active arm. Preliminary analysis shows significantly higher performance in memory encoding and a trend of higher performance in semantic dual-task gait at 7 days post 5 sessions of HF-rTMS in the active compared to the sham group.
Conclusions: These preliminary results are encouraging. Implications and future direction will be discussed.
Keywords: rTMS, high-frequency, Motoric-cognitive, seniors

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INTRA- AND INTER-NETWORK EFFECTS OF NAVIGATED TRANSCRANIAL MAGNETIC STIMULATION USING LOW- AND HIGH-FREQUENCY PULSE APPLICATION TO THE DORSOLATERAL PREFRONTAL CORTEX − A COMBINED RTMS-FMRI APPROACH

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Introduction: Although transcranial magnetic stimulation (TMS) is routinely applied in neuroscience and clinical settings, not much is known about its effects on brain networks. We therefore set up this pilot study using repetitive navigated TMS (rTMS) combined with resting-state functional magnetic resonance imaging (rs-fMRI) to explore frequency-dependent stimulation effects on an intra- and inter-network level.
Methods: Six healthy subjects (median age: 23.5 years) underwent two rTMS sessions (1 Hz and 10 Hz), seven days apart, and pre- and post-stimulation rs-fMRI. rTMS was delivered to the left dorsolateral prefrontal cortex (DLPFC), with the exact stimulation target being determined by Independent Component Analysis (ICA). Alterations of functional connectivity strength (FCS) were evaluated using seed-based correlation analyses within and between the salience network (SN), central executive network (CEN), posterior and anterior default mode network (DMN).
Results: Low-frequency rTMS resulted in significant intra-network alterations only for the anterior DMN and the left hemisphere. In contrast, high-frequency rTMS led to changes within all four networks of interest. Moreover, the posterior and anterior DMN largely showed opposite effects to rTMS, and the anterior DMN was rather isolated from the other networks, which was especially true for low-frequency rTMS. Changes in FCS due to low-frequency rTMS were even detectable seven days after stimulation.
Conclusion: This is the first study using neuronavigated TMS with ICA-based target selection to explore frequency-dependent stimulation effects in a combined rTMS-fMRI approach. Future studies including higher subject numbers may define the underlying mechanisms for the different responses to low- and high-frequency rTMS.
Keywords: dorsolateral prefrontal cortex, functional connectivity, navigated transcranial magnetic stimulation, large-scale network

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EEG NETWORK-SPECIFICITY OF RESPONSE TO FMRI-GUIDED TMS PERTURBATION OF THE DEFAULT MODE AND DORSAL ATTENTION NETWORKS IS CORRELATED WITH COGNITION

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Our understanding of the functional architecture of large-scale brain networks has traditionally been driven by the characterization of spatial correlations in the dynamics of the BOLD signal in resting-state functional Magnetic Resonance Imaging (fMRI). However, as this signal reflects slow evolving hemodynamic activity, it typically fails to capture network dynamics at the timescale of normal cortical physiological function. Furthermore, most measures of resting-state connectivity simply identify correlations in brain activity, and the causal significance of the identified relationships remains unclear. Here we non-invasively characterized resting-state fMRI networks dynamics at high spatio-temporal resolution using fMRI-guided, neuronavigated Transcranial Magnetic Stimulation (TMS) and simultaneous electroencephalography (EEG). Individualized targets were identified based on projecting group-average functional cortical atlas (n=1000) consisting of 7 networks onto the individualized cortical surface, and then weighted by the confidence map for each network. Voxels with the highest confidence in angular gyrus and superior parietal gyrus were selected for individualized stimulation of the default mode network (DMN) and dorsal attention network (DAN) respectively, using single-pulse TMS. Using source reconstructed EEG data in surface space, we were able to quantify distinct modulation of fast evolving network activation patterns as a function of the probed cortical nodes. TMS of DMN and DAN nodes induced network specific responses, with increased evoked activity in the stimulated network relative to the non-stimulated network. Furthermore, these network-specific TMS-evoked cortical dynamics were also reproducible across sessions. Notably, higher specificity of the TMS-induced engagement of target network(s) positively correlated with cognitive abilities, i.e. fluid and crystallized intelligence, with perturbation-induced network activation being more strongly correlated with cognitive profile than resting-state EEG dynamics. Taken together, our data suggest that the EEG response to targeted external perturbation with TMS captures unique features of individual brain network dynamics that are relevant for cognitive functioning.
Keywords: TMS-EEG, EEG source space, resting state fMRI, Cognition.

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MULTI-LOCUS TMS TRANSDUCER FOR PROBING ORIENTATION DEPENDENCY OF MECHANISMS IN THE PRIMARY MOTOR CORTEX

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Mechanisms underlying short-interval intracortical inhibition (SICI) and facilitation (SICF) in the motor cortex seem to be sensitive to conditioning-pulse orientation. Available devices require manual coil rotation to adjust the electric field orientation, making it impractical to apply two consecutive pulses with different orientations in millisecond scale. We developed a multi-locus transcranial magnetic stimulation (mTMS) transducer to control the pulse orientation electronically and investigated the orientation dependency of the mechanisms associated with the motor evoked potential (MEP) generation, SICI, and SICF. The mTMS transducer was manufactured by stacking two perpendicular figure-of-eight coils. The pulse direction is changed electronically by adjusting the amplitudes of simultaneously-triggered pulses in these coils, driven by a custom stimulator. Thirteen healthy subjects participated in the study. The hotspot, optimal orientation, and resting motor threshold (rMT) of the right abductor pollicis brevis muscle were measured. MEP amplitude stimulus-orientation curve was built by applying five 110%-rMT pulses every 3°; 0° as the current flowing in posterior-anterior (PA) direction perpendicular to the central sulcus. To assess SICI and SICF, paired-pulses were applied with 0.5, 2.5, 6, and 8 ms interstimulus intervals. Conditioning- and test-pulse intensities were 80- and 110%-rMT, respectively. Twenty paired-pulses were administered in each condition, with the conditioning-pulse orientation set to anterior-posterior (AP), PA, lateral-medial, or medial-lateral. Test pulses were always PA-oriented. The MEP amplitudes had consistent maxima around the PA and AP orientations. SICI was evident for conditioning pulses in all directions. SICF was observed only for PA- and AP-oriented conditioning pulses. Neural elements responsible for SICF seem to be aligned with the cortical columns, whereas a distinct mechanism of SICI activation makes it independent of pulse direction. Possibly, SICF and SICI mechanisms are initiated in the sulcus wall and the gyrus, respectively. The demonstrated control of stimulus orientation opens a possibility for new TMS protocols.
Keywords: Multi-locus TMS, Optimal orientation, Inhibition, Facilitation