Psychiatry Research 271 (2019) 259–264

Contents lists available at ScienceDirect

Psychiatry Research

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

Review article

Transcranial direct current stimulation for the treatment of obsessive-compulsive disorder? A qualitative review of safety and efficacy

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ARTICLE INFO

Keywords:
Treatment-resistance
OCD
tDCS
Cathode
Anode

ABSTRACT

Obsessive-compulsive disorder (OCD) is a highly disabling psychiatric disorder characterized by recurrent obsessions and compulsions. It has a lifetime prevalence of 1–3% in the general population and commonly has a chronic course. First-line treatments consist of selective serotonin reuptake inhibitors and cognitive-behavioral therapy but up to 60% of patients respond partially or not at all to these treatments. This paper reviewed the literature on the safety and efficacy of transcranial direct current stimulation (tDCS) for the treatment of obsessive-compulsive disorder and discussed future directions for research and clinical application. Criteria for inclusion were open or controlled studies on tDCS and OCD that used validated rating scales along with well-described stimulus parameters. In the majority of the limited number of published studies, most patients with treatment-resistant obsessive-compulsive disorder had either moderate or marked benefit with this technique different stimulation targets, sometimes sustained for many months. This technique might be efficacious in the treatment of obsessive-compulsive disorder, although it is difficult to draw definitive conclusions about its efficacy, future well-designed sham-controlled studies are needed to confirm the safety and efficacy of tDCS for the treatment of this condition.

1. Introduction

Obsessive-compulsive disorder (OCD) is a highly disabling psychiatric disorder characterized by recurrent obsessions and compulsions (American Psychiatric Association, 2013). OCD has a lifetime prevalence of 1–3% in the general population (Ruscio et al., 2010; Almeida-Filho et al., 1997). Commonly, OCD symptoms begin during childhood and have a chronic course, causing severe impairments in interpersonal, social and occupational functioning as well as in quality of life (Bystritsky et al., 2001; Steketee, 1997; Fontenelle et al., 2010; Subramaniam et al., 2012).

First-line treatments for OCD consist of selective serotonin reuptake inhibitors (SSRIs) and cognitive-behavioral therapy (CBT). Unfortunately, many patients are unable to tolerate medication side effects. Up to 60% of patients respond partially or not at all to first or second line treatments given in combination, or not, with CBT. Such conditions require alternative therapeutic approaches such as serotonin-norepinephrine reuptake inhibitors, augmentative atypical antipsychotics or glutamate-modulating agents (Aouizerate et al., 2006).

Given that OCD is very often a difficult condition to treat, alternative therapeutic approaches are highly needed. Among these, neuromodulation techniques have been investigated and according to three recent meta-analyses (Zhou et al., 2017; Trevizol et al., 2016; Berlim et al., 2013), moderate to large effect sizes for short-term therapeutic effects for OCD were found mostly for low-frequency and somewhat high-frequency repetitive transcranial magnetic stimulation by targeting the supplementary motor area (SMA), the orbitofrontal cortex (OFC) (Jaafari et al., 2012; Nauczyciel and Drapier, 2012), and to a lesser extent the left dorsolateral prefrontal cortex (LDLPFC), bilateral dorsolateral prefrontal cortex (DLPFC) and right dorsolateral prefrontal cortex (RDLPFC) for active treatment versus sham particularly in patients who were non-treatment resistant. It has also been shown that deep brain stimulation may show promise for treatment-resistant OCD but the results are limited by small sample size and insufficient randomized controlled studies (Naesströmee et al., 2016; van Westen et al., 2015; Alonso et al., 2015).

Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation technique which delivers low-amplitude direct currents (1–2 milliAmpere (mA)) to the brain between two large surface electrodes (anode and cathode) positioned on distinct areas of the scalp with a rubber headband (Wagner et al., 2007), which, depending on the polarity, intensity and duration of the current flow are capable of modulating cortical excitability by depolarizing or hyperpolarizing neuronal resting membrane potentials of different brain areas involved in cortico-subcortical loops (Nitsche and Paulus, 2000; Nitsche et al., 2008; Nitsche et al., 2003; Priori, 2003; Keeser et al., 2011). The currents penetrate the skull and enter the brain from the anode, travel through the tissues and exit via the cathode. The anodal electrode

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https://doi.org/10.1016/j.psychres.2018.11.033
Received 21 January 2018; Received in revised form 9 October 2018; Accepted 15 November 2018
Available online 16 November 2018

generally increases cortical excitability and the cathodal electrode decreases it (Nitsche and Paulus, 2000). The mechanisms of tDCS-induced depolarization/hyperpolarization remains poorly understood, but pharmacological studies have shown that the effect of tDCS may be linked to shifts in the membrane potential (Bindman et al., 1964). The effects of tDCS on cortical excitability are probably mediated by GABAergic and glutamatergic mechanisms (Liebetanz et al., 2002; Stagg and Nitsche, 2011; Monte-Silva et al., 2013), possibly leading to long-term depression and long-term potentiation-like mechanisms (Liebetanz et al., 2002). The technique is relatively safe with side effects limited to local tingling and skin irritation.

The safety and efficacy of tDCS have been investigated for the treatment of a variety of psychiatric disorders including depression and schizophrenia (Kuo et al., 2014; Kekic et al., 2016; Szymkowicz et al., 2016).

As far as the neurobiology of OCD is concerned, neuroimaging studies have demonstrated a malfunctioning of cortico-striato-thalamo-cortical circuitry, namely the fronto-striatal loop (impairments of behavioral inhibition/compulsions, impaired response inhibition), hyperactivity of the orbitofrontal-subcortical loops caused by a disruption in the balance of activity through these opposing basal ganglia pathways particularly during symptom provocation (impairments of cognitive inhibitory processes/obsessions), all including the SMA, anterior cingulate cortex (ACC), DLPFC, OFC and basal ganglia (Milad and Rauch, 2012; Del Casale et al., 2011). There is an increased activity in the OFC, DLPFC, medial prefrontal cortex, anterior cingulate gyrus (role in aberrant error monitoring and fear conditioning/expression), SMA which explains the use of inhibitory (cathodal tDCS) to treat OCD amongst other locations, increased activity of the basal ganglia and decreased activity in the right and left cerebellum and the parietal cortex (Del Casale et al., 2011; Milad and Rauch, 2012) along with increased regional cerebral blood flow (Zheng et al., 2011), all related to the severity of obsessive and compulsive symptoms in patients with OCD. The OFC plays a major role in the pathophysiology of OCD because obsessions and compulsions are mediated by hyper-activity of the orbito-frontal cortex either bilaterally (Alptekin et al., 2001) or unilaterally (left side) (Swedo et al., 1992).

Findings from neuroimaging studies also show that cognitive performance such as executive functioning, decision making, memory and visuospatial skills in OCD might be associated with the DLPFC and the OFC and have been reported to be disabled in OCD.

This paper reviewed the literature on the safety and efficacy of tDCS for the treatment of OCD and discussed future directions for clinical research in this growing area of attention (Fig. 1).

2. Method

Using the search terms “transcranial direct current stimulation”, “tDCS”, “obsessive-compulsive disorder”, and “OCD”, 14 controlled and open-label studies on humans published in peer-reviewed journals in English until December 2017 were retrieved through NCBI Pubmed and Science Direct searches. Criteria for inclusion were open or controlled studies on multiple sessions of tDCS and OCD meeting criteria for DSM-IV/5 or ICD-10 that used a least one validated rating scale along with well-described stimulus parameters and short as well as long-term outcomes (when possible) (See Table 1 Prisma checklist).

3. Results

Overall, these were studies on the safety and efficacy of tDCS in the treatment of obsessive-compulsive disorder (D'Urso et al., 2016; Todder et al., 2017; Bation et al., 2016; Dinn et al., 2016; Najafi et al., 2017; Beck et al., 1988) (Table 2). One study (Yekta et al., 2015) was not included in the review process because it was unclear in this publication whether patients who responded to the treatment had received active tDCS, sham tDCS or both.”

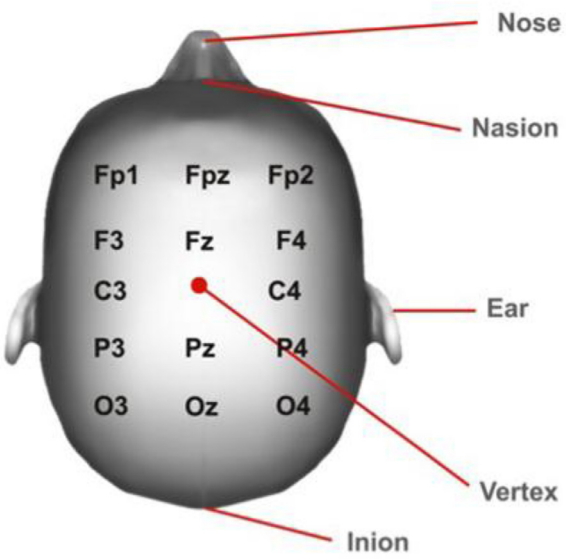

Fig. 1. Different localization used for transcranial direct current stimulation in the treatment of obsessive compulsive disorder; Fz corresponds to the supplementary area (cathodal tDCS over the pre-SMA/SMA in OCD), F3 to the left dorsolateral cortex, F4 to the right dorsolateral cortex (cathodal tDCS over the RDLPFC in OCD) and Fp1 to the left orbitofrontal cortex (cathodal tDCS over the left OFC in OCD).

A randomized, controlled, partial cross-over study (D'Urso et al., 2016) investigated the safety and efficacy of tDCS on OCD symptoms along with polarity-specific effects in twelve patients with OCD on stable doses of medications for one month before and throughout the trial. They initially received ten daily sessions of anodal ($N=6$) or cathodal ($N=6$) tDCS (2 mA, 20 min) with the active electrode placed bilaterally on the pre-SMA. In case of improvement or no change in symptoms severity, the patients were maintained on the same current polarity for ten more sessions. In case of symptoms worsening after the first ten sessions, patients were switched to the other polarity for ten additional sessions. Each subject received a total of 20 sessions of tDCS. There were few side effects such as mild headache, local tingling or itching and redness of the skin at the sites of the electrodes. After ten sessions, 50% of patients who initially received anodal stimulation were switched to cathodal tDCS while 100% of patients initially assigned to cathodal stimulation continued to receive the same treatment. After ten sessions of anodal tDCS, patients showed a worsening of symptoms whereas they significantly improved after ten sessions of cathodal stimulation with a 30% reduction in baseline severity score on the Yale-Brown obsessive-compulsive scale (Y-BOCS). The greatest symptoms improvement was seen in those patients who received 20 cathodal tDCS sessions. Sheehan disability scale (SDS; Sheehan et al. 1996) scores increased after anodal stimulation and decreased after cathodal stimulation.

A randomized, sham-controlled, cross-over study (Todder et al., 2017) investigated the use of tDCS on obsession-induced anxiety after symptom provocation in twelve patients with refractory OCD who received cathodal, anodal, and sham tDCS (2 mA, 20 min) over the medial prefrontal cortex (Fpz, international 10–20 EEG system) along with pharmacological treatment. The reference electrode was placed over the right shoulder. There were few, mild and transient adverse effects including facial pain and toothache in one patient, headache in another, and shoulder pain in a third patient. There was a statistically significant but short lasting reduction in the severity of the obsession-induced anxiety with active cathodal tDCS compared with anodal and sham stimulations.

An open study (Bation et al., 2016) assessed the safety and efficacy of tDCS in eight patients with treatment-resistant OCD on stable doses

Table 1
PRISMA Checklist table.

Dentification	Screening	Eligibility	Included
Records identified through database (NCBI Pubmed and Science Direct) searching ($N=14$)	Records screened ($N=14$)	Open or controlled studies on multiple sessions of tDCS and OCD meeting criteria for DSM-IV/5 or ICD-10, used a least one validated rating scale, well-described stimulus parameters, short as well as long-term outcomes (when possible) Full texts excluded: No evaluation OCD symptoms Not dealing with tDCS but tACS Only single session	Studies included in qualitative review ($N=13$)
Additional records identified through other sources ($N=0$)	Records excluded ($N=1$) Unclear in this study whether patients who responded to treatment had received active tDCS, sham tDCS or both	Full text articles assessed for eligibility ($N=13$)	

of medications for at least six weeks before entering the study. The patients underwent ten sessions (twice a day) of tDCS (2 mA, 20 min) with the cathode over the left OFC (FP1, EEG international system) and the anode over the right cerebellum. tDCS was well tolerated. One patient developed a skin lesion in over the placement of the cerebellar cathode with a slightly painful erythema which resolved within one week. There was an immediate and significant decrease of Y-BOCS score after ten sessions of tDCS and the beneficial effects lasted during the three months of follow-up. At end point, three months after the end of the tDCS sessions, 5 out of 8 patients had a decrease of ≥25% and 3 out of 8 patients had a decrease of ≥35% in Y-BOCS scores and were considered responders.

An open study (Dinn et al.. 2016) investigated the safety and efficacy of tDCS on obsessive and compulsive symptoms and on improving executive control in five medicated patients with treatment-resistant OCD who underwent 15 daily sessions over three weeks of tDCS (2 mA, 20 min) with the anode over the LDLPFC (F3) and the cathode over the right fronto-polar region (Fp2). The patients demonstrated significant OCD symptom reduction following the course of tDCS which was not maintained at one-month follow-up. There were non-significant changes in depressive and schizotypal symptoms following three weeks of tDCS although patients' daily ratings of depressive and generalized anxiety symptoms were significantly lowered.

An open study (Najafi et al., 2017) investigated the safety and efficacy of tDCS in forty-two patients with treatment-resistant OCD who underwent 15 sessions of tDCS for three weeks (2–3 mA, 30 min). Three cathodal leads were placed in downward position (triangle form) on the supraorbital region and FP2 (EEG system 10–20). Three anodal leads were placed on the parietal, temporal, and occipital areas (P1, C3, T7; triangle form). There were no major side effects and tDCS significantly decreased Y-BOCS scores by at least 60% over three weeks with a further decrease over one and three months follow-up.

4. Discussion

In the recent years, a limited number of controlled and open-label studies as well as case series have been published on the safety and efficacy of tDCS for the treatment of OCD. These were described in the previous section and are next discussed. Reviewed studies were either randomized, sham-controlled (D'Urso et al., 2016; Todder et al., 2017), open-label (Bation et al., 2016; Dinn et al., 2016; Najafi et al., 2017) and investigated the effects of tDCS alone or as an adjunctive treatment to pharmacotherapy.

Some studies assessed decision-making among other outcomes. Patients in different studies sometimes with comorbid psychiatric conditions were mostly treatment-resistant. Studies used different primary and secondary outcome measures. The design and stimulus parameters applied in the different studies were quite heterogeneous, making it relatively difficult to compare the efficacy of tDCS for OCD in these studies. Four different stimulation targets were chosen for tDCS: (1) cathodal tDCS (sometimes anodal) over the pre-SMA/SMA; (2) cathodal tDCS over the left OFC or right OFC, (3) cathodal tDCS over the RDLPFC and (4) cathodal tDCS over the medial prefrontal cortex.

The only two controlled studies (D'Urso et al., 2016; Todder et al., 2017) showed significant improvement of OCD symptoms in patients who underwent cathodal tDCS over the pre-SMA/SMA, the LDLPFC or the medial prefrontal cortex. Anodal tDCS over the pre-SMA/SMA was not efficacious for the treatment of OCD.

Open studies (Bation et al., 2016; Dinn et al., 2016; Najafi et al., 2017) with tDCS with the cathode over the left or right OFC and anodes on the parietal, temporal, and occipital areas (Najafi et al., 2017) resulted in an immediate and significant decrease in OCD symptoms with the beneficial effects lasting from one to three months.

As far as side effects are concerned, tDCS was generally safe and well tolerated. There were no major clinical or cognitive side effects. The only side effects in a minority of patients were mild headache, facial pain, local tingling or itching and redness of the skin at the site of stimulation spontaneously resolved.

Despite the fact that some studies did not discuss them, there are quite a number of limitations in these studies that one should be aware of. First of all, the limited sample sizes mostly when using a variety of stimuli for symptom reduction, the lack of sham conditions in most studies, the possibility of placebo responses in randomized controlled studies or carry-over effects of anodal or cathodal stimulation in cross-over studies, open studies, and the use of medications in some studies which all make it difficult to interpret the outcomes and clinical significance of the results. As far as the placebo is concerned, it is important to keep in mind that in highly resistant OCD, spontaneous remission is unlikely and placebo response is generally minimal (Pallanti and Quercioli., 2006). Studies involved rather short treatment durations and may have shown probably more beneficial outcomes if longer treatment duration had been applied. Brain state dependency is also another limitation that might have affected the clinical efficacy of tDCS. Most studies did not address the issue of long-term outcomes or maintenance tDCS in responders which is also of major limitation particularly if this technique might someday find its niche in daily clinical practice. In addition, pretty much like in the case of repetitive transcranial magnetic stimulation, the target locations are not precise even with the use of the 10–20 EEG International System. Therefore, the montage of electrodes might not be ideal confounding the outcome results.

The choice of the different targets for tDCS including the polarity of the electrodes is based on functional neuroimaging findings concerning the pathophysiology of OCD. For example, cathodal stimulation to inhibit pre-SMA activity is derived from the fact that the pre-motor/motor system is abnormally hyperactive and that there is a pathophysiological link between such hyper-excitability and OCD symptoms so the inhibitory modulation of pre-SMA by means of tDCS might reduce OCD symptoms (De Wit et al., 2012; Maltby et al., 2005; Nachev et al., 2008). As far as the DLPFC is concerned, this area plays a major role in

Table 2
tDCS studies in OCD.

Authors	Study design	Clinical and demographic data	Stimulus parameters	Rating scales and outcome measures	Results
D'Urso et al. (2016)	Randomized, sham-controlled, partial cross-over study safety, efficacy tDCS on OCD sx with polarity-specific effects in pts OCD	*N* = 12 pts OCD, stable doses meds for 1 mo before, throughout trial	Initially 10 daily sess. anodal (*N* = 6) or cathodal (*N* = 6) tDCS (2 mA, 20 min), active electrode bilat. pre-SMA In case improvement or no change sx severity, pts maintained same current polarity for 10 more sess. In case sx worsening after 1st 10 sess., pts switched to other polarity for 10 more sess. Each pt total 20 sess. tDCS	Y-BOCS (Goodman et al., 1989), SDS (Sheehan et al., 1996) bi-weekly	10/12 pts completed study After 10 sess., 50% pts with initial anodal tDCS switched to cathodal tDCS, 100% pts initially with cathodal tDCS continued same tt After 10 sess. anodal tDCS, pts with worsening sx, pts signif. improved after 10 sess. cathodal tDCS with 30% ↓ baseline severity score Y-BOCS Greatest sx improvement pts with 20 cathodal tDCS sess. Few AEs: mild h/a, local tingling/itching, skin redness sites electrodes
Todder et al. (2017)	Randomized, sham-controlled, cross-over study potential use tDCS to regulate obsession-induced anxiety immediately after sx provocation in pts refractory OCD	*N* = 12 pts refractory OCD, 7 m, mean age 38.5 ± 12 yrs, no response to ≥ 2 SSRIs or clomipramine), no response to CBT, psychotropic meds not changed ≥ 2 mos before study	3 similar stimulation sess., total 9 sess., interval ≥ 48 hs between sess., cathodal, anodal, sham tDCS medial prefrontal cortex with pharmacological tt, 2 mA, 20 min., active electrode over Fpz, reference electrode over rt shoulder, after stimulation mode completed, 1-wk interval without any stimulation	VAS 1° outcome measure Before and after tDCS, pts graded intensity anxiety after short exposure to provoking stimulus with VAS Clinical questionnaires (Y-BOCS, HAM-A (Hamilton, 1959), MADRS (Montgomery and Asberg, 1979), CGI (Guy, 1976) applied before each stimulation mode	10 pts completed study Statistically signif., short lasting ↓ severity obsession-induced anxiety with active cathodal tDCS vs. anodal and sham stimulations AEs few, mild, transient: facial pain, toothache 1 pt, h/a 1 pt, shoulder pain 1 pt
Bation et al. (2016)	Open study safety, efficacy tDCS cathode OFC, anode cerebellum in pts tt-resistant OCD	*N* = 8 pts tt-resistant OCD, no response to 3 SSRI, 2 augmentations with antipsychotics, with clomipramine and CBT, on stable doses meds for ≥ 6 wks before study, 7 pts on SSRI during tDCS and f/u (1 fluoxetine, 1 paroxetine, 2 sertraline, 3 clomipramine), 1 pt drug-free	10 sess., twice/d tDCS (2 mA, 20 min), cathode lt OFC (FP1), anode rt cerebellum (3 cm below inion, 1 cm rt from midline)	Y-BOCS, VAS, MADRS assessed 4 times: before tDCS, 3 times after (immediately after, 1 and 3 mos after 10th tDCS sess. 1° outcome score Y-BOCS at 4 times ass't 2° outcome MADRS score, VAS score	Immediate, signif. ↓ Y-BOCS score (26.4%) after 10 sess. tDCS, beneficial effects lasted 3 mo f/u No effects tDCS depressive sx including at end point 3 mos after end tDCS, 5/8 pts ↓ ≥ 25%, 3/8 pts ↓ ≥ 35% Y-BOCS score, responders tDCS well tolerated, 1 pt skin lesion over cerebellar cathode, slightly painful erythema resolved within 1 wk
Dinn et al. (2016)	Open study safety, efficacy tDCS on OCD sx, in improving executive control in pts tt-resistant OCD	*N* = 5 medicated pts tt-resistant OCD, 4 f, 1 m, mean age 40.4 ± 8.4 yr, no response psychotherapy, fluvoxamine, fluoxe- tine, pregabalin, duloxetine, venlafaxine, sertraline, risperidone, quetiapine	15 daily sess., 3 wks tDCS (2 mA, 20 min) anode LDLPFC (F3), cathode t fronto-polar region (Fp2)	Neuro-cognitive, clinical/personality testing before and after tDCS, 1- and 3-mo f/u Turkish version OCI (Foa et al., 2002), BDI,Turkish version LSAS (Liebowitz, 1987), SPQ-B (Axelrod et al., 2001), VAS before each sess.	Pts signif. OCD sx ↓ after tDCS, not maintained at 1 mo f/u Non-signif. changes depressive, schizotypal sx after 3 wks tDCS, pts' daily ratings depressive, generalized anxiety sx signif. ↓
Najafi et al. (2017)	Open study safety, efficacy tDCS in pts tt-resistant OCD	*N* = 42 pts tt-resistant OCD	15 sess. tDCS, 3wks(2–3 mA, 30 min), 3 cathodal leads downward position (triangle form) supraorbital region and FP2, 3 anodal leads parietal, temporal, occipital areas (P1, C3, T7; triangle form)	Y-BOCS	tDCS signif. ↓ Y-BOCS scores by ≥ 60% over 3 wks, further ↓ over 1 and 3 mos f/u No major AEs

Legend: AD: antidepressant; AEs: adverse effects; BAI: Beck anxiety inventory; bilat.: bilateral; BIS: Barratt Impulsiveness Scale; BART: balloon analogue risk task; BDI-II: Beck depression inventory; CBT: cognitive-behavioral therapy; CGI: Clinical Global Impression Scale; d: day; diff.: different; ERP: exposure and response prevention; f: female; fMRI: functional magnetic resonance imaging;;f/u: follow-up; gp: group; h/a: headache; HAM-A: Hamilton anxiety scale; HDRS:Hamilton depression rating scale; LDLPFC: left dorsolateral prefrontal cortex; LSAS: Liebowitz Social Anxiety Scale; lt: left; m: male; mA: milliAmpere; MADRS: Montgomery-Asberg Depression Rating Scale; MDD: major depressive disorder; min: minute; min.: minimal; mod.: moderate; mo(s): month(s); n: number; OCD: obsessive-compulsive disorder; OCI: Obsessive-Compulsive inventory; OFC: orbitofrontal cortex; pt(s): patient(s); resp.: respectively; RDLPFC: right dorsolateral prefrontal cortex; rt: right; SDS: Sheehan Disability Scale; sess.: session; signif.: significant; SMA: supplementary motor cortex; SNRIs: selective norepinephrine reuptake inhibitors; SPQ-B: Schizotypal Personality Questionnaire B; SSRIs; selective serotonin reuptake inhibitors; sx: symptoms;tDCS: transcranial direct current stimulation; tt: treatment;unilat.: unilateral; VAS: visual analog scale; vs.: versus; wk(s): week(s); Y-BOCS: Yale-Brown Obsessive- Compulsive Scale; yr: year; ↑: increase; ↓: decrease.

cognitive control and behavior, thus influencing several neuronal networks involved in behavioral and emotional processing. tDCS may influence cognitive control over obsessions and compulsions differently than modulation of orbitofrontal and pre-SMA activity along with helping to improve anxiety and depression symptoms. Considering the high overlap with comorbid depression and anxiety disorders with the DLPFC as a hub region, alternative electrode montages primarily involving prefrontal brain regions could modulate OCD symptoms and eventually concomitant affective disorders by restoring cognitive control, and executive functions in remote areas. Hyperactivity in the OFC and dys-connectivity between the cerebellum areas (hypo-active in OCD) and the OFC (Anticevic et al., 2014; Hou et al., 2012) also plays a key role in the pathophysiology of OCD. A decrease in OFC activity has even been correlated with symptoms improvement after medical or surgical treatment (Maia et al., 2008).

According to a recent study (Senço et al., 2015), a tDCS montage with the cathode over the pre-supplementary motor area and extracephalic anode seems to activate most of the areas related to OCD leading tom potential improvements in obsessive and compulsive symptoms, although the reviewed studies showed that tDCS montages over other areas might also be beneficial for OCD patients.

5. Conclusions

OCD is a condition that does not always respond to current pharmacological and psychotherapeutic approaches. Alternative approaches such as cathodal tDCS over the pre-SMA/SMA, cathodal tDCS over the RDLPFC and cathodal tDCS over the left OFC might alleviate obsessive and compulsive symptoms although no definitive conclusion as to the efficacy of this technique can be drawn given the paucity of randomized studies. Further sham-controlled studies with increased statistical power, rigorous standards of randomization, blinding procedures, optimal stimulus parameters, and clinical outcome as well as global functioning measures are needed to confirm the short and long-term safety and efficacy of tDCS in the treatment of such condition. Also studies with large sample sizes should compare he safety and efficacy of cathodal tDCS over the pre-SMA/SMA, over the RDLPFC, over the left OFC and the medial prefrontal cortex.

Funding

No source of funding.

Declaration of Interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2018.11.033.

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