SHORT ARTICLE

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Transcranial direct current stimulation (tDCS) in obsessive-compulsive disorder (OCD): the state of the art

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Summary

Obsessive Compulsive Disorder (OCD) is a major cause of illness in the field of mental health. A significant proportion of patients fail to achieve a satisfactory response after receiving standard therapies.

In this short article, we discuss and provide an update on the possible role of a non-invasive brain stimulation technique (transcranial direct current stimulation - tDCS) as an alternative treatment approach for OCD.

Seven randomized controlled trials investigating tDCS in OCD are examined. tDCS seems to be a promising treatment for OCD, particularly if targeting the Orbitofrontal Cortex (OFC), with a favorable side effects profile.

Despite the encouraging findings, it should be pointed out that all studies included patients already taking medications for OCD, therefore it is difficult to say if tDCS could work as a stand-alone therapy or as an add-on treatment.

Keywords: OCD, transcranial direct current stimulation, tDCS

Obsessive compulsive disorder (OCD) is a major cause of illness in the field of mental health and morbidity related to mental disorders [1,2]. First-line therapies for this condition include selective serotonin reuptake inhibitors (SSRIs) or cognitive behavior therapy (CBT) with exposure and response prevention (ERP) [3]. Nevertheless, a significant proportion of patients (about 40%) fail to achieve a satisfactory response despite receiving these therapies [3,4]. OCD is supported by a well defined neuroanatomical foundation, as shown in the study conducted by Tyagi and colleagues [5]. Non-invasive brain stimulation is being investigated as an alternative approach. Previous studies have primarily investigated the effects of repetitive transcranial magnetic stimulation (r-TMS) [6] and transcranial direct current stimulation (tDCS) [7] on specific dysfunctions within the orbitofronto-striato-thalamic neuro-circuitry that are believed to be associated with OCD. These dysfunctions occur in various brain regions, including the dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex (ACC), supplementary motor area (SMA), orbitofrontal cortex (OFC), and medial prefrontal cortex [3,7]. tDCS, or transcranial direct current stimulation, is a kind of neurostimulation that is safe and effective for treating OCD. It has the potential to be developed as a self-administered intervention. tDCS administers a low-intensity electric current (usually 1-2 milliamperes) to the scalp, which traverses the brain tissue and induces depolar-

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ization or hyperpolarization of neurons in the specific area of the brain being targeted. These alterations in neural activity may result in modifications in brain function and behavior. The duration of the effects of tDCS might range from few minutes to several hours after stimulation. Multiple studies have examined the effectiveness of tDCS in decreasing symptoms of OCD, with encouraging results. There have been seven randomized controlled trials (RCTs) in OCD that were done using sham controls. These trials employed different methodologies, resulting in significant diversity. The majority of the studies [7-13] included patients who were receiving medication for OCD, provided that their pharmacological therapy remained consistent. In the randomized controlled experiment (RCT) conducted by Bation et al. [8], N = 21, the use of active tDCS resulted in a substantial reduction in OCD symptoms compared to sham tDCS, immediately after the 10th tDCS session, indicating a strong immediate impact. However, there were no notable differences between the active and sham groups in terms of changes in Y-BOCS score or the number of responders one and three months after tDCS. This indicates a lack of substantial maintenance impact. In their study, Gowda and colleagues [9] administered anodal tDCS to the pre-SMA and cathodal tDCS to the right supraorbital region in patients who did not respond to serotonin reuptake inhibitors (SRIs). OCD resistance was widely characterized as experiencing treatment failure in at least one experiment including selective SSRIs. The use of active tDCS resulted in a much higher response rate and a considerable reduction in symptoms compared to the use of sham stimulation. In a comparable investigation [10] with patients who did not show improvement after receiving at least one prior primary pharmaceutical therapy (SRI) (N = 43), the application of active tDCS was shown to be more successful in decreasing symptoms of OCD compared to a sham treatment. In the randomized controlled trial conducted by Yoosefee et al. [11], all patients were administered fluoxetine; the study included a total of 30 participants in the active tDCS group and 30 participants in the sham group. The results showed no significant difference in OCD symptoms between the two groups. The tDCS treatment, when used as an augmentation technique with SSRI medication, was shown to be no more effective than a placebo when added to SSRI monotherapy. The study conducted by Adams and colleagues [12], investigated participants who were first provided with traditional ERP psychoeducation. The fluctuations in individual's subjective emotional discomfort throughout the ERP challenge were used as a measure of therapeutic safety learning. Individuals with OCD who underwent active tDCS demonstrated faster acquisition of therapeutic safety learning ($p < .05$) during the ERP challenge compared to those who received a sham treatment. The study done by Balzus et al. [13] used a randomized, double-blind, sham-controlled, crossover design trial. The researchers examined the impact of tDCS on the ability to monitor performance in persons with OCD and healthy participants. They used electroencephalography (EEG) to evaluate a specific brain response known as the error-related negativity (ERN). The application of cathodal tDCS resulted in a decrease in the amplitude of the ERN compared to the sham tDCS condition. Cheng and colleagues [14] aimed to assess the effectiveness of tDCS in treating OCD. Additionally, the researchers examined changes in cortical excitability and inhibition using concurrent transcranial magnetic stimulation-electroencephalography (TMS-EEG) measurements following the treatment (N- = 20). Following transcranial direct current stimulation, individuals with OCD had a significant decrease in their ratings on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Interestingly, the strength of TMS-induced N100, which is thought to be linked to GABAb receptor function, showed a significant reduction after tDCS. In a recent study, named FEATSOCS [7], the authors investigated the feasibility of using tDCS in treating OCD (N = 20). These participants received three sessions of tDCS treatment, specifically targeting the bilateral SMA and lateral orbitofrontal cortex (L-OFC). The treatment was administered in a clinic-based setting and compared to a sham treatment. The sequence in which the treatments were given was randomly determined and counterbalanced. Each session consisted of four 20-minute stimulations with a current of 2 mA. These stimulations were given over two consecutive days, with a break of at least four weeks between each course. The research lacked sufficient statistical power to detect a significant difference in group effects. tDCs shown a high level of safety, acceptability, and tolerance. The Y-BOCS scores showed numerical improvement from the first measurement to 24 hours after the last stimulation. The most significant improvement was seen in the lateral orbitofrontal cortex (L-OFC) group, with a Cohen's d effect size of -0.5 (95% CI -1.2 to 0.2) compared to the Sham group. The findings indicate that the L-OFC may be the most effective region for stimulation in future research. The FEATSOCS study also examined the practicality of gathering cognitive results using the CANTAB battery. Specifically, it focused on assessing motor-impulsivity (stop signal reaction time - SSRT) and cognitive inflexibility in relation to extra dimensional set shifting (Intra/Extra-Dimensional-Set-Shifting-Task: ID/ED) (unpublished data – paper in submission). These measurements were used to determine the underlying mechanisms of effect as it is crucial to note that individuals with OCD not only have clinical symptoms but also demonstrate deficiencies in some components of executive function, such as motor disinhibition and inflexible thinking, which have significant implications for their overall well-being. However, there is presently a scarcity of research about the cognitive impacts of tDCS for OCD and further studies, possibly using a home-based approach and testing neurocognitive domains, are warranted. In conclusion, tDCS seems to be a promising treatment for OCD, particularly if targeting the OFC [7]; however it should be

noted that all studies included patients taking medications for OCD (although medical treatment had to be stable for at least three months), therefore it is difficult to say if tDCS could work as a stand-alone therapy or as an add-on treatment. Moreover, the appropriate stage of administration of tDCS is still under debate: could it work better as a primary option, considering also its very few side effects, or as secondary/tertiary therapy, if previous ones have failed? The mechanism of effect of tDCS is still not completely clear, therefore investigating neurocognitive outcomes, other than symptoms severity, and using imaging techniques in future studies could shed light over the mechanistic action of tDCS in OCD.

Conflict of interest statement

The authors declare no conflict of interest.

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Authors' contributions

L.P.: data collection and writing. U.A.: conceptualization of ideas; formulation or evolution of overarching research goals and aims: writing.
All authors reviewed the final manuscript.

Ethical consideration

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