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Inconsistent outcomes of transcranial direct current stimulation (tDCS) may be originated from the anatomical differences among individuals: A simulation study using individual MRI data

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***Abstract*—Transcranial direct current stimulation (tDCS) is a kind of neuromodulation protocol, which transmits small amount of DC currents through scalp electrodes to facilitate or inhibit particular areas of the brain. Although many studies have demonstrated that tDCS can effectively modulate excitability of various brain sites, the outcomes of the tDCS treatment are not consistent among subjects to whom identical electrode montages were applied. So far, no studies have clearly elucidated the main cause of this individual variability. The hypothesis of our study was that the individual variability in the tDCS effect might be originated due to the anatomical differences among subjects. To verify our hypothesis, we investigated the relationship between the current density value at dorsolateral prefrontal cortex (DLPFC) simulated using finite element method (FEM) and the behavioral outcomes of a simple working memory (WM) task. A 3-back WM task experiment was conducted with twenty-five healthy subjects before and after the DC stimulation, when the cathode and anode electrodes were attached to right supraorbital area and F3 location, respectively, for all subjects. The results showed that participants who showed enhanced WM task performance after tDCS had a significantly larger current density on DLPFC, suggesting that the inconsistent behavioral outcomes of tDCS might be partially due to the anatomical differences among subjects.**

I. Introduction

Transcranial direct current stimulation (tDCS) is one of the representative noninvasive neuromodulation techniques, which can modulate the excitability of a specific brain area by delivering low-intensity direct current (DC) to the brain [1]. It is well known that anodal and cathodal stimulations facilitate and inhibit cortical excitability, respectively, although the exact mechanisms of tDCS have not yet been revealed [2]. tDCS has been extensively studied as a potential treatment tool for many mental diseases, such as depression, epilepsy, stroke, Alzheimer's disease, chronic pain, and tinnitus [3-7]. tDCS can also be applied to healthy subjects to enhance a specific mental performance. For example, studies have demonstrated that stimulating dorsolateral prefrontal cortex (DLPFC) with tDCS can manipulate working memory (WM) performance [2, 8, 9]. However, although the enhancement of behavioral outcomes due to tDCS proved to be statistically significant, some individuals still do not show any meaningful changes after tDCS. So far, no previous studies have clarified the cause of this individual variability.

The main hypothesis of the present study was that the individual variability in the tDCS effect can be partially due to the differences in the anatomical structure of each individual. We set this hypothesis based on the fact that the current density formed in the individual brain is significantly influenced by the different anatomical properties of each individual such as thickness of skull, shape of cortical folding structures, shape of the head, and so on [10, 11]. In this study, to prove our hypothesis, we investigated the relationship between the behavioral outcomes and the current density values at DLPFC simulated using finite element method (FEM). Twenty five healthy subjects participated in the 3-back WM task experiment before and after the 20-min DC stimulation.

II. Methods

A. Subjects

Twenty-five (25) healthy subjects with mean age of 22.4 ± 1.4 (18 males and 7 females) volunteered for the experiment. All subjects were in a healthy condition, and were not on any medication or drug. They also had no history of neurological, psychiatric or other severe diseases that might otherwise affect the experimental results. Two of the participants were excluded from the study due to the low MRI quality. All participants signed a written informed consent approved by the Institutional Review Board (IRB) of Samsung Medical Center prior to their participation in the study.

B. Experimental Procedure

All participants performed a 3-back verbal WM task before and after applying tDCS. The 3-back verbal WM task consisted of 28 Korean syllabuses that were randomly presented on each trial. The subjects had to press a button when a syllabus matched the one presented three times prior to the current one (Figure 1 (a)). The reaction time was also recorded using E-prime (Psychology Software Tools, PA, USA).

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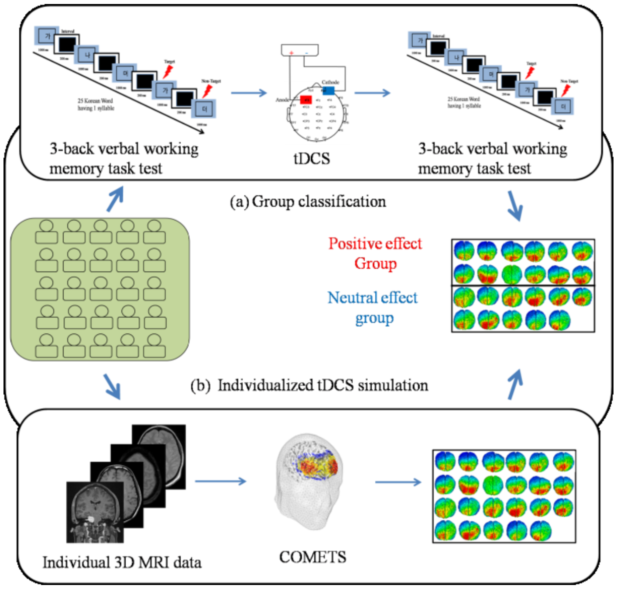

Figure 1. A schematic illustation of the study protocol. (a) the participants were classified into two categories – a group of individuals who showed positive tDCS aftereffect, the other group of individuals who did not show any significant enhancement in the behavioral outcomes. (b) The current density distribution elicited by tDCS was evaluated using individual MRI T1 data. Group comparison of the current density values at DLPFC was then perfomed.

Each participant underwent 20-min tDCS after performing the initial WM task. The anode and cathode electrodes were placed on F3 and right supraorbital region, respectively (see Figure 2). The stimulation current of 1.0 mA was delivered to the brain using Eldith DC-Stimulator (Neuroconn GmBH, Ilmenau, Germany) with 5 x 7 cm rectangular sponge electrode pads. After the tDC stimulation, the participants underwent another session of 3-back verbal WM task with different syllabuses.

Based on the results of the first 3-back WM task experiment, we excluded 7 subjects whose task performance (accuracy) were too good (above 90%) or too bad (below 30%) to maintain the homogeneity of the participants. The remaining participants were divided into two groups, a positive-effect (PE) group and neutral-effect (NE) group according to the following criteria:

1) If post-tDCS WM task performance significantly enhanced compared to the pre-tDCS performance, they were categorized as a PE group.

2) Even the accuracy did not significantly increased, if the reaction time of the post-tDCS decreased, they were also categorized as a PE group.

According to the above criteria, nine participants were classified as a PE group and eight were categorized as an NE group.

C. tDCS Current Analysis

Current density elicited by tDCS was computed using an FEM-based MATLAB toolbox, COMETS, developed by our group (http://www.cometstool.com, Figure 1.(b)). COMETS is a MATLAB toolbox that can analyze local electric fields

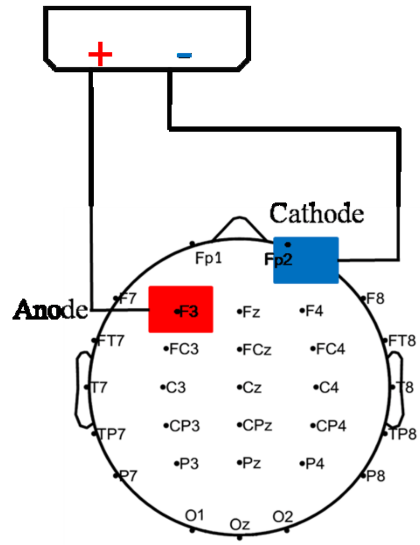

Figure 2. Schematic diagram of the tDCS. Anode denoted positive current electrodes and cahode denoted negative current electrodes. In our experiment, anodes which was our target electrode located in F3 to stimulate DLPFC but cathode was located in supraorbital, which was used as ground.

generated by tDCS using individual head model.

For the accurate evaluation of conductive current flow inside the brain, finite element (FE) head models were constructed from individual MRI data. Each FE head model consisted of three areas - skin, skull, and cerebrospinal fluid (CSF)/cortex. The conductivity values for skin, skull, and CSF/brain were set to 0.22, 0.014, and 1.79 S/m, respectively [12]. For the segmentation of MRI data, CURRY7 for Windows (Compumedics, Inc., Charlotte, NC) was used.

III. RESULTS

The average current density at DLPFC were 7.045 ±

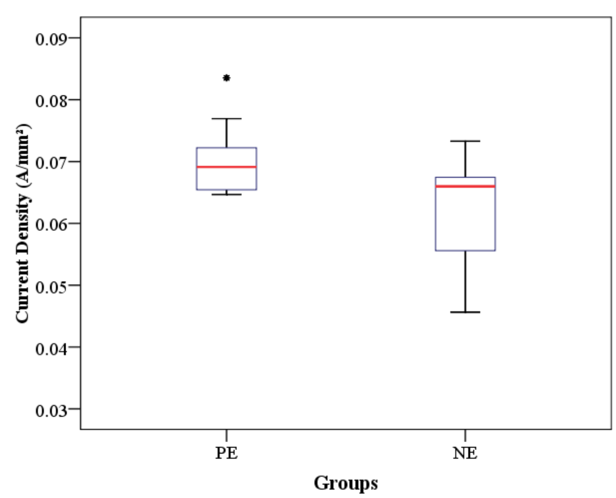

Figure 3. The average current density of DLPFC elicited by tDCS stimulaion. (PE: positive effect group, NE: neutral effect group).

0.629 ($\times 10^{-2}$ A/m^2) for the PE group (n = 9) and 6.212 ± 0.935 ($\times 10^{-2}$ A/m^2) for the NE (n = 8) group (Figure 3). The current density at DLPFC during tDCS were significantly larger in the PE group than the NE group (p = 0.0229, one-tail independent t-test; p = 0.0570, one-tail Wilcoxon rank sum test), indicating that the effect of tDCS was dependent on the amount of the stimulation current delivered to DLPFC, which resulted from the anatomical differences of each individual.

IV. Conclusions

In this study, preliminary results on the relationship between the tDCS effect in the WM task performance and the current density at DLPFC were presented. Our results showed that the differences in the anatomical structures of individual subjects resulted in different current density values at DLPFC, and eventually affected the behavioral outcomes of the DC stimulation. Our results may have a limitation - combining CSF and brain regions into a single tissue might result in errors in the field analysis results. Despite this limitation, our preliminary results suggest that individualized tDCS stimulation considering anatomical data would help to enhance the effect of tDCS.

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