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Although repetitive transcranial magnetic stimulation (rTMS) is an FDA approved treatment method for major depressive disorder (MDD), the mechanisms of action are not yet known. It could be possible that the propagation of TMS effects follows structural connections. We investigated whether structural connectivity between the subject-specific stimulation position in the left dorsolateral prefrontal cortex (DLPFC) and the cingulate cortex, derived from diffusion MRI (dMRI) data, could serve as a biomarker to predict treatment response.

Accelerated intermittent theta burst stimulation (aiTBS) was applied to the left DLPFC in forty MDD patients. Anatomical- and dMRI data were recorded before, directly after, and two weeks after aiTBS treatment. The Desikan-Killiany atlas was used to parcellate the brain and manually a node was added representing the subject-specific stimulation position. Baseline structural connectivity between the stimulation-node and the cingulate cortex, quantified using various metrics (fractional anisotropy, mean diffusivity, volume of tracts, number of tracts, and weighted density), was correlated with changes in depression severity, measured with the 17-item Hamilton Depression Rating Scale. Besides direct structural connections, also indirect connections with up to two internodes were studied. A distinction was made between immediate clinical effects, directly after the stimulation protocol, and delayed clinical effects, measured 2 weeks after the stimulation protocol.

Indirect structural pathways (two internodes) between the patient-specific stimulation site and the left caudal and bilateral posterior cingulate cortex showed predictive potential for the immediate clinical response to aiTBS. The delayed clinical effects of aiTBS could be predicted by the structural connectivity to the right caudal and left posterior part of the cingulate cortex.

These findings are in line with earlier assumptions that the clinical effects of (left DLPFC) neurostimulation may depend on 'preserved' structural frontocingular connections. Even though the results are promising, further investigation including replication studies with larger patient numbers is warranted.

Keywords: accelerated iTBS, diffusion MRI, major depressive disorder

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CTBS INCREASES THE FREQUENCY OF NARROW-BAND GAMMA BURSTS IN THE CONTRALATERAL PRE-FRONTAL CORTEX IN A PRIMATE MODEL OF RTMS

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Repetitive modes of TMS (rTMS) modulate behaviour in both humans and non-human primates (NHP). Although widely used in basic and clinical neuroscience, a precise understanding of the neurophysiological effects of rTMS in brain networks, and how such effects influence behaviour, is largely lacking. To overcome this gap, we study a NHP model of rTMS, focusing on the well-studied oculomotor network. Here, we report the effects of continuous theta-burst-stimulation (cTBS) to the right prefrontal cortex (PFC) on neuronal activity in the left PFC during performance of an oculomotor task.

We recorded neural activity from the left PFC (area 8Ar) with a Utah array during performance of an intermixed pro- and anti-saccade task. After a first block of 200 trials, we delivered 600 pulses of cTBS (50Hz bursts of 3 pulses, inter-burst frequency of 5 Hz) above motor threshold, followed by a second block of trials. In one monkey, we have analyzed changes in behavior and neural activity across cTBS applied to either the right PFC (15 sessions), M1 (a brain control; 10 sessions), or above the head (an AIR control, 11 sessions). Behaviorally, we observed significantly shorter leftwards anti-saccade reaction times after cTBS-PFC. At the neuronal level, the firing rate remained on average unmodulated, but the rate of narrow-band oscillatory bursts in the low-gamma (40-80Hz) selectively increased during cTBS-PFC and cTBS-M1 versus cTBS-AIR. The increase in low-gamma bursts lasted for ~10 minutes, resembling the behavioural effect. Our results suggest that an increase in gamma-band burst rates, which has been associated with increased interregional neuronal communication and enhanced working memory, may reflect contralateral disinhibition following cTBS-PFC. To our knowledge, this is the first study showing both behavioural and neurophysiological effects at the network level following cTBS.

Keywords: cTBS, TMS, NHP, PFC

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PROPAGATION OF TMS PULSES VERSUS FUNCTIONAL BRAIN CONNECTIVITY

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Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique that is used to induce changes in cortical activity. Besides local TMS effects under the stimulation coil, overall effects of stimulation have been found in distributed areas throughout the brain. The aim of this study was to quantify the propagation of TMS effects in terms of the brain's resting-state MR functional connectivity (FC).

TMS-EEG recordings were performed in six healthy subjects. Single-pulse TMS was applied to six stimulation sites (dorsolateral prefrontal cortex (DLPFC), motor cortex, and parietal cortex bilaterally) at 120% resting motor threshold. EEGlab and custom matlab scripts were used to compute the TMS-evoked potentials (TEPs). EEG source imaging was performed to convert the TEPs to source space using subject-specific head models. The AAL atlas was used to parcellate the brain into 84 nodes. TEP sizes in every node were quantified using root-mean-square values in the 15-400 ms interval after the stimulation. For every subject and for every stimulation site, FC maps were derived from the functional group connectome data (n=1000), using the individual stimulation positions as seed. Correlations between the TEP sizes and FC were computed on individual level, thereby excluding the nodes under the coil to focus on the actual propagation of the stimulus.

Two subjects showed significant correlations between FC maps and TEP size after stimulating the motor cortices. In the same subjects, negative correlations were found in the left DLPFC. No significant links were found when stimulating the right DLPFC and either parietal cortices in any of the subjects.

There is a large inter-individual variability in the dependence of the propagation from FC. This might be caused by differences in TEP distributions or as a result of correlating individual TEP data with group FC maps. More subjects should be included to extend this research.

Keywords: TMS-EEG, functional connectivity

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THE USE OF RTMS TO AUGMENT WALKING RECOVERY AFTER STROKE

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The goal of non-invasive brain stimulation to directly target brain circuitry to increase neural plasticity and improve coordinated activation of muscles after walking rehabilitation. Neuromodulation using rTMS has been incredibly successful in treating depression and has had some success with improving upper extremity (UE) motor control after stroke through either exciting (E-rTMS) ipsilesional or inhibiting (I-rTMS) contralesional activity. However, similar successes with rTMS for walking have not been achieved in the very few attempts made to date. We recently completed investigation of 14 individuals with chronic stroke who underwent single sessions of E-rTMS, I-rTMS, and SHAM-rTMS examining neurophysiological and biomechanical outcomes as well as spatiotemporal walking data. E-