Assessing effectiveness and specificity of DLPFC rTMS using an unbiased resting-state approach

Tik M.1,2, Hoffmann A.1,2, Sladky R.1,2, Tomova L.3, Hummer A.1,2, Navarro de Lara L.1,2, Biswal B.4, Bukowski H.3, Pripfl J.3, Lamm C.3, Windischberger C.1,2
1Medical University of Vienna, Center for Medical Physics and Biomedical Engineering, Wien, 2Medical University of Vienna, MR Center of Excellence, Wien, 3University of Vienna, Social Cognitive and Affective Neuroscience Unit (SCAN), Wien, 4UMDNJ-New Jersey Medical School, Department of Radiology, Newark

Background: While the precise mechanism of action is still unclear, rTMS is an effective FDA-approved treatment in depression and shows beneficial behavioral effects in a range of pathologies. This study is the first to investigate effectiveness and specificity of rTMS over left DLPFC using a large-scale sham-controlled resting-state (RS) approach.

Methods: 60 healthy subjects (age: 25.01±4.6 years, f/m: 31/29) underwent rTMS DLPFC and sham stimulation. Resting state (rs) fMRI scans were acquired before and twice after stimulation. We investigated BOLD signal changes in functional connectivity (fc) following 10 Hz rTMS (24 × 5s trains, ITI 20s, 1200 pulses @ 90%MT) during a classic resting state paradigm. We examined rsfc changes by using an unbiased approach based on a set of 20 well-established resting state networks derived from multicenter-data independent component analysis by Biswal et al. (2010a).

Results: Comparisons between pre and post stimulation revealed that 19 out of a total of 20 IC networks remained unchanged, i.e. showed no statistically significant differences before and after rTMS irrespective of real/sham stimulation (Fig. 1 A, blue). Only one network (IC17, red dashed) which includes the ACC and PFC showed DLPFC rTMS-related connectivity changes (while staying stable throughout the whole procedure in sham session, Fig. 1 B, C): The ACC had increased connection strength in the post-rTMS scan within this network, particularly with the DLPFC (stimulation site), bilateral insula and striatum.

Conclusions: For the first time this study shows in a model-free approach that rTMS over left DLPFC modulates functional connectivity within a specific network while other networks stay stable. This network is typically associated with attention, mood, reward processing and psychiatric conditions that are linked to maladaptive changes in these domains. This could have further implications on treatment, screening and treatment response monitoring of psychiatric conditions.

Figure 1. Receipting specific effects of DLPFC rTMS. A) To investigate how rTMS affects connectivity within the whole brain we used maps resulting from the netICA analysis by Biswal et al., 2010. We used the mean time-course of those masks to replicate these networks for the 6 acquired RS runs and further tested for changes pre and post real (DLPFC) and sham stimulation in all of the resulting 20 networks. 19 networks stay stable irrespective of stimulation site (sham/real) and runs (before, 15 min and 30 min after stimulation). B, C) One specific network (IC17) comprising DLPFC real stimulation site and ACC shows specific alteration. D) Time course correlations with a spherical 5 mm seed ROI around ACC (hotspot of C)