Constrained maximum intensity optimized multi-electrode tDCS targeting of human somatosensory network

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Abstract — **Transcranial direct current stimulation (tDCS) is a noninvasive method that delivers current through the scalp to enhance or suppress brain activity. The standard way of applying tDCS is by the use of two large rectangular sponge electrodes on the scalp. The resulting currents often stimulate a broad region of the brain distributed over brain networks. In order to address this issue, recently, multi-electrode transcranial direct current stimulation with optimized montages has been used to stimulate brain regions of interest (ROI) with improved trade-off between focality and intensity of the electrical current at the target brain region. However, in many cases only the location of target region is considered and not the orientation. Here we emphasize the importance of calculating the individualized target location and orientation by combined electroencephalography and magnetoencephalography (EMEG) source analysis in individualized skull-conductivity calibrated finite element method (FEM) head models and stimulate the target region by four different tDCS montages. We have chosen the generator of the P20/N20 component, located at Broadmann area 3b and oriented mainly from posterior to anterior directions as our target for stimulation because it can be modeled as a single dipole source with a fixed position and orientation. The simulations will deliver optimized excitatory and inhibitory electrode montages that are in future investigations compared to standard and sham tDCS in a somatosensory experiment. We also present a new constrained maximum intensity (CMI) optimization approach that better distributes the currents over multiple electrodes, therefore leads to less tingling and burning sensations at the skin and thus allows an easier realization of the sham condition, without significantly reducing the current intensity parallel to the target.**

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I. INTRODUCTION

Transcranial direct current stimulation (tDCS) is a non-invasive method to induce excitatory or inhibitory effects in different cortical areas of the human brain [1-4]. The conventional way for tDCS is to apply an electrical current (≤ 2mA) through two large patch electrodes (25–35cm^2). For somatomotor applications the standard two patch electrode montage with one electrode over the primary motor cortex (anode) and the other electrode over supraorbital area (cathode) [1-3], is mostly used to apply a maximum electric field to the brain regions of interest (ROI). However, as the currents are broadly distributed resulting in the stimulation of non ROI's, targeting a specific ROI, like the underlying sources of the somatosensory P20/N20 components of the somatosensory evoked responses might profit from more focality and directionality. Recently multi-electrode tDCS optimization methods have gained interest in order to achieve an efficient trade-off between focality, directionality and intensity of the stimulation current parallel to the target [5-7, 12]. However, most of the multi-electrode optimization approaches, when modeling a specific brain region, only consider the location and do not consider individual target orientation differences between subjects. Here, we explore different current focalities and intensities achieved among subjects in a somatosensory experiment and simulation study using combined electroencephalography (EEG) and magneto-encephalography (MEG) source analysis in finite element method (FEM) based skull-conductivity calibrated realistic head models first to calculate the target location and orientation and then then using four optimization methods with different goal functions, from which one, constrained maximum intensity, CMI, is a new approach. Based on the results from this study we will choose the individualized CMI-optimized TES montages for a future stimulation study of the somatosensory cortex.

II. MATERIALS AND METHODS

A. Data acquisition

Four right handed subjects (4 males, age 32, 51, 27, 22 respectively) participated in this initial study. Somatosensory evoked potentials (SEP) and somatosensory evoked fields (SEF) were recorded following electrical stimulation of the right hand first index finger using combined MEG (275 gradiometers) and EEG (80 electrodes). The electrical stimulus had an electrical pulse width of 0.2 ms and a

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randomly varied inter-stimulus interval between 350 ms - 450 ms to avoid habituation and obtain a clear pre-stimulus interval. The experiment had 4 runs of 10 minutes and the data were acquired with a sampling rate of 1200 Hz with online low pass filtering of 300 Hz. For more realistic tDCS simulations we also digitally recorded from a neoprene cap the 39 possible sensor positions of a starstim (Neuroelectrics, Barcelona, Spain) tDCS system corresponding to the international 10/10 system for all subjects with a Polhemus measurement device. Since our hardware is limited to eight 3.14 cm^2 Ag/AgCl gelled electrodes, in a later main stimulation experiment, without loss of much accuracy, we will only use the eight most important electrodes from optimization placed into 8 of the 39 holes in the neoprene cap.

TABLE 1. CURRENT DENSITY (A/M^2) IN TARGET (IT), IN NON-TARGET (INT) REGIONS, DIRECTIONALITY (DIR) AND PARALLITY (PAR) ACROSS 4 OPTIMIZATION APPROACHES FOR ALL 4 SUBJECTS.

Subjects	**2-Patch**			
	IT (A/m^2)	***INT (A/m^2)***	***DIR (A/m^2)***	***PAR***
S1	0.0783	0.0278	0.0278	36
S2	0.1129	0.0400	0.0400	35
S3	0.1428	0.0424	0.0424	30
S4	0.0825	0.0320	0.0320	39
	MI			
S1	0.0737	0.0328	0.0572	78
S2	0.1762	0.0284	0.1341	76
S3	0.2298	0.0482	0.1783	78
S4	0.0811	0.0208	0.0653	81
	CMI			
S1	0.0716	0.0270	0.0540	75
S2	0.1613	0.0344	0.1231	76
S3	0.2141	0.0447	0.1703	80
S4	0.0844	0.0280	0.0633	75
	ADMM			
S1	0.0142	0.0019	0.0109	77
S2	0.0315	0.0027	0.0239	76
S3	0.0401	0.0014	0.0310	77
S4	0.0199	0.0014	0.0146	73

B. Realistic head modeling and source analysis

T1-weighted (T1w), T2-weighted (T2w) Magnetic Resonance Images (MRI) and voxels of 1 x 1 x 1 mm^3 (MAGNETOM 3.0T Siemens Medical Solutions) for each subject were used for the construction of a six compartment (skin, skull compacta (SC), skull spongiosa (SS), cerebrospinal fluid (CSF), gray and white matter), segmented head model. Diffusion weighted MRI (dMRI, 1.9 mm edge length, two flat diffusion gradient images with reversed frequency and phase encoding directions for artifact correction and diffeomorphic non-linear registration and 20 directional images was used and processed to include white matter conductivity tensors in each head model following the steps in [8, 9]. Individual Skull conductivity calibration has been carried out to enable combined analysis of SEP and SEF data [8] and for appropriate estimation of individual P20/N20 target location and orientation, a FEM model based source analysis is performed using the following preprocessing steps: 20 to 250Hz digital bandpass filtering of EMEG after the removal of noisy channels, 50Hz digital notch filtering to remove power line noise harmonics, separation of processed recordings into 50 ms pre and 150 ms post stimulus intervals and the average across all the SEP/SEF single trials after visual inspection of noisy channels. Following the steps in [8], the P20/N20 underlying source in Brodmann area 3b was reconstructed, i.e., for each subject with individual source location and orientation.

C. tDCS simulation methods

In order to find the optimum montage that may result in an excitatory or inhibitory effect for the mainly tangentially oriented P20/N20 target we first used four optimization methods, namely, 2-patch [1-4], max intensity (MI) [5], constrained max intensity (CMI) approach and an Alternating Direction Method of Multipliers approach (ADMM) [7]. Our own Matlab (MathWorks, Natick, MA, USA) implementations were used for optimizations, the SimBio[1] toolbox for FEM computations and SCIRun[2] for visualization. The methods are described as follows

1) Standard 2-Patch: We simulated two 5 cm x 5 cm sponge-rubber like patches, with thickness 4 mm and saline like conductivity of 1.4Sm^{-1} as described in [11]. To make the simulation realistic we chose the FP2 and C3 positions from the tDCS cap sensor Polhemus measurement and center the patches at these positions on the segmented head model. The patches were modeled as a square cube 5 cm x 5 cm x 4 mm (thickness) patch by taking the location of FP2 and C3 electrodes as the center of the patch in a three dimensional coordinate system.

2) MI: The MI approach [5] produces an optimized bipolar montage of positive (anode) and negative (cathode) that injects a total current of 2 mA. As described in [5] the problem is defined as an optimization of the following equations

$$\boldsymbol{s}^{\boldsymbol{max}} = \max_{s} e^T C\boldsymbol{s}, \text{ subject to } \|\tilde{\boldsymbol{s}}\|_{\boldsymbol{1}} \leq 2\boldsymbol{s}_{\boldsymbol{Total}}$$

with $\tilde{\boldsymbol{s}} = [s_1, s_2, \ldots\ldots, s_{N-1}, -\sum_{i=1}^{N} s_i]^T$

where $s = s_1, s_2, \ldots\ldots, s_{N-1}$ and $\sum_{i=1}^{N} s_i$ accounts for the reference electrode, e is the target vector, C is the FEM influence matrix that maps surface currents to target current, $\boldsymbol{s}$ is the vector of injected currents at the N = 39 cap positions, $\boldsymbol{s}_{\boldsymbol{Total}}$ will be 2 mA here and in later experiments. As

[1] https://www.mrt.uni-jena.de/simbio/index.php/Main_Page

[2] http://www.sci.utah.edu/cibc-software/scirun.html

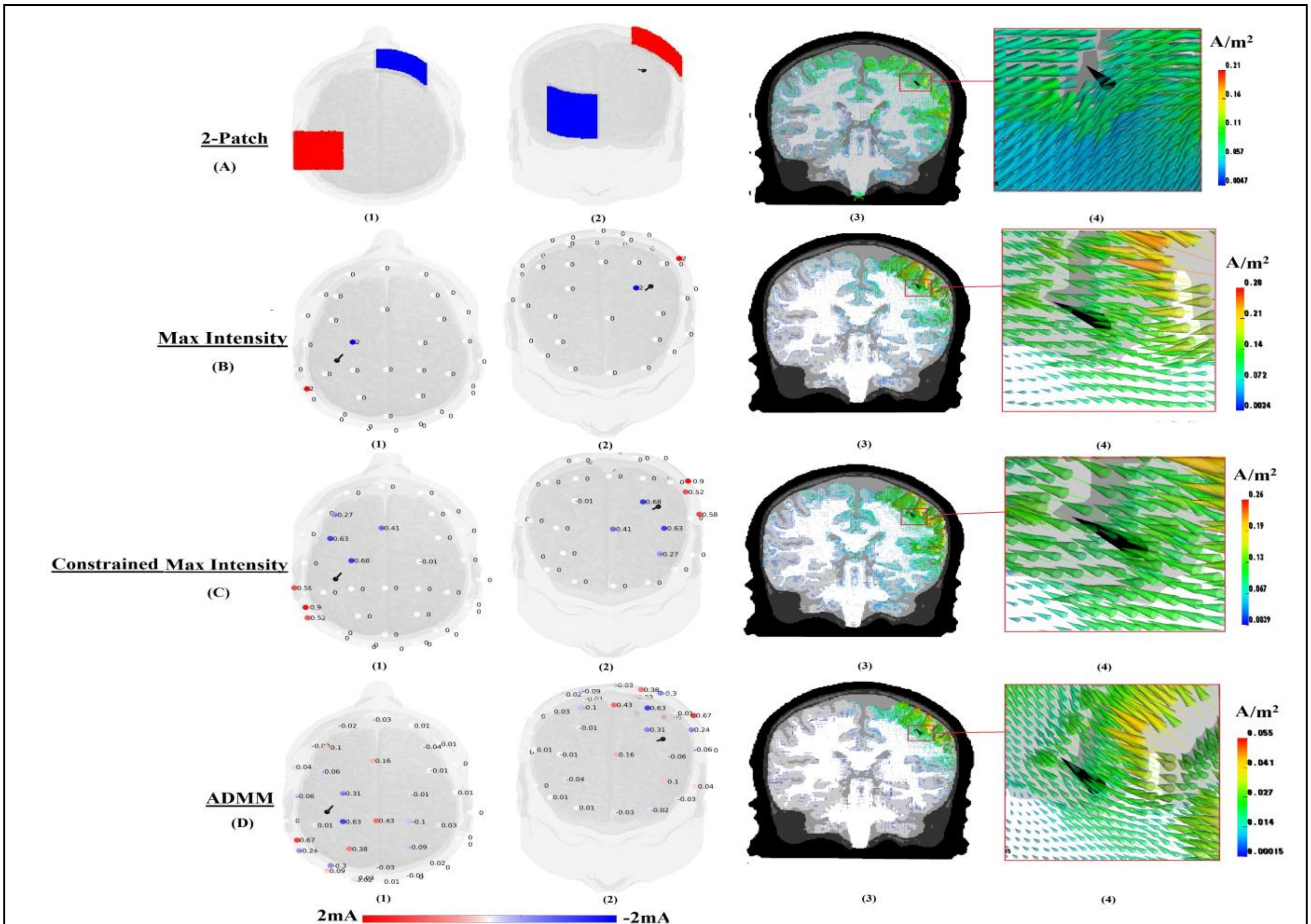

Figure 1. Current density distributions and montages with currents on stimulation electrodes for subject 2. The first and second columns A1-D1 and A2-D2 show the simulated montages with stimulation currents in top and frontal view respectively. The third column A3-D3 shows the current distributions for the 4 methods and the fourth column A4-D4 shows the current density vectors at the target.

described in [5] the max intensity approach optimally maximizes the intensity of the currents in the target with regard to the orientation of the target vector which is in the mainly tangentially-oriented P20/N20 source. Note that while intensity is optimal, focality is suboptimal, since it is not formulated in the MI approach. Also injection of 2mA through one small electrode with an area of (3.14 cm^2) can also lead to potential discomfort.

3) CMI: The CMI approach introduced for the first time here, mainly follows the MI approach, but using additional regularization it distributes the injected currents over multiple electrodes, thus reduces the current amplitude at each electrode and thereby will enable an easier realization of the sham condition. The additional constraints implemented in the CMI approach are expressed as follows

$\boldsymbol{s^{max}} = \max_{S} e^T C\boldsymbol{s} - \boldsymbol{\lambda} \|\tilde{\boldsymbol{s}}\|_2$, subject to $\|\tilde{\boldsymbol{s}}\|_1 \le 2\boldsymbol{s_{Total}}$, and $\|\tilde{\boldsymbol{s}}\|_\infty \le \boldsymbol{s_{Limit}}$
with $\tilde{\boldsymbol{s}} = [s_1, s_2, ..., s_{N-1}, -\sum_{i=1}^{N} s_i]^T$

where the additional regularization parameter $\boldsymbol{\lambda}$ controls the current distribution. For our experiment, the starstim system can stimulate with 8 electrodes so $\boldsymbol{\lambda}$ is chosen in a way that 8 electrodes are used. $\boldsymbol{s_{Limit}}$ is added to limit the amount of current injected or extracted by each stimulation electrode. In this case 1.5 mA is chosen as the $\boldsymbol{s_{Limit}}$ to minimize potential subject discomfort.

4) ADMM: The ADMM method was taken from [7]. The ADMM approach mainly focuses on the optimization of focal stimulation at the target while reducing the intensity at non target regions. ADMM method is expressed as follows

$$\max_{s} \int_{\Omega_t} < A\boldsymbol{s}\, , e > dx \; - \; \alpha \int_{\partial\Omega} \boldsymbol{s}^2\, \Omega \; dx \; - \; \beta \, \|\boldsymbol{s}\|_{L^1(\partial\Omega)}$$

subject to $w|A\boldsymbol{s}| \le \varepsilon$

where A is the FEM influence matrix that maps from sensors to all brain currents, w is a weighting matrix that allows higher currents in target regions and restricts currents in non-target regions, α and β are L1 and L2 regularization parameters respectively and ε is the tolerance for brain safety constraint. To solve the above equation systems, the ADMM optimization algorithm is in detail described in [7].

D. Evaluation

In order to choose the optimum method for our tDCS experiment, we quantify the current fields produced by each method as a measure of intensity of average current density in the target area (IT), intensity of average current density in non-target regions (INT), the inner product of current density and target vector indicating the current densities in the direction of the target vectors (DIR) and the percentage of current density that is oriented parallel to the target vector (PAR). These measures are also described in more detail in [7].

III. RESULTS

Individual P20/N20 targets were reconstructed as shown for subject 2 in Fig.1 (black cone). We also visualize in figure 1 for subject 2 how different methods can have different current density distributions and directions at the target. From figures A4 –D4 it can be seen that the direction of the current density at the dipole target changes with different montages with the standard 2-patch having the worst directionality at the target while the ADMM, MI and CMI show more parallel current density vectors in the direction of the dipole target orientation. It is further supported by the calculation in Table 1 as the 2-patch shows the worst PAR compared to other methods. From figures A3-D3 it can be seen that the 2-patch method shows the broadest field distributions while the ADMM approach shows more focality. Although the ADMM achieves the highest focality, it has lower intensity parallel to the target than MI and CMI, while MI and CMI are optimal with regard to IT, DIR and PAR, but less good with regard to INT, i.e., less focal at the target. So to have an optimum trade-off between intensity at the target and PAR the MI and CMI show promising results. MI and CMI nearly show the same target stimulation results, but CMI achieves these with a lower current per electrode and makes much better use of the multi-channel system, which will reduce the differences between sham and CMI compared to sham and MI at the electrode level, thus enabling an easier sham condition in our later experiment. At 2mA we will not lose subjects, but we will always enable easier sham because we reduce the current per electrode with CMI, while keeping the currents in the brain and especially the target at nearly the same level.

IV. DISCUSSIONS AND FUTURE WORK

In this work we run a somatosensory experiment with 4 subjects and individually reconstructed the underlying sources of the P20/N20 component with regard to location and orientation using combined SEP/SEF data and calibrated multi-compartment anisotropic realistic head models [8]. We developed CMI as a new and promising optimization approach that achieves nearly the same high field intensity parallel to the targets, while better making use of the multi-channel tDCS hardware, distributing the injected currents over multiple electrodes, thereby limiting the absolute value of the injected current per electrode. On the one hand, this will enable an easier realization of a sham condition, while on the other hand, this might also allow to use higher $\boldsymbol{s_{Total}}$ without stronger tingling or burning at the skin level [10]. We compared our new CMI approach to other optimization methods from the literature, namely MI and ADMM, and also to standard 2-patch and found results that support our hypotheses with regard to the superiority of CMI. We consider CMI to be a good optimization method choice for our later somatosensory stimulation experiment, where we will only readout amplitude modifications from the target area so that there is less interest in low INT values. However, in other experimental setups or in clinical applications with frequent stimulation sessions, the lower INT values and higher focality of ADMM might be preferable. In future to show validity of the CMI approach, all subjects will take part in a tDCS experiment. The experiment will be designed similar to [3, 4], but using MEG for a more sensitive readout of effects.

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