Computational modeling of transcranial direct current stimulation (tDCS) in obesity: Impact of head fat and dose guidelines

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Dennis Q. Truong [a], Greta Magerowski [b], George L. Blackburn [b], Marom Bikson [a], Miguel Alonso-Alonso [b,c,*]

[a] Neural Engineering Laboratory, Department of Biomedical Engineering, The City College of City University of New York, 160 Convent Ave, Steinman Hall, T-403B, New York, NY, USA
[b] Center for the Study of Nutrition Medicine, Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Ave, Feldberg 880, Boston, MA, USA
[c] Berenson-Allen Center for Noninvasive Brain Stimulation, Division of Cognitive Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Ave. Ks-158, Boston, MA, USA

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ABSTRACT

Recent studies show that acute neuromodulation of the prefrontal cortex with transcranial direct current stimulation (tDCS) can decrease food craving, attentional bias to food, and actual food intake. These data suggest potential clinical applications for tDCS in the field of obesity. However, optimal stimulation parameters in obese individuals are uncertain. One fundamental concern is whether a thick, low-conductivity layer of subcutaneous fat around the head can affect current density distribution and require dose adjustments during tDCS administration. The aim of this study was to investigate the role of head fat on the distribution of current during tDCS and evaluate whether dosing standards for tDCS developed for adult individuals in general are adequate for the obese population. We used MRI-derived high-resolution computational models that delineated fat layers in five human heads from subjects with body mass index (BMI) ranging from "normal-lean" to "super-obese" (20.9 to 53.5 kg/m^2). Data derived from these simulations suggest that head fat influences tDCS current density across the brain, but its relative contribution is small when other components of head anatomy are added. Current density variability between subjects does not appear to have a direct and/or simple link to BMI. These results indicate that guidelines for the use of tDCS can be extrapolated to obese subjects without sacrificing efficacy and/or treatment safety; the recommended standard parameters can lead to the delivery of adequate current flow to induce neuromodulation of brain activity in the obese population.

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1. Introduction

Obesity is a major public health concern worldwide. In the United States alone, 78 million adults and approximately 12.5 million children and adolescents were obese between 2009 and 2010 (Ogden et al., 2012). Research indicates that these numbers will continue to rise. The largest increase will be in severe obesity, with its accompanying surge in comorbid conditions and related healthcare costs (Finkelstein et al., 2012; Wang et al., 2011). The medical, social, and economic consequences of obesity have focused global attention on the condition and spawned numerous public health initiatives. Still, therapeutic options remain limited. New treatment strategies are required to halt the rise in obesity and limit future economic and societal costs.

A growing body of evidence, mostly from human neuroimaging studies, suggests that dysregulation in brain regions that process cognitive and reward aspects of food and eating behavior may be a key component of obesity (Alonso-Alonso and Pascual-Leone, 2007; Appelhans, 2009; Carnell et al., 2012; Dagher, 2012; Volkow et al., 2013; Zheng et al., 2009). Thus, modulating brain activity with neurotechnologies may open new therapeutic avenues. Compared to other neuromodulatory techniques, transcranial direct current stimulation (tDCS) offers significant advantages due to its relative safety, noninvasiveness, low-cost, and portability (Nitsche et al., 2008).

By delivering a weak direct current to the scalp via two electrodes – anode and cathode – tDCS can modulate the transmembrane potential of neurons, modify excitability, and induce plasticity changes. Over time, these can translate into clinical effects in diverse patient populations (Brunoni et al., 2012; Nitsche and Paulus, 2011; Nitsche et al., 2008). Preliminary, single-session data support a potential role for tDCS in the modulation of appetite and eating behavior in humans. In a randomized, sham-controlled, crossover study conducted in 23 subjects, Fregni et al. (2008) reported an acute decrease in food craving, as well as a reduction in snack consumption and eye gaze fixation to food following 20 min of tDCS applied over the prefrontal cortex. Similarly, a study in 19 subjects by Goldman et al. (2011) found that prefrontal

* Corresponding author at: Berenson-Allen Center for Noninvasive Brain Stimulation, Division of Cognitive Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Ave. Ks-158, Boston, MA 02215, USA. Tel.: +1 617 667 0240; fax: +1 617 975 5322.
  E-mail address: malonso@bidmc.harvard.edu (M. Alonso-Alonso).

tDCS caused a transient increase in the self-reported ability to resist food and a reduction in food cravings, particularly for sweet foods and carbohydrates; however there was no effect on ad libitum food intake. More recently, Montenegro et al. (2012) replicated the reduction of the desire to eat in 9 overweight subjects following a single session of prefrontal tDCS, and they also found an enhancement of the effect when tDCS was combined with a bout of aerobic exercise. Altogether, these three small studies provide initial rationale for the use of tDCS in clinical trials in the field of obesity.

To optimize stimulation parameters in obese subjects requires knowing the potential influence of head fat on current density distribution. It is well-established that head anatomy and variations in tissue layers, including fat (Shahid et al., 2011; Truong et al., 2012), affect how current density is distributed in the brain (Bikson et al., 2012a,b; Sadleir et al., 2010; Wagner et al., 2007). The identical tDCS montage applied to subjects with different head anatomy can produce varied intensity and pattern of current flow, which in turn may influence efficacy or safety. Even across anatomically typical adults, variation in peak cortical current density can vary > two-fold (Datta et al., 2012).

Therefore, the presence of a thickened layer of fat around the head in obese individuals could influence brain current flow and result in neuromodulation during tDCS administration. Investigating if and how to alter tDCS dose to accommodate variations in BMI is timely. Interest in the use of this technology in obese subjects is growing, for both the modulation of craving-related processes, and more broadly, for neuropsychiatric treatment of patients who often have obesity as a comorbidity. The purpose of this study was to systematically examine the role of head fat on the distribution of current during tDCS using MRI-derived high-resolution computational models, and to evaluate whether tDCS dosing standards developed for adults in general are adequate for the obese population.

2. Methods

2.1. Subjects

To determine the effect of head fat on current density distribution during tDCS, we created models from MRI images of five human subjects categorized according to BMI, from normal (18.5–24.9 kg/m^2) to super obese (>50 kg/m^2). Subjects were a 35-year-old female with a BMI of 53.5 kg/m^2 (S1), a 47-year-old female with a BMI of 43.4 kg/m^2 (S2), a 22-year-old female with a BMI of 38.3 kg/m^2 (S3), and a 25-year-old female with a BMI of 20.9 kg/m^2 (S4). We also included a 36-year-old male subject with a BMI of 25.1 kg/m^2 (S#) who participated in prior tDCS computational modeling studies (Bikson et al., 2010; Datta et al., 2012). Subjects S1–S4 underwent an MRI as part of research studies related to eating behavior and obesity. Study procedures were approved by the Institutional Review Board of Beth Israel Deaconess Medical Center.

2.2. MRI data collection and segmentation

We performed high-resolution T1-weighted magnetization prepared rapid gradient echo (MPRAGE) MRI scans at the Center for Biomedical Imaging, Boston University School of Medicine, using a 3-T Philips Achieva scanner (Philips Medical Systems, Best, The Netherlands) equipped with a Synergy-L Sensitivity Encoding (SENSE) head coil. Acquisition parameters were: TE = 3.2 ms; TR = 6.92 ms; flip angle = 8°; FOV = 256 mm; resolution = 256 × 256; slice thickness = 1.2 mm; no gap; and voxel size of 1 × 1 × 1.2 mm. The scans were segmented into 7 tissues: air, skin, fat, skull, cerebral spinal fluid (CSF), gray matter, and white matter.

Automated segmentation algorithms from Statistical Parametric Mapping (SPM8, Wellcome Trust Centre for Neuroimaging, London, UK) were used in conjunction with updated tissue probability maps (Rorden et al., 2012) to generate an initial segmentation of air, skin, skull, CSF, gray matter, and white matter. Additional post-processing

algorithms smoothed artifacts and corrected for discontinuities (Huang et al., 2012). We added fat segmentation through a threshold flood fill of skin (fat has high signal intensity on T1-weighted MRI images) and manually corrected lingering errors in continuity and detail in all tissues with ScanIP 4.2 (Simpleware Ltd, Exeter, UK). Tissue continuity was verified after the results of the automatic segmentation, visualizing the data extensively. Further manual adjustments were performed to guarantee continuity and improve the accuracy of the segmentation so that the tissue masks matched closely the real anatomy of the individual. All these procedures were carried out by two team members using the visualization options and tools provided in the ScanIP 4.2 software.

Two models (S# and S4) were artificially "fattened" by dilating the segmentation of fat. Fat was merged with the outer surface of skin, and then dilated isometrically up to 10 mm. This dilation caused fat to overtake the original skin surface by expanding outward. To recover the skin we made a duplicate of this merged fat and skin segmentation mask and dilated it an additional 3 mm to form the new skin surface. As a result of this transformation skin and fat were still distinct segmentation masks; fat became thicker, and the thickness of skin was fixed at 3 mm. No tissues other than skin and fat were altered in these models.

We measured the thicknesses of skin, fat, bone, and CSF for each model from the segmentation data. Measurements were performed over both motor strips (C3 and C4), 5 times each, and averaged. Tissue thickness was measured in three-dimensions by sampling a patch of tissue with a bounding box. The volume of the tissue within the bounding box was determined by summating the segmentation voxels (1 mm^3). This volume was then projected from the area of the diagonal plane within the bounding box so that thickness (length 'L') equals tissue volume divided by plane area (L = V / A). The measurements were recorded from 10:20 positions C3 and C4 where the plane was tangential to the scalp in a coronal slice.

2.3. Modeling of tDCS

Stimulation electrodes, sponge pads, and gels were modeled in SolidWorks (Dassault Systèmes Corp., Waltham, MA) and imported into ScanIP for meshing. Three montages were modeled: 5 × 7 cm pads with anode over the motor strip (C3) and cathode over the contralateral supra-orbital (M1-SO); 5 × 7 cm pads with anode over the inferior frontal gyrus (F8) and cathode over the contralateral supra-orbital (IFG-SO); and a high-definition (HD) electrode ring configuration designed for anodal stimulation over the motor strip (4 × 1 over C3; 5 cm radius from center electrode to outer electrodes). An adaptive tetrahedral meshing algorithm was used in ScanIP to generate meshes between 6 × 10^6 and 14 × 10^6 quadratic elements.

Finite element method (FEM) models were created in COMSOL multiphysics 3.5a (COMSOL, Inc., Burlington, MA) using the aforementioned meshes. Models were created using electrostatic volume conductor physics with material conductivities defined as follows: (in S/m): air, 1×10^{-15}; skin, 0.465; fat, 0.025; skull, 0.01; CSF, 1.65; gray matter, 0.276; white matter, 0.126; electrode, 5.99×10^7; saline-soaked sponge, 1.4; and conductive gel, 0.3. These conductivity values used were the same as previously published modeling work drawing on data from a combination of in vivo and in vitro measurements (Datta et al., 2011; Gabriel et al., 1996). We applied boundary conditions to simulate direct current stimulation. Internal boundaries between tissues were assigned the continuity condition (n * (J$_1$ − J$_2$) = 0), and the Laplace equation ($\nabla * (\sigma \nabla V) = 0$) was solved. The resulting cortical electric field was interpreted as a correlate for modulation (Bikson et al., 2004; Tranchina and Nicholson, 1986). The surfaces of the cathodes were grounded (V = 0), while the surfaces of the anodes had a current density of 1 A/m^2. All other exterior surfaces were electrically insulated. Peak electric field data are provided in the text as absolute values or as mean (μ) and standard deviation (σ).