


Efficacy of Transcranial Direct Current Stimulation in the Treatment: Resistant Patients who Suffer from Severe Obsessive-compulsive Disorder

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ABSTRACT

Background: During the past years, significant efforts have been made to explain the biological backgrounds of obsessive-compulsive disorder (OCD). Cortical-subcortical and neurotransmitter models are used for explaining the symptoms of OCD, so our hypothesis is that brain's transcranial direct current stimulation (TDCS) can regulate the brain activities of the OCD patients. Thus, based on the mentioned issues, this research seeks to investigate the efficacy of TDCS in treatment-resistant patients who suffer from severe OCD. **Materials and Methods:** The present study is a clinical trial research which was based on the available sampling method, 42 treatment-resistant patients who suffer from severe OCD were selected as research's samples (2015–2016). Medical intervention protocol in this study is TDCS cathode type that was done in 15 sessions for 3 consecutive weeks (each session was conducted for 30 min daily). Yale–Brown Obsessive-Compulsive Scale was used for evaluating the efficacy of TDCS method during the 1st, 5th, 10th, and 15th sessions and it was also used for checking the 1st and 3rd monthly follow-up phases. **Results:** Variance within-group analysis (repeated measure) showed that the mean differences in the different stages of evaluation are significant (seven stages of evaluation). **Conclusion:** TDCS can be introduced as an appropriate, strong tool for regulating the brain - behavioral systems and it can also be introduced as a suitable alternative treatment for treatment-resistant patients who suffer from severe OCD.

Key words: Brain - behavioral systems, obsessive-compulsive disorder, transcranial direct current stimulation

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INTRODUCTION

Obsessive-compulsive disorder (OCD) is a complicated neuropsychiatric disorder which includes the main characteristics such as excessive intrusive thoughts and a set of overt and covert behaviors that are used for reducing the stress and anxiety. This disorder is characterized by the decreased quality of life and high degree of dysfunction in the social and occupational activities.^[1,2] The OCD prevalence in the general population is 2–3%; OCD is the fourth common psychiatric disease that is resistant to the common drug treatment in the 40–60% of cases.^[3,4]

Recently, remarkable efforts have been made to explain the biological foundation of OCD. The cortical-subcortical model based on its active role causes the repetitive and compulsive behavior, this model through modifying the path of information from implicit memory to the explicit memory will bring excessive unwanted thoughts for OCD patients. New evidences have suggested that dysfunction of activity in the orbitofrontal, striatum, and thalamus circuit will increase the activity in the orbital, frontal cortex, cingulate gyrus engine, and caudate nucleus and it also decreases the activity in the cerebellum and parietal cortex.^[5] The central-amygdala model believes that avoiding conditional fearing is the cause of OCD, so this model provides appropriate explanation for motivational, emotional, and anxiety components of OCD.

Recently, medicines have been the center of attention because of their efficacy on the gamma-aminobutyric acid (GABA), glutamate system, and serotonin reuptake inhibitors. However, drugs' side effects and residual symptoms of OCD at middle level will decrease patients' tendency in taking them.^[6] The other medical ways such as electroconvulsive therapy, psychosurgery, brain deep stimulation, and vagus nerve stimulation have little efficacy and can cause memory dysfunction, anesthesia complications, and convulsions, so in spite of what has been said, it needs special equipment.^[7-8]

Transcranial direct current stimulation (TDCS) is a different approach for the treatment of OCD patients that nowadays has promising results. This method is completely noninvasive and featured of being easy to work, smooth transitions, suitable for portable usage, and has high clinical potential through a direct and low electrical current (1–3 mA) on the skull that causes temporary changes and cortical stimulation in the brain (facilitated or inhibited nerve spontaneous activity).^[9,10] This device's (TDCS) design features (or physical parameters) including electrical current, each electrode position, electrode size, stimulation

time, current polarization (anode or cathode), and the number of sessions are related to the rate of efficacy.^[11,12] Cathode and anode stimulation, respectively, decreases and increases brain's stimulation.^[13]

Maximum usage of cathode and anodic probes can be made by different ways. Contacting electrical current between anode and cathode electrodes changes and regulates the potentials of neuron's membrane of cortex in the electrode places. Anode stimulation increases serotonin and GABA and cathode stimulation decreases glutamate and GABA. Dopaminergic neurotransmitters will also be stimulated for hours after stimulation if electrical stimulation lasts for 20 min.^[5]

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TDCS through changing neuron's stimulation and modifying the potential of neuron's membrane can lead to the depolarization or hyperpolarization, so these activities can increase or decrease brain's function.^[17] Functional effects of TDCS are directly limited to electrode places.^[11] No major lateral side effects have been reported for using this method in humans. The most commonly reported side effects include irritation, mild itching, and weak pain at the site of the electrode, and in some cases, headache, fatigue, nausea, and rarely sleep disturbances are also seen.^[9,18,19]

Due to the simultaneous stimulation of cortex in psychiatric disorders, TDCS treatment (cathode) can inhibit the function of these areas in the brain.^[20] Some results have shown that electrical stimulation of right frontal cortex can decrease anxiety and depression and improve sleep quality and obsessive signs.^[21,22] Thus, based on the association between right hemisphere and mentioned process, we can say that "likely" there is a relationship between skull electrical stimulation of the right hemisphere with situational improvement of OCD patients. In spite of confirming the results of various studies on using TDCS method for the treatment of depression that has common pathophysiology relationship with OCD,^[23] so our knowledge in this type of treatment (using TDCS for decreasing OCD symptoms) is low. In a case study, the efficacy of TDCS in improving depression and anxiety symptoms was proved, but its efficacy was not proved about OCD symptoms.^[24] In another case study that was done to evaluate the effectiveness of noninvasive treatments in

improving psychological disorders, inconsistent results about the efficacy of TDCS method were acquired in which persuasive information about OCD treatment was very much limited.^[25]

Due to the resistance of OCD to a variety of treatments, compared to other psychiatric disorders, this study unlike other studies conducted until now seeks to use TBSTBS method. Hence, using TBS with more probes and lower cross-section level creates 2–3 mA intensity in each probe, thus right now, the measure of absorbed energy per time unit is nearly 3 times greater compared while using two probes. Thus, the present study aims to investigate “whether TDCS is safe, simple, and noninvasive and has low side effects and is effective for treatment-resistant OCD?” so, our hypothesis is:

TDCS is effective in the treatment-resistant severe OCD.

MATERIALS AND METHODS

This study is a clinical trial research (IRCT2015042721965N1). The study was approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1394.259) and the necessary permissions from the research council, Guilan University of Medical Sciences, were obtained. The population included all treatment-resistant OCD patients who referred to the Tolou subspecialty clinic in the Rasht province in 2015–2016. A total of 42 (19 males and 23 females) patients through the available sampling method were selected for the study. The mean and standard Deviation of group age was 29.10 ± 10.14 and variation ranged from 15 to 64. Marriage status of the group was as follows: 11 individuals were single (26.2%) and 31 were married (73.8%). Their educational level was as follows: an individual was illiterate (2.4%), 24 had a diploma degree (57.1%), 6 had postdiploma degree (14.3%), 9 had BA degree (21.4%), and the rest had MA and upper degree (4.8%). Between group's members, 14 were employed (33.3%) and most of them (39 ones) were urban residents (97.5%).

Inclusion criteria include (1) OCD diagnosis according to the axis I in relation to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) (based on psychiatrist's and clinical psychologist's diagnosis), the history of taking selective serotonin reuptake inhibitor (SSRI) drugs (two types) with adequate doses, and receiving cognitive behavior therapy (CBT) that did not work for patients. (2) The minimum score based on Yale–Brown scale is 25. (3) Taking drugs (such as anti-depressants [Numerical Rating Scale of pain SSRI], benzodiazepine, and anti-psychotics) 4 weeks prior to

participation in the study. (4) Patient's age range from 16 to 65 years. Exclusion criteria were: (1) Having serious coexisting medical conditions. (2) Suffering from organic brain disease. (3) Having a history of seizures. (4) Mental retardation. (5) Alcohol or drug usage in the last 6 months. (6) Having active phases in the psychotic disorders such as schizophrenia and bipolar disorder. (7) Being under psychotherapy treatment. (8) Pregnancy and lactation. (9) OCD patients who never received drug treatment.

Tool

Yale–Brown Obsessive-Compulsive Scale: This scale is one of the instruments that is used for measuring OCD and its severity. Goodman *et al.* devised this 10-item scale (5 items associated to the obsession and the rest associated to the compulsion) in 1989. The scale's scores range from 0 to 40. The score from 0 to 7 indicates sub-clinical; 8–15 as mild; 16–23 as moderate; 24–31 as severe; and 32–40 as extreme. The validity and reliability of the scale have been reported “acceptable.”^[26]

Transcranial direct current stimulation device

Brain stimulation through electrical current is a widespread applied technology for cerebral diseases. In the present study, for brain stimulation, we used TDCS device that was devised by Paym-e Gilan Mehr (knowledge-based company in Iran). The source of current is 18 V alkaline batteries. The other features of device are as follows: size of device is 32 cm × 21 cm × 11 cm; its weight is 5.1 kg; the maximum intensity is 3 mA and the maximum voltage is 18 V. The electrodes (cathode and anode) are installed to the scalp of the head to transfer constant electrical current to the brain through the skull. Electrodes can be made from carbon and they can be conductive. The size of each electrode in this study is 5.5 cm². They were passed through a sponge that was soaked in sodium chloride 9% to increase electrical current conductivity and prevent electrodes from temperature increase. The electrical current, electrode size, and the duration of stimulation in the device are controllable.

Implementation

Before starting the experiment, the participants should be aware about the research's purpose, probability of damages in addition, and confidentiality of their information, and also the examinees should sign consent paper for their participation in the study.

Medical intervention protocol in this study is TDCS cathode type that was done in 15 sessions for 3 consecutive weeks (each session was conducted for 30 min daily [24 h was considered for each session interval for minimizing the impacts of test levels]).

In this study, we used stimulation and inhibition methods. Thus, TDCS through relative changing and adjusting frontal lobe and gyrus (cingulate) region increases the activities of thalamic part and parietal cortex, so these processes cause bilateral stimulation of dorsolateral prefrontal cortex that finally leads to brain activity regulation. For this purpose, three leads of cathodes and three leads of anodes were used. The cathode leads were placed in downward position (in the triangle form) on the supraorbital region and FP2 (electroencephalogram [EEG] 10–20). The anodal leads were placed on the parietal, temporal, and occipital areas (P1.C3.T7) in the triangle form, the triangle apex was upward and its bases were outward and downward. The FP2 area was 10–20 in the EEG system.

During all sessions, some gel was used in the probes for increasing electrical conductivity, and then electrical current was passed on the skull for 30 min with 2–3 mA intensity. Normal saline solution was used for decreasing probability of the skin irritation during passing electrical current. By the way, during the sessions, music and film were also used to increase patient's relaxation.

The examinees were evaluated during the 1st, 5th, 10th, and 15th sessions and also they were checked during the 1st and 3rd monthly follow-up phases based on a structured clinical interview (according to the DSM-V); Yale–Brown Obsessive-Compulsive Scale was used and patients were interviewed by the clinical psychologist and psychiatrist.

The descriptive (mean and standard deviation [SD]) and inferential (repeated measure analysis) statistical data were analyzed through SPSS version 22 software.

RESULTS

Table 1 shows the mean and SD scores of the OCD patients' based on Yale–Brown scale, four sessions (1st, 5th, 10th, and 15th) and two follow-up phases (1st and 3rd monthly phases).

Repeated measures analysis was used to evaluate the statistical significance of the observed differences. Due to the significances of four multivariate tests such as Wilks' lambda, Hotelling's trace, Roy's largest root, and Pillai's trace ($F = 168.055, P < 0.01$), the Mauchly's test was used for sphericity evaluation. Therefore, according to log base root, Mauchly's test at level 0.95 is significant. Hence, Epsilon point was used (Greenhouse-Geisser) to normalize the data distribution [Figure 1].

Table 2 shows that the mean of differences in the different measuring levels is significant. The obtained effect size is equal to 0.78.

Table 1: Descriptive indicators of obsessive-compulsive variable

Measurement	Mean±SD	n
Session 1	29.0714±2.76205	42
Session 5	21.8571±5.21523	42
Session 10	14.0238±6.11072	42
Session 15	10.6190±5.77612	42
1 st month follow-up	9.2857±6.12984	42
3 rd month follow-up	6.5000±6.75440	42

SD – Standard deviation

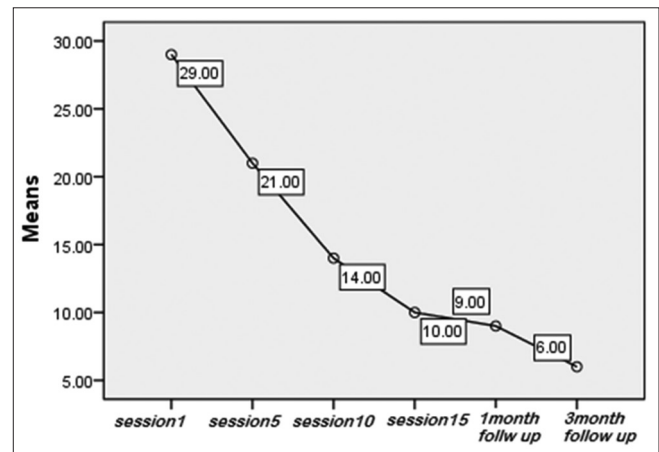


Figure 1: The efficacy of transcranial direct current stimulation in the treatment-resistant patients who suffer from severe obsessive-compulsive disorder

DISCUSSION

The present study showed that 15 sessions (duration of each session was 30 min) of TDCS treatment with the maximum of 2–3 mA intensity per second could improve OCD in treatment-resistant patients without having major side effects. The results of the present study were consistent with that of Bation *et al.*,^[5] Mondino *et al.*,^[27] and Yekta *et al.*^[28] A study by Volpato *et al.*^[25] showed that TDCS has no efficacy in reducing OCD symptoms, so this result was inconsistent with the results of the present study.

It should be noted that “most of the studies that have been done until now just used a pair of probes with electrical current <3 mA, but in the recent study, three probes were used.” Using three probes regulates current intensity and keeps the range between 1 and 3. This method keeps the energy in the cingulate gyrus 3 times more than the normal level. Bation *et al.*^[5] tried TDCS 2 times per a day to solve the limitation of adding current intensity and remove the limitation of energy absorption in the targeted tissue, but the amount of absorbed energy was less than the present study results. In addition, the limitations in the number of sessions cause decreased treatment efficacy. Obsession is resistant to the common treatment; it requires high

Table 2: Internal effects of the examinees in the repeated measures

Source	SS	df	MS	F	Significant	η^2	Observed power
Procedure	15,530.2	3.504	4432.77	152.93	0.000	0.789	1
Error	4163.61	143.644	28.986				

SS – Sum of squares; MS – Mean square

doses of medicine, so in spite of insufficiency in the current intensity in this study (1–3 mA), the present study by focusing on cingulate area and energy absorption has got enough efficacies. Hence, intensity of stimulation and energy absorption rate can be considered as an important factor in the long-term potential. Due to the brain prefrontal intervention on the OCD pathophysiology, the TDCS method can be useful for decreasing the symptom of OCD. The TDCS through affecting the resting potential of membrane and adjusting the synaptic transmitters and through regulating glutamine and Gamma-Aminobutyric acid (GABA) neurotransmitters decreases the OCD symptoms in the patients.

The hyperactivities of orbitofrontal cortex (OFC) (especially right anterolateral cortex) and low degrees of activities in the anterior cingulate are effective in OCD, so in the present study, through TDCS, we decrease the measure of thought repetition and the other overvalued ideas such as cleanness and tidiness in the patients. In addition, the hyperactivities of the OFC, caudate nucleus, and thalamus that lead to some excessive certain routine such as checking and hand washing were decreased after receiving TDCS treatment. Thus, TDCS can be introduced as a strong and appropriate tool for regulating brain-behavioral systems and can be introduced as an alternative treatment for treatment-resistant OCD patients.

Using appropriate sample size, more treatment sessions, highly focusing on energy per unit volume, and having 1st and 3rd monthly follow-up phases are the advantages of the present study. Lack of control on the expectations and promising effects due to the modernity of this technology are the disadvantages of the present study. Therefore, we suggest that, in the future researches, promising effect should be taken into account and the efficacy of TDCS method should be tested for the other common psychiatric disorders.

CONCLUSION

TDCS treatment could improve OCD in treatment-resistant patients without having major side effects. TDCS can be introduced as an appropriate, strong tool for regulating the brain-behavioral systems and it can also be introduced as a suitable alternative treatment for treatment-resistant patients who suffer from severe OCD.

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Conflicts of interest

There are no conflicts of interest.

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