Psychiatry Research 279 (2019) 399–400

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Letter to the Editor

Transcranial alternating current stimulation for the treatment of major depression during pregnancy

Dear editors,

Major depressive disorder (MDD) is the most frequent psychiatric morbidity in pregnancy. Although psychotherapeutic interventions are often insufficient, many women renounce medication for fear of severe adverse effects, i.e. teratogenicity (Kurzeck et al., 2018). Recently, studies applying non-invasive transcranial brain stimulation (NTBS) have shown promising results for the treatment of MDD (Brunoni et al., 2019).

As the electric field distribution is supposed to be limited to the brain, NTBS could be predestined for the treatment of MDD in pregnancy. In contrary to transcranial direct current stimulation (tDCS) with application of a steady current, transcranial alternating current stimulation (tACS) is a newly developed stimulation technique with a typically sinusoidal waveform. It is thought to alter the brain´s endogenous oscillatory patterns by changing neuronal membrane potentials (Kuo and Nitsche, 2012) and thus might be suitable in disorders with altered electroencephalography (EEG) activity. Gamma band activity (about 40 Hz) is involved in cognitive functions and is impaired in various psychiatric disorders (Fitzgerald and Watson, 2018). Recently, a pilot study applying alpha- and gamma-tACS in depressed subjects showed that tACS may be a feasible and efficacious treatment in MDD (Alexander et al., 2019). However, there is only sparse data evaluating the efficacy and safety of NTBS in depression during pregnancy (Kurzeck et al., 2018).

Here, we report the case of a 38-year-old female patient suffering from recurrent MDD during the second pregnancy. In her first episode, at the age of 35 during the first pregnancy, she was treated with tDCS and reached remission in terms of HAMD and BDI (unpublished data). In the present episode, occurring in week 6, she was suffering from depressed mood, social withdrawal, decreased energy, insomnia, and suicidal ideation. Following the patient's wish for abstaining from medication and her preference for NTBS, she was offered tACS after giving informed consent for an individual treatment attempt.

Gamma-tACS with DC offset (20 min, frequency 40 Hz, 48 000 cycles, 2 mA range, offset at 1 mA without ramp-in/ramp-out) was delivered by a neuroConn DC-Stimulator Plus after placing saline-soaked sponge electrodes (35 cm^2) over both dorsolateral prefrontal cortices (F3-F4 position). Clinical assessment and cognitive tasks were performed before first (baseline), after 5th, after 9th stimulation (1 stimulation missed for gastrointestinal symptoms), and 2 weeks after the stimulation period.

At baseline, she presented with a HAMD-21 score of 19, a BDI score of 24, a Positive Affect Score of 15 and a Negative Affect Score of 26 in the Positive and Negative Affect Schedule (PANAS). Trail Making Test (TMT) was performed in 25 s (TMT-A), and 82 s (TMT-B).

After 9 stimulations, HAMD was 11, BDI = 12, Positive Affect = 22, and Negative Affect = 17. TMT-A was performed in 19 s, and TMT-B in 50 s. Gamma-tACS was well tolerated with only mild phosphenes during stimulation and no further side effects. Two weeks after the stimulation period HAMD was 10, BDI = 9, Positive Affect = 30, and Negative Affect = 15. TMT-A was performed in 15 s and TMT-B in 35 s. At follow-up three months later, the patient had reached remission (HAMD = 3; BDI = 7) when she was pregnant in week 27 without any complications reported.

To our knowledge, this is the first report to use gamma-tACS for MDD during pregnancy. Moderate symptoms of depression were improved during treatment until remission at follow-up. Cognitive task performance was improved, in line with previous studies pointing towards an effect of tACS on cognitive functions (Kuo and Nitsche, 2012).

However, clinical improvement could also be driven by non-specific interventional and placebo effects as the patient had already responded to tDCS treatment before. To date, the evidence regarding the effect of distinct tACS frequencies on psychiatric symptoms in the literature is inconclusive and further studies are required (Alexander et al., 2019). Still, this case report supports the feasibility and tolerability of gamma-tACS for MDD during pregnancy and emphasizes the need for further systematic investigation of the mechanisms.

Declaration of Competing Interest

UP has a private practice with neuroCare Group Munich and received paid speakership from neuroCare Group. FP is a member of the European Scientific Advisory Board of Brainsway Inc., Jerusalem, Israel, and has received speaker's honoraria from Mag&More GmbH and the neuroCare Group. His lab has received support with equipment from neuroConn GmbH, Ilmenau, Germany, and Mag&More GmbH and Brainsway Inc., Jerusalem, Israel. The other authors declare no conflict of interest.

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https://doi.org/10.1016/j.psychres.2019.06.009
Received 1 May 2019; Received in revised form 7 June 2019; Accepted 8 June 2019
Available online 09 June 2019
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Anja Wilkening[a,*], Anna Kurzeck[a], Esther Dechantsreiter[a], Frank Padberg[a], Ulrich Palm[a,b]

[a] *Department of Psychiatry and Psychotherapy, University of Munich, Nussbaumstr. 7, 80336 Munich, Germany*

[b] *Medical Park Chiemseeblick, Rasthausstraße 25, 83233 Bernau am Chiemsee, Germany*

E-mail address: anja.wilkening@med.uni-muenchen.de (A. Wilkening).

* Corresponding author.