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Transcranial direct current stimulation in patients with skull defects and skull plates: High-resolution computational FEM study of factors altering cortical current flow

Abhishek Datta [a,*], Marom Bikson [a], Felipe Fregni [b,c,*]

[a] Neural Engineering Laboratory, Department of Biomedical Engineering, The City College of New York of CUNY, New York, NY 10031, USA
[b] Laboratory of Neuromodulation, Spaulding Rehabilitation Hospital, Harvard Medical School, Boston, MA 02114, USA
[c] Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 02215, USA

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ABSTRACT

Preliminary positive results of transcranial direct current stimulation (tDCS) in enhancing the effects of cognitive and motor training indicate that this technique might also be beneficial in traumatic brain injury or patients who had decompressive craniectomy for trauma and cerebrovascular disease. One perceived hurdle is the presence of skull defects or skull plates in these patients that would hypothetically alter the intensity and location of current flow through the brain. We aimed to model tDCS using a magnetic resonance imaging (MRI)-derived finite element head model with several conceptualized skull injuries. Cortical electric field (current density) peak intensities and distributions were compared with the healthy (skull intact) case. The factors of electrode position (C3-supraorbital or O1-supraorbital), electrode size skull defect size, skull defect state (acute and chronic) or skull plate (titanium and acrylic) were analyzed. If and how electric current through the brain was modulated by defects was found to depend on a specific combination of factors. For example, the condition that led to largest increase in peak cortical electric field was when one electrode was placed directly over a moderate sized skull defect. In contrast, small defects midway between electrodes did not significantly change cortical currents. As the conductivity of large skull defects/plates was increased (chronic to acute to titanium), current was shunted away from directly underlying cortex and concentrated in cortex underlying the defect perimeter. The predictions of this study are the first step to assess safety of transcranial electrical therapy in subjects with skull injuries and skull plates.

Introduction

Transcranial electrical stimulation using weak direct currents – transcranial direct current stimulation (tDCS) – is a promising method of brain modulation that has been increasingly tested as a tool to modulate plasticity in neuropsychiatric diseases (Boggio et al., 2009b). Relatively simple to apply, tDCS involves application of direct current through at least one electrode positioned on the scalp. The mechanisms of tDCS are associated with the intensity and direction of current flow through the cortex, leading to neuromodulation and lasting changes in cortical excitability. The polarity specific shifts in cortical excitability have been suggested to be due to membrane polarization (Ardolino et al., 2005; Radman et al., 2009) leading to modulation of sodium and calcium channel conductance and a change in NMDA-receptor activation (Liebetanz et al., 2002; Nitsche et al., 2003). Clinical tDCS has shown to induce beneficial effects in preliminary studies in different neuropsychiatric conditions such as pain (Fregni et al., 2006a; 2007), motor rehabilitation (Fregni et al., 2005b; Hummel et al., 2005), cognitive function (Fregni et al., 2005a; Iyer et al., 2005), major depression (Boggio et al., 2007) and craving disorders (Boggio et al., 2009a).

Because of these initial positive results, tDCS has the potential to be used for the rehabilitation of patients with brain lesions who also have skull defect (with or without skull plates) such as patients with traumatic brain injury (TBI) or patients who undergo neurosurgery. In fact, some of the neurological sequelae are presumably consequences of disrupted cortical activity following the traumatic event, and tDCS in this circumstance can be a useful tool to reactivate and restore activity in essential neural networks associated with cognitive and motor processing. In our pilot study combining tDCS with robotic motor training aimed at upper extremity motor recovery, in a small group of TBI survivors with no skull defects, we showed that tDCS can enhance the effects of upper extremity motor training (Chew et al., 2009). tDCS has similar potential to also improve cognition in these patients. Finally, because of preliminary data showing that tDCS reduces epileptogenic activity as indexed by epileptiform discharges in humans and seizure threshold in animals (Fregni et al., 2006b;

* Corresponding authors. A. Datta is to be contacted at T-463 Steinman Hall, Grove School of Engineering, The City College of CUNY, 160 Convent Ave, New York, NY 10031, USA. Fax: +1 212 650 6727. F. Fregni, Spaulding Rehabilitation Hospital, 125 Nashua Street, Boston, MA 02114, USA. Fax: +1 617 975 5322.
E-mail addresses: abhishek.datta@gmail.com (A. Datta), ffregni@partners.org (F. Fregni).

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Liebetanz et al., 2006), this technique might be useful for patients with refractory epilepsy who underwent surgery and have skull plates or applied to patients who needed to undergo decompressive craniectomy for trauma and cerebrovascular disease.

Although evidence supports the investigation of tDCS in TBI or patients with other major neurological deficits and skull defects, one perceived limitation for the use of tDCS in these patients is the modified current flow by the skull defects and use of skull plates. During tDCS, the current applied at the scalp must pass through the resistive skull before reaching the brain, and the specific relationship between electrode position, skull geometry, and the underlying tissue properties are thought to determine the location and magnitude of current flow (Datta et al., 2009a). It remains unknown how skull defects and use of skull plates associated with TBI would affect current flow through the brain and how to modify tDCS dose and/or electrode locations in such cases. For example, a hole through the skull that is filled with relatively highly conductive fluid or tissue, might present an attractive "shunt" pathway for current entering the brain. The underlying cortex would then be exposed to a higher intensity of focused current flow. This in turn might be either beneficial in targeting the underlining brain region or hazardous if the increased current levels resulted in undesired neurophysiologic or pathological changes.

Computational finite element method (FEM) models of tDCS allow prediction of current flow through the cortex (Miranda et al., 2006; Wagner et al., 2007). We previously developed a high-resolution MRI-derived model of tDCS with increased precision and accuracy (Datta et al., 2009a). Here we modify this model to include conceptualized (cylindrical) skull defects and plates and analyze resulting changes in cortical current flow; therefore our aims were to: (i) determine cortical current density distributions in subjects with skull defects; (ii) determine whether the size of skull defect influences the amount and location of current induced in the brain and (iii) determine whether skull plates (i.e. acrylic or titanium plates) also change (and in which direction) the amount of current being delivered to the brain. Our predictions provide a general framework to determine what factors modulate current flow to the brain in cases of specific skull injuries, and thus a rational basis for customizing electrical stimulation dose based on individual parameters and desired outcome.

Methods

Models

To consider the role of skull defects on brain current flow during tDCS, we developed finite element (FE) models that addressed the role of electrode configuration and skull defect size/properties. All models were based on a single MRI-derived head model from a healthy adult subject, where idealized (cylindrical) skull defects were added. For Part 1, we considered two electrode configurations (C3-supraorbital or O1-supraorbital), two defect sizes (2.5 cm and 10 cm diameter), two defect locations in relation to the electrodes (under and between the stimulation pads), and four defect states (acute tissue, chronic tissue, titanium skull plate, and acrylic skull plate). In Part 2, we considered only the effect of incrementally changing the defect size. In each case, the electric fields induced on the cortical surface were compared to the healthy (no defect) case.

MRI guided finite element head model

The volume conductor 3D model (having 1 mm^3 resolution) used in this study was developed previously by our group to calculate tDCS induced electric fields. The entire process involving segmentation of high-resolution 3 T MRI scans, mesh creation and the eventual export to a finite element method solver (SIMPLEWARE LTD., UK) was detailed previously (Datta et al., 2009a); importantly the entire workflow preserves the high resolution of the MRI scans. The model is referred to as the 'healthy head model' in this paper (Fig. 1) and the electrical properties of the tissues are assigned representative isotropic average values (in S/m): brain: 0.2; CSF: 1.65; skull: 0.01; and scalp: 0.465. The muscle, fatty tissue, eyes and blood vessel compartments were assigned the same tissue properties as that of scalp. In this study, the tDCS induced cortical currents of a healthy head was used as a control to evaluate the effects of skull injury. In Part 1, we modeled two electrode *configurations* in combination with a range of skull *defects* and skull *plates*, as specified below. For each model, the combination of electrode configuration and skull injury type and location, together determine the model *montage*. For Part 2, we focused on the role of varying skull defect size under an electrode. Outside of the injury, head properties were unchanged across montages.

Part 1: electrode properties and configurations

We modeled conventional "sponge-based" electrodes having an area of 35 cm^2 (7×5 cm) which is a size commonly used in clinical studies (Fregni et al., 2005a, 2006a) and calculated the induced currents in the cortex resulting from application of 1 mA total current (corresponding to an average electrode surface current density of 0.28 A/m^2).

We modeled two electrode configurations (Fig. 1):

(A) M1-supraorbital: The anode electrode was placed over the primary motor cortex with its center localized 5 cm lateral from the vertex (corresponding to C3) and the cathode electrode was placed over the contralateral supraorbital area.
(B) Occipital-supraorbital: The anode electrode was placed on O1 (primary occipital cortex) and the cathode electrode was placed over the contralateral supraorbital area.

The latter electrode configuration allowed us to model the presence of large skull defects and skull plates between the stimulation electrodes. During conventional tDCS, rectangular sponges are typically soaked in saline and the abutting electrode is energized. The sponge was thus assigned the electrical conductivity of saline ($\sigma = 1.4$ S/m) and the stimulation electrodes were modeled as conductors ($\sigma = 5.8\times10^7$ S/m). The electrodes had a thickness of 1 mm and the thickness of the sponge varied from 1 to 2.5 mm (Datta et al., 2009a). An important note here is that electrode *location* is important in relation to skull defects and skull plates.

Part 1: skull defects — acute and chronic defects

Skull defects were modeled as idealized cylindrical "holes" in the skull. We considered the following two defect sizes in this study: (1) a large hole having a diameter of 10 cm that can be associated with decompression craniectomy, in cases of surgery for hemorrhage drainage in which the removed skull is not placed back, or large skull fracture (Rish et al., 1979) and (2) a small hole with a diameter of 2.5 cm that is usually found as a consequence of a neurosurgical procedure or a small skull fracture (Sekhar and Fessler, 2006). Distinct locations of the holes — either under or between the stimulation electrodes were modeled. In cases where the hole in the skull was underneath the stimulation electrode, the center of the injury was aligned with the center of the electrode (for instance, over the primary motor cortex, corresponding to the location of C3). In cases where the holes were between the stimulation electrodes, the center of the injury corresponded to approximately midway between the anode and cathode electrodes.

We analyzed two different scenarios for tissue filling up defects. In the *acute* defect state, CSF ($\sigma = 1.65$ S/m) was used to fill the hole in the skull (Wagner et al., 2007); CSF has been shown in imaging and