Transcranial Direct Current Stimulation of Dorsolateral Prefrontal Cortex in Patients with Obsessive Compulsive Disorder to Improve Decision Making and Reduce Obsession Symptoms

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ABSTRACT

Objective: Recent studies on treating obsessive compulsive disorder (OCD) have investigated noninvasive brain stimulation techniques like transcranial direct current stimulation (tDCS) to enhance patients' performance. This study aimed to analyzed the affect of anodal and cathodal tDCS applied over the dorsolateral prefrontal cortex (DLPFC) on higher cognitive process and reduce obsession symptoms in patients with OCD.

Methods: the current study is analysis of variance. In this regard, 20 patients with obsessive compulsive disorder (n=20) were randomly assigned to receive either experimental (active) or control (sham) tDCS. Measuring cognitive functions, the participants done a set of decision making neuropsychological tasks; and for obsession symptoms, the Yale-brown obsessive compulsive and Beck anxiety scale (BAI) were used. we applied anode electrode over the right DLPFC (F4), and cathode electrode over the left DLPFC (F3) region in 15 sessions within 20 minutes.

Results: After 15 sessions of applying tDCS, patients showed significant improvement in decision making tasks. Similar results were determined obsession symptoms.

Conclusion: The data were analyzed by SPSS 18.0.0 software, using analysis of variance methods.This study demonstrated that anodal tDCS over left DLPFC, concurrent with cathodal tDCS over right DLPFC, improved cognitive impairment and reduced obsession symptoms in patients with OCD.

1. Introduction

Obsessive compulsive disorder (OCD) is a disabling mental disorder characterized by recurrent, intrusive thoughts and repetitive and stereotypical rituals either in response to the obsessions in order to reduce distress and anxiety or performed according to rigid rules (American Psychiatric Association, 2000). An ongoing debate about the nature of cognitive deficits thought to underlie the disorder's behavioral dysfunctions has elucidated few consistent findings (kuelz, 2004). The dominant neurobiological model of OCD proposes a central role for dysregulation of cortico–striato–thalamic circuits in the pathophysiology of the symptoms (Volpato et al, 2012). Previous studies suggested that the prefrontal cortex (PFC) consisting dorsolateral PFC (DLPFC) and orbitofrontal (OFC) area contributed in cognitive disturbances of obsessive compulsive disorder. Find-

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ings from neuroimaging studies show that congnitive performance such as decision making and memory irregularities in OCD are supposed to associate with prefrontal cortex (Page, 2009; Dittrich, 2010). The DLPFC and OFC are primarily associated with "cognitive" or "executive" functions, whereas ventromedial prefrontal cortex (VMPFC) is largely associated with "emotional" or "affective" functions (Page, 2009; Dittrich, 2010), suggesting that cognition and emotion, which are seriously malfunctioned in OCD, are associated with altered cortical activity in the prefrontal cortex.

Although the results of the studies are not consistent, but the results of SPECT and PET show more evidence about the role of thalamus circuits, putamen and pallidus cores in OCD of children' patient, whereas the adult studies show the considerable role of orbitofrontal cortex and prefrontal cortex in OCD (Huijser et al., 2011; Ruch et al., 1994; MacMaster et al., 2008; Dittrich et al, 2010).

The role of uncertainty in decision-making has yet to be systematically investigated in OCD (Cavedini et al., 2006) and indecisiveness has even been posited to be a basic characteristic of OCD (Summerfeldt et al., 2004a). It seems that in OCD patients the volume of ventral frontal regions increase with age, where as the dorsal region decrease considerably (hujiser et al, 2011). Beside this we can see the hyperactivity in DLPFC region and hypoactivity in ventrolateral region, thus the symptoms of OCD can be derive from this imbalance.

Thus, OCD involves failures in two main inhibitory processes, namely cognitive (responsible for the obsessions) and behavioral (responsible for the compulsions) ones (Chamberlain, 2005). Recent research has supported two cortical–subcortical pathways in OCD pathogenesis: (a) the frontostriatal loop (dorsolateral-caudate–striatum–thalamus) responsible for impairments of behavioral inhibition and (b) the orbitofrontal loop (orbitofrontal, medial prefrontal, and cingulate) responsible for impairments with cognitive inhibitory processes. Several studies suggested certain inter-hemisphere effects. An EEG study (Kuskowski et al., 1993) demonstrated that OCD show lower right hemispheric activation patients compared to healthy control.

Functional neuroimaging studies have focused on the circuit starting from the prefrontal region and continuing through the basal ganglia, particularly the caudate nucleus and thalamus, and ending in the vicinity of the prefrontal region again (Insel, 1992). In structural brain investigations, same neuroanatomical structures associated with this circuit have drawn attention. Consequently, in these imaging investigations, some regions have been established as key brain areas, including the orbitofrontal cortex (OFC), thalamus, caudate nucleus, and anterior cingulate cortex. However, to date, the role of dorsolateral prefrontal cortex (DLPFC) volume has not been evaluated in OCD. The DLPFC is an important section of the prefrontal cortex, associated with executive functions, attention, nonverbal memory, and visuospatial skills, which have been reported to be disabled in OCD.

For example, some investigations have shown that patients with OCD had impaired measures of executive functions (Flor-Henry et al., 1979; Savage et al., 1999), whereas others have demonstrated nonverbal memory deficits (Christensin, 1999; Dirson et al., 1995). Moreover, Russell et al. (2003) examined prefrontal cortex neurochemistry in pediatric patients with OCD and found a significant increase (21% higher) in N-acetylaspartate (NAA) in their left but not right DLPFC compared to control subjects, without any significant differences in choline (Cho) or creatine (Cr) levels. This investigation suggests a neurochemical alteration in the DLPFC in patients with OCD. However, no volumetric study has evaluated that region; hence, we conducted the present study to examine DLPFC volumes in patients with OCD.

The noninvasive brain stimulation techniques have been used to regulate the dysfunctional cortex in OCD (Jaafari et al., 2012; Hoek, & Sommer, 2010). Most of the researchers use rTMS in their studies, but there is another technique which applies weak direct current on brain, called tDCS (volpato et al, 2012). tDCS has been succefully used in other psychopathological disorders, such as depression (Nitsche & Paulus, 2001) and also variety of cognitive performance like declarative memory (Javadi & Walsh, 2012), working memory (Boggio, Ferrucci, et al., 2006; Fregni et al). Based on neuroimaging all the information about OCD, we proposed a specific tDCS montage. Therefore, this study aimed mainly to investigate the effect of tDCS decision making, which is the most impaired neuropsychological domain in OCD. and reduction of obsession symptoms. The anodal stimulation applied over right DLPFC and cathodal stimulation over the left DLPFC. Lastly, as to our knowledge there is not any experimental tDCS studies in OCD domain, thus , this study aimed to examine decision making aspects, one of the most impaired cognitive domains in OCD.

2. Methods

A total of 20 participants, aged 20-45 years, with OCD diagnosis recruited through accidental sampling. The target population was all OCD patients referring at Atieh Clinic in Tehran, Iran and the results will generalized to obsessive compulsive patients. The results were analyses by SPSS 18.0.0 analysis, using analysis of variance. Demographic characteristics are shown in Table 1. Inclusion criteria were as follows: (1) failure in response to SSRIs pharmacotherapy for at least 2 weeks before tDCS sessions; (2) not on any psychotropic medications during the study; (3) moderate to severe obsession compulsion scores on the Yale-brown obsessive compulsive Scale (YBOC); (4) BAI scores of at least 20 (scored by an experienced psychiatrist); and (5) OCD diagnosis based on a clinical interview by an experienced psychiatrist, according to DSM-IV criteria. Then, they were administered the Yale-brown obsessive compulsive Scale (YBOC) and the Beck anxiety inventory (BAI) test (Beck et al., 1988).

Participants were randomly assigned in two groups (experimental or active tDCS, n=10; control or sham tDCS, n=10). The patients underwent cathodal and anodal stimulation over left and right DLPFC, respectively.

The anodal electrode was positioned over area F4 (right DLPFC) according to the 10–20 EEG international system, and the cathode electrode was positioned over F3 (left DLPFC). The stimulation was transferred by a saline soaked pair of surface sponge electrodes (35 cm^2). Treatment consisted in a 15 day tDCS (20 minutes per day). In the sham stimulation the electrode positioned as same as active group but the stimulator turned off after 30 seconds. Cognitive functions and obsession symptoms were assessed before the first tDCS session as baseline, and after the 15th tDCS session for any group (Salehi et al, 2015).

decision making was assessed using the Cambridge neuropsychological test automated battery (CANTAB; CeNeS, Cambridge, UK). has been used for a large variety of clinical populations, such as neurodegenerative diseases, psychiatric disorders, neurosurgical case a special focus on neuropsychological functions (Fray& Robbins, 1996).

CanNTAB is a reliable assessment test which include different kind of tests such as problem solving, executive function, attention, learning, and memory (Robbins et al, 1994; de Jager et al, 2002; Egerhazi et al, 2013; Kuzmickiene and Kaubrys, 2015).

In this study, a test of CANTAB battery (15–20 minutes duration), selected from the CANTAB decision making tests was used: CGT.

This battery was selected to evaluate decision making in patients with OCD (Kim, et al, 2014). The CGT test assesses decision making by presenting a row of 10 boxes across the top of a screen, some of them are red and some blue. At the bottom of the screen, there are rectangles containing the words 'Red' and 'Blue'. The participant must guess whether a yellow token is hidden in a red or a blue box (Deakin et al., 2004). The likely neural substrate for this task is the orbitofrontal prefrontal cortex.

It lasts about ten 30-minute times and the outputs include risk taking, quality of decision making, deliberation time, risk adjustment, delay aversion, and overall proportion bet. The IST test assesses decision making by presenting with a 5x5 array of grey boxes on the screen, and 2 larger colored panels below these boxes. The participants are instructed to play a game for points, which they can win by making a correct decision about which color is in the majority under the grey boxes. They must touch the grey boxes one at a time, which opens up to reveal one of the two colors shown at the bottom of the screen. Once a box was touched, it would remain open. When the participants made their decision about which color is in the majority, they must touch the panel of that color at the bottom of the screen to indicate their choice. After the participants indicated their choice, all the remaining grey boxes on the screen would reveal their colors and a message was

Table 1. Descriptive statistics of demographic data.

Group	Sample size	Age, Y (mean)	Onset age, Y (mean)	Baseline BAI score (mean)	Baseline YBOC score (mean)
Experimental	10	27.5	19.6	33.20	19.5
Control	10	26.5	23.2	33.80	18.60

Table 2. Levene's test for CGT Scores.

Variables	df	f	Sig.
CGT quality of decision making	1	0.01	0.89
CGT deliberation time	1	0.41	0.52
CGT risk taking	1	0.41	0.52
CGT risk adjustment	1	0.56	0.46
CGT delay aversion	1	1.09	0.31
CGT overall proportion bet	1	0.18	0.67

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displayed to inform the participants whether or not they were correct. The colors change from trial to trial. At the end of a trial, the grey boxes were displayed on the screen again at a speed which depends on how fast the trial was completed, so that there is always at least 30 seconds between trials.

The 8 IST outcome measures cover errors, latency, total correct trials, mean number of boxes opened per trial, and probability of the participant's decision being correct based on the available evidence at the time of the decision.

Obsession compulsion symptoms and anxiety were evaluated using: the BAI (Beck anxiety inventory) and YBOC(Yale- brown obsessive compulsive scale). Before applying stimulation we obtained the baseline and then remeasure after 15 sessions. The original form of BAI, which is used in this study, is a 21-question multiple-choice self-report inventory ask about common symptoms of anxiety that the subject has had during the past month. Scoring the BAI is based on a 0-3 point scale. The YBOC has 10 scales which measures the obsession compulsion and its intensity. Both measures are designed for indicating the presence of symptoms in the past days.

We used PASW Statistics 18.0 for data analysis. The data from clinical and psychological measures and cognitive task were analyzed with ANCOVA.

3. Results

The effects of tDCS on the CGT were investigated. Regarding deliberation time, the ANCOVA results showed that there was no significant difference ($F=0.56$, $P>0.05$).

The effects od tDCS on IST were investigated. For IST Mean box opening latency(win condition), no significant difference was observed ($F= 0.97$, $P> 0.05$).

4. Discussion

The clinical data of this study demonstrated that administration of tDCS over DLPFC for 15 consecutive days improved decision making,

Which functionally is associated with prefrontal cortex function (Studer et al., 2015; Chan et al., 2014) and also significantly reduced obsession compulsion symptoms. Evidently, It can be said that due to large alterations in cortical activity of the PFC in patients with OCD (Banca

Table 4. Levene's test for IST scores.

Variables	df	f	Sig.
IST discrimination errors	1	1.30	0.58
IST sampling errors	1	0.17	0.12
IST mean box opening latency	1	4.28	0.06
IST mean color decision latency	1	2.51	0.13
IST mean P (correct)	1	1.63	0.21
IST mean number of boxes opened per trial	1	1.44	0.24
IST total correct	1	0.08	0.08

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Table 3. ANCOVA after control of pretest scores.

Variables	df	f	Sig.
CGT quality of decision making	1	26.26	0.01
CGT deliberation time	1	0.56	0.78
CGT risk taking	1	0.56	0.01
CGT risk adjustment	1	17.26	0.01
CGT delay aversion	1	5.61	0.03
CGT overall proportion bet	1	11.58	0.01

et al., 2014), there is enhancement in decision making of the patients. we applied anodal tDCS over the right DLPFC simultaneously with cathodal stimulation of the left DLPFC.

There is an interhemispheric imbalance with higher activation in the left frontal regions and lower activation in the right regions of OCD patients (Harrison 2003; Nitsche; et al. 2009). Seemingly, there is a higher than normal cortical activity in the left DLPFC and a lower than normal activity in the right DLPFC, which is responsible for impaired decision making in patients with OCD. We modulated this imbalanced activity in the left and right PFC by applying anodal tDCS on the right DLPFC and cathodal tDCS on the left, and observed improved performance in decision making tasks after a 15-session tDCS protocol.

All in all, the finding of this study suggest that this protocol of tDCS is more effective in modulating imbalance of activity in DLPFC which has positive effects on , decision making impairment, one of the most damaged cognitive functions in OCD (Banca et al., 2014), and also had effect on reduction of obsession compulsive symptoms which is in accordance with previous brain stimulation studies of OCD. In other words, by applying anodal stimulation over right DLPFC and cathodal stimulation over left DLPFC, we increase and decrease activity in these regions respectively in OCD patients. Although numerous studies showed effectiveness of tDCS on executive functions (Boggio, Ferrucci, et al., 2006; Ferrucci, Mameli, et al., 2008; Fregni et al., 2006; Jo et al., 2009), but there is less studies about decision making using tDCS; and no study about OCD patients.

Although of potential clinical application to reduce obsessive compulsive symptoms, the findings of this study are from a small group, so there are limitation in generalizing results and need replication with a longer treatment duration of tDCS. Moreover, as we didn't follow up the results in long duration, it can be another limitation of our study which should be consider in future. Furthermore, for the reason of improvement in decision making is not clear, using various lind of neuroimaging measures can be helpful to discover it.

Table 5. ANCOVA after control of pretest scores.

Variables	df	f	Sig.
IST discrimination errors	1	6.37	0.02
IST sampling errors	1	6.16	0.02
IST mean box opening latency	1	0.97	0.33
IST mean color decision latency	1	4.78	0.04
IST mean P (correct)	1	5.12	0.03
IST mean number of boxes opened per trial	1	9.914	0.01
IST total correct	1	11.52	0.01

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