FUNCTIONAL CONNECTIVITY- AND E-FIELD-OPTIMIZED TMS TARGETING: A PILOT TMS-FMRI VALIDATION AT THE SINGLE-SUBJECT LEVEL

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Effectiveness of personalized, functional connectivity (FC)-guided TMS treatments (Cole et al. 2021) can profit from optimizing coil position and orientation based on E-field simulations. However, existing optimization routines (e.g., SimNIBS; (Saturnino et al. 2019)) typically only consider the E-field in a small patch surrounding a single target coordinate, thus ignoring whole-brain topography of both subject-specific FC map and E-field. To increase target specificity of FC-guided TMS, we developed an optimization approach that takes into account the available spatial information and tested its validity in a single-subject TMS-fMRI experiment, indirectly targeting ventromedial prefrontal cortex (vmPFC) via its FC with left dorsolateral prefrontal cortex (LdlPFC).

Using SimNIBS, we simulated TMS-induced E-fields for multiple coil positions and orientations surrounding an individualized, vmPFC-anticorrelated LdlPFC coordinate (Figure 1B+C). Within our approach, the optimal combination of coil position and orientation simultaneously maximized (Cole et al. 2021) overlap between E-field and negative FC cluster in LdlPFC and (Saturnino et al. 2019) E-field strength in the target cluster, while minimizing overlap with non-target (e.g., positive FC) areas (Figure 1C). For concurrent TMS-fMRI, we used two TMS-compatible 7-channel RF surface coil arrays and a MR-compatible TMS coil that was neuronavigated to the optimized position and orientation (Figure 1A). TMS pulses were applied during gaps between volumes at suprathreshold intensity.

Our optimization approach resulted in a very good overlap between subject-specific vmPFC-based FC map and simulated E-field, with minimal off-target coverage. Concurrent TMS-fMRI revealed specific TMS-induced BOLD modulations in both the directly stimulated LdlPFC target area and the indirectly targeted bilateral vmPFC (Figure 1D).

Preliminary TMS-fMRI data indicates that our FC- and E-field-based TMS optimization approach ensures precision and specificity of stimulation-induced brain activation in both directly targeted and functionally connected regions. We will further validate this approach in a larger sample, yet concentrating on single-subject level evaluations. We hope that this approach will further increase specificity and effectiveness of personalized TMS.

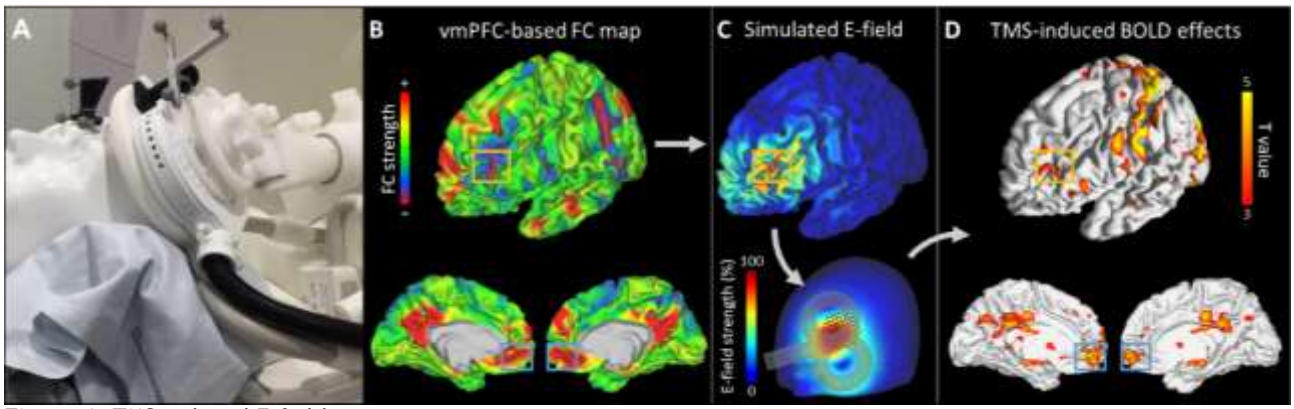

Figure 1. TMS-induced E-fields

References:

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EMOTION PROCESSING TASK AS A NEW STRATEGY FOR LOCATING INDIVIDUALIZED TMS TARGETS

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Introduction: Dysfunctions in emotion processing and regulation are common in subjects suffering from MDD, paradigms involving emotion processing and regulation might be ideal for revealing the corresponding neurocircuitry. Functional MRI localisers using emotion processing paradigms reveal individual dorsolateral prefrontal cortex (DLPFC) activation clusters. This method could be advantageous as these regions may then be used as targets for TMS treatment. In this study, we compared targets derived from individual functional localisers to targets commonly used in TMS for MDD.

Methods: Twenty-eight patients diagnosed with acute MDD (16f/12m, mean age: 28.7±7.1) participated in the study and performed a facial emotion discrimination task (EDT). Data acquisition was performed on an ultra-high 7 Tesla whole-body MR scanner (Siemens Magnetom 7T). The Euclidean distances to seven commonly used DLPFC targets were calculated for each patients EDT activation peak within the group-level DLPFC activation cluster.

Results: DLPFC activation maxima were successfully derived in all subjects. Group-averaged distances of the different targeting approaches to the EDT maxima ranged from 16 mm to 40.5 mm. Targeting approaches that are generally considered less effective (e.g. 5 cm method and EEG-F3 targeting) showed the highest spatial distances to individual functional activation peaks. The spatial reproducibility of the EDT was stable for most subjects, however, in some subjects the spatial variability was quite high (Figure 1). The variability could be improved by performing multiple runs to achieve reliable DLPFC localisation (Geissberger et al. 2020).

Conclusion: We conclude that the EDT may be used to obtain single-subject activation clusters within the DLPFC in a clinical sample. Based on this, individually localized DLPFC with fMRI show considerable inter-subject variability and therefore using the same target for all subjects is suboptimal. We therefore suggest future usage of functional localisers for determining stimulation targets as we showed they can be reliable and reproducible in patients.

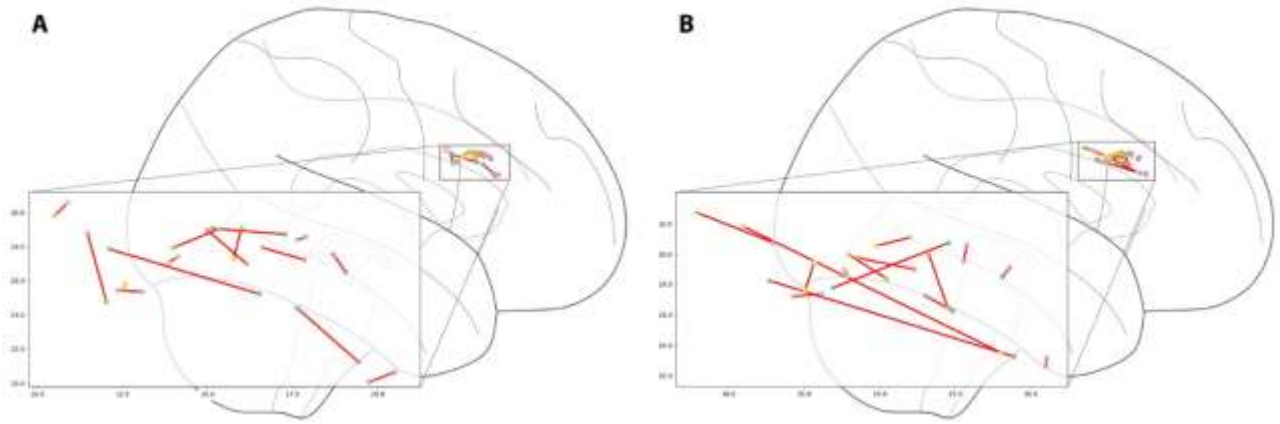

Figure 1. (a) Intra-session distances of single-subject activation maxima in l-DLPFC cluster between two runs. Dots are marking runs, while red lines represent each subject. (b) Inter-session distances of single-subject activation maxima in l-DLPFC cluster. Dots are marking sessions, while red lines represent each subject. Data is represented in a lateral view of the right hemisphere glass brain

References:

1. *Geissberger N, Tik M, Sladky R, Woletz M, Schuler A, Willinger D & Windischberger C: Reproducibility of amygdala activation in facial emotion processing at 7T. NeuroImage 2020; 211:116585*