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Imaging of current flow in the human head during transcranial electrical therapy

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ABSTRACT

Background: It has been assumed that effects caused by tDCS or tACS neuromodulation are due to electric current flow within brain structures. However, to date, direct current density distributions in the brains of human subjects have not been measured. Instead computational models of tDCS or tACS have been used to predict electric current and field distributions for dosimetry and mechanism analysis purposes.
Objective/Hypothesis: We present the first *in vivo* images of electric current density distributions within the brain in four subjects undergoing transcranial electrical stimulation.
Methods: Magnetic resonance electrical impedance tomography (MREIT) techniques encode current flow in phase images. In four human subjects, we used MREIT to measure magnetic flux density distributions caused by tACS currents, and then calculated current density distributions from these data. Computational models of magnetic flux and current distribution, constructed using contemporaneously collected T_1-weighted structural MRI images, were co-registered to compare predicted and experimental results.
Results: We found consistency between experimental and simulated magnetic flux and current density distributions using transtemporal (T7-T8) and anterior-posterior (Fpz-Oz) electrode montages, and also differences that may indicate a need to improve models to better interpret experimental results. While human subject data agreed with computational model predictions in overall scale, differences may result from factors such as effective electrode surface area and conductivities assumed in models.
Conclusions: We believe this method may be useful in improving reproducibility, assessing safety, and ultimately aiding understanding of mechanisms of action in electrical and magnetic neuromodulation modalities.

Introduction

Transcranial electrical stimulation (tES) strategies such as tDCS or tACS, have been indicated for stroke rehabilitation, treatment of epilepsy, and improving cognitive, motor or memory performance in healthy subjects [1]. However, the underlying mechanisms of tDCS and tACS remain unclear. It has been assumed tES effects are greatest, and electric fields and current densities are largest, in brain structures near stimulating electrodes. In tDCS at 1 mA intensity, excitatory effects are associated with structures under more positively polarized electrodes and inhibitory effects with those under more negatively polarized electrodes [2]. It is hypothesized that externally applied fields depolarize or hyperpolarize resting membrane voltages in targeted tissue, leading to increased excitability or inhibition respectively. However, there is evidence of increased excitability at 2 mA, regardless of polarity [3]. Effects may also depend on total stimulation time [4]. Further, tACS applied at frequencies up to 80 Hz may entrain neural networks, with excitatory or inhibitory effects that depend on frequency, current intensity and phase of current application relative to underlying activity [5].

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High-resolution anatomically-detailed computational models are frequently used to model tES current distributions and inform mechanism theory. Model tissue conductivities are typically derived from measurements on bulk excised tissues [6,7]. However, while surface field measurements have been made using ECoG arrays [8], systematic model validation has not yet been possible. Knowledge of complete current distributions formed within the brain during tES would clarify study outcomes and allow more detailed explorations of mechanism. Further, effects of different current application protocols, electrode designs, individual neuroanatomy, cerebrospinal volume and many other study factors could easily be resolved.

Recently developed MR electrical impedance tomography (MREIT) [9] methods make it possible to reconstruct conductivity and current density distributions in subjects using only one component (B_z) of magnetic flux density vectors. One MREIT method, DT-MREIT [10], can be used to reconstruct full anisotropic conductivities and current density distributions using MREIT and diffusion tensor image data gathered from the same subject, and has recently been demonstrated in canines [11].

Functional MRI has been used to characterize responses to tES [12–14] and it has been noted that current administration creates artifacts on MR images [15]. One group used fMRI methods to identify voxel clusters correlating with current flow [16] and plotted magnetic flux density distributions caused by tDCS during entire MR acquisitions. However, to date, there have been no reports of tES current density imaging in humans.

In this paper, we demonstrate the first MREIT current density images (MREIT-CDI) in human heads. Data was gathered from four human subjects undergoing tACS-like stimulation procedures at frequencies of 10 Hz and 1.5 mA intensity. We used MREIT methods to recover magnetic flux density distributions caused by the current flow, and reconstructed in-plane current density distributions caused by both bilateral (T7-T8) and anterior-posterior (Fpz-Oz) montages. While AC stimulation was employed, electromagnetic field distributions and tissue conductivities at this frequency should be very similar to those found in tDCS [17]. We show correspondences between experimental B_z data and that predicted by computational models constructed using high-resolution T1-weighted MR images obtained in the same imaging session. We then computed measures of current density distribution (projected current density, J^P) within a focus plane for each subject and compared these with model predictions. Because literature conductivity values are almost exclusively derived from excised human or animal tissue samples, and these measurements in the human head are entirely novel, we did not extensively analyze differences between predicted and experimental measurements.

MREIT-CDI techniques may be useful in validating tES models and confirming protocol consistency. These techniques can be used to directly examine the effect of individual neuroanatomic variation, allowing detailed examination of correlations between current distributions and brain structures. Development of this capacity would immediately illuminate mechanism investigations. When current density data is processed further to form conductivity images, the results may have more profound implications in wider fields, such as EEG source imaging, where precise estimations of tissue conductivities are critical to reducing source location uncertainty.

Material and methods

Subject selection

All procedures were performed according to protocols approved by the University of Florida (UF) and Arizona State University Institutional Review Boards. Four healthy normal right-handed male volunteers were recruited (mean age 20, range 19–21), screened to exclude metallic implants, agreed to participate, then admitted to the study.

Subjects completed a mini–mental state examination (MMSE) [18], to rule out dementia and neurological deficits (MMSE scores > 24 were required for inclusion), and right-handedness was confirmed (Edinburgh Inventory [19] scores >+40 were required for inclusion). Subjects completed brief questionnaires before and after interventions to assess mood, and tACS-related physical sensations. No subject reported any adverse events, either acutely or in follow up meetings approximately 24 h after interventions.

MR imaging setup

All data were measured using a Philips 32-channel head coil in a 3 T MRI Philips Achieva scanner at the Advanced Magnetic Resonance Imaging and Spectroscopy Facility, UF McKnight Brain Institute. We gathered co-registered high resolution T_1-weighted and diffusion weighted data on all subjects for computational model construction and comparison with MREIT results. MREIT acquisitions employed a Philips mffe protocol, modified to produce TTL-logic pulses after each MR excitation pulse, triggering a MR-safe battery-operated constant current source (DC-STIMULATOR MR, neuroConn, Ilmenau, Germany). Fig. 1 shows a schematic of the measurement setup. We verified that 'no current' (NC) measurements using the MREIT sequence did not affect processed signal phase, and that expected current-induced B_z maps were recovered using an agarose phantom (Figs. S1 and S2).

Subject protocol

Prior to scans, neuroConn carbon-rubber electrodes (~25 cm^2), enclosed in sponges, were soaked in saline (0.9% NaCl) and squeezed to remove excess solution. Immediately before electrode placement on Fpz, Oz, T7 and T8 locations, a 5-ml volume of saline was applied to both sides of each sponge. Small amounts (ca. 1 ml) of saline were also applied to the scalp under hair at electrode sites. Electrodes were applied approximately 30 min before tACS procedures.

Fig. 2(i) shows schematic electrode placements for Subject A. Electrodes were secured with elastic bandage (Vetrap, 3 M). Stimulator connections were completed after subjects entered the scanner. Stimulation was administered using both an Fpz-Oz and T7-T8 montage. Details of stimulation parameters are described in the sections below.

Subjects were requested to report stimulation-related side effects while in the scanner. Phosphene perception was rated on a 1–10 scale, with 1 corresponding to 'no detectable flashing' and 10 corresponding to 'white field'. Phosphene fields were recorded as either 'peripheral' or 'central'. Any subject perceptions of cutaneous stimulation were also recorded.

MR imaging procedures

After pilot scan acquisition, a 3D FLASH T_1-weighted structural image was acquired with a 240 mm (FH) x 240 mm (AP) x 160 mm (RL) field-of-view (FOV) and 1 mm isotropic resolution, centered laterally on the mid-brain. Fig. 1(b) shows the Philips mffe sequence modified for MREIT-CDI. MREIT-CDI datasets were acquired in three 5 mm contiguous slices (NS = 3) with an in-plane FOV of 224 mm (RL) x 224 mm (AP) and a data matrix size 100 × 100 x 3 (resolution 2.24 × 2.24 × 5 mm^3). MREIT slice positions were aligned to the T_1-image volumes and chosen to encompass electrodes (Fig. 2(i)). MREIT scans were performed for each slice sequentially, and