

Exploration of the effect of race on cortical current flow due to Transcranial Direct Current Stimulation: Comparison across Caucasian, Chinese, and Indian standard brains*

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Abstract— It is well known that genetic and environmental factors amongst others make different ethnic populations dissimilar reflected by the difference in overall skull and brain volume, shape, and size. We sought to investigate in this study the effects of race related morphological changes by comparing across standard Caucasian, Chinese and Indian templates on brain current flow due to transcranial Direct Current Stimulation.

Findings indicate up to 1.4 fold variation in induced electrical field magnitude in both target and non-target regions across the electrode montage and average heads considered. The observed variation is similar to the variation observed in adults of Caucasian race indicating that variation observed due to race are not significantly more than within race variation.

I. INTRODUCTION

Transcranial Direct Current Stimulation (tDCS) is a non-invasive modality that modulates underlying cortical activity using weak currents (1-2 mA typically) in a polarity-specific fashion [1-2]. Clinical tDCS been shown to induce beneficial effects for a host of neurological and neuropsychiatric conditions and for rehabilitation after stroke. Infact, evidence-based analysis on therapeutic use indicates probable efficacy for the treatment of major depression without drug resistance and for fibromyalgia pain [12]. Furthermore, tDCS is safe, easy to apply, low cost and allows adjunctive use/pairing with other interventions.

During any transcranial current stimulation technique, the induced electric field in the cortex is significantly altered from what is applied on the scalp based on how the current traverses through the intermediate tissue structures. Considering constant electrode size/montage, this current traversal is determined primarily by tissue geometry (shape, thickness, etc.) and relevant property (electrical conductivity) [3]. It is known that there are significant differences in size and shape of the skull across races [4]. For instance, it has been reported that the frontal bone is thicker while the

parieto-occipital bone is thinner in white males in comparison to black males [5]. Similarly, differences in brain size and shape have been observed across Chinese and Caucasian groups by a host of imaging studies [6]. The Caucasian brain was shown to be longer and the Chinese brain rounder while on the brain structural level, volume differences were noted across several gyri.

These geometrical differences will invariably modify the current flow into the cortex thereby leading to a different “effect” for the same tDCS stimulation intensity. This as a consequence implies that an individual’s race is expected to play a role in the cortical current flow due to tDCS. While effects of tDCS depend on myriad factors including brain state, stimulation timing in relation with task, cortical engagement, the intensity and the spatial extent of induced current remains the foremost factor.

This study aims to gain insight into the effect of race by comparing tDCS induced electric field (EF) as computed by finite element method (FEM) models. Specifically, average head templates for three ethnic groups (Caucasian, Chinese, and Indian) are considered. We build race-specific FE models derived from these templates and evaluate differences across the two most commonly used tDCS electrode configurations: C3-Fp2 (C3-SO) and F3-Fp2 (F3-SO).

II. METHODS

The steps for generating the MRI-based FE models ensuring preservation of input data resolution are based on extensive prior work by our group [3, 9, 10, 11]. These involve:

MRI acquisition and pre-processing

An Indian brain atlas was constructed from 157 Adults (males=98, females=59, and 18-35 years) as part of a larger effort to build several templates (age, gender-specific, etc.). After applying rigid linear registration with a MNI-152 template, the images were registered to first construct a raw template before eventual non-linear registration. The resultant images were averaged to create the final template [8].

A Chinese brain atlas (Chinese_56) was obtained from the Laboratory of Neuro Imaging (LONI), University of Southern California. The atlas was derived from 56 males (24.46 \pm 1.81 years) using a modified LONI pipeline using linear and non-linear transformation [6]

The classic Caucasian brain atlas (ICBM-152) was obtained from the Montreal Neurological Institute (MNI, Montreal, Canada) [7]. The ICBM-152 template is an

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unbiased non-linear average of MRIs of 152 adult human subjects (males and females included) spanning 18-90 years.

Segmentation and electrode placement

The segmentation of MRI data into tissue categories (e.g. skin, skull, CSF, gray matter, white matter, and air cavities) was performed using a combination of a probabilistic segmentation routine, tissue probability map and a custom Matlab script [13]. The residual continuity and anatomical detail errors were corrected for in ScanIP (Simpleware Ltd.,UK). Due to the need to include the entire cranium for realistic current flow models, the field of volume of the templates were extended. Stimulation electrodes created as CAD files were then incorporated within the skin mask to model the electrode configurations: a) C3-Fp2: Electrodes positioned over the C3 and the right supra-orbital regions simulating the classic motor cortex-contralateral orbita (M1-SO) stimulation [1] and b) F3-Fp2: Electrodes positioned over the F3 and the right supra-orbital regions simulating another widely used configuration. The electrodes comprised of a bottom saline layer and a top conductor layer simulating typical sponge-pad tDCS administration.

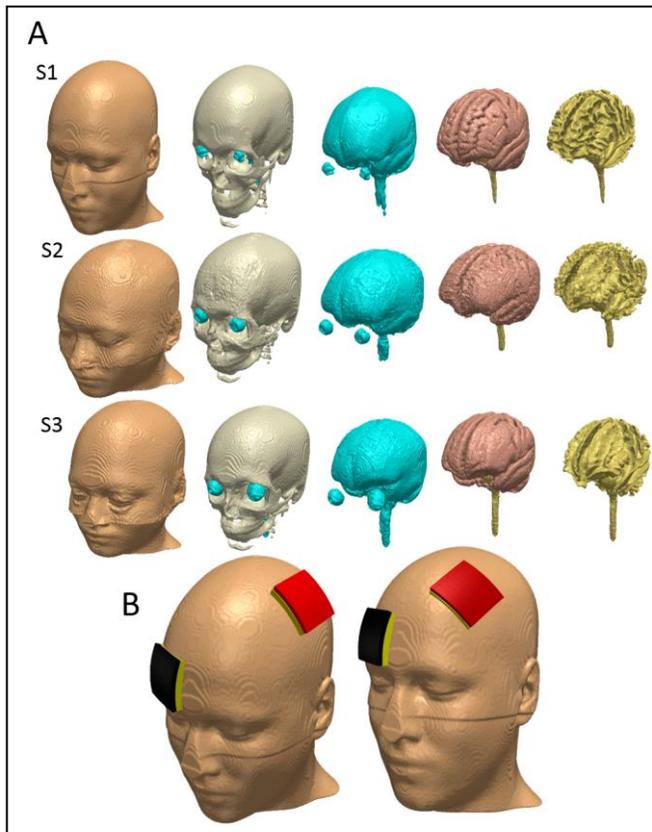


Figure 1. A: Segmentation masks of the average heads: S1: Average Caucasian S2: Average Chinese S3: Average Indian. B: The electrode montages considered in the study: M1-SO and F3-SO.

Finite element modeling

FE meshes of high quality factor were generated from the tissue and electrode masks using ScanIP. These meshes were then imported into a FE solver (COMSOL Multiphysics) and respective electrical conductivities assigned (in S/m): skin (0.465); skull (0.01); CSF (1.65); gray matter (0.276); white matter (0.126); air ($1e-7$); electrode ($5.8 e7$); sponge (1.4) [3].

The relevant boundary conditions are then imposed: 1 mA at the active (anode) electrode, ground condition at the reference (cathode) electrode and all other external surfaces treated as insulated. The C3 and F3 electrodes were treated as anode while the SO electrode was treated as cathode. The standard Laplacian equation is solved using the linear system solver of conjugate gradients with a tolerance setting of $1E-6$.

Current flow patterns obtained from individual-specific MRI are influenced significantly by gyri and sulci folding evident from the discrete EF peak or clustering phenomena [3]. Average templates however blur cortical morphology such that analysis on the gyral / sulcal level is not meaningful. Nonetheless, the consideration of average datasets is expected to provide valuable information on overall current flow- which is a function of shape, size, and thickness of the skull as well as the brain. We therefore generate 3D surface EF magnitude plot on the entire surface of the brain tissue. In addition, 2D cross-section EF magnitude maps are generated on representative coronal slices. Furthermore, since tDCS protocols are typically planned by positioning the active electrode directly “over a region of interest”, the induced EF at regions underneath the active electrode is naturally of more interest. We therefore determined peak induced values from surface directly underneath the active electrode and refer to them as “target” peak values. Likewise, we also obtained “non-target” peak values from regions *not* underneath the active electrode.

III. RESULTS

Consistent with several prior modeling efforts, both the montages considered were characterized by diffuse (non-focal) current flow. As observed in FE models derived from individual MRI [3], the models derived from average templates generally indicate increased current flow in regions anterior to the active electrode or *between* the two electrodes. Of all the combinations tested, only the average Chinese head resulted in relatively higher current flow *underneath* -when the active pad was positioned over C3 (Figure 2 S2 B1)

The average Caucasian head led to the lowest non-target induced cortical EF for the M1-SO montage (0.35 V/m) while the average Indian head led to the lowest non-target (global) induced cortical EF for the F3-SO montage (0.29 V/m).

TABLE 1. INDUCED EF PEAK VALUES (V/M) ACROSS THE TWO STIMULATION MONTAGES FOR EACH OF THE AVERAGE HEADS

| | C3-Fp2 (M1-SO) | | F3-Fp2 (F3-SO) | |
|---------------|----------------|------------|----------------|------------|
| | Target | Non-Target | Target | Non-Target |
| AVG CAUCASIAN | 0.17 | 0.35 | 0.12 | 0.34 |
| AVG CHINESE | 0.23 | 0.43 | 0.13 | 0.4 |
| AVG INDIAN | 0.23 | 0.39 | 0.15 | 0.29 |

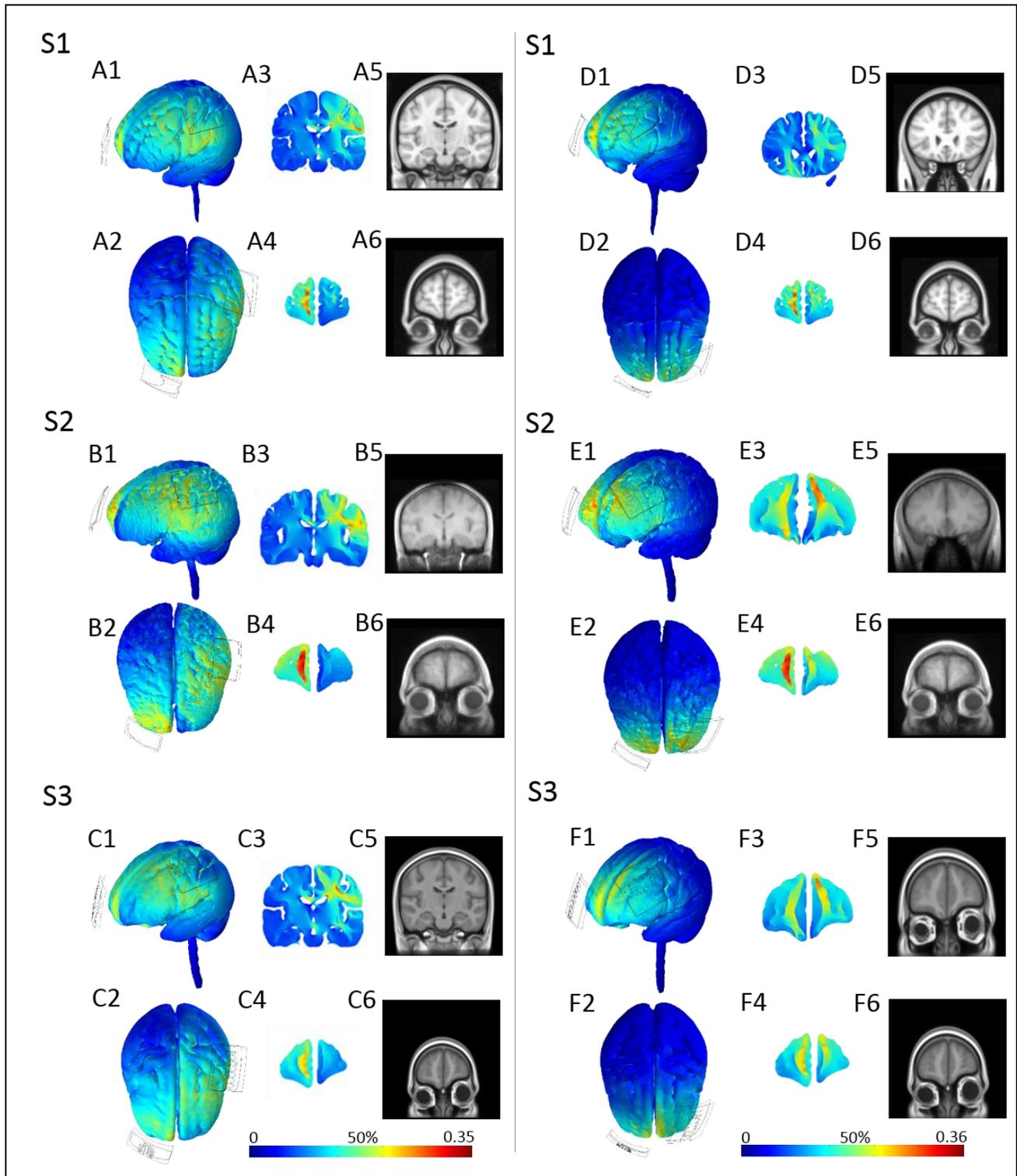


Figure 2: Induced cortical electric field magnitude surface and cross-section plots for M1-SO (left column) and F3-SO (right column). **S1:** Average Caucasian **S2:** Average Chinese **S3:** Average Indian. For each configuration we plotted the left side view and the top view. The cross-sectional images were obtained from a section directly underneath the active electrode and a section anterior to the active electrode (in the frontal area).

The average Chinese head led to the highest non-target EF across both montages (0.43 V/m and 0.4 V/m). With respect to target (local) activation, the average Caucasian head led to the lowest magnitude across both the electrode configurations. Taking the target peaks together, a maximum of ~ 1.3 fold difference in EF is observed across the templates for the M1-SO montage (0.17-0.23 V/m). A maximum of ~ 1.2 fold difference in EF is observed across the templates for the F3-SO montage (0.12-0.15 V/m). Taking the non-target peaks together, a maximum of ~ 1.2 and ~ 1.4 fold EF difference is observed across the templates for the M1-SO and the F3-SO montage respectively.

The sample cross-sectional plots (one taken directly underneath the active pad and the other in a frontal region) confirm the diffuse bilateral nature of the current flow with race-specific variation in patterns across deep structures. The

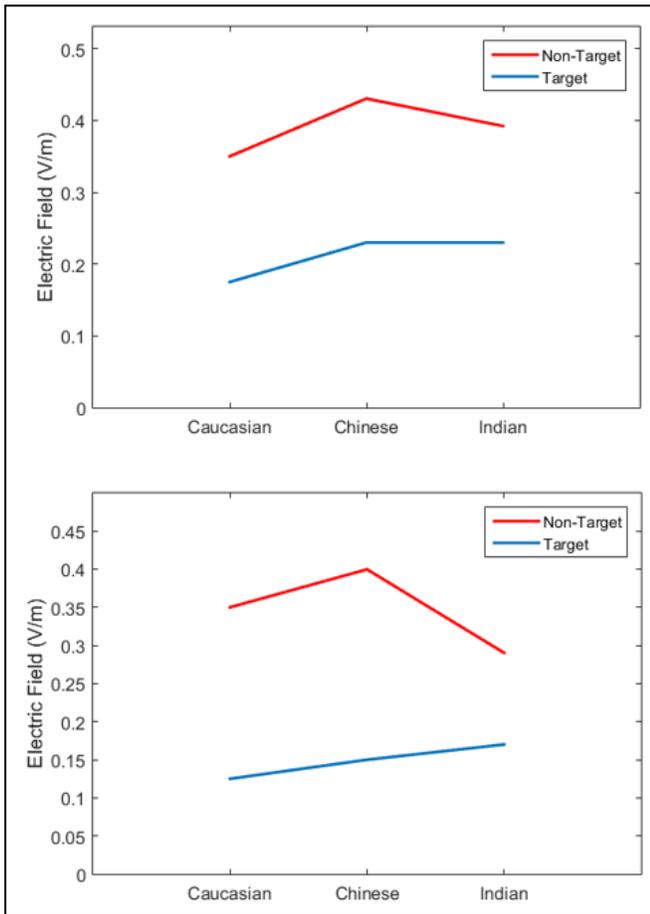


Figure 3. Variation of peak electric field in target and non-target regions across average heads (upper panel: M1-SO; lower panel: F3-SO). Target region represents area directly underneath the active electrode.

average Chinese head for instance indicates the highest EF magnitude in deeper structures (Figure 2 S2 E3 and S2 B4)-which is a reflection of the highest induced EF in the non-target superficial regions.

Overall, the peak cortical EF magnitudes in target areas was significantly lower than the non-target areas for both conventional montages across all average heads (Figure 3). These results are again consistent to predictions across healthy individuals of Caucasian race [3]. For the F3-SO montage in general, the peak induced EF in non-target region

is significantly higher than target region ($\sim 3x$ increase for average Chinese and average Caucasian) as opposed to M1-SO montage.

IV. DISCUSSION

This study demonstrates for the first time via computational models that race related structural differences will impact current flow patterns. A maximum variation of 1.4 fold is predicted across all the templates and the montages considered. This variation is comparable to the ~ 1.5 fold observed across individuals of one race (Caucasian) when looking at the peak electric field magnitude- indicating that the difference due to ethnic factors are not higher than inter-individual difference within a race.

It is known that the averaging process during template creation blurs anatomical details such as gyri/sulci structure. The gyri and sulci morphology however is paramount for realistic individual current flow modeling. Therefore, while comparison across race-specific templates sheds important information about the overall degree of potential changes due to race, it is recommended to rely on individual MRIs for current flow modeling and targeting.

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