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Original article

Comparison of electric field strength and spatial distribution of electroconvulsive therapy and magnetic seizure therapy in a realistic human head model

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ABSTRACT

Background: This study examines the strength and spatial distribution of the electric field induced in the brain by electroconvulsive therapy (ECT) and magnetic seizure therapy (MST).
Methods: The electric field induced by standard (bilateral, right unilateral, and bifrontal) and experimental (focal electrically administered seizure therapy and frontomedial) ECT electrode configurations as well as a circular MST coil configuration was simulated in an anatomically realistic finite element model of the human head. Maps of the electric field strength relative to an estimated neural activation threshold were used to evaluate the stimulation strength and focality in specific brain regions of interest for these ECT and MST paradigms and various stimulus current amplitudes.
Results: The standard ECT configurations and current amplitude of 800–900 mA produced the strongest overall stimulation with median of 1.8–2.9 times neural activation threshold and more than 94% of the brain volume stimulated at suprathreshold level. All standard ECT electrode placements exposed the hippocampi to suprathreshold electric field, although there were differences across modalities with bilateral and right unilateral producing respectively the strongest and weakest hippocampal stimulation. MST stimulation is up to 9 times weaker compared to conventional ECT, resulting in direct activation of only 21% of the brain. Reducing the stimulus current amplitude can make ECT as focal as MST.
Conclusions: The relative differences in electric field strength may be a contributing factor for the cognitive sparing observed with right unilateral compared to bilateral ECT, and MST compared to right unilateral ECT. These simulations could help understand the mechanisms of seizure therapies and develop interventions with superior risk/benefit ratio.

1. Introduction

Electroconvulsive therapy (ECT) is a highly effective treatment that induces a generalized seizure in anesthetized patients by administering electric current to the brain via scalp electrodes. ECT has unparalleled antidepressant efficacy in the treatment of severe major depression [1]. However, its clinical use is limited by cognitive side effects such as retrograde amnesia [2–4]. Advances in ECT technique have reduced the side effects of ECT. These include the shift from long sinewave pulses to brief rectangular pulses [5,6] and subsequently to ultrabrief pulses [7–10], which reduced the strength of neural stimulation in the brain and improved tolerability [4]. As well, changes in electrode placement can reduce cognitive side effects. High-dose right unilateral (RUL) ECT has a comparable efficacy to bilateral (BL) ECT with a significant decrease in amnesia [11], potentially due to the increased focality of the RUL stimulus [12]. Other electrode configurations that increase focality and target frontal brain regions include bifrontal (BF) ECT [13] and experimental paradigms such as focal electrically administered

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seizure therapy (FEAST) [14,15] and frontomedial (FM) ECT [16]. However, even with relatively focal electrode placements, conventional ECT current amplitudes of 800–900 mA generate an electric field (E-field) strength that is substantially above the threshold for neural firing of most of the brain, and hence produce stimulation that is both non-focal and more intense than necessary for seizure induction [17]. Reducing the stimulus current amplitude can therefore make the ECT E-field more focal and closer to the neural firing threshold [12,18], while still being able to elicit generalized seizures, although the efficacy and side effects of such paradigms have been explored to a very limited extent in early studies [19] as well as recent small studies and case reports [14,16,20–22]. Such E-field characteristics are also achieved in magnetic seizure therapy (MST), which uses high-dose repetitive transcranial magnetic stimulation to induce a seizure, is associated with fewer cognitive side effects than conventional ECT, and has shown therapeutic efficacy in several studies [23–27]. For these conventional and experimental interventions, there is insufficient knowledge of the characteristics of the E-field induced in the brain by the various electrode and coil configurations as well as current amplitudes, which limits our ability to understand the mechanisms of these interventions and to rationally optimize their dosing.

Previously, using a spherical head model, we examined the stimulation strength and directly stimulated subvolume of the brain (focality) of various ECT electrode and MST coil configurations [17], showing that the E-field strength relative to threshold for MST is 3–6 times weaker and 10–60 times more focal compared with conventional ECT with 800 mA, 0.3 ms pulses. Spherical head models, however, are limited by the substantial simplification of the head anatomy, tissue heterogeneity, and anisotropic tissue properties. In another study using a realistic human head model, we investigated the induced E-field strength in various brain regions of interest (ROIs) by the BL, BF, RUL, and FEAST ECT electrode configurations [28]. However, that study used a truncated head model above the level of the auditory canal, and FM ECT and MST were not modeled. To date, the E-field generated by MST has not been studied in a realistic head model. Moreover, our prior study [28] and other ECT simulations in realistic head models [29,30] did not explore the E-field characteristics relative to neural activation threshold or the effect of current amplitude adjustment.

Addressing these questions, in this paper we extend our previous work to investigate the characteristics of the E-field induced in the brain by ECT and MST. We create an anatomically realistic finite element model of the whole head to simulate the E-field distribution induced by various ECT electrode configurations and an MST coil configuration. We evaluate and compare the stimulation strength and focality relative to an estimated neural activation threshold in the whole brain as well as in specific ROIs thought to be associated with therapeutic action and/or adverse side effects of ECT and MST. Finally, we consider the effect of the stimulus current amplitude on stimulation strength and focality. These simulations could help the interpretation of clinical studies and may guide the improvement of ECT and MST dosing paradigms.

Preliminary results from this study were previously presented in part in conference proceedings [31].

2. Materials and methods

2.1. Data acquisition and image preprocessing

The head model was derived from magnetic resonance imaging (MRI) data of one healthy human subject (male, right handed, age = 34 years). Written informed consent approved by the Institutional Review Board of Columbia University was obtained from the subject before the experiments. T1-weighted structural MRI and diffusion tensor imaging (DTI) datasets of this subject, including the skull base and a portion of the neck underneath, were acquired on a 3 T Philips Achieva scanner (Philips Medical Systems, Best, Netherlands) using an 8-channel head coil. A three-plane localizer and sagittal scout image were acquired to determine the location of the anterior commissure (AC) and posterior commissure (PC). The T1-weighted MRI images were obtained with a 3D spoiled gradient recalled echo (SPGR) (TR = 6.5 ms; TE = 3.0 ms; 256 coronal slices; $1 \times 1 \times 1$ mm^3 voxel; FA = 8°; 2 averages). We corrected the structural MRI image intensities for bias field inhomogeneity [32]. We then applied content-preserving anisotropic diffusion filtering to remove the image noise or artifacts while preserving content details and improving tissue boundaries [33,34].

The DTI data were acquired by employing a single-shot spin-echo echo-planar imaging (EPI) sequence (TR = 13,510 ms; TE = 70 ms; 112×112 acquisition matrix; FA = 90°; $2 \times 2 \times 2$ mm^3 voxel). The diffusion sensitizing gradients with a b-value of 1000 s/mm^2 were applied in 32 non-collinear directions. We corrected the DTI data for distortions due to eddy currents and subject motion artifacts. The diffusion tensor volumes were then co-registered to the T1-weighted MRI volume while the orientation of each diffusion tensor was preserved using the FSL's diffusion toolbox (FDT) from the FMRIB Software Library (FMRIB Analysis Group, University of Oxford, UK).

2.2. Tissue segmentation

To create a realistic volume conductor model of the whole head, the structural MRI images were segmented into several tissue regions (Table 1). We first removed non-brain regions using the skull-stripping algorithm of the BET tool in FSL [35]. This initial segmentation was further corrected for accurate brain extraction using manual editing tools in the ITK-SNAP software [36]. The deskulled MRI images were automatically segmented into subvolumes corresponding to gray matter, white matter, and cerebrospinal fluid (CSF) using the automated segmentation tool FAST in FSL [37]. The non-brain regions were manually segmented into 11 different tissue regions, including skin, muscle, skull compacta, skull spongiosa, vertebrae, spinal cord, lens, eyeball, sclera, optic nerve, and sinus, using a combination of segmentation editing tools of ITK-SNAP [36] and an in-house segmentation algorithm based on thresholding and mathematical morphological operations [28,33,34]. The complete head model and its constituent tissues are displayed in Fig. 1.

2.3. ECT electrode and MST coil configurations

For ECT, three conventional ECT electrode configurations (BL, BF, and RUL) [13] and two experimental configurations (FEAST and FM) [14,16] were modeled (see Fig. 2). For BL ECT, the two electrodes were placed bilaterally at the frontotemporal positions located 2.5 cm above the midpoint of the line connecting the

Table 1
Tissue electrical conductivities (S/m) used in the model.

Tissue	Conductivity	Tissue	Conductivity
Skin	0.43	Lens	0.32
Muscle	0.32	Eyeball	0.5
Skull compacta	0.0063	Sclera	0.5
Skull spongiosa	0.04	Spinal cord	0.15
Cerebrospinal fluid (CSF)	1.79	Vertebrae	0.012
Gray matter	0.33	Optic nerve	0.14
White matter (iso.)	0.14	Sinus	0