × 1 ring tDCS: A neurophysiological study. *Brain Stimulation*, *6*(4), 644–648. https://doi.org/10.1016/j.brs.2012.09.010

Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest package: Tests in linear mixed effects models. *Journal of Statistical Software*, *82*(13), 1–26. https://doi.org/10.18637/jss.v082.i13

Lee, H. K., Ahn, S. J., Shin, Y. M., Kang, N., & Cauraugh, J. H. (2019). Correction to: Does transcranial direct current stimulation improve functional locomotion in people with Parkinson's disease? A systematic review and meta-analysis. *Journal of Neuroengineering and Rehabilitation*, *16*(1), 1–13. https://doi.org/10.1186/s12984-019-0582-0

Leenus, D. J. F., Cuypers, K., Vanvlijmen, D., & Meesen, R. L. J. (2015). The effect of anodal transcranial direct current stimulation on multi-limb coordination performance. *Neuroscience*, *290*, 11–17. https://doi.org/10.1016/j.neuroscience.2014.12.053

Lenth, R. V. (2021). emmeans: Estimated marginal means, aka least-squares means. R package version 1.6.3. In *R Foundation for statistical computing*. https://cran.r-project.org/package=emmeans

Lucena, M. F. G., Teixeira, P. E. P., Pinto, C. B., & Fregni, F. (2019). Top 100 cited noninvasive neuromodulation clinical trials. *Expert Review of Medical Devices*, *16*(6), 451–466. https://doi.org/10.1080/17434440.2019.1615440

Luke, S. G. (2017). Evaluating significance in linear mixed-effects models in R. *Behavior Research Methods*, *49*(4), 1494–1502. https://doi.org/10.3758/s13428-016-0809-y

Manji, A., Amimoto, K., Matsuda, T., Wada, Y., Inaba, A., & Ko, S. (2018). Effects of transcranial direct current stimulation over the supplementary motor area body weight-supported treadmill gait training in hemiparetic patients after stroke. *Neuroscience Letters*, *662*(July 2017), 302–305. https://doi.org/10.1016/j.neulet.2017.10.049

Natick MTMI. MATLAB (2018). *MATLAB 9.6 (R2019a)*. Natick, MA, MathWorks.

Messier, J., & Kalaska, J. F. (2000). Covariation of primate dorsal premotor cell activity with direction and amplitude during a memorized-delay reaching task. *Journal of Neurophysiology*, *84*(1), 152–165. https://doi.org/10.1152/jn.2000.84.1.152

Morey, R. D. (2008). Confidence intervals from normalized data: A correction to Cousineau (2005). *Tutorial in Quantitative Methods for Psychology*, *4*(2), 61–64. https://doi.org/10.20982/tqmp.04.2.p061

Morya, E., Monte-Silva, K., Bikson, M., Esmaeilpour, Z., Biazoli, C. E., Fonseca, A., Bocci, T., Farzan, F., Chatterjee, R., Hausdorff, J. M., Da Silva Machado, D. G., Brunoni, A. R., Mezger, E., Moscaleski, L. A., Pegado, R., Sato, J. R., Caetano, M. S., Sá, K. N., Tanaka, C., … Okano, A. H. (2019). Beyond the target area: An integrative view of tDCS-induced motor cortex modulation in patients and athletes. *Journal of Neuroengineering and Rehabilitation*, *16*(1), 1–29. https://doi.org/10.1186/s12984-019-0581-1

Mosayebi Samani, M., Agboada, D., Jamil, A., Kuo, M. F., & Nitsche, M. A. (2019). Titrating the neuroplastic effects of cathodal transcranial direct current stimulation (tDCS) over the primary motor cortex. *Cortex*, *119*, 350–361. https://doi.org/10.1016/j.cortex.2019.04.016

Müri, R. M., Rösler, K. M., & Hess, C. W. (1994). Influence of transcranial magnetic stimulation on the execution of memorised sequences of saccades in man. *Experimental Brain Research*, *101*(3), 521–524. https://doi.org/10.1007/BF00227345

Patel, R., & Madhavan, S. (2019). Comparison of transcranial direct current stimulation electrode montages for the lower limb motor cortex. *Brain Sciences*, *9*(8), 1–10. https://doi.org/10.3390/brainsci9080189

Poreisz, C., Boros, K., Antal, A., & Paulus, W. (2007). Safety aspects of transcranial direct current stimulation concerning healthy subjects and patients. *Brain Research Bulletin*, *72*(4–6), 208–214. https://doi.org/10.1016/j.brainresbull.2007.01.004

Quiles, V., Ferrero, L., Iáñez, E., Ortiz, M., & Azorín, J. M. (2022). Review of tDCS configurations for stimulation of the lower-limb area of motor cortex and cerebellum. *Brain Sciences*, *12*(2), 248. https://doi.org/10.3390/brainsci12020248

R Core Team. (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing. https://www.R-project.org/

Sadler, C. M., Kami, A. T., Nantel, J., & Carlsen, A. N. (2021). Transcranial direct current stimulation of supplementary motor area improves upper limb kinematics in Parkinson's disease. *Clinical Neurophysiology*, *132*(11), 2907–2915. https://doi.org/10.1016/j.clinph.2021.06.031

Talairach, J., & Tournoux, P. (1988). *Co-Planar Stereotaxic Atlas of the Human Brain: 3-Dimensional Proportional System: An Approach to Cerebral Imaging*. New York, Thieme Medical Publishers, Inc.

Wiethoff, S., Hamada, M., & Rothwell, J. C. (2014). Variability in response to transcranial direct current stimulation of the motor cortex. *Brain Stimulation*, *7*(3), 468–475. https://doi.org/10.1016/j.brs.2014.02.003

Yeom, H. G., Kim, J. S., & Chung, C. K. (2020). Brain mechanisms in motor control during reaching movements: Transition of functional connectivity according to movement states. *Scientific Reports*, *10*(1), 1–12. https://doi.org/10.1038/s41598-020-57489-7

How to cite this article: Zandonai, T., Bertucco, M., Graziani, N., Montani, V., & Cesari, P. (2022). Transcranial direct current stimulation (tDCS) modulates motor execution in a limb reaching task. *European Journal of Neuroscience*, *56*(4), 4445–4454. https://doi.org/10.1111/ejn.15756