34th Annual International Conference of the IEEE EMBS
San Diego, California USA, 28 August - 1 September, 2012

Transcranial Direct Current Stimulation in Pediatric Brain: A computational modeling study

Preet Minhas, Marom Bikson (*Member, IEEE*) Adam J. Woods, Alyssa R. Rosen, Sudha K. Kessler

***Abstract*— Transcranial direct current stimulation (tDCS) is a method of non-invasive brain stimulation which uses weak electric currents applied on the scalp to modulate activity of underlying brain tissue. In addition to being used as a tool for cognitive neuroscience investigations, tDCS has generated considerable interest for use as a therapeutic modality for neurologic disorders. Though the safety and tolerability of tDCS in adults is well-established, there is little information on the safety of tDCS in children. Because there are differences between children and adults in several key parameters (such as skull thickness and cerebrospinal fluid volume) which affect current flow through the brain, special consideration should be given to the stimulation parameters which are used in a pediatric study population. In this study we present cortical electrical field maps at different stimulation intensities and electrode configurations using a high-resolution-MRI derived finite element model of a typically developing, anatomically normal 12 year old child. The peak electrical fields for a given stimulus intensity in the adolescent brain were twice as high as in the adult brain for conventional tDCS and nearly four times as high for a 4X1 High-Definition tDCS electrode configuration. These data suggest that acceptable tDCS stimulation parameters may be different in children compared to adults, and that further modeling studies are needed to help guide decisions about applied current intensity.**

I. Introduction

Transcranial direct current stimulation (tDCS) is a non-invasive tool for modulation of neuronal activity using weak electrical currents applied to the scalp, using 25-35 cm^2 sponge-covered rubber electrodes (conventional tDCS) or arrays of conductive gel covered discs (High-Definition tDCS). There is a growing body of evidence suggesting that the changes in cortical neuronal activity induced by tDCS can be used therapeutically for neurologic and psychiatric disorders, many of which affect children and adults. However, reports of the use of tDCS in children have been extremely limited at this point, in part because of the safety concerns that always come with extending the use of new technologies from adults to children [1],[2],[3].

*Research supported by: The Children's Hospital of Philadelphia and Clayton's Hope Foundation. A.J. Woods receives support from: NIH NINDS T32NS007413.

P Minhas is with the City College of New York, New York, New York (phone: 212-650-6791; fax: 212-650-6727; e-mail: pminhas.8923@gmail.com). M Bikson is with the City College of New York, New York, New York 10031 (email: bikson@ccny.cuny.edu)

SK Kessler, AR Rosen, and AJ Woods are with Children's Hospital of Philadelphia and the University of Pennsylvania, Philadelphia, PA 19104 USA. (email: kesslers@email.chop.edu; rosenar@email.chop.edu; adwoods@mail.med.upenn.edu).

The safety and tolerability of tDCS when used within accepted safety guidelines is well established in adults [4], [5],[6],[7]. There are several parameters that determine the effects of tDCS – current intensity applied at the scalp, electrode size, electrode locations, and duration of stimulation [9],[10]. Previous modeling studies of current flow through the brain resulting from tDCS have shown patterns of current flow also depend on anatomic considerations [11]. Because the skull and brain mature over time, with age dependent differences in skull thickness, CSF volume, and white and gray matter volumes, the effects of tDCS with specified parameters may differ substantially in children compared to adults [12],[13].

Computational models using finite element methods can be used to predict the relationship between tDCS effects at specified parameters and induced brain current flow (cortical electric fields). In this study, we present the first high-resolution model of current flow through a child's brain. Conventional and 4x1 High-Definition tDCS montages are evaluated at different current intensities compared to the same stimulation parameters in an adult head model.

II. Methods

A. MRI derived head model

To determine peak electric fields and total current flow distribution in children relative to adults, we developed an individualized high resolution (1mm) MRI derived finite element model for a 12-year old child. A standard high-resolution adult model (of 35 years) previously developed by our group was used as a comparison [14]. High-resolution 3T MRI scans of the adolescent were obtained and segmented into six tissues (CSF, gray, white, bone, skin, and air), using both automated (FSL) and manual segmentation tools (SIMPLEWARE Ltd., Exeter UK) (Figure1).

The stimulation sponge pads, rubber electrodes, disc electrodes, and gel were imported into ScanCAD (SIMPLEWARE Ltd., Exeter UK) as .STL files and manually placed on the scalp. The volumetric mesh was generated from the segmented data. The final mesh, consisting of >5,000,000 tetrahedral elements (>9,000,000 degrees of freedom), was imported into COMSOL Multiphysics 3.5 (Comsol Inc., MA). The model was solved using a linear system solver of conjugate gradients with a relative tolerance of 1×10^6. The electrical properties of the tissues were defined by the average isotropic conductivity (S/m): gray matter: 0.276 S/m; white matter: 0.126 S/m; CSF: 1.65 S/m; skull: 0.01 S/m, scalp: 0.465 S/m.

B. Electrode configurations

We modeled two electrode configurations:

(A) M1-supraorbital: Conventional sponge based electrodes with an area of 25 cm^2 were modeled. The anode was placed over the primary motor cortex with its center corresponding to C3 (on a 10-20 EEG cap). The cathode was placed over the contralateral supraorbital area (Figure 2).

(B) 4x1 HD-tDCS ring: Disk electrodes (11 mm in diameter) submerged in gel were modeled. The anode was placed over the primary motor cortex corresponding to C3. Four returns were arranged in a circular fashion around the anode, each at a disc center to disc center radius of 5 cm. This separation corresponds to the electrode separation using a 10-20 EEG cap system in an adult. However, because the circumference of the adult head is larger than that of the child, the 5 cm separation in the child does not equate to the same separation when using the 10-20 EEG cap system. Therefore, a smaller sized ring configuration (disc center to disc center radius of 2.5 cm) was also modeled in the child. (Figure 2).

C. Initial and Boundary Conditions

The Laplace equation $\nabla \cdot (\sigma \nabla V) = 0$ (V: potential, σ: conductivity) was solved with the following boundary conditions: (1) inward current flow = J_n (normal current density) applied to the exposed surface of the anode electrode, (2) ground applied to the exposed surface of the cathode electrode(s), and (3) all other external surfaces treated as insulated. Current densities corresponding to 1 and 2 mA of total current for the rectangular pad configuration and 0.5 to1.5 mA (in increments of 0.5) total current for the 4x1 ring configuration were respectively applied. The electric field magnitude was plotted on the cortical surface for both the adult and child for both electrode configurations and respective currents. Additionally, coronal cross-sectional slice plots of EF magnitude were generated for the 4x1 ring configuration.

III. Results

A. Comparison of intervening tissue:

Because the thickness of the intervening tissues between scalp and brain are important determinants of current behavior, we calculated differences in skin thickness and skull thickness in the child and adult heads based on the MRI image. The skin thickness in the region underlying C3 (anode for conventional and High-Definition tDCS) was 5.5 mm in the child and 6.3 mm in the adult. The skull thickness under the electrodes was 2.9 mm in the child and 3.9 mm in the adult. Figure 1 shows the segmented compartments (bone, skull, CSF, gray matter, and white matter) for both the child and adult. Cross sections were taken through the 3D rendered tissues to measure skull and scalp thickness (using tools in SIMPLEWARE, Ltd., UK).

B. Current Flow

We calculated the electric field/current density magnitude in the brain for both the child and adult for conventional (25 cm^2 pads) and High-Definition tDCS (Figure 2).

Stimulation, with an intensity of 2 mA, using 25 cm^2 square pads resulted in a peak electric field of 0.70 V/m and 1.04 V/m, beneath the anode, in the adult and child respectively (Figure 2). Thus, for the same conventional tDCS stimulation intensity, the peak electric field in the child was ~1.5 times higher than in the adult. However, the peak electric field on the scalp was similar for both the adult and child (6.2 V/m and 6.5 V/m, respectively- corresponding to a current density of 1.7 A/m^2, and 1.8 A/m^2, respectively). Reducing the stimulation intensity in the adolescent simulation from 2 mA to 1 mA, resulted in a peak electric field of 0.52 V/m (as expected from linearity, Figure 2), for the adolescent, which was ~1.3 times lower than in the adult case for 2 mA of stimulation.

For the 4x1 High-Definition ring configuration the peak electric field was 0.16 V/m and 0.56 V/m (for a disc center to disc center radius of 5cm), at 1 mA, in the adult and child respectively (Figure 2). At the smaller ring size (disc center to disc center radius of 2.5 cm) the child had a peak electric field of 0.41 V/m. Modulation of the cortical tissue appeared to extend much deeper (toward the ventricles) at 1.5 mA of current in the child compared to the adult.

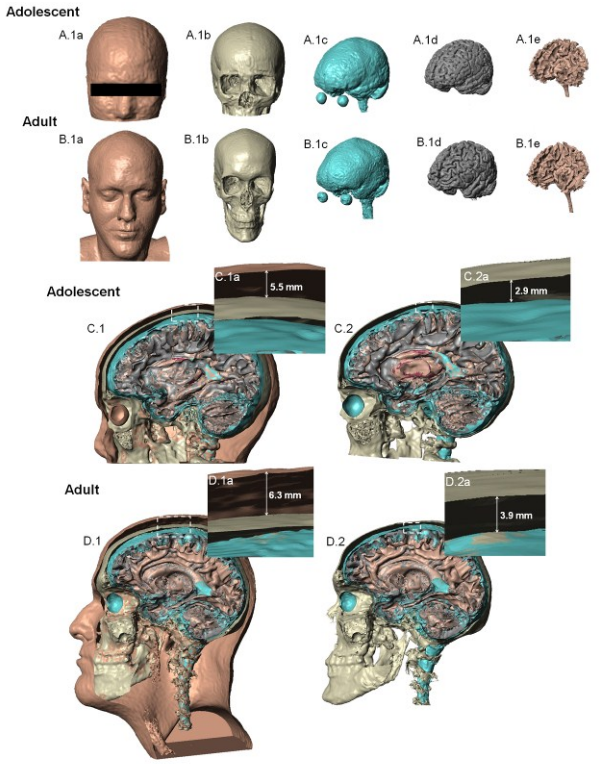

Figure 1. Segmented tissue masks (skin, skull, CSF, gray matter, and white matter respectively) for the child and adult are shown in the first two rows. Skin and skull thickness are among important factors that determine the flow of current through the brain. The skin thickness was 5.5 mm and 6.3 mm for the adolescent and adult respectively. The skull thickness was 2.9 mm and 3.9 mm for the adult and child respectively.

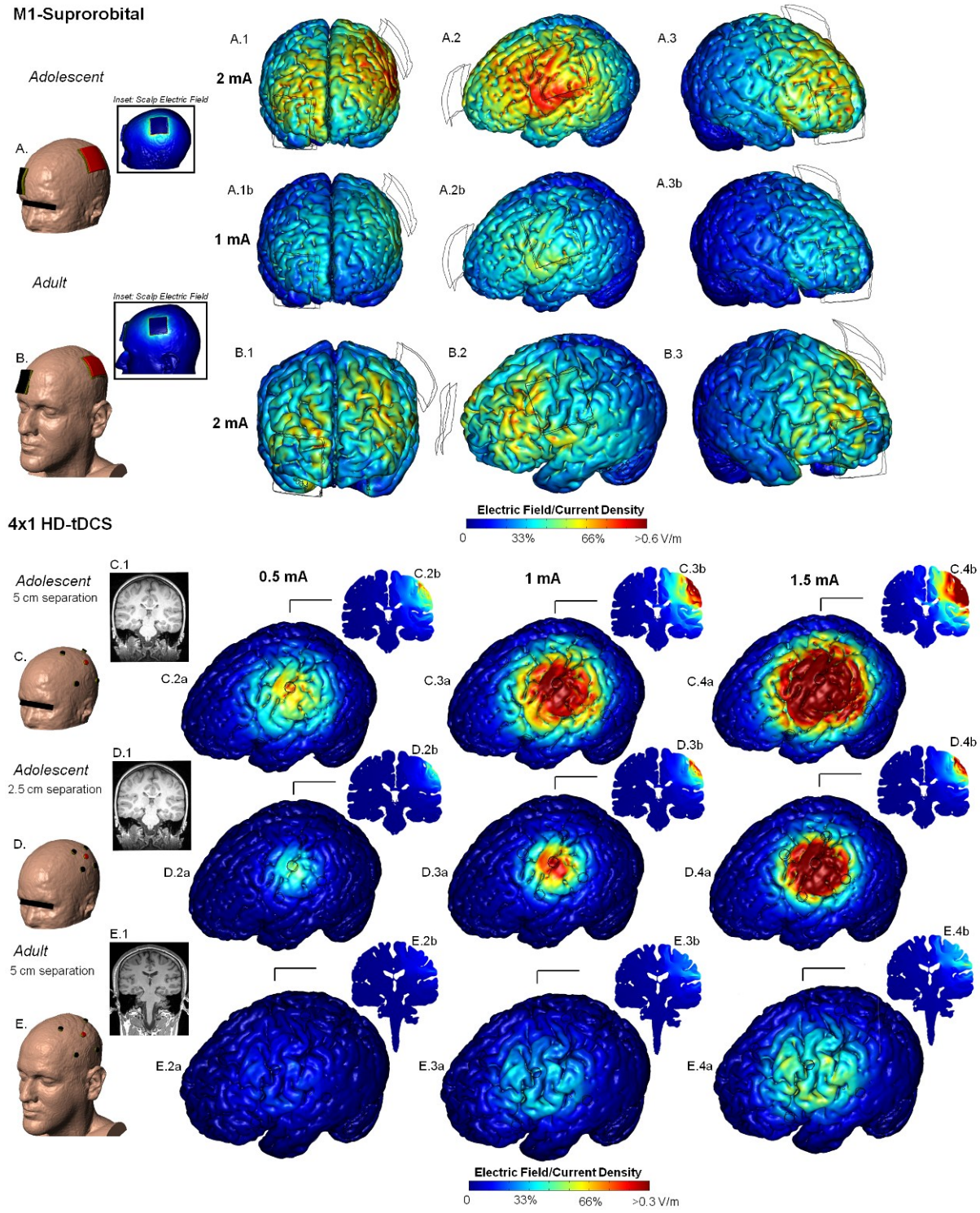

Figure 2. Predicted electric field magnitude plotted on to the cortical surface of the adolescent and adult for conventional and 4x1 High-Definition tDCS at different current dosages. **tDCS:** For conventional tDCS the center of anode (red) was positioned on the motor strip and cathode (black) was positioned over the contraletral supraorbital area (**A, B**). For 4x1 high definition tDCS the center of the anode (red) was positioned on the motor strip and the four returns (black) were placed around the center in a circular fashion with a 5cm distance from the center of the anode to the center of the return (**C,E**). An additional smaller ring (2.5 cm separation) was modeled for the child (see methods) (**D**). At 2 mA, the peak electric field was1.04 V/m in the adolescent and 0.70 V/m in the adult. False color maps are shown in the front, left and right view respectively (**A.1-3, B.1-3**).The second row shows a false color map of induced electric fields at 1 mA current in the adolescent in the front, right and left view, respectively (**A.1b-3b).** *Insets* show electric field on the scalp (10X scale). The peak electric fields on the scalp for the adult and child at 2 mA are 6.2 V/m and 6.5 V/m respectively. **HD-tDCS:** The peak electric field, at 2 mA, for 4x1 HD-tDCS was 1.12 V/m in adolescent and 0.32 V/m in the adult, at a 5 cm separation. A smaller ring was modeled for the adolescent. This separation corresponds to the 5 cm separation in the adult (see methods). False color maps of 0.5 mA, 1 mA, and 1.5 mA of current are shown, respectively, in the adolescent and adult, at 5cm separation **(C.2a, C.3a, C.4a, D.2a, D.3a, D.4a, E.2a, E.3a, E.4a**). Cross-sectional coronal electric field plots, corresponding to the coronal MRI slice, were taken from the center of the brain (beneath the anode). Brain modulation was comparatively deeper for the adolescent than the adult at all three current intensities **(C.2b, C.3b, and C.4b**).

IV. Discussion

The results of this study suggest that while general patterns of current flow may be similar in adult and child brains for specific electrode montages, the peak electric fields achieved with a given tDCS current intensity are greater in the child brain. These results have potentially important implications for investigators designing studies utilizing tDCS in pediatric populations and provide a valuable first-approximation towards efficacy and safety parameters. However, it is also important to note that although electric field is an important metric establishing efficacy and safety, it is not sufficient in itself- nor does it account for region specific (anatomical) or (patho)physiological differences across subjects. For example, stimulation waveform and duration should be taken in to account.

To date, there are a limited number of published studies reporting tDCS in children; these studies applied stimulation up to 20 minutes at intensities varying from 1 mA to 2 mA using bilateral (anodal and cathodal stimulation over the brain) or cathodal stimulation [1],[2],[3]. Similar to tDCS studies performed on adults, these studies reported no adverse effects or significant side effects beyond itching or tingling at the site of stimulation [4],[5],[6],[7]. Because the peak brain electrical fields under the anodal regions may have been substantially higher than expected in adults, this may suggest that higher peak electrical fields can be tolerated without apparent adverse effects. Nevertheless, caution is warranted in applying stimulation intensities above 1.5 mA in pediatric populations.

However, for the same tDCS dose, the predicted current density on the scalp is similar for the adult and child, consistent with similar safety/tolerability for *skin-level effects*. Interestingly this suggests that it is possible to reduce tDCS current intensity in children to produce the same peak brain electric fields as in adults, but with reduced peak skin current density. It is also important

This study compared a high resolution model for a specific adult and child. Additional limitations include those intrinsic to finite element modeling: (a) precision and accuracy of segmentation of tissues (b) assumed isotropic conductivity values (not taking into account inhomogeneity and anisotropy). Furthermore, the assigned tissue conductivity values are presumed to be the same in the adult head model and pediatric head model, though in reality, there may be differences in the conductivity properties of skin or white matter, for example, in a child compared to an adult. Finally, differences in tissue/brain sensitivity to electrical stimulation (e.g. neurophysiology) were not considered.

Because the differences demonstrated in this study between an adolescent brain and adult brain were significant, we suspect that even greater differences may be detected in models of still younger subjects. Future directions in this line of investigation may include head models from younger healthy subjects as well as subjects with abnormal anatomy or brain lesions.

References

[1] E.T.Varga, D. Terney, M. D. Atkins, M. Nikanorova, D. S. Jeppesend, P. Uldalle et al., "Transcranial direct current stimulation in refractory continuous spikes and waves during slow sleep: A controlled study" *Epilepsy Research*, vol. 97, pp. 142-145, 2011.

[2] S. Yook, S. Park, J. Seo, S. Kim, and M. Ko, "Suppression of Seizure by Cathodal Transcranial Direct Current Stimulation in an Epileptic Report . A case report" *Ann Rehabil Med*, vol.35, pp. 579-558, 2011.

[3] A. Mattai, R. Miller, B. Weisinger, D. Greenstein, J. Bakalar, J. Tossell et al., "Tolerability of transcranial direct current stimulation in childhood-onset schizophrenia" *Brain Stimulation*, vol.4, pp.275-80, 2011.

[4] M.A Nitsche, D. Liebetaz, N. Lang, A. Antal, F. Teruga, W. Paulus, "Safety criteria for transcranial direct current stimulation (tDCS) in humans" *Clin* Neurophysiol, vol.114, pp.2220–2, 2003.

[5] C. Poreisz, K. Boros, A. Antal, W. Paulus, "Saftey aspects of transcranial direct current stimulation concerning healthy subjects and patients" *Brain Research Bulletin*, vol.4(6), pp.208-214, 2007.

[6] S. K. Kessler, P. E. Turkeltaub , J. Benson, R. H. Hamilton, "Differences in the experience of active and sham transcranial direct current direct stimulation" *Brain Stimulation*. In press.

[7] P. C. Gandiga, F. C. Hummel, L. G. Cohen, "Transcranial DC Stimulation(tDCS): A tool for double-blind sham controlled clinical studies in brain stimulation", *Clin Neurophys*, vol.117(4), pp. 845-850, 2006.

[8] A. Datta, M. Bikson, F. Fregni, "Transcranial direct current stimulation in patients with skull defects and skull plates: High-resolution computational FEM study of factors altering cortical current flow" *Neuroimage*, vol.52(4), pp.1268-78, 2010.

[9] A. Datta, M. Elwassif, F. Battaglia, M. Bikson , "Transcranial current stimulation focality using disc and ring electrode configurations: FEM analysis" *Journal of Neural Engineering*, vol 5, pp.163-174, 2008.

[10] A. Datta, M. Bikson, F. Fregni. "Transcranial direct current stimulation in patients with skull defects and skull plates: High-resolution computational FEM study of factors altering cortical current flow" *Neuroimage*, vol..52 no.4, pp.1268-78, 2010.

[11] A. Datta, J. Baker, M. Bikson, F. Fridriksson. "Individualized model predicts brain current flow during transcranial direct-current stimulation treatment in responsive stroke patient", *Brain Stimulation* vol. 4, pp.169-74, 2011.

[12] Brain Development Group. "Total and Regional Brain Volumes in a Population-Based Normative Sample from 4 to 18 Years: The NIH MRI study of Normal Brain Development" *Cerebral Cortex*, vol. 22, pp.1-12, 2012.

[13] H. Wanifuchi, T. Shimizu, T. Maruyama, "Age related changes in the proportion of intracranial cerebrospinal fluid space measured using volumetric computerized tomography scanning" *J Neurosurg*, vol.97, pp.607-610, 2002.

[14] A. Datta, V. Bansal, J. Diaz, J. Patel, D. Reato, M. Bikson. Gyri – precise head model of transcranial DC stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad. *Brain Stimulation*, vol.2 no.4, pp.201-207, 2009.