A case study of weekly tACS for the treatment of major depressive disorder

Dear Editor,

At the conclusion of our recent clinical trial (NCT02339285) of tACS (transcranial alternating current stimulation) for the treatment of major depressive disorder [1], we received requests from patients for continued stimulation motivated by their clinical improvement. In response, we acquired approval from the institutional review board at the University of North Carolina at Chapel Hill to offer 12 weeks of weekly stimulation at the request of the study participant. Stimulation from the original experiment was continued such that the patients and experimenters were still blinded to the condition of stimulation (10Hz-tACS, 40Hz-tACS, placebo-tACS).

The pilot data reported here constitutes — to our knowledge — the largest dose of tACS ever delivered to a single participant in a clinical trial: 40-min for five consecutive days in the main experiment and 40-min for 12 consecutive weeks in the follow-up extension, for 680 minutes of total stimulation time for each participant. We acquired daily self-reported depression severity ratings on a 10-point Likert scale, and collected monthly clinician-administered Montgomery-Åsberg Depression Rating Scale (MADRS) assessments. Three participants enrolled in the

Fig. 1. Effect of tACS on depression symptoms in a single participant. The initial study, five consecutive days of stimulation, resulted in a response to tACS based on (A) clinical assessment via MADRS [0–36 scale]. (B) Daily depression self-report [1–10 scale]. The extension study, twelve consecutive weekly stimulation sessions, resulted in remission based on (C) MADRS. (D) Daily depression self-report. Solid yellow line depicts the time of stimulation. Dashed grey line depicts a response to tACS (MADRS of 18). Dashed black line depicts remission (MADRS of 9). Terminology: Month (M), Day (D), Follow-up (F).

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extension study. After unblinding, we found that one of the three participants received 10Hz-tACS, the condition that was successfully blinded and showed a significant response in our initial experiment. The other two participants received stimulation in a control frequency (40Hz) that did not show a therapeutic effect in the main experiment. Thus, these participants are not discussed here. For the participant that received 10Hz-tACS, the MADRS and daily depression rating in response to tACS are reported in Fig. 1.

The patient reported a lifelong history of depression and presented initially with severe symptoms of depression (MADRS score of 35). At the completion of the 5-day initial experiment, her depression symptoms were reduced to 15 at the two-week follow-up (F1) and 13 at the four-week follow-up (F2). While the patient demonstrated a response to tACS (defined as 50% symptom reduction), she did not go into remission (defined as a MADRS score of 9 or less). Months after completion of the first experiment, the participant enrolled in the extension experiment motivated by her response to treatment. After eight weeks of stimulation (month 3, M3), the patient responded to treatment (MADRS score of 16, a 20-point decline from the baseline of 36). After twelve weeks of stimulation, the patient was in remission (MADRS score of 7). Near the end of treatment in May 2017, the patient reached out to our study coordinators to express that she was experiencing profound improvements in her personal life after feeling entirely incapacitated from her depression prior to enrollment in the clinical trial. After completion of the twelve weekly sessions, the patient wrote to express that her life had changed profoundly. At the end of August 2017 (over two months after the end of treatment), the patient reported an experience of “total contentment” and lasting effects. The patient reached out again in January 2018 (six months post-treatment) and wrote that she had experienced a full relapse into depression.

These findings suggest that the acute effects observed in the initial trial wear off with time, and that weekly bifrontal 10Hz-tACS, a more manageable therapeutic intervention than daily tACS, can effectively result in remission of depression. Although the case study reported here is limited to a single experience and, thus, is not generalizable, the findings are promising regarding both the feasibility and potential therapeutic benefit of weekly bifrontal 10Hz-tACS.

Declaration of competing interest

F.F. is the lead inventor of IP on brain stimulation filed by UNC. F.F. is the founder, CSO, and majority owner of Pulvinar Neuro LLC. The company had no role in this study. F.F. is also an author under Elsevier and receives royalty payments.

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References