32nd URSI GASS, Montreal, 19-26 August 2017

Variability in TDCS Electric Fields: Effects of Electrode Size and Configuration

Ilkka Laakso* (1), Satoshi Tanaka(2), Marko Mikkonen(1), Soichiro Koyama(3), and Akimasa Hirata(4)
(1) Aalto University, Espoo, Finland
(2) Hamamatsu University School of Medicine, Hamamatsu, Japan
(3) Fujita Health University, Toyoake, Japan
(4) Nagoya Institute of Technology, Nagoya, Japan

Abstract

Variability in the efficacy of transcranial direct-current stimulation (TDCS) may be affected by variations in electric fields, which depend on both experimental parameters and individual anatomical features of the head and brain. Electrode configurations that minimize inter-subject differences in electric fields would be useful for controlling variability in experimental TDCS studies. This study investigated the effects of electrode size and configuration on the variability in the electric fields. Individual MRI-based models of 44 subjects and the finite-element method were used. Motor cortical TDCS was modelled for four electrode montages.

1. Introduction

Transcranial direct current stimulation (TDCS) modulates the brain activity by delivering weak direct currents to the brain through electrodes attached to the intact scalp. Because TDCS is well tolerable and affordable [1, 2], it is promising as an alternative treatment strategy for diverse neurological or psychiatric diseases [3]. For instance, TDCS has shown effectiveness for drug-resistant depression [4], chronic pain [3], or stroke recovery [5].

However, important limitations of TDCS are that its mechanisms are not fully understood and there is a large inter-individual variability in the responses to TDCS [6, 7]. Recent computational studies have suggested that inter-individual differences in skull and brain anatomy may contribute to this variability by creating varying electric fields in each brain [8, 9]. In experiments, these variations are problematic because the stimulus delivered to each individual's brain varies even in otherwise identical experimental conditions. The variations in the electric fields originate from factors such as individual anatomy of the brain, cerebrospinal fluid (CSF), and skull [8, 9], and it is difficult to take these factors into account without time-consuming computer simulations.

Therefore, it would be beneficial to design an electrode configuration that minimizes inter-individual variations in the electric fields. The purpose of the present study was to examine whether the variability in the TDCS electric fields can be reduced by changing the electrode size or configuration. To answer this question, we studied the variability of the electric fields using MRI-based individually-constructed computational models of 44 subjects. The target was the hand motor area of the primary motor cortex.

2. Methods and Models

2.1 Subjects and Imaging

We used the T1 and T2 weighted MRI data of 44 subjects (age: mean±SD: 23.3±4.5, range: 19–38 years, 12 female) reported in our previous study [10]. All MRI scans were acquired using a 3 T MRI scanner.

2.2 Cortical Reconstruction and Registration

We used a method described previously [10] to generate surface representations of each subject's brain which were then registered with the Montreal Neurological Institute (MNI) average brain template to allow mapping of individually calculated electric fields to the standard brain space. Briefly, cortical surfaces were reconstructed from the MR images using the FreeSurfer image analysis software [11, 12]. The individual subjects' brain surfaces were then registered using FreeSurfer to the default FreeSurfer brain template (FS40). To present the results in the standard space, FreeSurfer was used to generate the brain surface of the MNI ICBM 2009a nonlinear asymmetric template [13], which was then registered with the FS40 template. The final mapping was generated by combining the mappings from the individual brains to the FS40 template and the inverse mapping from the FS40 template to the MNI template.

2.3 Volume Conductor Models

T1- and T2-weighted MRI of 44 subjects were segmented using in-house software [8, 10]. The segmented models consisted of 11 tissues, which were assigned the following conductivity values (for references, see [10]): grey matter 0.2 S/m, white matter 0.14 S/m, blood 0.7 S/m, compact bone 0.008 S/m, spongy bone 0.027 S/m, CSF 1.8 S/m, muscle 0.16 S/m, skin 0.08 S/m, fat 0.08 S/m, eye humour 1.5 S/m, and dura 0.16 S/m.

2.4 Numerical Electric Field Modelling

The DC electric field can be represented as the gradient of the electric scalar potential. The scalar potential ϕ satisfies $\nabla\cdot\sigma\nabla\phi = -i$, where σ (S/m) is the conductivity and i (A/m^3) is the current source.

The equation was solved numerically using the finite-element method using the voxels of the volume conductor model as the elements and piecewise linear basis functions, as described previously [14]. The degrees of freedom were the values of the potential at the corners of each voxel. The equation system was solved to the relative residual of 10^{-6}. The electric fields were calculated from the gradient of the scalar potential at each vertex of a polygonal surface located 1 mm below the grey matter surface.

2.5 Electrode Montages

The electrodes were modelled based on a realistic two-compartment model [20, 10]. They consisted of sponges saturated with normal saline (thickness 6 mm, conductivity 1.6 S/m). A 1-mm thick rubber sheet (conductivity 0.1 S/m) was inserted in the sponge. A connector modelled as a disk with a radius 5 mm was placed on top of the rubber sheet, serving as a current source, with a source or sink current distributed uniformly on the disk.

Four electrode configurations were considered for each subject. In the first configuration, the anode was a 5 cm x 7 cm rectangular sponge, which is the electrode type proposed in the pioneering study of Nitsche and Paulus [15], and the most commonly used electrode in subsequent studies [16]. In the second and third configurations, the anode was either a 3 cm x 3 cm rectangular or a 0.8-cm diameter circular sponge. The rationale for using smaller electrodes is that reducing the size of the electrode has been shown to have a focusing effect on the physiological responses to TDCS [17]. For all the above anode locations, the cathode was a 5 cm x 7 cm rectangular sponge electrode positioned over the contralateral (right) orbit, as is commonly done in experimental TDCS studies [16]. In the following, these electrode montages are denoted ‘large’, ‘medium’, and ‘small’, according to the size of the anode. The fourth configuration was a high-definition TDCS electrode montage, consisting of one anode surrounded by a ‘ring’ of four cathodes placed at a distance of 3 cm from the anode [18, 19]. The electrodes were small circular sponges with a diameter of 0.8 cm. For all configurations, the stimulating current was set to 1 mA.

2.6 Stimulation Target

The target of stimulation was the hand area of the primary motor cortex (Fig. 1). The target site corresponded to the centre of the characteristic ‘inverted omega’ shape of the hand motor area. The target site in each subject was determined using the mapping from the MNI template brain to each individual brain. The centre of the anode was placed at the closest point on the scalp to the target site in the brain.

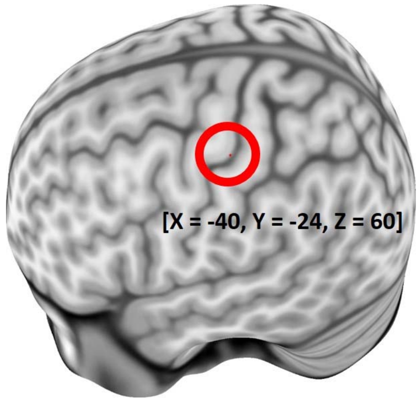

Figure 1. Target site in the MNI template brain.

3. Results

Figure 2 shows the four electrode configurations and the calculated electric fields for three exemplary subjects. As seen in the figure, reducing the electrode size had the effect of increasing the electric field near the target site and decreasing the electric fields elsewhere in the brain, thus increasing the focality of stimulation. Using small electrodes in the ring configuration reduced the electric field compared to the small electrode with the contralateral reference electrode. However, the ring configuration effectively eliminated the electric fields in non-target brain regions. It is notable that conventional large electrode produced relatively large electric fields in the frontal regions, and the maximum was not generally found near the target site. Reducing the electrode size moved the maximum towards the target site.

The inter-subject registration method was used to map the individually calculated electric fields to the MNI brain template. Figure 3 shows the mean and relative standard deviation of the absolute value of the electric field calculated over all 44 subjects. The tendency of increased focality for smaller electrode sizes is clear. However, the relative standard deviation data indicates the trade-off of increased focality: as the electrode size is reduced, the inter-subject variability of the electric fields in the target area increases. The likely reason is that the electric fields become more sensitive to small anatomical differences near the anode. The ring configuration is particularly sensitive to variations, doubling the relative standard deviation near the target region compared to the conventional configuration with a large anode.

At the target site (Fig. 1), the electric fields (mean±SD) were 0.29±0.06 V/m, 0.44±0.11 V/m, and 0.62±0.18 V/m for the large, medium and small anode sizes, and 0.39±0.16 V/m for the ring configuration. These values are different from the maximum values shown in Fig. 3 because of deeper location of the target site.

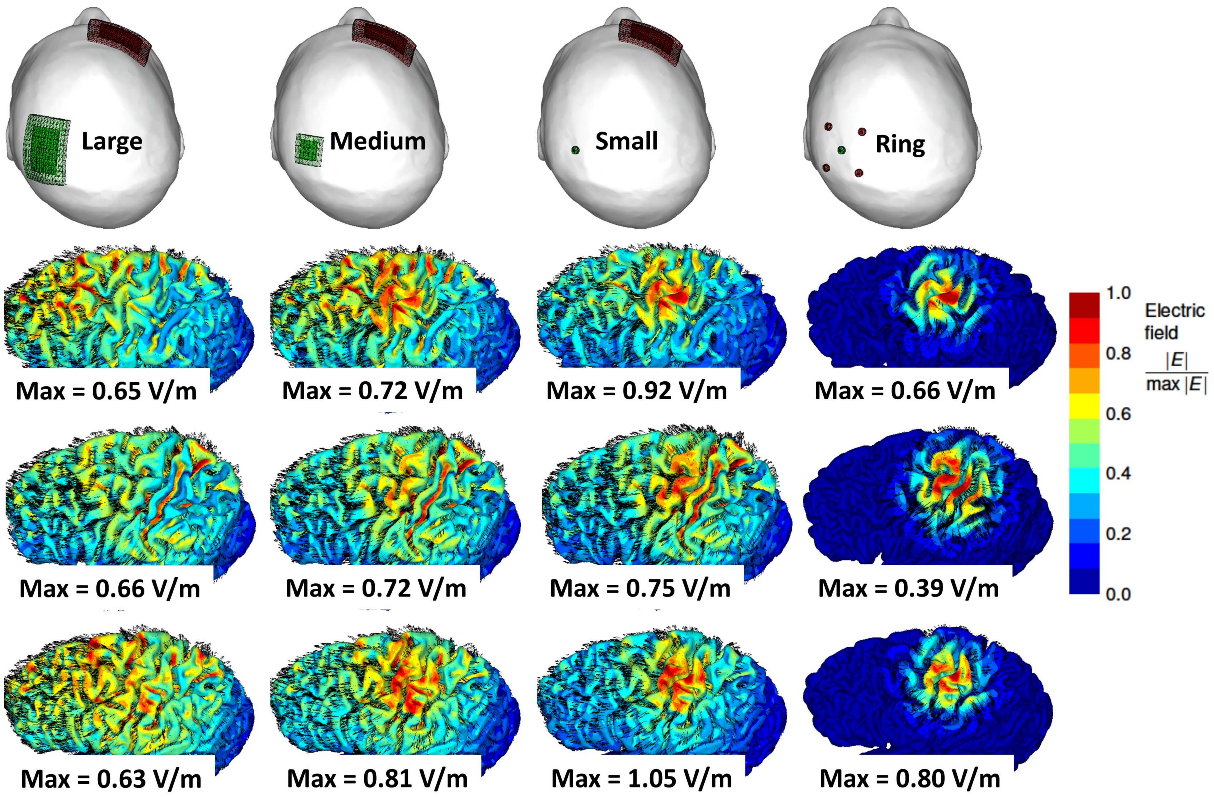

Figure 2. Electrode configurations (top row) and the electric fields in three exemplary subjects (rows 2–3).

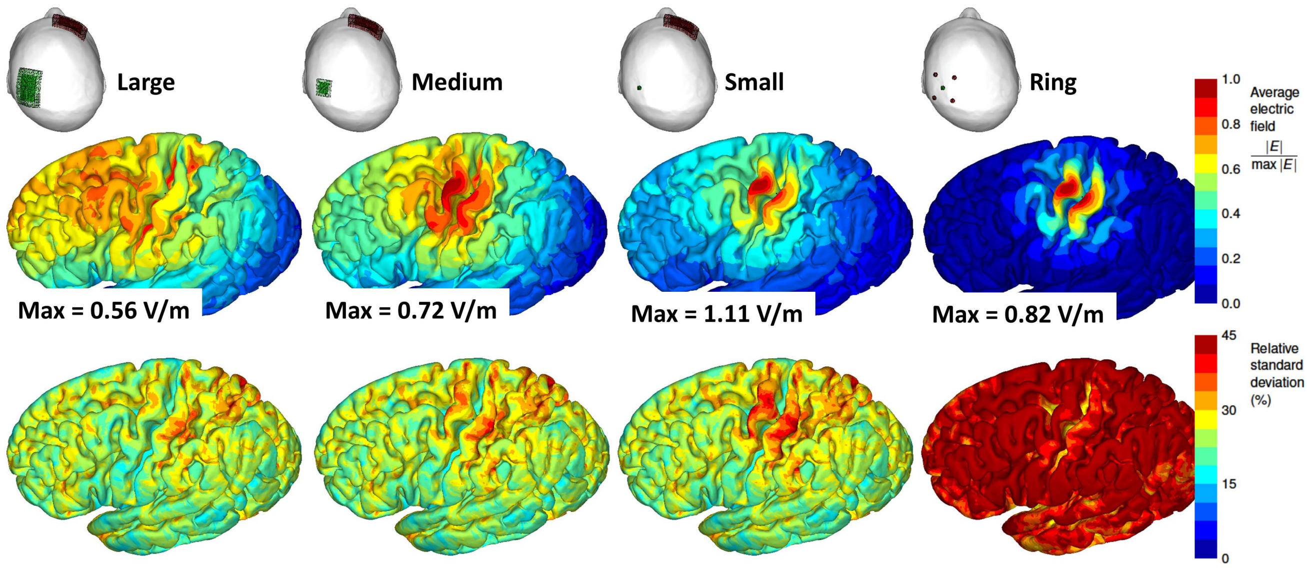

Figure 3. Average electric fields of 44 subjects and the relative standard deviation for four electrode configurations.

In experiments, the ring electrode configuration has been shown to produce comparatively similar effects to the conventional montage with a large anode [19]. The results herein show that the electric fields are relatively similar in magnitude, especially in the deeper region where the target site was located. In another experimental study [17], a 0.1 mA current applied through a 3.5 cm^2 anode has been shown to produce more focal effects than a 1 mA current with a 35 cm^2 anode. Therefore, based on the results presented herein, there would have been a factor of five difference in the magnitude of the electric field in addition to differences in the field distribution.

4. Conclusions

We confirmed that a smaller electrode size can be used to improve the focality of TDCS electric fields. However, the improvement comes at the cost of increased inter-subject variability in the electric fields. Therefore, reducing the electrode size does not appear to be an effective strategy to reduce the variability observed in TDCS studies. This has important implications for the planning of experimental TDCS studies. Namely, if larger electrodes are used, the electric fields are less variable, but the affected site in the brain may be difficult to determine due to the spatial spread of the electric fields. On the contrary, smaller electrodes can focus the stimulation but inter-subject variability becomes more difficult to control. An effective but time-consuming strategy to control both focality and variability would be to use small electrodes and tune the stimulation current and the electrode location individually based on computational modelling.

5. References

1. S. Tanaka and K. Watanabe, “Transcranial direct current stimulation–a new tool for human cognitive neuroscience,” *Brain Nerve*, vol. 61, pp. 53–64, Jan 2009.

2. A. R. Brunoni, M. A. Nitsche, N. Bolognini, M. Bikson, T. Wagner, L. Merabet, D. J. Edwards, A. Valero-Cabre, A. Rotenberg, A. Pascual-Leone, R. Ferrucci, A. Priori, P. S. Boggio, and F. Fregni, “Clinical research with transcranial direct current stimulation (tDCS): challenges and future directions,” *Brain Stimul*, vol. 5, pp. 175–195, Jul 2012.

3. M.-F. Kuo, W. Paulus, and M. A. Nitsche, “Therapeutic effects of non-invasive brain stimulation with direct currents (tDCS) in neuropsychiatric diseases,” *Neuroimage*, vol. 85 Pt 3, pp. 948–960, Jan 2014.

4. D. Meron, N. Hedger, M. Garner, and D. S. Baldwin, “Transcranial direct current stimulation (tDCS) in the treatment of depression: Systematic review and meta-analysis of efficacy and tolerability,” *Neurosci Biobehav Rev*, vol. 57, pp. 46–62, Jul 2015.

5. J. Marquez, P. van Vliet, P. McElduff, J. Lagopoulos, and M. Parsons, “Transcranial direct current stimulation (tDCS): does it have merit in stroke rehabilitation? a systematic review,” *Int J Stroke*, vol. 10, pp. 306–316, Apr 2015.

6. S. Wiethoff, M. Hamada, and J. C. Rothwell, “Variability in response to transcranial direct current stimulation of the motor cortex,” *Brain Stimul*, vol. 7, no. 3, pp. 468–475, 2014.

7. V. López-Alonso, B. Cheeran, D. Rio-Rodriguez, and M. Fernández-Del-Olmo, “Inter-individual variability in response to non-invasive brain stimulation paradigms,” *Brain Stimul*, vol. 7, no. 3, pp. 372–380, 2014.

8. I. Laakso, S. Tanaka, S. Koyama, V. De Santis, and A. Hirata, “Inter-subject variability in electric fields of motor cortical tDCS,” *Brain Stimul*, vol. 8, no. 5, pp. 906–913, 2015.

9. A. Opitz, W. Paulus, S. Will, A. Antunes, and A. Thielscher, “Determinants of the electric field during transcranial direct current stimulation,” *Neuroimage*, Jan 2015.

10. I. Laakso, S. Tanaka, M. Mikkonen, S. Koyama, N. Sadato, and A. Hirata, “Electric fields of motor and frontal tDCS in a standard brain space: A computer simulation study,” *NeuroImage*, vol. 137:, pp. 140–51, August 2016.

11. A. M. Dale, B. Fischl, and M. I. Sereno, “Cortical surface-based analysis. i. segmentation and surface reconstruction,” *Neuroimage*, vol. 9, pp. 179–194, Feb 1999.

12. B. Fischl, M. I. Sereno, R. B. Tootell, and A. M. Dale, “High-resolution intersubject averaging and a coordinate system for the cortical surface,” *Hum Brain Mapp*, vol. 8, no. 4, pp. 272–284, 1999.

13. V. Fonov, A. C. Evans, K. Botteron, C. R. Almli, R. C. McKinstry, D. L. Collins, and Brain Development Cooperative Group, “Unbiased average age-appropriate atlases for pediatric studies,” *Neuroimage*, vol. 54, pp. 313–327, Jan 2011.

14. I. Laakso and A. Hirata, “Fast multigrid-based computation of the induced electric field for transcranial magnetic stimulation,” *Phys Med Biol*, vol. 57, no. 23, pp. 7753–65, 2012.

15. M. A. Nitsche and W. Paulus, “Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation,” *J Physiol (Lond)*, vol. 527 Pt 3, pp. 633–639, Sep 2000.

16. M. A. Nitsche, L. G. Cohen, E. M. Wassermann, A. Priori, N. Lang, A. Antal, W. Paulus, F. Hummel, P. S. Boggio, F. Fregni, and A. Pascual-Leone, “Transcranial direct current stimulation: State of the art 2008,” *Brain Stimul*, vol. 1, no. 3, pp. 206–23, 2008.

17. M. A. Nitsche, S. Doemkes, T. Karaköse, A. Antal, D. Liebetanz, N. Lang, F. Tergau, and W. Paulus, “Shaping the effects of transcranial direct current stimulation of the human motor cortex,” *J Neurophysiol*, vol. 97, pp. 3109–3117, Apr 2007.

18. A. Datta, V. Bansal, J. Diaz, J. Patel, D. Reato, and M. Bikson, “Gyri-precise head model of transcranial direct current stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad,” *Brain Stimul*, vol. 2, no. 4, pp. 201–7, 2009.

19. H.-I. Kuo, M. Bikson, A. Datta, P. Minhas, W. Paulus, M.-F. Kuo, and M. A. Nitsche, “Comparing cortical plasticity induced by conventional and high-definition 4 × 1 ring tDCS: a neurophysiological study,” *Brain Stimul*, vol. 6, pp. 644–648, Jul 2013.

20. G. B. Saturnino, A. Antunes, and A. Thielscher, “On the importance of electrode parameters for shaping electric field patterns generated by tDCS,” *Neuroimage*, vol. 120, pp. 25–35, Oct 2015.