transcranial Direct Current Stimulation: personalizing the neuromodulation

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***Abstract*— The beneficial effects of transcranial direct current stimulation (tDCS) has been demonstrated, but the neuroscientific community is working to increase its efficiency. A promising line of advancement may be reducing the inter-individual variability of the response through the personalization of the stimulation, adapted to fit the structural and functional features of individual subjects. In this paper, we approach the personalization of stimulation parameters using modeling, a powerful tool to test montages enabling the optimization of brain's targeting.**

I. Introduction

tDCS is a noninvasive technique able to induce changes in neural excitability. A weak current flow is delivered by scalp electrodes through head tissues, eliciting neuromodulation into the brain. Over the years, different kinds of montages have been used in order to increase efficiency and focality of stimulations. Size and position of the electrodes have played a crucial role in administration of dose into subject's brain, as much as current intensity and waveform (direct, alternating, random noise) [1, 2, 3]. So, our first experiment was the customization of the stimulating electrode [4]. In a previous work, we tested the feasibility of a procedure to aim to specific cortical targets through transcranial electric stimulation (tES). This procedure detailed how to shape and position the personalized stimulating electrode based on the three-dimensional reconstruction of structural MRI of each subject. More recently, we also showed that, this innovative personalized electrode, shaped on individual brain MRI data, targeting 5-day anodal transcranial Direct Current Stimulation (tDCS) over primary somatosensory cortical area, induced a relevant reduction of multiple sclerosis fatigue symptoms [5]. So through modeling, we compared the electric field induced in the neural tissue by a personalized electrode, shaped to target either the primary somatosensory (S1) or motor (M1) area with a non-personalized one. Our second personalization, was reaching the optimal positons of sponge electrodes on a subject affected by aphasia, having a lesion in the Broca's area, caused by a stroke. Our goal, was choosing the montage able to elicit the higher electric field (EF) in the perilesional area. In fact, it has not yet been clarified which of the varied electrode montages investigated, is the most effective in enhancing language recovery. The third and fourth experiment are function-guided personalization experiments. In these experiments, we used high definition (HD) electrodes, small circular elements able to deliver current in a restricted region. In fact, placing the HD anode or cathode (respectively for an anodal and cathodal stimulation) over the target and four references around it (4 x 1 ring montage), it is possible to contain the generated EF in a circular delimitated area [6, 7]. So, in our third experiment we modeled the just described ring electrode configuration on an epileptic subject's head, stimulating the cortical region containing the seizure focus. Since a cathodal stimulation can decrease the neural excitability, the objective of the experiment was to use such stimulation to reduce the power and the number of the epileptic spikes. In the last experiment, we ran a virtual EEG session putting a current dipole inside the brain, simulating a sensory evoked potential. Then we collected the voltage distribution data over the scalp and we used those parameters to invert the stimulation, applying current to the scalp. In this way we obtained an optimization of the stimulation in terms of focalization and minimal intensity applied.

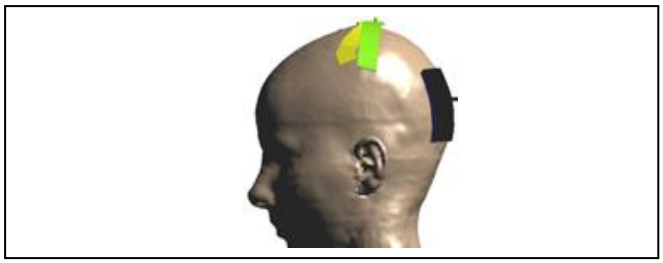

Figure 1. Experiment 1: *Lateral view of the personalized (yellow) non-personalized (green) electrode used to target M1.*

II. Materials and Methods

A. Experiment 1

We used two realistic human models from the "Virtual Family" [8], based on high resolution MRI of healthy volunteer. By a virtual reproduction of the ad-hoc neuronavigation procedure to shape and place the personalized electrode, we targeted bilateral primary motor (M1) or somatosensory cortex (S1) alternatively with the personalized and non-personalized electrode, with the reference always on the occipital area. We then estimated the distribution of the electric field across the brain structures by a computational electromagnetic approach. All the electrodes were modelled as pad conductors (σelet= 5.9*107 S/m) with a thickness of 1 mm placed over a layer (with a thickness of 5 mm) of conductive gel (σGel=1.4 S/m) with the same shape of the conductor (figure 1).

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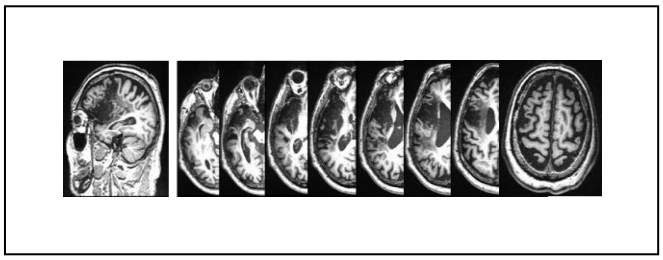

Figure 2. Experiment 2: *Sagittal and axial structural MRI slices of the modeled head of a subject having a lesion in the Broca's area.*

B. *Experiment 2*

Finite element model (FEM) of the head of a single left frontal stroke patient (figure 2) was developed in order to study the pattern of the cortical EF magnitude and inward/outward radial EF (associated with excitation/inhibition) under five different electrode sponge montages: Anodal-tDCS (A-tDCS) over the left Wernicke's area (Montage A) and over the left Broca's area (Montage B); Cathodal tDCS (C-tDCS) over the right homologue of Wernicke's area (Montage C), and of Broca's area (Montage D), where for all montages A-D the "reference" electrode was placed over the supraorbital contralateral forehead; stimulation with A-tDCS over the left Broca's and C-tDCS over the right Broca's homologue (Montage E) [9, 10].

C. *Experiment 3*

A FEM of an epileptic subject's head was realized to study the correlation between modeling results and real stimulation effects on the same patient, in order to verify the injected EF parameters over the cortex. The aim of the stimulation was to inhibit the cortical excitability of the region of the seizure focus. To do that, we ran a real EEG session and, recording the time course of the spikes, we were able to locate the source of the seizures. Then, we modeled the HD montage with a central cathode placed over the epileptic focus and four HD anodes positioned 5 cm from the center. We delivered -2 mA normal current through the central cathode, setting the 4 ring anodes as ground (figure 3).

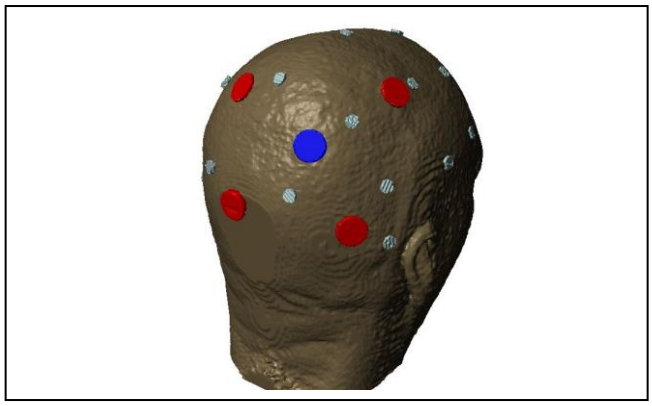

Figure 3. Experiment 3: Cathodical *HD 4 x 1 montage, modeled over the epileptic patient centered over the seizure focus.*

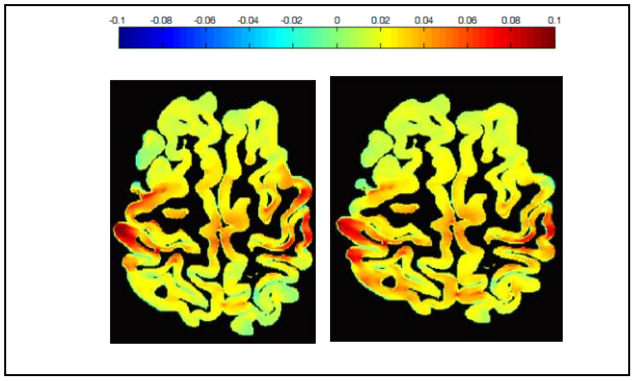

Figure 4. Experiment 1: *Distributions of the difference between the electric field distribution due to the personalized and non personalized electrode used to target M1(left) and S1(right). The selected slices are at -2 cm from the projection of Cz over the cortex.*

D. *Experiment 4*

We modeled a head of a healthy subject and we included an electric dipole into the brain. The dipole was composed by 2 opposite 0.5 V charges, a mm distant from each other. More specifically, it was located in the left somatosensory cortex, where the right hand representation was recognized. We recorded the voltage distribution generated over the scalp and we used those values to apply four different kinds of current stimulation. All the stimulations, delivered a total current intensity of 2 mA through HD electrodes. We applied: the same scalp voltage distribution over the scalp using 336 electrodes, the laplacian distribution of the voltage using 336 electrodes and two bipolar distributions, with the electrodes respectively placed over the maximum and minimum positions of the two previous distributions.

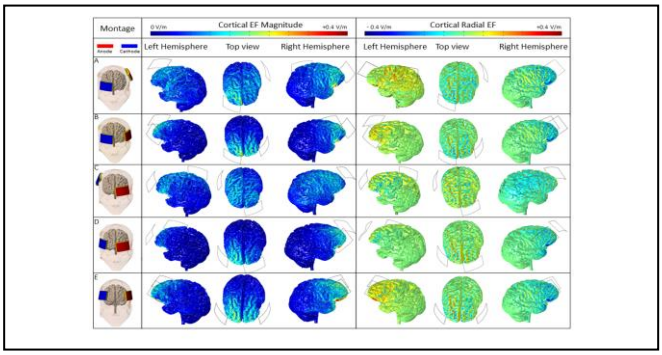

Figure 5. Experiment 2: *Effect of electrodes' position on cortical electric fields induced by five different montages. An individualized FEM head model was created from MRI scans of an adult male at 1 mm3 resolution. First column: Sample segmentation head mask showing five electrode montages. Second column: three different views of the EF Magnitude normal to the brain surface showing how each area of the brain is involved in the stimulation. The color maps were generated between 0 and +0.4 V/m. Third column: three different views of the Radial EF elicited through each gyrus. This measure is sensible to the direction of the current flow. The color maps were generated between -0.4 V/m and +0.4 V/m.*

III. RESULTS

A. Experiment 1

The personalized electrode was able to modulate more deeply and strongly the area of the central sulcus than the non-personalized one, particularly in the lateral regions along the central sulcus for both M1 and S1 targeting. Furthermore, the personalized electrode used to target S1 modulated the postcentral gyrus more selectively. On the contrary, the personalized electrode used to target M1 broadened its effects over both the pre and postcentral gyrus (figure 4).

B. Experiment 2

In all cases, the "reference" electrode over the contralesional supraorbital forehead is not inert and influences the current path through the entire brain. Montage B, although similar to montage D, exerted the greatest effect over the left perilesional cortex, which was still stronger in montage E.

C. Experiment 3

The ring HD stimulation modeled, having the cathode placed between P3 and O3, was able to deliver the maximum negative EF over the epileptic focus (-0,03 V/m). We look forward to know the response of the real stimulation applying the same modeling parameters and then studying the correlation among the results to optimize such parameters.

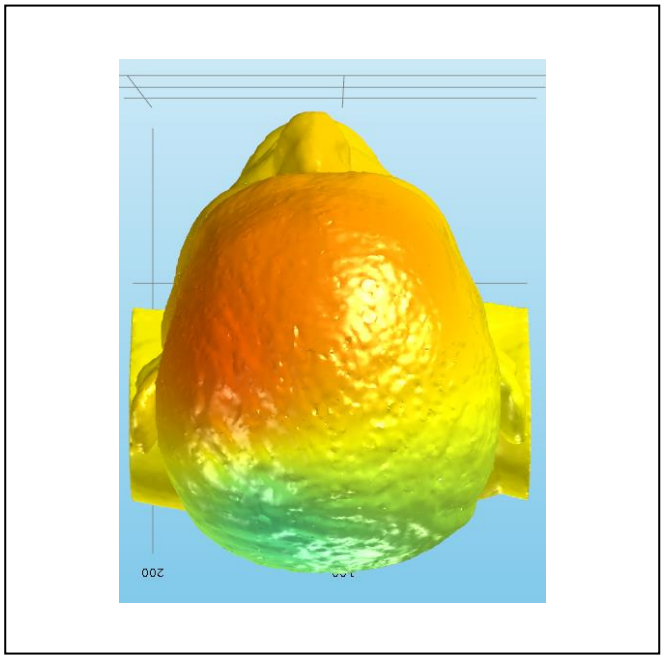

Figure 6. .Experiment 4: Voltage distribution over the scalp generated by the S1 electric dipole.

D. Experiment 4

The current stimulations delivered by 336 electrodes using the voltage distribution over the scalp was able thoroughly to recreate such voltage distribution. Even so, it generated the less accurate EF distribution over the cortex, with the minimum value to the target (1.39E-05 V/m). The laplacian 336 electrodes stimulation, showed a scalp distribution more closer than the original one, but a higher value to the cortical target (2.03E-05 V/m) and a lower total brain EF.

They are two promising signs of a better focalization. Nevertheless, the highest value to the target was reached by both the bipolar stimulations (4.39E-05 V/m), but the second one delivered a much lower total EF into the brain (4.9E-05 V/m versus 9.81 V/m). So, with the last stimulation we obtained the best ratio between target EF value and dose injected into the subject's brain.

IV. CONCLUSION

In this paper we modelled the electric field distribution due to four different kinds of tDCS personalization, with the aim to study the possible impact of the personalized tDCS on the electric field distribution, in order to increase the efficiency of this promising technique. In particular, we showed a personalization of the electrode based on the structural conformation of a cortical region, a specific sponge montage studied in function of a brain lesion's position, a HD montage guided by a real EEG session to identify the position of an epileptic focus and a static EEG simulation to reach the more efficient HD stimulation. In conclusion, the personalized tDCS, leaded by both the functional or anatomical information, seems to be crucial to obtain more encouraging clinical results. Furthermore it will help to better comprehend the network or cellular mechanisms activated by the transcranial current stimulation, comparing modeling and real stimulations on the same subjects.

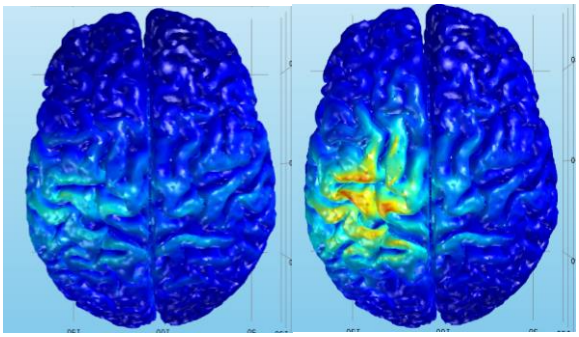

Figure 7. Experiment 4: Autoscale of the cortex EF distribution elicited by delivering 2 mA of current stimulation, starting from the laplacian voltage distribution over the scalp. On the left the EF induced by 336 electrodes and on the right the bipolar stimulation with the electrodes placed over the maximum and minimum.

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