

TMS and negative symptoms

T. Wobrock<sup>1</sup>, A. Hasan<sup>2</sup>, P. Falkai<sup>2</sup>, J. Cordes<sup>3</sup>, W. Gaebel<sup>3</sup>, B. Langguth<sup>4</sup>, M. Landgrebe<sup>4</sup>

<sup>1</sup>Centre of Mental Health, County Hospitals Darmstadt-Dieburg, Groß-Umstadt, Germany ; <sup>2</sup>Dept. of Psychiatry and Psychotherapy, Ludwig-Maximilians-University Munich, Munich, Germany ; <sup>3</sup>Dept. of Psychiatry and Psychotherapy, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany ; <sup>4</sup>Dept. of Psychiatry and Psychotherapy, University of Regensburg, Regensburg, Germany

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**Background:** In schizophrenia negative symptoms often persist and determine an unfavourable course. Reviews including studies with small sample sizes indicate improvement of negative symptoms in schizophrenia patients by repetitive transcranial magnetic stimulation (rTMS), but provide heterogenous results. To prove the clinical efficacy of rTMS on negative symptoms trials with larger samples of patients are needed.

**Methods:** In a multicentre randomized, sham-controlled, rater- and patient-blind clinical trial including 197 patients we investigated the efficacy and tolerability of a 3 week 10 Hertz (Hz) rTMS add-on to antipsychotic therapy (in total 15000 stimuli, stimulation intensity 110 % of the individual motor threshold) over the left dorso-lateral prefrontal cortex (LDLPFC) immediately after treatment and during a 12 weeks follow-up. **Results:** According to our primary outcome parameter we observed a significant decline in negative symptoms (negative sum score of the PANSS) in the verum and sham group (N = 124), but could not find a significant superior reduction in the verum group at day 21. At day 28 significant more patients in the verum compared to the sham group showed a clinical meaningful reduction of PANSS negative subscore ( $\geq 20\%$ ) (N = 89; 57.5 % vs. 32.7 %,  $p = 0.033$ ), however this effect did not persist at further follow-up. **Discussion:** High-frequency (10 Hz) rTMS of LDLPFC over 3 weeks provided only a small benefit in the reduction of negative symptoms, however HF-rTMS was well tolerated. We discuss our results in comparison to current meta-analyses and previous studies. **Trial registration:** ClinicalTrials.gov NCT00783120.