

The therapeutic benefit of the repetitive transcranial magnetic stimulation on the specific symptoms of schizophrenia

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Summary

Transcranial magnetic stimulation is the modern non-invasive method based on the principle of electromagnetic induction. The TMS is widely used in research, diagnostics and treatment of neuropsychiatric disorders. Previous studies imply that repetitive TMS (rTMS) might be useful also in the treatment of some specific symptoms of schizophrenia. The thesis consists of three studies focused on the evaluation of the therapeutic effect of rTMS on specific symptoms of schizophrenia, particularly on negative symptoms and auditory hallucinations.

Study 1. The double-blind sham-controlled study of high-frequency rTMS (20Hz) for negative symptoms in schizophrenia

The high-frequency repetitive transcranial magnetic stimulation (HF-rTMS) over the prefrontal cortex is a promising method for the treatment of negative symptoms of schizophrenia. Using double-blind, sham-controlled, parallel design, we evaluated the effect of HF-rTMS over the left dorsolateral prefrontal cortex (DLPFC) on negative symptoms in patients with schizophrenia. Sixteen schizophrenia patients with predominantly negative symptoms on stable antipsychotic medication were treated with 20Hz rTMS (90% of motor threshold, 2000 stimuli per session) over ten days within 2 weeks with six weeks follow-up. The effect was assessed using PANSS, CGI, MADRS and neuropsychological tests. We failed to find any significant effect of active rTMS. Sham rTMS showed a trend for improvement over time on positive and negative subscales of PANSS and MADRS. Between-group comparisons failed to reveal any significant differences on any rating scales except a positive subscale of PANSS after 8 weeks. Results from our study did not confirm that HF-rTMS over the left DLPCF affects the negative symptoms of schizophrenia and alternative rTMS approaches are discussed.

Study 2. Effect of low-frequency rTMS on electromagnetic tomography (LORETA) and regional brain metabolism (PET) in schizophrenia patients with auditory hallucinations.

Auditory hallucinations are characteristic symptoms of schizophrenia with high clinical importance. It was repeatedly reported that low frequency (≤ 1 Hz) repetitive transcranial magnetic stimulation (rTMS) diminishes treatment-resistant auditory hallucinations. A neuroimaging study elucidating the effect of low-

frequency rTMS in auditory hallucinations has not yet been published. Low-frequency rTMS (0.9Hz, 100% of motor threshold, 20 min.) applied to the left temporo-parietal cortex was used for ten days in the treatment of medication-resistant auditory hallucinations in schizophrenia (N=12). The effect of rTMS on electrical current density The Low Resolution Electromagnetic Tomography (LORETA) and brain metabolism (18FDG PET) was measured before and after two weeks of treatment. We found a significant improvement in the total and positive symptoms (PANSS), and on the hallucination scales (HCS, AHRS). The rTMS decreased the brain metabolism (18FDG PET) in the left superior temporal gyrus and in interconnected regions and effected increases in the contralateral cortex and in the frontal lobes. We detected a decrease of current densities (LORETA) for the beta 1 and 3 bands in the left temporal lobe whereas an increase was found for beta 2 contralaterally. Our findings implicate that the effect is connected with decreased metabolism in the cortex underlying the rTMS site while facilitation of metabolism is propagated by transcallosal and intrahemispheric connections. The LORETA indicates that the neuroplastic changes affect the functional laterality and provide the substrate for a metabolic effect.

Study 3. Clinical and Electrophysiological Effect of Low-Frequency rTMS in Schizophrenic Patients with Auditory Hallucinations

A growing body of evidences indicates that low-frequency repetitive transcranial magnetic stimulation (rTMS) directed to the left temporo-parietal region might be a effective treatment for auditory hallucinations (AHs) in patients who do not respond to antipsychotic medication. However, little is known about the electrophysiological effect on regional functional activity subsequent to the rTMS treatment. Nineteen schizophrenic patients with antipsychotic-resistant AHs were randomized to either active (n=10) or sham (n=9) rTMS. Low-frequency rTMS (0,9Hz, 100% MT, 1200 stimuli per session) was administered over the left temporo-parietal region for ten days. In case of sham rTMS a coil was tilted at 90°. EEG data were recorded within tree days before and after rTMS treatment. The localization of the differences in electrical activity (current density) was assessed by voxel-by-voxel paired t-tests of the low resolution brain electromagnetic tomography (LORETA) images. The clinical effect was assessed by the Positive and Negative Syndrome Scale (PANSS) and the Auditory Hallucination Rating Scale (AHRS) by a rater blind to the treatment condition. After two weeks of treatment, AHRS scores were significantly improved for patients receiving active rTMS compared to the sham group (median reduction: 40% vs. 12%; p=0.01). LORETA analysis revealed an decrease of current densities in alpha 2, beta 1 and beta 2 bands in the left frontal, temporal and parietal lobes in case of active group. No significant differences in electrical activity were observed in sham group. Active rTMS but not sham stimulation attenuated an auditory hallucinations and was associated with an decrease activity in faster bands on the left hemisphere.