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Determinants of the electric field during transcranial direct current stimulation

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ABSTRACT

Transcranial direct current stimulation (tDCS) causes a complex spatial distribution of the electric current flow in the head which hampers the accurate localization of the stimulated brain areas. In this study we show how various anatomical features systematically shape the electric field distribution in the brain during tDCS. We constructed anatomically realistic finite element (FEM) models of two individual heads including conductivity anisotropy and different skull layers. We simulated a widely employed electrode montage to induce motor cortex plasticity and moved the stimulating electrode over the motor cortex in small steps to examine the resulting changes of the electric field distribution in the underlying cortex. We examined the effect of skull thickness and composition on the passing currents showing that thinner skull regions lead to higher electric field strengths. This effect is counteracted by a larger proportion of higher conducting spongy bone in thicker regions leading to a more homogenous current over the skull. Using a multiple regression model we could identify key factors that determine the field distribution to a significant extent, namely the thicknesses of the cerebrospinal fluid and the skull, the gyral depth and the distance to the anode and cathode. These factors account for up to 50% of the spatial variation of the electric field strength. Further, we demonstrate that individual anatomical factors can lead to stimulation "hotspots" which are partly resistant to electrode positioning. Our results give valuable novel insights in the biophysical foundation of tDCS and highlight the importance to account for individual anatomical factors when choosing an electrode montage.

Introduction

Transcranial direct current stimulation (tDCS) is a widely used brain stimulation technique with various applications in different areas of neuroscience and clinical research. It is typically employed by attaching two large pad electrodes (with a few centimeters edge length) to the head and passing a weak electric current in the range of a few mA through them. It has been shown that tDCS can induce changes on motor cortex excitability (Nitsche and Paulus, 2000) that are dependent on stimulation strength and duration (Nitsche and Paulus, 2001). In slice preparations it has been demonstrated that weak DC fields can shift thresholds for action potential generation and exert an influence on spike timing (Bikson et al., 2004; Radman et al., 2007). While the exact mechanisms of action are still under discussion it is generally agreed that the local electric field and its orientation with respect to neuronal structures are main determinants of the stimulation effects that differ between various stimulation (Miranda et al., 2013; Radman et al., 2009). As direct measurements of these electric fields are difficult to implement various efforts have been made to estimate the electric field distribution by means of computational modeling. Simulation approaches range from spherical models (Datta et al., 2008; Miranda et al., 2006) to more realistic MRI derived head models (Datta et al., 2009; Sadleir et al., 2010) in order to demonstrate the effects of electrode shape, conductivity anisotropy (Suh et al., 2012), different skull layers (Neuling et al., 2012) or artificial skull openings (Datta et al., 2010) on the injected electric field.

However, few studies have tried to quantify how much the spatial distribution of the electric field on the cortical surface is predetermined by individual anatomical features as well as electrode position. That is, to which extent does individual anatomy in addition (or opposing) to the electrode placement dictate the stimulated brain areas?

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In the current study we explore the impact of several anatomical factors such as skull thickness and sulcal depth in combination with effects of electrode position on the electric field pattern in the brain. We employ anatomically realistic FEM models that are based on MR images and accurately capture the gyrification of gray matter (GM), the conductivity anisotropy of white matter (WM), the thickness of the cerebrospinal fluid (CSF) layer, the different skull layers, the eye regions and the nasal cavities. We focus on simulating the electric field distribution that might occur during a standard tDCS experiment aimed at inducing motor cortex plasticity. By investigating the effects of systematic displacements of the electrode position on the electric field distribution, we characterize how anatomical constraints interact with the electrode placement. In particular, we assess how stable the stimulated areas in the brain are when varying electrode positions. We demonstrate that our results are consistent across FEM models of two individual heads and are robust across a wide range of simulated electrode thicknesses and conductivities.

Methods

MR data acquisition

Structural (sMRI) and diffusion (dMRI) magnetic resonance images were acquired for two healthy participants (one male, one female, 27 & 26 years) without history of neurological or psychiatric diseases. The data was collected using a 3T TIM Trio scanner (Siemens Healthcare, Erlangen, Germany) equipped with a 12-channel head coil at the MPI for Biological Cybernetics (Tübingen, Germany). The study was approved by the local ethics committee of the Medical Faculty of the University of Tübingen and data collection was performed after receiving written informed consent.

T1- and T2-weighted MR images were obtained, both with and without fat suppression. 3D MP-RAGE was used for the T1-weighted images (192 sagittal slices, matrix size = 256 × 256, voxel size = 1 mm^3, flip angle 9°, TR/TE/TI = 2300/2.98/1100 ms without fat suppression, TR/TE/TI = 2300/4.21/1100 ms with selective water excitation). The T2-weighted images consisted of 2D turbo spin echo acquisitions (96 sagittal slices, matrix size = 256 × 256, voxel size = 1 × 1 × 2 mm^3, flip angle 110°, TR/TE = 11,990/102 ms, turbo factor 11, with and without fat suppression). The signal from subdural fat and the spongy bone of the skull was reduced in the fat suppressed images. This simplified the accurate reconstruction of the border between CSF and skull and helped the accurate segmentation of the eye regions. The dMRI images used a twice refocused SE-EPI sequence (72 axial slices, matrix size = 128 × 128, voxel size 1.9 × 1.9 × 2.1 mm3, TR/TE = 10,500/105 ms, 6/8 phase partial Fourier, GRAPPA acceleration factor 2, 7 averages) with 20 diffusion directions and a b-value of 2000 s/mm^2. Interspersed were 7 acquisitions with b = 0 s/mm^2.

Segmentation

FEM head models were created for two subjects. In a first run, different tissue types including WM, GM, CSF, skin and skull were segmented in an automated manner using SimNibs (Windhoff et al., 2013). Special attention was given to tissue interfaces as important physical effects occur there due to abrupt changes in conductivity and charge accumulation (Miranda et al., 2003; Thielscher et al., 2011).

The first version of the head models was further refined in a semi-automatic process. This was based on anatomical masks for the vitreous body of the eyes, the surrounding eye regions and the skull (including the nasal cavities) which had been prepared in MNI space before. The masks for the vitreous bodies of the eyes and the eye regions were hand-drawn based on the T1 MNI template and covered on purpose spatially slightly larger areas. The skull mask was based on the skull reconstructions of the Ella and Duke models of the virtual family (Christ et al., 2010) that had been registered to MNI space by non-linear warping (FSL FNIRT). It was further improved by manual corrections. After non-linear registration of the whole-head T1 image onto the MNI template (FSL FNIRT), the masks could be accurately registered onto the individual MRIs. The standard settings for FSL FNIRT were modified by (among others) allowing stronger maximal deformations to ensure good registration results in the non-brain parts of the image. The transformed mask of the vitreous bodies was applied to the fat suppressed T2-image and the final geometries were extracted by histogram-based thresholding. The mask for the surrounding eye regions was applied to the non-fat suppressed T2 and histogram-based thresholding was again used to determine the final geometries. If necessary, the skull mask was manually corrected after transformation into the individual space to make sure that the outer shape fitted well with the skull boundaries as visible in the T1 and T2 images. The spongy part of the skull was then segmented by applying the mask to the non-fat suppressed T1 image, followed by histogram-based thresholding. A minimal thickness of 1 mm was ensured for the compact bone. Spurious voxels with high intensities were excluded by means of spatial clustering and applying a threshold for the minimum cluster size (Fig. 1D shows exemplary sagittal slices with the final skull compartments indicated in color). The final volume masks were used to create triangle surfaces using the methods described in Windhoff et al. (2013) and a tetrahedral volume mesh was built. The resolution of tetrahedral elements was enhanced near the electrodes as well as at GM/WM tissue interfaces. This semi-automatic process allows for a time-efficient construction of geometrically accurate head models that include important anatomical features for tDCS simulations. A cut-through image of the FEM head model showing the different tissue volumes is depicted in Fig. 1A. Conductivity anisotropy for WM and GM was estimated from the diffusion tensor using a volume normalized approach as described in Opitz et al. (2011). In short it is assumed that the eigenvectors are the same for the diffusion as well as for the conductivity tensor. The eigenvalues are transferred such that the mean conductivity of the anisotropic case is identical with the isotropic one. Please note that this approach leaves the conductivity in GM close to the isotropic case as fractional anisotropy is generally low in GM. However, it allows for a smooth transition of the principal conductivity direction at the border between GM and WM.

Simulations

For both subjects the anode was placed directly above the hand area of M1 and the cathode over the contralateral supraorbital region as typically employed in tDCS studies aimed at inducing motor plasticity. The electrode size was set to 7 cm × 5 cm (35 cm^2), which is commonly used in experimental studies. The longer edge of the anode was aligned parallel to the central sulcus such that it approximately covered the precentral gyrus. In order to study the effect of slight changes in electrode placement we moved the anode in steps of 5 mm anterior and posterior as well as medial and lateral (from −2 cm to +2 cm in both directions). Furthermore, we rotated the anode around its center in 15 degree steps until a complete 180 degree turn was completed as further rotations would result in the same montage again due to symmetry. In total, 28 different electrode montages were simulated for each subject. For an illustration of the simulated montages see Fig. 1B. The cathode position was left unchanged across simulations. Electrode thickness for both anode and cathode was 5 mm.

The following conductivity values were used for simulation unless indicated otherwise: σ_{skin} = 0.25 S/m (average between outer skin and fat as given in Truong et al. (2012)), $\sigma_{compactbone}$ = 0.008 S/m (Miranda et al., 2013), $\sigma_{spongybone}$ = 0.025 S/m (Dannhauer et al., 2011), σ_{CSF} = 1.79 S/m, σ_{GM} = 0.276 S/m and σ_{WM} = 0.126 S/m (Thielscher et al., 2011), $\sigma_{eyeball}$ = 0.50 S/m and $\sigma_{eyeregion}$ = 0.25 S/m (Gabriel et al., 1996b) and $\sigma_{electrodes}$ = 1.79 S/m. Anisotropic