Effects of noninvasive anodal transspinal direct current stimulation of the cervical segments on motor learning in healthy subjects

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***Abstract*—The aim of this study was to estimate the effect of noninvasive anodal transpinal spinal direct current stimulation (a-tsDCS) at the C7-Th1 level of the spinal cord (C7-Th1) on the corticospinal system and on the modulation of motor skills. The effect of tsDCS was assessed using motor-evoked potentials (MEP) from transcranial magnetic stimulation (TMS) in the primary motor cortex (M1). The study was done on 54 healthy subjects aged 22+/-4 years. Our results showed that the application of 11-minute a-tsDCS at the cervical spinal cord level with a current of 1.5 mA had no effect on the improvement in manual dexterity in the 9-HPT test and had no effect on visual-motor association learning in the SRT test. Moreover, the factor of motor learning during stimulation does not affect the MEP from TMS. Overall, these results point to the need to develop further protocols for the effects of tsDCS on upper limb motor skills.**

Keywords—non-invasive brain stimulation, transspinal stimulation, TMS, motor skills

I. Introduction

Hand movement is an important aspect of daily life and can be disturbed in neurological disorders in which the function of the cortical and corticospinal neuronal circuits is significantly involved [1]. A potential method of rehabilitation is tsDCS, which is a non-invasive method of moderating the activity of the spinal cord and different descending and ascending neuronal systems. However, at the moment there is no clear understanding of the effects of this stimulation [2].

It is proposed that tsDCS modulates the excitability of the corticospinal system (CSS), the main system that regulates motor functions. The corticospinal tract (CST), is the pathway by which the brain controls voluntary movements of the limbs and precise movements of the fingers and hands. CSS excitability can be examined by measuring motor evoked potentials that can be elicited in target muscles by applying single-pulse TMS over the primary motor cortex (M1) muscles representation. MEP amplitude provides time-accurate and muscle-specific determination of corticospinal excitability circuits in the cortex and spinal cord [3],[4].

Published studies demonstrate that cervical tsDCS leads to an increase in MEP amplitude and its effect persists for up to 2 hours after cessation of stimulation, reflecting in CSS excitability [5]. Since tsDCS influences CSS excitability, it can be assumed that tsDCS will affect motor skill production, but this effect is not well understood. According to a recent study, a-tsDCS improves motor unit recruitment [6], improved the effect of a training session on locomotor learning, and also

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resulted in greater retention of learning compared to imitation [7].

In the upper extremities, tsDCS of the cervical spinal cord combined with vigorous exercise restored upper extremity function in people with complete and incomplete motor spinal cord injury [8].

In this study we estimated the effect of a-tsDCS (C7-Th1) of the spinal cord on the new motor skills development of the upper extremities in healthy people. Also, the contribution of the motor learning component in the TMD elicited MEP amplitude was assessed.

II. MATERIALS AND METHODS

A. Subjects

The study involved 54 healthy adults aged 22+/-4 years.

B. Experiment design

The experiment was carried out in two stages: 24 healthy adults were involved at the first stage, all subjects were divided into 2 groups, for the first group, the a-tsDCS protocol was applied, the stimulating electrode was located above the C7-Th1 segment, and the discharge electrode was on the clavicle. Stimulation parameters: 1.5 mA for 11 minutes, the second group was subjected to sham tsDCS. MEP were recorded from TMS at three time intervals before stimulation, immediately after tsDCS, and 15 minutes after tsDCS.

Other 30 healthy adults were involved at the second stage, all subjects were also divided into 2 groups (stimulation and sham), received similar stimulation with the first group, but during the 11-minute tsDCS session, the subjects performed motor tests such as the criterion for assessing manual dexterity: a test with 9 holes (9- HPT) and the Serial Reaction Time (SRT) task. They also registered MEP from TMS in three time intervals similar to the first stage.

C. Parameters of TMS

Magnetic brain stimulation was performed using a MagPro X100 MagVenture transcranial magnetic stimulator; stimulation was navigated using the Localite TMS Navigator system. An AxilumRobotics TMS-Cobot was used to control the positioning, orientation, and contact of the TMS coil with the subject's head under the control of an optical tracking system. This system allows guaranteed (error less than 0.1 mm) to stimulate one and the same point in the brain. TMS focused over the left field of M1 is performed using a C-B60 figure-of-eight coil. To generate the MEP, TMS was used in the “hot spot” of the first dorsal interosseous (FDI) muscle in M1 with single impulses with an intensity of 115% of the resting motor threshold.

D. Parameters of tsDCS

tsDCS is performed using the system for non-invasive electrical brain stimulation BrainStim. Stimulation parameters: current value - maximum 1.5 mA per electrode, voltage up to 15V. During the session, the anode electrode was placed at the level of the cervical spine (segmenta cervicalia C7, which is determined by palpation, in combination with anatomical landmarks). The cathode electrode is placed on the right clavicle. We used two electrodes with an area of 5 × 5 cm, an anode electrode and 5 × 10 cm cathode. Before mounting the electrodes, a gel is applied for better electrical conductivity.

The electromyogram is registered with the help of an additional BrainAmp EXG block. Surface electromyography (EMG) was recorded from the right FDI muscles.

E. Data Analysis

Peak-to-peak amplitudes were calculated for TMS-induced FDI muscle MEP responses and were analyzed offline using custom code written in MATLAB (version R2020a, The Mathworks Inc., Natick, MA, USA). Each phase of the study (before tsDCS, immediately after tsDCS, and after 15 minutes) contained twenty MEP responses that were averaged. MEP amplitudes after stimulation and 15 minutes later were then normalized as a ratio to the mean MEP amplitude before tsDCS.

F. Statistical Analysis

The dynamics of the performance in both motor tests was evaluated by linear mixed-effect models. In particular, factor Group (df = 1, either Stimulation or Sham) and factor Day (df = 1, either first session or second session) were used as fixed effects, whereas participant’s ID was used as a random intercept effect. Performance of the Stimulation group during the experimental session of the first day was used as a baseline condition for the model. Main effects of the model were assessed by ANOVA. Approximations of degrees of freedom for fixed effects were obtained by means of Satterthwaite approximation using lmerTest package [9] following recommendation by [10].

The difference in MEP modulation in the experimental session with and without training was evaluated by a linear mixed-effect model, as well. In this case, factor Group (df = 1, either Stimulation or Sham), factor Training (df =1, either ‘Yes’ or ‘No’) and factor Time (df = 2, recordings performed either before tsDCS (Tbefore), immediately after tsDCS (T0), or 15 min After tsDCS(T15)) were used as fixed effects, whereas participant’s ID was used as a random intercept effect. Within the model, we compared the significance of interaction coefficients, using MEP amplitudes recorded before the tsDCS session (Tbefore) as a baseline condition. The resulting p-values were corrected with respect to the false discovery rate (FDR) according to Benjamini and Hochberg adjustment [11].

III. RESULTS

TABLE I. MAIN EFFECTS OF THE STATISTICAL MODELING FOR THE PARTICIPANT’S PERFORMANCE IN GPT TEST

	Sum Sq	df (n)	df (d)	F value	Pr(>F)
Day	22.37	1	30.44	8.55	.006
Group	1.08	1	48.34	0.41	.523

Day x Group	4.42	1	30.44	1.69	.204

df(n) - degrees of freedom (nominator); df (d) - degrees of freedom (denominator).

TABLE II. MAIN EFFECTS OF THE STATISTICAL MODELING FOR THE PARTICIPANT'S PERFORMANCE IN SRT TEST

	Sum Sq	df (n)	df (d)	F value	Pr(>F)
Day	43818.27	1	20.62	22.71	<.001
Group	4938.324	1	45.05	2.56	.117
Day x Group	1003.395	1	20.62	0.52	.479

df(n) - degrees of freedom (nominator); df (d) - degrees of freedom (denominator).

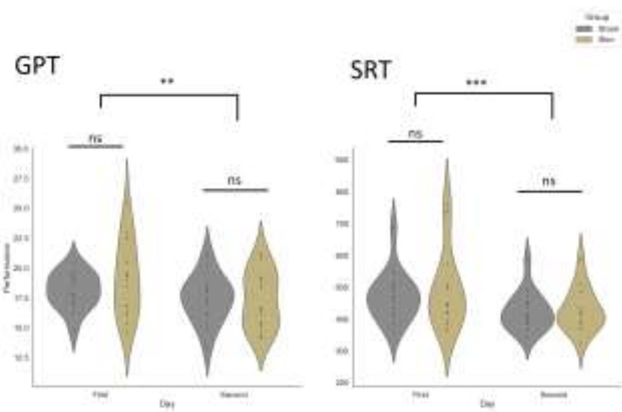

Fig. 1. Performance of participants in both GPT (left panel) and SRT (left panel tests). **p<.01; ***p<.001

The linear mixed model fit of the MEP amplitudes recorded before (Tbefore), immediately after (T0), and with 15 minutes delay after the stimulation or sham session (T15) was performed by restricted maximum likelihood (REML criterion at convergence = 49613.65). Importantly, the model did not reveal the significance of the slope interaction coefficients between factors Training and Time neither for the Stimulation group at the level T0 (β = 47.58, SE = 76.17, df = 3078.04, t = 0.62, p = .53) and at the level T15 (β = -86.87, SE = 78.20, df = 3081.44, t = -1.11, p = .78), nor for Sham group at the level T0 (-56.16, SE = 83.92, df = 3078.03, t = -0.70, p = .99) and at the level T15 (β = 207.97, SE = 83.92, df = 3078.03, t = 2.47, p = .053). Accordingly, we demonstrated that the dynamics of MEP amplitudes does not differ between sessions with and without motor training.

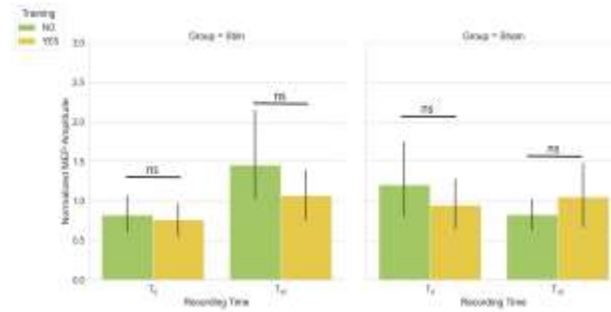

Fig. 2. MEP amplitudes recorded immediately after (T0), and with 15 minutes delay after the stimulation session (T15) normalized by MEP amplitudes recorded before stimulation. The results are provided separately for participants receiving (yellow) and not receiving (green) motor training. Left panel: anodal tsDCS; right panel: sham stimulation.

IV. DISCUSSION

In this randomized, sham-controlled study, we tried to determine whether a-tsDCS (C7-Th1) spinal cord level has an effect on the acquisition of new motor skills in healthy individuals. We also tried to determine whether the MEP changes when there is a factor in learning new motor skills during tsDCS. Our study showed that a-tsDCS (C7-Th1) for 11 minutes at 1.5 mA does not affect the development of new motor skills in healthy people, learning occurs similar to sham. An individual's ability to coordinate fingers and manipulate objects effectively (dexterity score) on the 9-hole test (9-HPT), as well as learning to correlate between visual cue position and desired response on the Serial Reaction Time Test (SRT) to stimulation, did not differ from sham. We also determined that the motor learning factor during stimulation did not affect the change in MEP. Linear mixed model analysis showed that MEP amplitude did not change with motor training during tsDCS in either the simulation group or the placebo group. This suggests that the motor learning factor during tsDCS does not cause additional changes in the excitability of the CSS.

The results of Siobhan K. Donges showed [12] that the effects of real and sham DS stimulation did not differ for motor evoked potentials or cervicomedullary motor evoked potentials for any muscle.

However, it has been previously demonstrated that tsDCS leads to modulation of CSS excitability. In our previous studies, we have shown that tsDCS at the level of the cervical enlargement of the spinal cord can cause a change in the amplitude of MEP compared to the amplitude induced by placebo stimulation [13], similar results were obtained in some other studies [5],[14]. A study by Oluvole O. Avosika et. al demonstrated that tsDCS improved the acquisition and retention of motor skills in healthy subjects and prolonged the exercise-mediated decline in excitability of the alpha motor neuron pool. As in the animal study [15] with C4 spinal cord injury has been shown to improve locomotion and forepaw manipulation in animals stimulated with tsDCS significantly enhanced motor cortex-induced responses after injury.

This study showed no improvement in motor skills control in healthy subjects with a-tsDCS (C7-Th1) for 11 minutes at 1.5 mA, possibly due to mounting and parameterization. It has previously been shown that changing the montage [14],[16] polarity, intensity, duration, concomitant treatment or task can qualitatively change the results of stimulation. Examining the effect of cervical tsDCS on motor skill development requires further study.

Based on this, we made an assumption: the mechanisms underlying plastic changes in the spinal cord caused by tsDCS are not ambiguous and very mosaic. It can be assumed that they are related to the fact that tsDCS can affect the conduction properties of the corticospinal system, as well as the activity of neurons in the ascending and descending spinal tracts, modulating excitability in their cortical targets, including motor areas, as evidenced by changes in the resting motor threshold.

V. Conclusion

1) Application of a-tsDCS at the level of the upper spinal cord segments (C7-Th1) for 11 minutes at 1.5 mA does not affect the development of new motor skills in healthy people in the 9-hole manual dexterity tests (9-HPT) and Sequential Reaction Time Test (SRT).

2) The factor of motor learning during tsDCS on the cervical region does not affect the change in the MEP.

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