Prefrontal transcranial direct current stimulation (tDCS) for treatment of schizophrenia with predominant negative symptoms: A double-blind, sham-controlled proof-of-concept study

Ulrich Palm1, Daniel Keesser1,2, Alkomiet Hasan1, Michael J. Kupka2, Janusch Blautzik2, Nina Sarubin1,3, Filipa Kaymakanova1, Ina Unger1, Peter Falkai1, Thomas Meindl2, Birgit Ertl-Wagner2, Frank Padberg1

1 Department of Psychiatry and Psychotherapy, Ludwig Maximilian University Munich, Germany; 2 Institute for Clinical Radiology, Ludwig Maximilian University Munich, Germany; 3 Hochschule Fresenius, University of Applied Sciences, Germany; * both authors contributed equally

Background

Negative symptoms in schizophrenia include a dysfunction of various brain regions like the dorsolateral prefrontal cortex (DLPFC) and cognitive deficits. Recently, non-invasive brain stimulation has proven to modulate DLPFC action and transcranial direct current stimulation (tDCS) is investigated as a treatment option in schizophrenia.

Methods

In this study, twenty schizophrenia patients with predominantly negative symptoms received 10 sessions of add-on active (2 mA, 20 min) or sham tDCS (anode: left DLPFC; cathode: right supraorbital). Primary outcome was change in the Scale for the Assessment of Negative Symptoms (SANS) sum score; secondary outcomes were reduction in Positive and Negative Syndrome Scale (PANSS) scores and improvement of depressive symptoms, cognitive processing speed, and executive functioning. Sixteen patients underwent additional functional connectivity magnetic resonance imaging (fcMRI) before and after the 1st and 10th sessions to investigate changes in resting state networks.

Clinical and Imaging Results

Per-protocol analysis showed a significant greater decrease in SANS score with active (1-34.4%) than with sham tDCS (-1.1%) (Fig. 1 A), and the affective subscale improved significantly more in the active group. PANSS sum scores decreased significantly more with active (-25.4%) than with sham stimulation (-2.2%) (Fig. 1 B). In the active group, after the 1st tDCS fcMRI revealed significant deactivation in the default mode network, localized in the subgenual cortex that remained stable after the 10th tDCS, and temporary changes in the left DLPFC in the frontal parietal network and in a cluster comprising the left insula, putamen, and anterior cingulate regions. (Fig. 2 A-C). PANSS changes in the active group were correlated to changes in the default mode network. (Fig. 2 D).

Conclusions

The results of this proof-of-concept trial indicate that prefrontal tDCS is a promising intervention for treatment of schizophrenia with predominant negative symptoms.

References
