

Neural Correlates of rTMS Treatment of Negative Symptoms

A. Aleman¹, J. Dlabac-de Lange², E. Liemburg², H. Knegtering³

¹Neuroscience, University of Groningen, Groningen, Netherlands ; ²Psychiatry, University medical Center Groningen, Groningen, Netherlands ; ³Psychiatry, Lentis Mental Health Center, Groningen, Netherlands

Repetitive Transcranial Magnetic Stimulation (rTMS) of the frontal cortex has been shown to improve negative symptoms in schizophrenia in a number of small studies, although inconsistent results have also been reported. Neuroimaging has shown bilateral hypofrontality in schizophrenia, and rTMS may improve brain activation. We therefore aimed to investigate whether 10 Hz stimulation of the bilateral dorsolateral prefrontal cortex during 3 weeks would yield substantial treatment effects and would improve frontal activation.

Methods: This study concerned a multicenter double-blind randomized controlled trial in 32 patients with schizophrenia or schizoaffective disorder. All had moderate to severe negative symptoms (Positive and Negative Syndrome Scale (PANSS) negative subscale ≥ 15). Patients were randomized to a 3-week course of active or sham rTMS. Primary outcome was severity of negative symptoms as measured with the Scale for the Assessment of Negative Symptoms (SANS) and the PANSS negative symptom score. Twenty-four patients participated in the pre- and posttreatment fMRI measurement. Analyses concerned changes in brain activation as measured with functional magnetic resonance imaging (fMRI) during the Tower of London (ToL) task from pre-treatment to post-treatment.

Results: Brain activation increased more in the active group in the right DLPFC and the right medial frontal gyrus as compared to the sham group. Different activation change was also found in the left posterior cingulate, with decreased activation in the active and increased activation in the sham group. The changes in brain activation were accompanied by a significant improvement of negative symptoms in the treatment group ($p=0.04$).

Conclusions: Our findings suggest that treatment with rTMS over the DLPFC may potentially increase task-related activation in frontal areas and improve negative symptoms in patients with schizophrenia.