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Generating, validating and applying volume conductor models for electric field simulations to determine and optimize the brain regions targeting by transcranial brain stimulation

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approach has helped us understand normal brain states, their operation and conditions like healthy aging, dementia and epilepsy. Using a combination of computational modeling and dynamical systems analysis we provide a mechanistic description of the formation of resting state manifold via the network connectivity. We demonstrate that the symmetry breaking by the connectivity creates a characteristic flow on the manifold, which produces the major data features across scales and imaging modalities. These include spontaneous high amplitude co-activations, neuronal cascades, spectral cortical gradients, multistability, and characteristic functional connectivity dynamics. When aggregated across cortical hierarchies, these match the profiles from empirical data and explain features of the brain's microstate organization. Examples for clinical translation are taken from drug resistant epilepsy and brain stimulation using Temporal Interference. Virtual Brain Twins are part of the European infrastructure called EBRAINS, which supports researchers worldwide in digital neuroscience.

Research Category and Technology and Methods

Translational Research: 19. Modeling and computational methods

Keywords

Digital twin, Temporal Interference, Epilepsy, EBRAINS

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FS2F.6

COMPUTATIONAL MODELS FOR THE TREATMENT OF REFRACTORY EPILEPSY WITH DEEP BRAIN STIMULATION

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Symposium title

Simulating brain stimulation at different spatial scales

Abstract

Epilepsy is a chronic neurophysiological disorder that affects 1% of the world's population. While most of the patients are effectively treated with medication, surgical options can be explored, ranging from resective surgery to neuromodulation such as Deep Brain Stimulation (DBS), targeting the anterior nucleus of the thalamus (ANT). Despite its safety and effectiveness, ANT-DBS has a success rate of only 68%, posing several clinical and scientific challenges.

My research aims to improve the efficacy and the fundamental understanding of DBS in treating epilepsy by integrating personalized computational models at different spatial scales. We use a unique combination of clinical data from patients implanted with DBS, using scalp electroencephalogram (EEG) and simultaneous intracranial recordings (iEEG) from the thalamus.

We built personalized volume conduction models using scalp EEG data during DBS stimulation and performed source reconstructions on ANT-DBS evoked potentials. With simultaneous scalp and intracranial recordings (i.e., when the DBS is switched off), we designed a multiscale computational model based on individual scans of the patients. Using The Virtual Brain (TVB), we implemented two different models, a virtual DBS patient and a virtual epileptic patient. We fitted the relative parameters to the scalp and intracranial EEG, when the DBS was switched on or off, respectively.

Preliminary results consist of i) personalized DBS maps related to DBS evoked potentials for five patients and ii) replicated time-locked evoked activity induced by DBS on the scalp and the duration and amplitude of interictal epileptiform discharges (IEDs) recorded intracranially.

We will compare DBS maps to epilepsy maps resulting from reconstructed IEDs, and combine the virtual DBS and epileptic patients to explore the associations between the DBS settings and the efficacy of DBS therapy for epileptic patients.

Research Category and Technology and Methods

Translational Research: 19. Modeling and computational methods

Keywords

Computational models, DBS, epilepsy, EEG

http://dx.doi.org/10.1016/j.brs.2024.12.110

FS2F.7

RELEVANCE OF E-FIELDS BELOW ACTIVATION THRESHOLD FOR DEEP BRAIN STIMULATION

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Symposium title

Simulating brain stimulation at different spatial scales

Abstract

Deep brain stimulation (DBS) can successfully relieve motor symptoms in many individuals with Parkinson's disease, but its exact mechanism of action is not understood yet. Previous theories have assumed that only the direct and indirect effects of the tissue of volume activated (VTA), in which the E-field of DBS elicits spikes, are relevant. Consequently, E-fields outside of the VTA, for example in cortical areas, have been neglected.

In this talk, I will elaborate on a new potential mechanism of action of DBS. I suggest that weak E-fields below the activation threshold modulate activity in regions remote from the DBS target, most importantly, in the motor cortex. Specifically, weak E-fields may under certain conditions desynchronize motor cortical activity, effectively breaking up large-scale synchrony with the activated subcortical areas of the target.

We show preliminary volume conduction simulation results of whole-head E-fields for DBS, quantifying E-fields in cortical areas. For typical monopolar DBS settings in Parkinson's disease, E-field magnitudes in motor cortical areas can reach more than 0.6 V/m. Thus, the magnitude of cortical E-fields can be in the range of common E-field magnitudes of transcranial alternating current stimulation (tACS) or higher.

Finally, ongoing work includes studying the influence and therefore functional relevance of such weak E-fields on the (de-)synchronization of cortical neurons using dynamic models.

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Research Category and Technology and Methods

Translational Research: 1. Deep Brain Stimulation (DBS)

Keywords

deep brain stimulation, transcranial alternating current stimulation, E-field, synchrony

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FS2F.8

GENERATING, VALIDATING AND APPLYING VOLUME CONDUCTOR MODELS FOR ELECTRIC FIELD SIMULATIONS TO DETERMINE AND OPTIMIZE THE BRAIN REGIONS TARGETING BY TRANSCRANIAL BRAIN STIMULATION

Axel Thielscher [1,2], Oula Puonti [1], Lars G. Hanson [2,1], Jesper D. Nielsen [1], Teresa Cunha [2,1], Torge Worbs [2,1], Kristoffer H. Madsen [1,2], Frodi Gregersen [1]. [1] *Danish Research Centre for Magnetic Resonance, Denmark;* [2] *Technical University of Denmark, Denmark*

Symposium title

Simulating brain stimulation at different spatial scales

Abstract
Electric field simulations are used to characterize the brain regions affected by transcranial electric and magnetic stimulation (TES, TMS) and to optimize the applied electric field distributions. They rely on volume conductor models that are usually derived from structural MR images and represent the major tissue compartments of the head and brain. The accuracy of the volume conductor models directly impacts the accuracy of the simulated fields. This relates to the anatomical accuracy of the MR image segmentation, and the accuracy of the chosen ohmic tissue conductivities that are average values taken from a sparse literature.
My talk will start with a brief overview of our simulation pipeline spanning from MR image processing to electric field simulation and estimation of the effects of the stimulation currents on neural activity. I will then cover two complementary aspects of volume conductor modeling in more detail: First, I will give an overview of our new deep-learning-based MR image segmentation methods that combine speed with robustness to changes in the MR image contrast and typical MR artefacts. I will discuss volumetric segmentation methods for the major head and brain tissues, and surface-based methods that are particularly aimed at the accurate segmentation of the pial and white matter surfaces. The outputs of both methods are combined to obtain a final high-resolution volume conductor model.
Second, I will summarize our recent advances to validate the electric field simulations using MR current density imaging (MRCDI). MRCDI is based on the measurements of the tiny magnetic fields (around 1 nT) that are caused by the current flow induced by TES. Comparisons of the measured with simulated fields allow non-invasive in-vivo assessments of the accuracy of the volume conductor models. Importantly, our proof-of-concept results suggest that simulation accuracy can benefit from individualization of the tissue conductivities.
Research Category and Technology and Methods
Translational Research: 19. Modeling and computational methods
Keywords
TES, TMS, Image segmentation, Magnetic resonance current density imaging

http://dx.doi.org/10.1016/j.brs.2024.12.112

FS2G.1

TARGETING THE EXECUTIVE CONTROL NETWORK VIA THE LEFT DORSOLATERAL PREFRONTAL CORTEX FOR THE TREATMENT OF ALCOHOL USE DISORDER

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Symposium title
Cheers to Promising New Avenues in TMS for Alcohol Use Disorder
Abstract
Transcranial magnetic stimulation (TMS) is a promising treatment tool for Alcohol Use Disorder (AUD) that can modulate neural circuits associated with AUD and relapse risk. Several cortical targets that may lead to improved treatment outcomes have been proposed, including enhancing top-down cognitive control. To this end, we aim to evaluate the efficacy of stimulation to the left dorsolateral prefrontal cortex (L.DLPFC) to reduce alcohol relapse.

Study 1: A total of 17 Veterans with AUD (1 female) were enrolled in a double-blind, sham-controlled trial (20 sessions; intermittent theta burst stimulation; 2 sessions/day; 7–10 days; 600 pulses/session) delivered to the L.DLPFC. *Study 2*: A total of 49 Veterans with AUD (1 female) were enrolled in a study of the same design but double the dose - 1200 pulses/session. Pre- and post-treatment assessments included self-report questionnaires and fMRI tasks to probe target engagement. Likelihood of relapse to alcohol was assessed via standard Odd's Ratios.

Study 1: Relative to sham, individuals who received 600 pulses of DLPFC TMS were less likely to relapse within the first 3 months following TMS (OR=12.0, p=0.07). Change in brain response to alcohol cues (Cohen's d) was reduced following real TMS and increased following sham within the left insula (−0.19 v. 0.51), thalamus (−0.28 vs. 0.77), and ventral striatum (−0.29 v. 0.23). There was no change at the DLPFC stimulation site following real TMS (0.03). *Study 2*: Relative to sham, individuals who received 1200 pulses of DLPFC TMS were less likely to relapse within the first 6 months following TMS (OR=4.4, p=0.05).
These data suggest that TMS strategies targeted at increasing executive control effectively reduce alcohol consumption, relative to sham. Potential risks and benefits of this approach as well as future directions to optimize this strategy will be discussed.
Research Category and Technology and Methods
Translational Research: 10. Transcranial Magnetic Stimulation (TMS)
Keywords
iTBS, veterans, alcohol use disorder, relapse

http://dx.doi.org/10.1016/j.brs.2024.12.113

FS2G.2

IDENTIFYING OPTIMAL TMS TARGETS TO REDUCE ALCOHOL CUE-REACTIVITY IN AUD: A HEAD-TO-HEAD COMPARISON OF MPFC AND DLPFC STIMULATION

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Symposium title
Cheers to Promising New Avenues in TMS for Alcohol Use Disorder
Abstract
Alcohol Use Disorders (AUD) are prevalent and challenging to treat, with 60% of individuals relapsing within the first 6 months despite available behavioral and pharmaceutical interventions. High relapse rates are likely due to factors that affect limbic and executive circuits in the brain, including vulnerability to salient cues and loss of cognitive control. These behavioral processes are regulated by frontal-striatal circuits with key nodes in the medial prefrontal cortex (MPFC) and the dorsolateral prefrontal cortex (DLPFC). These two cortical sites represent fruitful treatment targets for transcranial magnetic stimulation (TMS). To date, the majority of studies have focused on stimulating the DLPFC. However, theta burst stimulation (TBS) to the MPFC has also shown recent promise as a tool to decrease brain reactivity to alcohol cues. The purpose of this study was to evaluate the relative efficacy of a single-session of TMS to the DLPFC versus the MPFC on brain reactivity to alcohol cues in individuals with AUD. Sixty-eight individuals with AUD (57M/11F) completed three TMS sessions on separate days: 1) 10Hz DLPFC, 2) iTBS MPFC and 3) sham stimulation. Following each session, brain reactivity to alcohol cues was measured using fMRI. To evaluate functional connectivity, images were analyzed using the CONN toolbox. Fisher's transformed correlation coefficients were extracted between the MPFC and the following AAL atlas ROIs: insula, caudate, putamen, pallidum, anterior cingulate cortex, amygdala, superior occipital cortex. Functional connectivity during alcohol versus neutral beverage cue blocks were assessed for each participant. A general linear model revealed that, relative to sham, MPFC stimulation had a larger attenuating effect on alcohol cue reactivity than the DLPFC protocol (F=17.18, p<0.001). These findings suggest that cTBS to the MPFC may be more effective than TMS to the DLPFC in reducing brain reactivity to alcohol cues, supporting further research into MPFC-targeted TMS treatments for AUD.
Research Category and Technology and Methods
Clinical Research: 10. Transcranial Magnetic Stimulation (TMS)
Keywords
Alcohol Use Disorder, Functional connectivity, Cue-reactivity

http://dx.doi.org/10.1016/j.brs.2024.12.114

FS2G.3

TARGETING THE MEDIAL PREFRONTAL AND ANTERIOR CINGULATE CORTICES WITH DEEP TMS IN ALCOHOL USE DISORDER: CLINICAL, FMRI, DTI, AND EEG OUTCOMES

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