Neuroscience Letters 584 (2015) 347–350

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Short communication

What is the optimal anodal electrode position for inducing corticomotor excitability changes in transcranial direct current stimulation?

Minji Lee[a,1], Yun-Hee Kim[a,b,*], Chang-Hwan Im[c,2], Jung-Hoon Kim[c,2], Chang-hyun Park[b,3], Won Hyuk Chang[b,4], Ahee Lee[a,5]

[a] Department of Health Sciences and Technology, Samsung Advanced Institute for Health Science and Technology, Sungkyunkwan University, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Republic of Korea
[b] Department of Physical and Rehabilitation Medicine, Center for Prevention & Rehabilitation, Heart Vascular and Stroke, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Republic of Korea
[c] Department of Biomedical Engineering, Hanyang University, Haengdang 1-dong, Seongdong-gu, Seoul 133-791, Republic of Korea

HIGHLIGHTS

- The optimal tDCS electrode position was determined by electric current stimulation.
- The simulation provided the electrode position posterior to the MEP hot spot.
- The stimulation-derived position induced higher MEP amplitude than the MEP hot spot.

ARTICLE INFO

Article history:
Received 7 August 2014
Received in revised form 28 October 2014
Accepted 31 October 2014
Available online 3 November 2014

Keywords:
Transcranial direct current stimulation (tDCS)
Motor cortical excitability
Electric current density

ABSTRACT

Transcranial direct current stimulation (tDCS) non-invasively modulates brain function by inducing neuronal excitability. The conventional hot spot for inducing the highest current density in the hand motor area may not be the optimal site for effective stimulation. In this study, we investigated the influence of the center position of the anodal electrode on changes in motor cortical excitability. We considered three tDCS conditions in 16 healthy subjects: (i) real stimulation with the anodal electrode located at the conventional hand motor hot spot determined by motor evoked potentials (MEPs); (ii) real stimulation with the anodal electrode located at the point with the highest current density in the hand motor area as determined by electric current simulation; and (iii) sham stimulation. Motor cortical excitability as measured by MEP amplitude increased after both real stimulation conditions, but not after sham stimulation. Stimulation using the simulation-derived anodal electrode position, which was found to be posterior to the MEP hot spot for all subjects, induced higher motor cortical excitability. Individual positioning of the anodal electrode, based on the consideration of anatomical differences between subjects, appears to be important for maximizing the effects of tDCS.

1. Introduction

As non-invasive brain stimulation, transcranial direct current stimulation (tDCS) has the capacity to modulate cortical function and optimize brain plasticity by inducing changes in neuronal excitability [10,13]. Low direct currents are applied to the scalp through anodal and cathodal electrodes. Depending on the stimulation polarity, anodal tDCS induces facilitation, while cathodal tDCS induces inhibition of brain excitability [4]. The effects of tDCS are typically measured through changes in the amplitude of motor evoked potentials (MEPs). MEP amplitude increases after anodal tDCS and decreases after cathodal tDCS [10,12].

* Corresponding author. Tel.: +82 2 3410 2824/2818; fax: +82 2 3410 0052.
E-mail addresses: minji.lee@skku.edu (M. Lee), yun1225.kim@samsung.com, yunkim@skku.edu (Y.-H. Kim), ich@hanyang.ac.kr (C.-H. Im), gmsinhwa@naver.com (J.-H. Kim), park.changhyun@hanmail.net (C.-h. Park), wh.chang@samsung.com (W.H. Chang), ahee.lee@gmail.com (A. Lee).
[1] Tel.: +82 2 3410 2832; fax: +82 2 3410 2820.
[2] Tel.: +82 2 2220 2322; fax: +82 2 2296 5943.
[3] Tel.: +82 2 3410 3762; fax: +82 2 3410 0052.
[4] Tel.: +82 2 3410 2818; fax: +82 2 3410 0052.
[5] Tel.: +82 2 3410 2832; fax: +82 2 3410 0052.

http://dx.doi.org/10.1016/j.neulet.2014.10.052
0304-3940/

tDCS offers an effective treatment to improve motor and cognitive function [1], but further work is needed to establish optimal application methods. Numerous stimulation parameters can influence the efficacy of tDCS, including the placement, size, and type of electrodes, as well as the intensity and duration of stimulation. Modulation of these parameters can help streamline the focality and intensity of currents needed to target brain regions [5,17]. Simulation of electric currents based on computational head modeling is considered an effective means of selecting optimal stimulation parameters [2,8,16]. This method utilizes anatomical head images based on magnetic resonance imaging (MRI) data to observe changes in the electric field distribution depending on the modulation of stimulation parameters [3,11,15].

Among various simulation parameters, the position of electrodes is potentially important for determining the effects of tDCS. The highest current may not be necessarily formed at the center of the anodal electrode, as the finite size of electrodes affects the electric field distribution near the stimulation site [7]. If the center of the anodal electrode does not correspond to the scalp point of the highest current density, the conventional hot spot (the scalp position from which a contralateral MEP of maximum amplitude and lowest threshold is obtained) may not be the optimal stimulation site.

In this study, we investigated changes in motor cortical excitability depending on the center position of the anodal electrode. We hypothesized that the conventional hot spot may not be the stimulation site for maximally facilitating motor cortical excitability in anodal tDCS. We searched for optimal anodal electrode position with electric current simulation, and then assessed whether stimulation over the simulation-derived site induced higher motor cortical excitability than stimulation over the conventional hot spot.

2. Material and methods

2.1. Subjects

Sixteen young healthy subjects (26.2 ± 2.1 years, 10 males, and 6 females) participated in this study. They were randomly recruited among individual who satisfied inclusion criteria for the experiment. All reported no history of neurological or psychiatric disorders, and all were right handed as assessed by the Edinburgh handedness inventory [14].

2.2. Application of tDCS

The experiment was performed with a single-blinded crossover design. All subjects received tDCS using three different conditions, with a 24 h washout period between adjacent conditions: (i) real stimulation with the anodal electrode located at the conventional hand motor hot spot (MEP hot spot) (C1); (ii) real stimulation with the anodal electrode position identified by electric current simulation as the point with the highest current density in the hand motor area (simulation hot spot) (C2); and (iii) sham stimulation (C3). The order of conditions was randomized and counterbalanced across the subjects. The anodal electrode was located over the left hand motor area with different exact positions for each condition, and the position of the cathodal electrode was fixed at the right supraorbital area. We applied tDCS at 1 mA intensity for 20 min using a DC-STIMULATOR® (NeuroConn, Ilmenau, Germany). Direct currents were delivered through a saline-soaked pair of surface sponge, 4.3×4.3 cm, rubber electrodes.

For C1, the hand motor hot spot was determined as the position displaying the lowest resting motor threshold when MEPs were recorded over the right first dorsal inter-osseous muscle during application of single-pulse transcranial magnetic stimulation (TMS) over the left hand motor area. We delivered TMS using a Magstim Rapid2 magnetic stimulator (Magstim, Cardiff, UK) with a 70-mm figure-eight-shaped coil. For C2, the simulation hot spot was positioned based on the simulation of local electric fields as described below. For C3, we used the same electrode positions as C1, and applied tDCS at the same intensity during first 15 s, and then stopped the stimulation to deliver no more current for the remaining time [6]. MEP amplitude measurements were made without knowledge of treatment condition.

2.3. Simulation of local electric fields for tDCS

Step1: acquisition of MRI data

For each subject, a 3D head model was generated from T1-weighted MRI data, which was acquired using a turbo field echo sequence (number of slices = 124, slice thickness = 1.60 mm, matrix size = 512×512, in-plane resolution = 0.47 mm $\times$ 0.47 mm) with a Philips ACHIEVA MR scanner (Philips Medical Systems, Best, The Netherlands).

Step 2: generation of a head model

The T1-weighted image was transformed to a 3D head model by creating a boundary element method model in CURRY (Neuroscan, Sterling, VA, USA). Electric fields were simulated over the 3D head model using COMETS® (Computation of electric field due to transcranial current stimulation, http://www.COMETStool.com), which derives a current density distribution by considering individual anatomical differences in the components such as skin, skull, and brain in accordance with the principles of tDCS [18].

Step 3: simulation of tDCS

With the 10–20 system applied over the 3D head model, 1 mA intensity electric fields were generated by tDCS through 4.3×4.3 cm electrodes. The anodal electrode was located at one of 49 points around the MEP hot spot determined for C1, with the cathodal electrode positioned at the right supraorbital area. The position of the 49 points was decided by repeating an isotropic 4% shift in the coronal or sagittal direction from the MEP hot spot in the international 10–20 system. By changing anodal electrode position, we measured the current density at the hand motor area by averaging seven values within it. The position of the seven points was manually determined on the 3D head model. The seven points composing a hexagonal form (six points at the nodes of the hexagon and one point at the center of the hexagon) with equidistance between each other covered the hand motor area as compactly as possible. We selected the anodal electrode position that induced the highest current density in the hand motor area as the stimulation site for C2.

2.4. Measurement of motor cortical excitability

We assessed the subjects' motor cortical excitability by measuring the amplitude and latency of contralateral MEPs evoked by TMS over the MEP hot spot before and after each stimulation for all stimulation conditions. The amplitude referred to the distance from the baseline to wave peak in microvolts, whereas the latency was defined as the period from the starting of single pulse TMS to the emergence of wave peak in miliseconds. MEPs were recorded five times, and each measure was computed as the average across the five trials. Provided the measures before and after stimulation, the improvement ratio was also calculated: (after stimulation–before stimulation)/before stimulation.

To infer whether there were differences in motor cortical excitability changes depending on the three stimulation conditions, we performed repeated measures ANOVA with two factors: the three stimulation conditions (C1–C3) and two time points (before and after stimulation). When appropriate, post hoc comparisons

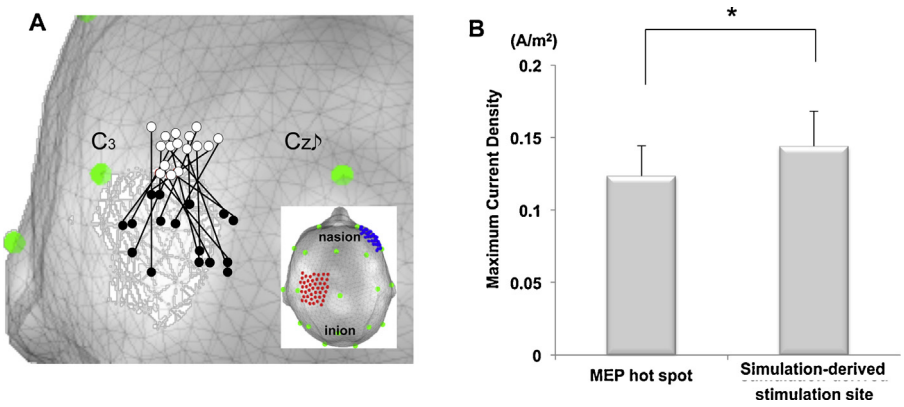

Fig. 1. (A) Anodal electrode position determined in each subject by electric current stimulation (stimulation hot spot; black dots) in relation to the hot spot measured by motor evoked potentials (MEP hot spot; white dots). In the inset, white dots indicate the anodal electrode, whereas blue dots mean the cathodal electrode on a 3D head model. (B) A comparison of current density induced in the hand motor area between the MEP hot spot and simulation hot spot. Error bars mean standard deviations. *, statistical significance with p value <0.05. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

were carried out between the two time points for each stimulation condition and between each pair of conditions at each time point using paired sample t-tests. Statistical significance was determined at a p-value of 0.05 with a false discovery rate correction.

3. Results

3.1. Simulation hot spot

The stimulation hot spot, determined as the position of the anodal electrode for C2, varied among the subjects. In relation to the MEP hot spot, the simulation hot spot was localized on the posterior in all subjects (Fig. 1A). The average current density at the hand motor area was higher by 11.7% for stimulation on the simulation hot spot than on the MEP hot spot ($t = -5.186$, $p < 0.001$, Fig. 1B).

3.2. Comparison of motor cortical excitability changes

There was an interaction between the three stimulation conditions and two time points in the amplitude of MEPs ($F = 7.459$, $p = 0.006$). MEP amplitude increased after stimulation for both real stimulation conditions (C1 and C2) (C1: $t = -3.959$, $p < 0.001$; C2: $t = -4.488$, $p < 0.001$). There was no difference between the three stimulation conditions before stimulation ($F = 0.005$, $p = 0.995$), but MEP amplitude for C2 was higher than for C1 ($t = -2.699$, $p = 0.017$) as well as for C3 ($t = 3.546$, $p = 0.003$) after stimulation (Fig. 2A, Table 1). The improvement ratio of MEP amplitude was higher for both real stimulation conditions (C1 and C2) than for the sham stimulation condition (C3) (C1 vs. C3: $t = 2.715$, $p = 0.016$; C2 vs. C3: $t = 3.684$, $p = 0.002$), and was also higher for C2 than for C1 ($t = -2.689$, $p = 0.017$) (Fig. 2B). There was no interaction effect for MEP latency in repeated measure ANOVA.

4. Discussion

We observed different effects of tDCS on motor cortical excitability depending on the position of the anodal electrode. Motor cortical excitability was better modulated when applying anodal tDCS over a simulation-derived stimulation site posterior to the conventional hot spot.

For the simulation of electric currents generated by tDCS, anatomical differences such as skull thickness, subcutaneous fat levels, and cerebrospinal fluid density have been considered [9]. Due to the individual anatomical differences, we found that electric fields were differently generated even for the same stimulation site, and the anodal electrode position for generating maximal current density in the hand motor area varied between subjects.

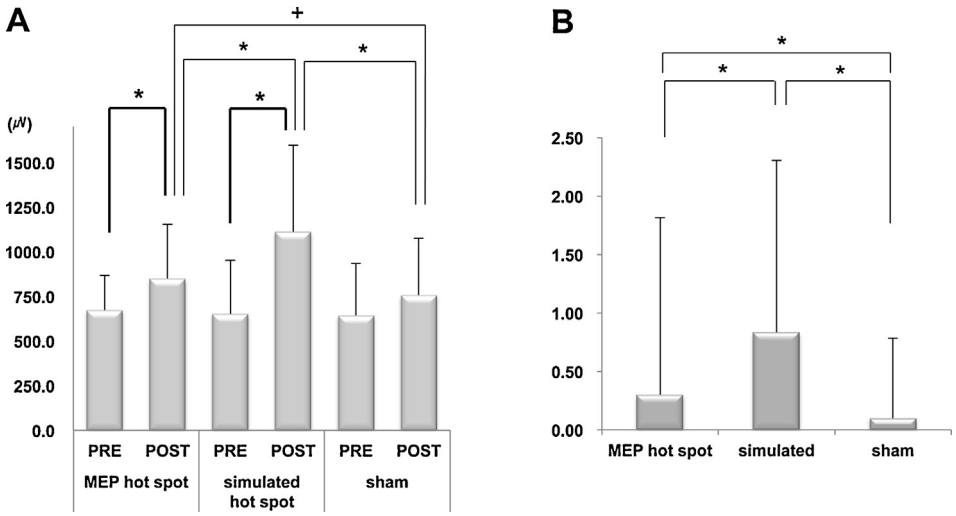

Fig. 2. Comparisons of (A) changes and (B) improvement ratio of the amplitude of motor evoked potentials between three stimulation conditions. Error bars mean standard deviations. *, statistical significance with $p < 0.05$ with a false discovery rate correction. +, significance trend with $p < 0.05$ without a false discovery rate correction.

Table 1
Measurement values (in μV) of the amplitude of motor evoked potential before and after stimulation in three stimulation conditions.

Condition		Mean ± standard deviation	95% confidence interval		Improvement ratio
			Lower limit	Upper limit	
MEP hot spot	Before stimulation	651.05 ± 177.18	564.23	737.86	0.30 ± 0.29
	After stimulation	848.34 ± 305.54	698.62	998.05	
Simulated hot spot	Before stimulation	650.38 ± 302.18	502.31	798.44	0.83 ± 0.75
	After stimulation	1111.74 ± 486.78	873.22	1350.26	
Sham	Before stimulation	642.38 ± 290.79	499.89	784.86	0.09 ± 0.15
	After stimulation	701.91 ± 324.00	543.15	860.67	

Even so, across all subjects, the simulation-derived anodal electrode position was commonly found to be posterior to the conventional hot spot determined by MEPs. We attribute the posterior shift of the optimal stimulation site to edge effects in applying tDCS [17], with increases in the current density toward the perimeter of the anodal electrode due to higher resistance. We postulate that the hand motor area approximated the perimeter of the anodal electrode when the stimulation site was positioned posterior to the conventional hot spot, so that it had higher current density for stimulation over the simulation-derived stimulation site. If the position of the cathodal electrode was changed to a different site, the electric field distribution between the anodal and cathodal electrodes would be altered and the shift of optimal position of the anodal electrode could also change.

MEP latency did not differ after tDCS application on the MEP hot spot as well as on the stimulation hot spot. The aftereffect of anodal tDCS on facilitating cortical excitability could be seen as changes in MEP amplitude, but not as changes in MEP latency specifically for healthy subjects.

This study has some limitations to consider for future investigations. First, we examined the effects of anodal electrode position exclusively in terms of physiological measures. The effects should be confirmed for behavioral outcomes such as motor performance by evaluating a task performed by the subjects. Second, the effects of cathodal electrode position should be considered to identify the optimal combination of anodal and cathodal electrode positioning. Third, in our simulation each 3D head model consisted of three components: skin, skull, and cerebrospinal fluid/cortex such that gray and white matter was not separately considered in the head model. Regarding the incompleteness in the head model, the simulation toolbox will be developed towards including more individual components.

When using tDCS as a therapeutic tool for patients such as with stroke, the most effective modulation of brain excitability would be crucial. Although previous studies using the MEP hot spot have provided the effects of tDCS on the recovery of motor function, it may be possible to further enhance the tDCS effects by using a more optimal stimulation site rather than the MEP hot spot. In this regard, it is notable that simulation-based search for an optimal stimulation site could be applied to most of patients, while the MEP hot spot is applicable to only part of patients who satisfy inclusion criteria for safety in measuring MEPs. The optimal montage of electrodes for maximum enhancement of brain function may vary between healthy and pathological brains, and the differences need to be fully investigated for application in patients with brain diseases.

5. Conclusions

Motor cortical excitability was improved by positioning the anodal electrode posterior to the conventional hot spot, with an electrode montage of the anode in the left hand motor area and the cathode in the right supraorbital area. Electric current stimulation that considers anatomical differences between subjects is useful for selecting the optimal stimulation site for tDCS.

Acknowledgments

This study was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP) (NRF-2014R1A2A1A01005128) and the Brain Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2006-2005330) and Samsung Medical Center grant, [#SMO1131391].

References

[1] S.S. Ayache, W.H. Farhat, H.G. Zouari, H. Hosseini, V. Mylius, J.P. Lefaucheur, Stroke rehabilitation using noninvasive cortical stimulation: motor deficit, Expert Rev. Neurother. 12 (2012) 949–972.
[2] S. Bai, S. Dokos, K.A. Ho, C. Loo, A computational modelling study of transcranial direct current stimulation montages used in depression, NeuroImage 87 (2014) 332–344.
[3] S. Bai, C. Loo, S. Dokos, A review of computational models of transcranial electrical stimulation, Crit. Rev. Biomed. Eng. 41 (2013) 21–35.
[4] A.J. Butler, M. Shuster, E. O'Hara, K. Hurley, D. Middlebrooks, K. Guilkey, A meta-analysis of the efficacy of anodal transcranial direct current stimulation for upper limb motor recovery in stroke survivors, J. Hand Ther. 26 (2013) 162–170, quiz 171.
[5] J.P. Dmochowski, A. Datta, M. Bikson, Y. Su, L.C. Parra, Optimized multi-electrode stimulation increases focality and intensity at target, J. Neural Eng. 8 (2011) 046011.
[6] W.W. Feng, M.G. Bowden, S. Kautz, Review of transcranial direct current stimulation in poststroke recovery, Top. Stroke Rehabil. 20 (2013) 68–77.
[7] A. Foerster, S. Rocha, C. Wiesiolek, A.P. Chagas, G. Machado, E. Silva, F. Fregni, K. Monte-Silva, Site-specific effects of mental practice combined with transcranial direct current stimulation on motor learning, Eur. J. Neurosci. 37 (2013) 786–794.
[8] R.N. Holdefer, R. Sadleir, M.J. Russell, Predicted current densities in the brain during transcranial electrical stimulation, Clin. Neurophysiol. 117 (2006) 1388–1397.
[9] J.C. Horvath, O. Carter, J.D. Forte, Transcranial direct current stimulation: five important issues we aren't discussing (but probably should be), Front. Syst. Neurosci. 8 (2014) 2.
[10] M. Kandel, J.M. Beis, L. Le Chapelain, H. Guesdon, J. Paysant, Non-invasive cerebral stimulation for the upper limb rehabilitation after stroke: a review, Ann. Phys. Rehabil. Med. 55 (2012) 657–680.
[11] P.C. Miranda, M. Lomarev, M. Hallett, Modeling the current distribution during transcranial direct current stimulation, Clin. Neurophysiol. 117 (2006) 1623–1629.
[12] F. Notturno, L. Marzetti, V. Pizzella, A. Uncini, F. Zappasodi, Local and remote effects of transcranial direct current stimulation on the electrical activity of the motor cortical network, Hum. Brain Mapp. (2013).
[13] J. O'Shea, M.H. Boudrias, C.J. Stagg, V. Bachtiar, U. Kischka, J.U. Blicher, H. Johansen-Berg, Predicting behavioural response to TDCS in chronic motor stroke, NeuroImage (2013).
[14] R.C. Oldfield, The assessment and analysis of handedness: the Edinburgh inventory, Neuropsychologia 9 (1971) 97–113.
[15] M.J. Russell, T. Goodman, R. Pierson, S. Shepherd, Q. Wang, B. Groshong, D.F. Wiley, Individual differences in transcranial electrical stimulation current density, J. Biomed. Res. 27 (2013) 495–508.
[16] R.J. Sadleir, T.D. Vannorsdall, D.J. Schretlen, B. Gordon, Transcranial direct current stimulation (tDCS) in a realistic head model, NeuroImage 51 (2010) 1310–1318.
[17] T. Wagner, F. Fregni, S. Fecteau, A. Grodzinsky, M. Zahn, A. Pascual-Leone, Transcranial direct current stimulation: a computer-based human model study, NeuroImage 35 (2007) 1113–1124.
[18] Y.-J. Jung, J.-H. Kim, C.-H. Im, COMETS: a MATLAB toolbox for simulating local electric fields generated by transcranial direct current stimulation (tDCS), BioMed. Eng. Lett. 3 (2013) 39–46.