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SHORT COMMUNICATION

Duration but not intensity influences transcranial direct current stimulation (tDCS) after-effects on cortical excitability

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Summary Recent studies have shown heterogeneous results regarding the influence of intensity and duration of motor transcranial direct current stimulation (tDCS) on cortical excitability. In this pilot crossover study including 14 healthy participants, we compared the effects of a single session of anodal-tDCS set with two commonly used durations (20 and 30 minutes) and intensities (1 and 2 mA) on short-interval intracortical inhibition (SICI) and intracortical facilitation (ICF). Regardless of the current intensity, 20 minutes of tDCS increased SICI (3 ms inter-stimulus interval ISI) and decreased ICF (7 ms ISI); 30 minutes of tDCS did not affect cortical excitability.

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Introduction

Transcranial direct current stimulation (tDCS) consists in delivering a weak direct current between two electrodes placed over the scalp of a subject in order to modulate cortical excitability. Depending on the polarity of the electrodes, differential effects of tDCS have been described: anodal-tDCS applied over the motor cortex increases cortical excitability whereas cathodal-tDCS decreases it [17]. Apart from the polarity of the electrode, several parameters should be taken into account to explain tDCS after-effects on motor cortical excitability. Among them, current intensity, stimulation duration, current density, electrode size and electrode montage have been evaluated in numerous studies, leading to somewhat controversial results [4,8,13,17,20]. For instance, some studies reported that longer duration and higher intensities of anodal-tDCS over the motor cortex led to higher tDCS after-effects on cortical excitability [14,15]. Conversely, some recent studies indicated that intensity did not differentially affect cortical excitability [6,10] and some other studies reported no effect of tDCS on motor cortical excitability whatever the stimulation condition (anodal, cathodal, sham) [8] or parameters [19]. However, if stimulation intensity does affect cortical excitability, this might show a non-linear effect [3]. In clinical populations, while the majority of studies have used a 20-minute tDCS duration, some studies have started to use longer durations (e.g., 30 minutes [12]). However, physiological effects of such stimulation parameters on cortical excitability are still unclear.

In this pilot study, we aimed to compare the effects of two durations (20 and 30 minutes) and two intensities (1 and 2 mA) of anodal-tDCS on motor cortical excitability. To measure cortical excitability, we used paired pulse transcranial magnetic stimulation (TMS) protocols evaluating short-interval intracortical inhibition (SICI) and intracortical facilitation (ICF).

Methods

Fourteen healthy volunteers (three males, 11 females, two left-handed, one ambidextrous) aged between 21 and 35 years (mean = 27.5 ± standard deviation = 4.6) were recruited. tDCS was delivered using a commercial NeuroConn DC-stimulator (GmbH, Germany) with two electrodes (35 cm^2) covered by saline-soaked sponges and fixed with rubber bands. tDCS was applied with two different current intensities: 1 mA, 2 mA, and two different durations: 20 minutes, and 30 minutes with 15 sec fade-in and fade-out periods. The anode was positioned over the left primary motor cortex (over the TMS motor hotspot) and the cathode over the right supraorbital region. In a crossover design, each participant underwent four sessions of tDCS separated by at least 5 days to avoid carry-over effects.

SICI and ICF were assessed at baseline and after the end of the tDCS session using a standardized paired-pulse TMS protocol. TMS was delivered using a monophasic Magstim Bistim^2 stimulator (MagStim Co Ltd, UK) with a figure-of-eight coil. The location of the motor cortex was determined as the site that produced the largest and most stable single motor evoked potential (MEP) at moderately suprathreshold stimulation intensities. The conditioning stimulus was set at 80% of the resting motor threshold intensity (RMT; defined as the percentage of maximum of stimulator output to produce MEP amplitudes of at least 50 μV in five out of ten consecutive trials) and the test stimulus at an intensity necessary to evoke ~1 mV MEP in the relaxed right first dorsal interosseous muscle. The intensities of the conditioning and test stimuli were not adjusted after tDCS. Inter-stimulus intervals (ISIs) between the pairs of stimuli were 2 and 3 ms for SICI and 7, 9 and 12 ms for ICF. In total, 65 randomized stimuli were applied, with 15 stimuli using the test stimulus alone and 10 stimuli for each ISI. The MEP amplitudes evoked by paired-pulse stimulation were expressed as a ratio to the MEP amplitude of the test stimulus for each ISI. Statistical analyses were performed using SPSS (version 22). Three-way repeated measures ANOVAs were performed separately for each ISI to assess the effects of three independent variables on MEP amplitude: tDCS duration with two levels (20 and 30 minutes), tDCS intensity with two levels (1 and 2 mA) and time with two levels (pre tDCS, post tDCS). In case of significance, post-hoc comparisons were performed. Significance level was set at $P < .05$.

Results

Significant differences were found only for the ISI of 3 ms (SICI) and 7 ms (ICF). No significant effects of tDCS were observed for 2, 9 and 12 ms ISI.

For 3ms ISI, no main effects of duration, intensity and time were reported on MEP amplitude. The three-way interaction among duration, intensity and time was not significant, nor were the interactions between intensity and time and duration and intensity. However, there was an interaction between duration and time, $F(1, 13) = 4.795$; $P = .047$; partial $\eta^2 = .269$. Post-hoc tests demonstrated that, regardless of the intensity, MEP amplitude was significantly lower after the 20-minute duration tDCS (0.426 ± 0.104) than at baseline (0.626 ± 0.119; $P = .031$). However, no difference was reported between baseline (0.471 ± 0.119) and post tDCS (0.474 ± 0.127) for the 30-minute duration ($P = .963$; Fig. 1).

For 7 ms ISI, no main effects of duration, intensity and time were reported on MEP amplitude. The three-way interaction between duration, intensity and time was not significant, nor were the interactions between intensity and time and duration and intensity. However, there was an interaction between duration and time, $F(1, 13) = 5.432$; $P = .037$; partial $\eta^2 = .295$. Post-hoc tests demonstrated that, regardless of the intensity, MEP amplitude was significantly lower after the 20-minute duration tDCS (1.284 ± 0.156) than at baseline (1.551 ± 0.176; $P = .033$). However, there was no difference between baseline (1.348 ± 0.129) and post tDCS (1.428 ± 0.150) for the 30-minute duration ($P = .569$, Fig. 1).

Discussion

In this study, we showed that anodal-tDCS duration but not intensity had a significant effect on cortical excitability. Namely, 20 minutes of anodal-tDCS significantly increased SICI (measured by a 3 ms ISI) and decreased ICF (measured

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