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Effect of transcranial direct current stimulation on cortico-muscular coherence and standing postural steadiness

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Abstract—**Non-invasive brain stimulation is a promising tool for inducing cortico-spinal excitability and facilitating motor function. The objective of this study was to investigate the effect of transcranial DC stimulation (tDCS) on cortico-spinal excitability of leg area, cortico-muscular coherence of tibialis anterior muscle, and standing postural steadiness there from. In single-blind, sham-controlled, crossover study, five healthy subjects were evaluated under two conditions – with 10min anodal tDCS and with 10min sham tDCS. Anodal tDCS induced statistically significant (P=0.001, N=20) cortico-spinal excitability, 45min and 60min after the end of tDCS as revealed by single pulse transcranial magnetic stimulation (TMS) of resting tibialis anterior muscle. Furthermore, anodal tDCS induced statistically significant (P=0.001, N=20) cortico-muscular coherence in tibialis anterior muscle during quiet standing with eyes closed, 45min and 60min after the end of tDCS. The % change in the stabilogram metrics after anodal tDCS during quiet standing with eyes closed showed that anodal tDCS strongly (P=0.0000) affected the change in centroid of CoP data-points in medio-lateral direction ($\%CoP_{ML}$) at 45min and 60min after tDCS session. Anodal tDCS had moderate effect (P=0.0113) on the change (decrease) in the path length of CoP trajectory ($\%CoP_{PL}$) at 60min after tDCS. Also, anodal tDCS had a strong (P=0.0000) effect on the change (decrease) in sway area ($\%CoP_{EA}$) at 45min and 60min after tDCS session.**

I. Introduction

Non-invasive brain stimulation (NIBS) such as transcranial direct current stimulation (tDCS) is a promising tool for inducing cortical excitability and facilitating motor function. It has been shown that NIBS can facilitate neuroplastic mechanisms [1, 2]. In the case of tDCS, the mechanism of action in improving learning is enhanced cortical excitability, which enhanced the probability of learning-related long-term potentiation (LTP)-like processes [3, 4]. Several studies have shown beneficial effect of tDCS on a set of hand functions that mimic activities of daily living in the patients with chronic stroke, and suggest that tDCS in combination with traditional rehabilitative therapy may play an adjuvant role [5, 6]. Tanaka et al. have shown that anodal tDCS transiently elevated leg pinch-force on the non-dominant side of healthy subjects during and up to 30min after the application [7]. Our overarching goal is to use tDCS for balance rehabilitation.

In this study, we focused on anodal tDCS which has already been shown to increase cortical excitability and improve motor learning and function [2, 8]. It was postulated that anodal tDCS may improve leg function and therefore enhance postural steadiness during quiet standing with eyes closed. The goal was to determine the effect of anodal tDCS on cortico-spinal excitability of the leg motor area as well as cortico-muscular coherence of tibialis anterior muscle and postural steadiness there from during quiet standing with eyes closed.

II. Methods

A. Subjects

Five healthy right-leg dominant males who were aged between 22 to 30 years volunteered for this study. All subjects gave their written informed consent for the experiments in compliance with the Helsinki Declaration. They had no known neurological disorder at the time of the study.

B. Experimental protocol

In this single-blind, sham-controlled, crossover study, the subjects were evaluated under two conditions – with 10min anodal tDCS and without anodal tDCS where sham stimulation was slowly ramped up in 15sec and down to zero in 15sec for blinding effect [7]. The study design was repeated-measure, randomized-order with sufficient 'wash-out' time in between the sessions. The muscle relaxation was ensured by providing a visual-feedback of the electromyogram (EMG) measured from the muscle belly.

A constant-current stimulator (PCM Equipments, India) delivered the currents via 3cmx3cm saline-soaked stimulating sponge electrode centered on the scalp at the position where TMS (Magstim, UK) of the motor cortex representing the non-dominant leg (i.e., left leg) elicited maximal motor evoked potential (MEP) in resting tibialis anterior muscle measured with bipolar Ag/AgCl electrode (amplifier gain=10^5). The location of the 80-mm figure-eight iron-core coil (called hot spot) was marked with washable ink pen to reduce variability in coil placement during the experiment. The saline-soaked 5cmx7cm reference sponge electrode was placed on the forehead above the contralateral orbit. During tDCS, the current was ramped up in 15sec to a steady-state of 2mA (0mA for sham stimulation) of 10min duration and then ramped down to zero in 15sec. The experiment consisted of either an anodal tDCS or a sham tDCS session each day, randomly assigned for 8 alternate days. The changes in

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cortico-spinal excitability were evaluated with MEP from resting tibialis anterior muscle with single-pulse TMS before and immediately after (Post 0) the completion of the tDCS session as well as at 15min (Post 1), 30min (Post 2), 45min (Post 3), and 60min (Post 4) after the tDCS session. The TMS intensity was set during baseline measures of each session such that the MEP was about 1mV at the hot-spot.

The postural steadiness was evaluated based on center of pressure (CoP) measurements using Wii Balance Board (Nintendo of America Inc., USA) just before and immediately after (Post 0) the completion of the anodal tDCS session as well as at 15min (Post 1), 30min (Post 2), 45min (Post 3), and 60min (Post 4) after the tDCS session. The CoP data acquisition software was developed for our purposes by Engineering Acoustics Inc., USA. During postural steadiness test, the subject was required to stand quiet for 60sec with comfortable stance width, arms by the sides, looking straight but eyes-closed while trying to reduce CoP excursions. An Ag/AgCl 10mm EEG cup electrode (Technomed, Europe) was placed at the hot-spot, held by an elastic chin-belt strapped around the head. EEG electrode impedance was kept below 5kohm by scratching the scalp and putting electrode gel in the cup electrode. A bipolar 2cm-apart EMG electrode was placed on the muscle belly of the corresponding (i.e., left leg) tibialis anterior muscle. EEG and EMG signals were amplified (OpenEEG, Olimex, Bulgaria), band-pass filtered at 1-200Hz and digitized (12-bit AD, USB-6008, National Instruments, USA) at a sampling rate of 1000Hz for offline analysis in Matlab (The Mathworks, Inc., USA).

C. *Analysis of postural steadiness data*

During each 60sec long postural steadiness test, the first ~14sec and last 10sec of the CoP, EEG, and EMG data were deleted due to possible end transients. EEG-EMG coherence was evaluated from 35 segments of 1.024sec per session for 4 sessions of either tDCS or sham. The magnitude squared coherence [9] was computed with Matlab ('mscohere' function, Signal Processing Toolbox, The Mathworks, Inc., USA) between EEG and EMG signal using Welch's averaged, modified periodogram method with a frequency resolution of 1Hz. The magnitude squared coherence is a function of frequency expressed as a real number between 0 and 1, with 1 indicating a perfect linear association at that frequency and 0 indicating a complete absence of linear association at that frequency. The coherence was considered to be significant if the theoretical threshold proposed by Rosenberg et al. [10] for the confidence limit at 95% was exceeded under the hypothesis of independence as approximated for our 35x4 observations by:

$$1-\left(1-\frac{95}{100}\right)^{\frac{1}{35\times4-1}}=0.021 \qquad (1)$$

The postural steadiness was evaluated based on stabilogram (standing balance) metrics such as mean medio-lateral CoP position (CoP_{ML}), mean anterior-posterior CoP position (CoP_{AP}), path length (CoP_{PL}) of the CoP trajectory and CoP sway area (CoP_{EA}) found from 95% confidence ellipse, were computed during each 35sec of CoP data with custom software written in Matlab (The Mathworks, Inc., USA).

Paired t-test (Matlab 'ttest' function, The Mathworks, Inc., USA) was performed for the differences in mean between tDCS and sham for the MEP-measure of cortical excitability, cortico-muscular coherence, and % change of stabilogram metrics from baseline values – $\%CoP_{EA}$, $\%CoP_{PL}$, $\%CoP_{ML}$, and $\%CoP_{AP}$ after 0min, 15min, 30min, 45min, and 60min of administrating tDCS/sham session, for all the subjects pooled together.

III. Results

The hot-spot for anodal tDCS was found roughly about 2cm posterior and 1cm lateral to the vertex for all subjects. The TMS intensity was 65.2±5% of the maximum output for all the subjects.

A. *MEP-based evaluation of cortical excitability*

The MEP measures during resting state of tibialis anterior before tDCS session (baseline), immediately after (post 0) and at 15min intervals for 60mins after that (post 1, post 2, post 3, post 4) are shown with box-plot in Figure 1a. Figure 1b shows the corresponding MEP measures for the sham sessions. The tDCS session induced statistically significant cortical excitability (t-test, P=0.001, N=20) at 45min and 60min after the tDCS session (Post 3 and Post 4 respectively) when compared to sham stimulation.

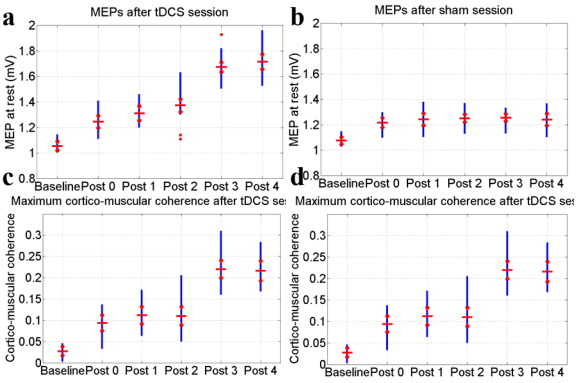

Fig. 1. a) Box-plot of MEP-based measurement of cortico-spinal excitability before tDCS session (baseline), immediately after (Post 0), and at 15min intervals after that (Post 1, Post 2, Post 3, Post 4).
b) Box-plot of MEP-based measurement of cortico-spinal excitability before sham session (baseline), immediately after (Post 0), and at 15min intervals after that (Post 1, Post 2, Post 3, Post 4).
c) Box-plot of maximum cortico-muscular coherence before tDCS session (baseline), immediately after (Post 0), and at 15min intervals after that (Post 1, Post 2, Post 3, Post 4).
d) Box-plot of maximum cortico-mucular coherence before sham session (baseline), immediately after (Post 0), and at 15mins intervals after that (Post 1, Post 2, Post 3, Post 4).

B. *Cortico-muscular coherence of tibialis anterior*

During postural steadiness test, 3 out of 5 subjects showed significant coherence (>0.021) between EEG and EMG in the frequency range of 14-30Hz before anodal tDCS and all 5 subjects showed significant coherence (>0.021) between EEG and EMG in the frequency range of 14-40Hz after tDCS. The anodal tDCS induced statistically significant (t-test, P=0.001, N=20) maximum cortical excitability (over 14-40Hz frequency range) at 45min and 60min (Post 3 and Post 4 respectively) shown in Figure 1c when compared to sham stimulation (Figure 1d).

Figure 2 shows a linear relation between the MEP-based measure of cortico-spinal excitability and corresponding maximum cortico-muscular coherence during the postural steadiness test. A linear fit (coherence=0.3*MEP (in mV)-0.29) is also shown in Figure 2.

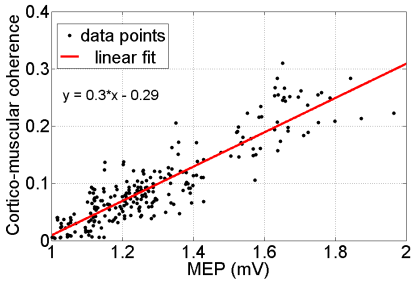

Fig. 2. MEP-measure of cortico-spinal excitability vs. corresponding maximum cortico-muscular coherence during postural steadiness test. The linear fit is shown with red-line.

C. *Stabilogram performance*

An illustrative stabilogram plot is shown in Figure 3. The centroid of the CoP cluster is towards left foot (-0.322m) in medio-lateral direction between the feet and in the front (0.233m) of the line joining the midpoint of the ankle joints. Since the MEP-measure of cortico-spinal excitability of leg area and cortico-muscular coherence of tibialis anterior muscle were statistically significant at 45min (Post 3) and 60min (Post 4) following anodal tDCS therefore the postural steadiness measures based on stabilogram metrics – CoP_{ML}, CoP_{AP}, CoP_{PL}, and CoP_{EA} – of all the subjects were pooled together for at baseline, Post 3, and Post 4 only (Table 1). The results from statistical t-test performed on the % change in the stabilogram metrics from baseline values showed that anodal tDCS strongly (P=0.0000) affected the change in centroid of CoP data-points from baseline value in medio-lateral direction ($\%CoP_{ML}$) when compared to sham session at Post 3 and Post 4. Also, anodal tDCS had a strong (P=0.0000) effect on the % change (decrease) in sway area ($\%CoP_{EA}$) from baseline values when compared to sham at Post 3 and Post 4. Anodal tDCS had only a moderate affect (P=0.0113) on the change (decrease) in the path length of CoP trajectory ($\%CoP_{PL}$) from baseline value when compared to sham at Post 4.

IV. Discussion

We showed that 2mA anodal tDCS for 10min over the cortical representation of tibialis anterior muscle induced statistically significant increase in MEP-based measure of cortico-spinal excitability and increase in cortico-muscular coherence of tibialis anterior muscle during quiet standing with eyes closed. Moreover, we showed that the cortico-muscular coherence was correlated with the MEP-measure of cortico-spinal excitability following anodal tDCS and may be used as a surrogate measure during motor task performance when TMS may be impractical.

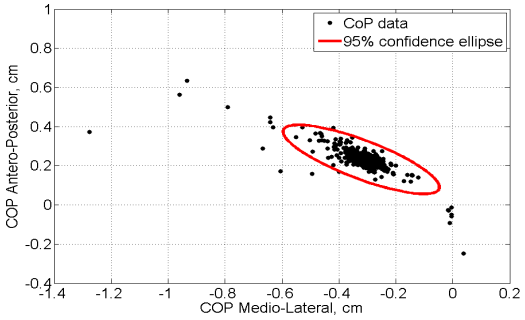

Fig. 3. An illustrative stabilogram plot showing CoP Medio-Lateral and CoP Antero-Posterior excursions and 95% confidence ellipse with CoP_{ML}, = -0.3216cm, CoP_{AP}=0.2328cm, CoP_{PL}, = 37.3cm, CoP_{EA}=0.091cm^2

TABLE I. Stabilogram metrics (mean±std.dev.): CoP_{ML}, CoP_{AP}, CoP_{EA}, and CoP_{PL} during Baseline, Post 3, and Post 4 measures

Stabilogram metric	Baseline (N=40)	Post 3 measure	
		tDCS (N=20)	sham (N=20)
CoP_ML (cm)	0.11±0.20	-0.32±0.09	0.11±0.08
CoP_AP (cm)	0.80±0.33	0.82±0.11	0.84±0.17
CoP_PL (cm)	39.09±13.32	26.38±7.13	30.38±12.13
CoP_EA (cm^2)	0.0658±0.0221	0.0421±0.0144	0.0804±0.0253
Stabilogram metric	**Baseline (N=40)**	**Post 4 measure**	
		tDCS (N=20)	**sham (N=20)**
CoP_ML (cm)	0.11±0.20	-0.24±0.10	0.07±0.07
CoP_AP (cm)	0.80±0.33	0.73±0.15	0.83±0.20
CoP_PL (cm)	39.09±13.32	22.74±5.73	30.47±13.33
CoP_EA (cm^2)	0.0658±0.0221	0.0271±0.0142	0.0636±0.0182

The postural steadiness measures during quiet standing with eyes closed provided some interesting results:

A. Anodal tDCS strongly (P=0.0000) affected the $\%CoP_{ML}$ at 45min and 60min following tDCS: The subjects were all right-leg dominant and tDCS was performed for the cortical representation of the tibialis anterior of their left leg. The tDCS increased the cortico-spinal excitability and cortico-muscular coherence of unilateral left tibialis anterior (and other left ankle muscles) and may have caused over-correction of bilateral symmetry in medio-lateral with mostly proprioceptive feedback during eyes-closed condition primarily by ankle joint actuation (ankle strategy) [11].

B. Anodal tDCS moderately (P=0.0113) affected the $\%CoP_{PL}$ at 60min following tDCS: The path length is due to sway of the CoP from its centroid which was reduced at 45min and 60min following tDCS when compared to sham. Winter et al. explained the sway during quiet standing with an ankle muscle stiffness model where the muscle stiffness

is controlled by muscle tone, which is the summation of recruited muscle twitches in the ankle muscles. [12]. Therefore it was hypothesized that tDCS-induced increase in cortico-spinal excitability and cortico-muscular coherence in left tibialis anterior (and may be other left ankle muscles) reduced the sway by increasing muscle tone and consequently muscle stiffness.

C. Anodal tDCS session strongly (P=0.0000) affected the %CoP_{EA} at 45min and 60min following tDCS: The 95% confidence ellipse area for CoP deviations (CoP_{EA}) from its centroid depended on the magnitude of sway. It was hypothesized based on an ankle muscle stiffness model [12] that tDCS-induced increase in cortico-spinal excitability and cortico-muscular coherence in left tibialis anterior (and may be other left ankle muscles also) reduced the sway by increasing muscle tone and consequently muscle stiffness.

It was interesting that although the CoP_{EA} decreased statistically significantly (P=0.0000) from following tDCS but CoP_{PL} did not decrease that significantly (P=0.0113). This was found to be due to an increase in the frequency of sway while the sway was bounded by a smaller area (confidence ellipse), as postulated in prior work as well [13]. Gatev et al. [14] suggested an integrated central (feedforward) and reflexive (feedback) control of ankle joint stiffness where sway is a necessary exploratory behavior and feedforward setting of muscle stiffness can avoid the lags in feedback loop. Therefore in an integrative model, the sway size may be reduced by ways other than reflexively increasing ankle impedance, stiffness or viscosity. For example, Loram and Lackie showed a minimization of sway size caused by an improvement in the accuracy of the anticipatory torque impulses [15]. We postulate that tDCS-induced cortico-spinal excitability and increase in cortico-muscular coherence improved the accuracy of feedforward torque impulses.

The role of feedback cannot be completely discounted as changes in reflex excitability with respect to postural sway during standing have also been shown [16]. Roche et al. have shown an increase of disynaptic inhibition at spinal level (reflex pathways) during anodal tDCS which relied on an increase of disynaptic interneuron excitability [17]. After the submission of our manuscript, Roche et al. showed that anodal tDCS induced effects on spinal network excitability similar to those observed during co-contraction [16]. This supported our hypothesis based on ankle muscle stiffness model that anodal tDCS activated descending corticospinal projections mainly increasing ankle joint stiffness. Therefore not only at the cortical level but anodal tDCS also induced effects on spinal network excitability which will have far-reaching applications in movement rehabilitation.

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