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Reduced Current Spread by Concentric Electrodes in Transcranial Electrical Stimulation (tES)

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ABSTRACT

Objective: We propose the use of a new montage for transcranial direct current stimulation (tDCS), called concentric electrodes tDCS (CE-tDCS), involving two concentric round electrodes that may improve stimulation focality.
Methods: To test efficacy and focality of CE-tDCS, we modelled the current distribution and tested physiological effects on cortical excitability. Motor evoked potentials (MEPs) from first dorsal interosseous (FDI) and abductor digiti minimi (ADM) were recorded before and after the delivery of anodal, cathodal and sham stimulation on the FDI hotspot for 10 minutes.
Results: MEP amplitude of FDI increased after anodal-tDCS and decreased after cathodal-tDCS, supporting the efficacy of CE-tDCS in modulating cortical excitability. Moreover, modelled current distribution and no significant effects of stimulation on MEP amplitude of ADM suggest high focality of CE-tDCS.
Conclusions: CE-tDCS may allow a better control of current distribution and may represent a novel tool for applying tDCS and other transcranial current stimulation approaches.

Introduction

Transcranial electrical stimulation (tES) is a non-invasive technique with great potential in basic and clinical research, for understanding the neural substrates of cognition and as a co-adjuvant in treating brain dysfunctions. The most used tES is transcranial direct current stimulation (tDCS), in which low intensity direct current is applied to modulate cortical excitability, acting on polarization of neurons [1–4].

A well known limitation of tDCS, as commonly employed, is its poor stimulation focality [5]. The application of two electrodes, one over the target area ("target" electrode) and one over a distant site (return electrode), induces spreads of current over an extensive portion of the brain affecting not only the area under both electrodes but also the areas between them [6]. The cortical area where the electric field is maximum depends on the location and distance of the two electrodes, and may not be directly under the active electrode [7,8]. Additionally, the position of the return electrode determines the direction of the current [9], which ultimately determines the physiological effects of the stimulation.

The lack of focality and the stimulation of the cortex under the return electrode associated with the standard bipolar montage was first addressed by using a smaller target electrode or/and a larger reference electrode [10]. More recently, a new type of montage was proposed, called high-definition tDCS (HD-tDCS), in which the active electrode is surrounded by several return electrodes. HD-tDCS is very promising because it may deliver a more focal stimulation and avoid the spreading of current over unwanted areas, as suggested by a modelling study [5] and an experimental study with suprathreshold transcranial electric stimulation [11]. However, there is still little direct evidence that modulation of excitability can be obtained with HD-tDCS [12,13]. In addition HD-tDCS requires the use of a dedicated adaptor (e.g., Soterix Medical, USA) or multichannel tDCS device (e.g., Starstim, Neuroelectrics, Spain) to distribute the current equally among the return electrodes.

Here, we have implemented an alternative version of the HD-tDCS montage by using two concentric electrodes (CE-tDCS) that can be used with a standard tDCS device, and tested its focality and efficacy on cortical excitability.

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Methods and materials

Subjects

Fifteen right-handed healthy volunteers (8 females, aged 19–32 years) participated in the study, after giving written informed consent. They reported no history of neurological or psychiatric disorders or any contraindication for non-invasive brain stimulation [14]. The study was approved by the Ethics Committee of IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy. The protocol was carried out in accordance with the approved guidelines and with the ethical standards of the Declaration of Helsinki.

Procedure

Three testing sessions, in which either anodal (A-tDCS), cathodal (C-tDCS) or sham-tDCS was applied, were conducted at least 2 days apart and counterbalanced across participants. Motor evoked potentials (MEPs) from the right first dorsal interosseous (FDI) and from the right abductor digiti minimi (ADM) were recorded before and after the application of tDCS over the contralateral primary motor cortex (M1) representation (hotspot) of the FDI, while participants were comfortably seated on an armchair in dim light.

tDCS was delivered at 1 mA for 10 min (10 s ramp up/ramp down) by a battery-driven DC stimulator (BrainStim, EMS, Italy). In the sham-tDCS the current was ramped up and down at the beginning and at the end of the session. Current was applied through two concentric electrodes as shown in Fig. 1A and 1B (target electrode: central round electrode, radius = 1.0 cm, area = 3.14 cm^2; return electrode: outer ring electrode, inner radius = 3.5 cm, outer radius = 4.0 cm, area = 11.78 cm^2). Electrodes were made of conductive rubber, installed in a non-conductive silicon casing, flexible enough to adapt the electrodes to the scalp and ensure the correct position of the return electrode relative to the target electrode. First we filled the electrode cage with an electroconductive gel (Elektrogel, Italy), then positioned the electrodes, with the target electrode over the FDI hotspot, and finally we fastened the electrodes with a tubular net-shaped elastic bandage in mesh tissue, making sure that the it did not push the electrode forward or backward. This procedure was aimed at reducing contact impedance and at creating a uniform adherence between the whole surface of the electrodes and the scalp, avoiding uneven distribution of the current [15].

MEPs were collected by applying twenty single transcranial magnetic stimulation (TMS) pulses (every 4–8 s) over FDI and twenty single TMS pulses over ADM, before and after tDCS. TMS intensity was kept constant to obtain a baseline peak-to-peak MEPs of about 1 mV in the FDI (mean TMS intensity: 59.1% MSO). The position of the coil (70 mm Figure-of-Eight, Magstim, UK) was controlled through a neuronavigation system (SofTaxic Optic, EMS, Italy). Electromyography (EMG) was recorded from the right FDI and ADM muscles through a belly-tendon montage, with a band-pass filter at 0.1–1000 Hz and digitized at a sampling rate of 5000 Hz (BrainAmp, Brain Products GmbH, Germany).

At the end of each session, the subjects were asked to complete a questionnaire and give a score from 0 = none to 4 = strong to rate their skin sensations during the stimulation [15].

Analysis and statistics

Epochs were baseline corrected to the 100 ms before the TMS pulse, filtered with a low cutoff at 10 Hz and a notch filter at 50 Hz. Epochs containing muscle artefacts and MEP responses smaller than 50 μV were discarded.

To test the effects of stimulation on both muscles, a repeated measure MANOVA was run on MEP amplitude with factors stimulation (A-tDCS, C-tDCS and sham-tDCS) and time (pre-TMS and post-TMS) as within-subject factors, and with FDI and ADM as dependent variables. Significant effects were followed up with separate univariate ANOVAs for each muscle and with post-hoc comparisons using Fisher's least significant difference method. The Kolmogorov–Smirnov test was applied to assess for normal distribution of variables. The Greenhouse–Geisser correction was used when appropriate.

We analyzed skin sensations given by the stimulations by comparing discomfort for each stimulation condition, i.e., the global sensation score obtained from the questionnaires (max score = 28), with a generalized linear model with Poisson distribution, which is suitable for discrete dependent variables.

Electric field modelling

The electric field produced by a CE-tDCS montage was first investigated by Datta et al. [7] using a spherical head model. Here, we calculated the electric field produced by the CE-tDCS used in our experiment in a realistic head model. This model was obtained by segmenting MR images (*Colin27* single-subject template available at BrainWeb, http://brainweb.bic.mni.mcgill.ca/brainweb) into five tissues: scalp, skull, cerebral spinal fluid (including the lateral ventricles), white matter and grey matter, as described elsewhere [16]. The hand knob was identified [16] and the central electrode was placed radially over the center of the FDI representation on the cortex, assumed to lie on the lateral part of the hand knob, as shown in Fig. 1. The center of the ADM representation was assumed to lie in the mesial part of the hand knob. Regions of interest (ROIs) with 1 cm radius were defined around the centers of the FDI and ADM representations to calculate average electric field values on the cortical surface.

Results and discussion

The distribution of the magnitude of the electric field on the cortical surface of our realistic head model is shown in Fig. 1C, and was similar to that induced by HD-tDCS [6]. The maximum magnitude was 0.25 V/m whereas average magnitudes in the FDI and ADM ROIs were 0.10 V/m and 0.08 V/m, respectively. The distribution of the normal component is shown in Fig. 1D; average values in the aforementioned ROIs were 0.06 V/m and 0.01 V/m, respectively. The average values of the tangential component were 0.06 V/m in both ROIs. The standard montage (two 35 cm^2 electrodes) induced higher average values for the magnitude of the E-field in both ROIs: 0.13/0.12 V/m for the FDI/ADM ROIs. The same trend was observed for the normal component of the field: 0.08/0.07 V/m for the FDI/ADM. The similar values in both ROIs indicate that the standard montage is less focal than both the CE- and HD-tDCS montages.

We have found that MEP amplitude was significantly dependent on the interaction between time and stimulation [$F(4, 11) = 4.22$, $p = 0.026$; Wilk's $\Lambda = 0.39$]. We run follow-up ANOVAs to test on which muscle the effect was stronger. Interestingly, these analyses revealed that the interaction between time and stimulation was significant only for the FDI muscle and it was not significant for the ADM muscle. For FDI, we found increased MEPs after A-tDCS and decreased MEPs after C-tDCS, and no significant changes after sham-tDCS [interaction stimulation × time: $F(2,28) = 5.67$, $p = 0.009$; all post-hoc tests comparing MEPs in post-TMS across stimulations $p < 0.05$]. Baseline MEP amplitudes and TMS intensities did not differ between stimulation conditions ($p > 0.05$). In other words we replicated the effects of tDCS that have been found with conventional montages (Fig. 2A).

For ADM, we found no significant effects of time by stimulation interaction on the cortical excitability [stimulation by time

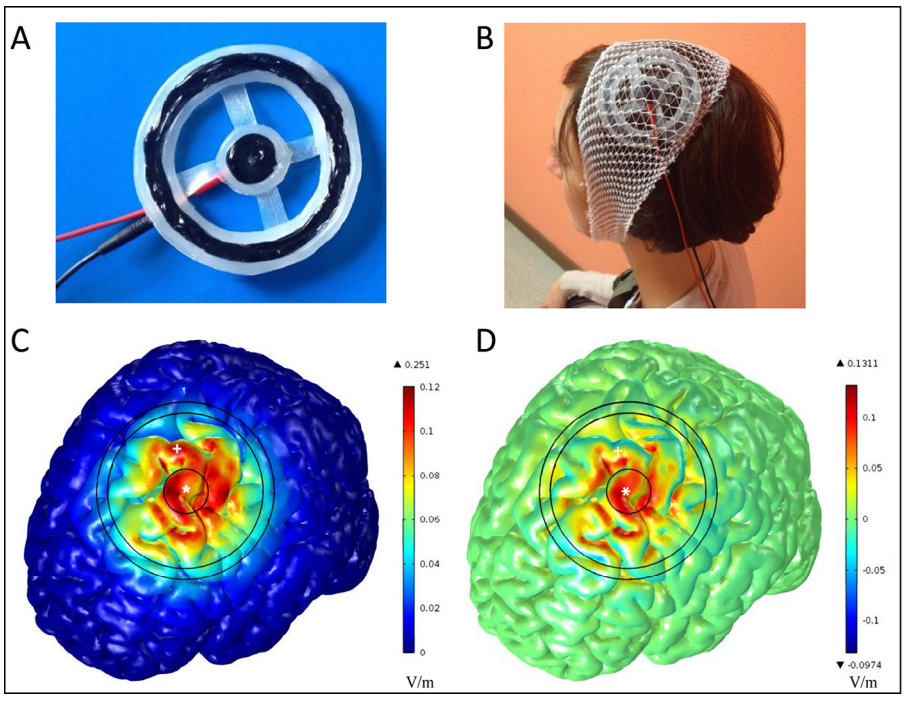

Figure 1. (A) Overview of the concentric electrodes (CE-tDCS) configuration. (B) Picture shows a representative subject with the CE-tDCS montage. The distribution of the electric field magnitude (C) and of its normal component (D) on the cortical surface. The positions of the centers of the first dorsal interosseous (FDI) representation, in the lateral part of the hand knob, and abductor digiti minimi (ADM) representation, in the mesial part of the hand knob, are indicated by the symbols * and +, respectively. The normal component flows into the cortex under the anode (red).

interaction $F(28,2) = 2.40$, $p = 0.11$], supporting the focal distribution of currents resulting from modelling the electric field. Although the choice of ADM as a control muscle has some limitation due to the possible different excitability compared to FDI, ADM has shown consistent modulation to tDCS [10], as reported in the first pioneer study on tDCS [17]. In our experiment, the lower amplitude of MEPs from ADM may raise the concern whether effects of tDCS on ADM could be revealed at this TMS intensity. However, a recent paper has shown that low amplitude MEPs may be optimal to reveal excitatory effects of plasticity-inducing protocols, whereas may be suboptimal to reveal inhibitory effects [18]. Nevertheless, we found no excitatory effects of A-tDCS on ADM. Therefore, these data support that CE-tDCS may induce focal distribution of currents.

When looking at MEPs recorded from the ADM, we only found a significant main effect of time [$F(1,14) = 5.16$, $p < 0.05$], revealing that MEPs decreased during the experimental session regardless of the stimulation (Fig. 2B). The mechanism underneath such decrease is unclear. Surround inhibition is a known mechanism within

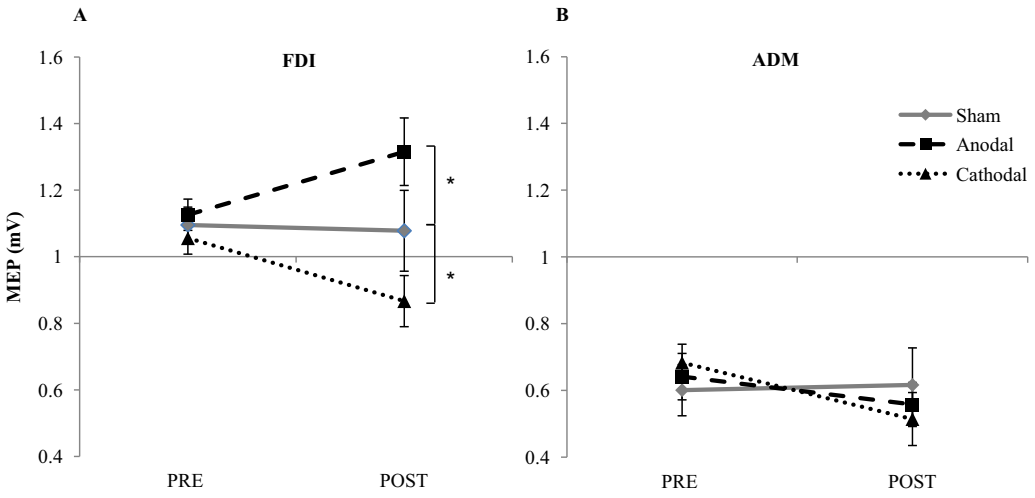

Figure 2. Motor evoked potential (MEP) magnitudes pre and post anodal-, cathodal- and sham-transcranial direct current stimulation. CE-tDCS was applied at 1 mA for 10 min. Error bars depict standard error and asterisks depict $p < 0.05$. (A) Mean and standard error for MEPs from the right first dorsal interosseous (FDI), in μV: Pre-sham: 1095 ± 54; pre-AtDCS: 1126 ± 47; pre-CtDCS: 1056 ± 48; post-sham: 1077 ± 121; post-AtDCS: 1315 ± 101; post-CtDCS: 867 ± 77. (B) Mean and standard error for MEPs from the right abductor digiti minimi (ADM), in μV: pre-sham: 600 ± 77; pre-AtDCS: 641 ± 70; pre-CtDCS: 682 ± 55; post-sham: 616 ± 111; post-AtDCS: 558 ± 66; post-CtDCS: 514 ± 80.

the motor system [19], in which neural signals to a central receptive field or target are facilitatory and eccentric signals are inhibitory. However, it is not a likely explanation because it would predict a decrease of ADM MEPs only in the A-tDCS condition. Differently, the decrease of ADM MEPs becomes apparent only as an overall effect when all stimulation conditions are considered. Therefore an alternative explanation may be a subtle decrease in arousal during the experiment.

The effects on FDI and conversely the lack of effects on ADM show that the effective electric field was mainly restricted to the area under the central electrode and did not substantially spread to the surrounding cortical regions. Together with the modelling results, these data suggest that the normal component of the electric field on the gyrus may be the effective one [20], because it is the only one that has considerably different values in the two ROIs. These data also confirm that the use of a small target electrode [8,10] can increase stimulation focality compared with standard montages employing bigger electrodes [21,22].

Despite the high current density of the central electrode and shunting, as shown in the model of the current distribution, the skin sensations reported by participants were relatively low (sham-tDCS: 2.29 ± 1.50; A-tDCS: 2.67 ± 2.47; C-tDCS: 2.33 ± 2.18). Importantly, participants were not able to distinguish between stimulations because of the itching sensations felt below the tDCS electrodes [Wald chi-square (d.f. 2) = 0.33, $p = 0.85$] [15].

It should be noted that the size of the MEP changes both for A-tDCS and C-tDCS (17% and 18% of baseline respectively) may be smaller than the ones reported with conventional montages [23,24], although extended measurement of the after-effects of CE-tDCS and a direct comparison of the data with conventional montages are needed for this conclusion. Smaller MEP changes may be due to the decreased average E-field in the target region compared to the conventional montage, due to greater shunting caused by the electrodes' proximity.

These data suggest that CE-tDCS leads to an effective and focal modulation of neural activity by limiting the current spread on the cortex. This ensures a better control during the stimulation in terms of current direction under the active electrode that, besides stimulation of a single area, may be of particular interest when stimulating two sites and when applying in phase and out of phase transcranial alternating current stimulation, because it allows to overcome confounds related to the return electrode [25]. Therefore, CE-tDCS can represent an additional tool which is able to offer important advantages to those who use standard tDCS, or tES in general, in their research activity.

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