Research Paper: Effect of Transcranial Direct Current Stimulation on Dorsolateral Prefrontal Cortex to Reduce the Symptoms of the Obsessive-Compulsive Disorder

Sina Shafiezadeh1, Mansoureh Eshghi1, Zahra Dokhaei1, Hossein Mohajeri1, Atiyeh MohammadShirazi1, Sara Mirsadeghi1, Peyman Hasani Abhari1,4*

1. Institute for Cognitive Science Studies, Tehran, Iran.
2. Faculty of Humanities, Tarbiat Modares University, Tehran, Iran.
3. Department of Brain and Cognitive Science, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran.
4. Department of Cognitive Rehabilitation, Brain and Cognition Clinic, Tehran, Iran.

* Corresponding Author:
Peyman Hasani Abhari, PhD.
Address: Department of Brain and Cognitive Science, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran.
Tel: +98 (912) 1750782
E-mail: abhari@iricss.org

ABSTRACT

Introduction: Obsessive-Compulsive Disorder (OCD) is one of the most common debilitating mental disorders with a prevalence rate of 2% to 3% in the general population. Previous studies have indicated abnormalities in the dorsolateral prefrontal cortex (DLPFC) of OCD patients; thus, we decided to use transcranial Direct Current Stimulation (tDCS) to decline these patients’ symptoms.

Methods: A total of 24 patients with OCD participated in this study with the hope of improvement after the application of tDCS. The subjects were randomly assigned to three groups of Sham, Right DLPFC, and Left DLPFC. tDCS was applied for five consecutive days and in each session, patients were subjected to 2 mA current flow for two 15 minutes followed by a 10-minute rest in between (every session lasted for 40 minutes).

Results: Subsequently, the changes in obsessive-compulsive level and cognitive functions were evaluated via Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and Depression, Anxiety, and Stress Scale 21 (DASS-21) by comparing the results before (pre-test) and after (post-test) tDCS treatment.

Conclusion: Ultimately, the scores of the Yale-Brown scale in the Left DLPFC group showed significant changes after treatment with tDCS (mean difference compared to the sham group: -6.18 and P≤0.05). Hereupon, this study demonstrated that transcranial direct current stimulation may cause improvements in symptoms of OCD.
1. Introduction

OCD is a rather common psychiatric disorder characterized by the presence of obsessions and/or compulsions. OCD is defined as unwanted intrusive and recurrent thoughts, urges, or images (obsessions) and repetitive behaviors or mental acts that the individual feels driven to perform in response to an obsession or according to rules that patients believe must be applied rigidly (compulsions) (D’Urso et al., 2016).

OCD may be associated with both genetic and adventitious factors with a prevalence rate of 2% to 3% in the general population (Brunelin et al., 2018; Meyer, 2013). This disorder also has a prevalence of 1-3% in children and teenagers and 75% of them suffer from other anxiety disorders, such as anxiety, oppositional defiant disorder, attention-deficit/hyperactivity disorder, and Tourette’s disorder (Öst et al., 2016).

Symptoms of OCD are intrusive and recurrent thoughts and urge leading to compulsive and repetitive behaviors or mental acts (Brunelin et al., 2018; D’Ursoa et al., 2016). Meyer believed that the emergence of these thoughts depends on religiosity, self-esteem, and personality characteristics (Meyer, 2013). In 30-50% of adults with OCD, the early symptoms would commence in childhood or early adulthood, and if not treated, it may lead to subjective distress as well as a social disability (D’Ursoa et al., 2016; Öst et al., 2016). By the devaluation of life quality, OCD has been ranked as one of the ten most handicapping conditions by the World Health Organization. Studies have revealed that the frustration caused by this disorder leads to high levels of subjective distress, social disability, and suicidal thoughts (Angelakis, Gooding, Tarrier, & Panagioti, 2015; D’Urso et al., 2016).

Psychopharmacologic and psychotherapeutic interventions or a combination of them are common treatments for OCD; however, they fail to function properly in almost 40% of patients (Brunelin et al., 2018). For that reason, non-pharmacological approaches, such as non-invasive brain stimulation therapies, comprising repetitive Transcranial Magnetic Stimulation (rTMS), and transcranial Direct Current Stimulation (tDCS) are mostly suggested (D’Ursoa et al., 2016; Mondino, Haesebaert, Poulet, Saoud, & Jérôme Brunelin, 2015). tDCS is an available method enhancing cortical excitability and spontaneous neuronal activity under an anode by generating a weak current between anode and cathode. It is suggested that this method enhances cortical excitability and activity by the generation of action potentials; thus, it could be effective in improving the symptoms of psychiatric disorders (Lefaucheur et al., 2017; Stagg, Antal, & Nitsche, 2018) which was first introduced in animal and human experiments in the 1950s, and added to the standard arsenal of methods to alter brain physiology as well as psychological, motor, and behavioral processes and clinical symptoms in neurological and psychiatric diseases about 20 years ago. In contrast to other noninvasive brain stimulation tools, such as transcranial magnetic stimulation, it does not directly induce cerebral activity, but rather alters spontaneous brain activity and excitability by subthreshold modulation of neuronal membranes. Beyond acute effects on brain functions, specific protocols are suited to induce long-lasting alterations of cortical excitability.
ability and activity, which share features with long-term potentiation and depression. These neuroplastic processes are important foundations for various cognitive functions such as learning and memory formation and are pathologically altered in numerous neurological and psychiatric diseases. This explains the increasing interest to investigate transcranial direct current stimulation (tDCS) and has been suggested to decrease symptoms of OCD (Bation, Poulet, Haesebaert, Saoud, & Brunelin, 2015; Senço et al., 2015).

Imaging studies have manifested abnormalities in the cortico-striato-thalamo-cortical pathways, especially, the Dorsolateral Prefrontal Cortex (DLPFC)-caudate nucleus-thalamus loop in patients with OCD. Also, several pieces of research brought out the clinical effectiveness of stimulating DLPFC in other psychiatric conditions (Brunelin et al., 2018). Accordingly, DLPFC is a promising approach for OCD treatment and we aimed at utilizing that in this study.

2. Methods

In this study, 24 patients, including seven women and 17 men participated, of whom 17 cases were married and 7 cases were single. There were three groups in this study, including the Sham, Right DLPFC (anode in F4 and cathode in FP1 area), and Left DLPFC (anode in F3 and cathode in FP2 area). The subjects were randomly distributed into groups: One woman and five men in the sham group, three women and seven men in the Right DLPFC group, and three women and five men in the Left DLPFC group (Table 1).

All patients were subjected to a 2 mA current flow for 30 minutes with a 10-minute rest in between (the total session period was 40 minutes). This protocol was performed daily for five days. To find a suitable location, an international 10–20 electrode placement system and 5×7 cm² electrodes pads were used.

For evaluation of changes in obsessive-compulsive level and cognitive functions, the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and Depression, Anxiety, and Stress Scale 21 (DASS-21) were used before and after therapy. Data were analyzed by SPSS v. 16. To compare the results of the Y-BOCS and DASS-21, the mean and standard deviation of pre-test and post-test in all groups were examined. Then, the Analysis of Covariance (ANCOVA) was applied to omit the pre-test learning effect. The LSD post-test was used to demonstrate which between-group differences were significant.

3. Results

The severity of OCD cases, who were confirmed with clinical diagnosis, were assessed with the Y-BOCS and their scores were considered as the pre-test scores. These scores were between 12 and 30 (with a mean of 21 and a standard deviation of 4.7), which showed that they suffered from mild to severe OCD. To examine the aspects of emotional disturbance, the DASS-21 was used. Table 2 describes the descriptive data of the sham, left DLPFC, and right DLPFC groups, including the means and standard deviations of both tests in each group.

To statically control the influence of pre-test, the ANCOVA was applied (Table 3), which showed at least one significant difference between groups. Therefore, the LSD post hoc test was done. A significant difference was observed between the left DLPFC and sham groups in the Y-BOCS scores (Table 4). No significant differences were observed in the DASS-21 scores between groups.

4. Discussion

Studies have shown that stimulating DLPFC has some beneficial effects in psychiatric conditions with an abnormality in this area (Brunelin et al., 2018). We aimed to reduce the clinical symptoms of OCD and attempted to employ a tDCS as a non-invasive method in two regions of left DLPFC and right DLPFC.

In this study, OCD patients experienced a protocol of tDCS treatment (2 mA current flow for 15 minutes with 10 minutes of rest in between for five days), and their depression, anxiety, stress level, and OCD symptoms were assessed using DASS-21 and Y-BOCS. Participants in both groups of Left and Right DLPFC showed no significant difference in scores of the DASS-21. Although

Table 1. Demographic data of the patients

| Variables | Sham Group | Right DLPFC Group | Left DLPFC Group | Total |
|-----------|------------|-------------------|------------------|-------|
| Men       | 5          | 7                 | 5                | 17    |
| Women     | 1          | 3                 | 3                | 7     |
our results showed no significant difference in the right DLPFC, another study on five patients using a different protocol for 15 days, demonstrated significant improvements (Dinna et al., 2016). One of the reasons for the absence of a significant improvement can be the high variation in scores that increases the standard deviation. This problem can be solved by increasing the number of cases in all groups. Also, a longer period of treatment may result in more satisfying results. One promising point, which strengthens these ideas is that there was no significant difference in pre-test and post-test scores of the sham group, as well. We observed a significant improvement in the Y-BOCS scores in the left DLPFC. This shows that this protocol has some positive effects on decreasing the difficulties caused by OCD.

Several studies have employed tDCS to reduce problems caused by OCD with different protocols and considering different areas of the brain (Bation, Mondino, Le Camus, Saoud, & Brunelin, 2019; Bation et al., 2016; Brunelin et al., 2018; D’Ursoa et al., 2016; Goradel, Poursamali, Mowlai, & Movahed, 2016; Meyer, 2013; Mondino et al., 2015; Najafi et al., 2017; Palm et al., 2017; Senço et al., 2015). Improvements following the

### Table 2. Descriptive data of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Depression, Anxiety, and Stress Scale 21 (DASS-21) in all groups

| Test                          | Mean±SD | Pre-test | Post-test |
|-------------------------------|---------|----------|-----------|
| Yale-Brown (Sham)             | 18.88±4.390 | 17.00±7.783 |
| DASS-21 (Sham)                | 29.75±10.209 | 24.62±14.071 |
| Yale-Brown (Left DLPFC)       | 21.50±4.660 | 0.38±0.744  |
| DASS-21 (Left DLPFC)          | 30.50±15.137 | 25.87±13.206 |
| Yale-Brown (Right DLPFC)      | 22.62±4.809 | 15.50±6.761 |
| DASS-21 (Right DLPFC)         | 20.87±14.980 | 14.25±13.551 |

### Table 3. Analysis of Covariance (ANCOVA) results

| Test                      | Sum of Squares | Average Squares | Degrees of Freedom | F   | P       |
|---------------------------|----------------|-----------------|--------------------|-----|---------|
| Modified model            | 714.41         | 238.13          | 3                  | 19.25 | 0.0001  |
| Covariate variable        | 700.07         | 700.07          | 1                  | 59.59 | 0.0001  |
| Independent variable      | 68.06          | 136.13          | 2                  | 5.50 | 0.012   |
| Error                     | 12.37          | 12.37           |                    |     |         |

### Table 4. The results of the LSD Post Hoc Test

| Variables    | Average Difference | P     |
|--------------|--------------------|-------|
| Left DLPFC   | -3.155             | 0.09  |
| Sham         | -6.18*             | 0.003 |
| Right DLPFC  | 3.155              | 0.09  |
| Sham         | -3.02              | 0.11  |
treatment with tDCS in different areas suggest that there is not only one specific area affected by OCD, but also it seems that OCD involves more complex and extended neurological pathways.

5. Conclusion

Applying tDCS as a non-invasive method in the left DLPFC area is effective for decreasing the difficulties of OCD.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed about the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information. They were free to leave the study whenever they wished, and if desired, the research results would be available to them.

Funding

The present study was funded by the Institute for Cognitive Science Studies (ICSS), Tehran, Iran.

Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

References

Alizadeh Goradel, J., Pouresmali, A., Mowlaie, M., & Sadeghi Movahed, F. (2016). The effects of transcranial direct current stimulation on obsession-compulsion, anxiety, and depression of a patient suffering from obsessive-compulsive disorder. Practice in Clinical Psychology, 4(2), 75-80. http://jpcp.uswr.ac.ir/article-1-304-en.html

Angelakis, I., Gooding, P., Tarrier, N., & Panagioti, M. (2015). Suicidality in Obsessive Compulsive Disorder (OCD): A systematic review and meta-analysis. Clinical Psychology Review, 39, 1-15. [DOI:10.1016/j.cpr.2015.03.002]

Bation, R., Mondino, M., Le Camus, F., Saoud, M., & Brunelin, J. (2019). Transcranial direct current stimulation in patients with obsessive compulsive disorder: A randomized controlled trial. European Psychiatry, 62, 38-44. [DOI:10.1016/j.eurpub.2019.08.011]

Bation, R., Poulet, E., Haesebaert, F., Saoud, M., & Brunelin, J. (2016). Transcranial direct current stimulation in treatment-resistant obsessive-compulsive disorder: An open-label pilot study. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 65, 153-7. [DOI:10.1016/j.pnpbp.2015.10.001]

Brunelin, J., Mondino, M., Bation, R., Palm, U., Saoud, M., & Poulet, E. (2018). Transcranial direct current stimulation for obsessive-compulsive disorder: A systematic review. Brain Sciences, 8(2), 37. [DOI:10.3390/brainsci8020037]

de Melo Felipe da Silva, R., Brunoni, A. R., Miguel, E. C., & Shavitt, R. G. (2016). Transcranial direct current stimulation for treatment-resistant obsessive-compulsive disorder: Report on two cases and proposal for a randomized, sham-controlled trial. Sao Paulo Medical Journal, 134(5), 446-50. [DOI:10.1590/1516-3180.2016.015010716]

Dinna, W. M., Aycicegi-Dinn, A., Goral, F., Karamursel, S., Yildirim, E. A., & Hacioglu-Yildirim, M., et al. (2016). Treatment-resistant obsessive-compulsive disorder: Insights from an open trial of transcranial Direct Current Stimulation (tDCS) to design a RCT. Neurology, Psychiatry and Brain Research, 22(3-4), 146-54. [DOI:10.1016/j.npbp.2016.06.003]

D’Urso, G., Brunoni, A. R., Anastasia, A., Micillo, M., de Bartolomeis, A., & Mantovani, A. (2016). Polarity-dependent effects of transcranial direct current stimulation in obsessive-compulsive disorder. Neurocase, 22(1), 60-4. [DOI:10.1080/13554794.2015.1045522]

D’Urso, G., Brunoni, A. R., Mazzaferrro, M. P., Anastasia, A., de Bartolomeis, A., & Mantovani, A. (2015). Transcranial direct current stimulation for obsessive-compulsive disorder: A randomized, controlled, partial crossover trial. Depression and Anxiety, 33(12), 1132-40. [DOI:10.1002/da.22578]

Lefaucheur, J. P., Antal, A., Ayache, S. S., Benninger, D. H., Brunelin, J., & Cogiamanian, F., et al. (2017). Evidence-based guidelines on the therapeutic use of transcranial Direct Current Stimulation (tDCS). Clinical Neurophysiology, 128(1), 56-92. [DOI:10.1016/j.clinph.2016.10.087]

Meyer, R. W. (2013). OCD symptoms and Adlerian psychology: a literature review [MA. thesis]. Minnetonka, MN: Adler Graduate School. https://allredadlater.edu/library/masters/2013/ryan-w-meyer

Mondino, M., Haesebaert, F., Poulet, E., Saoud, M., & Brunelin, J. (2015). Efficacy of cathodal transcranial direct current stimulation over the left orbitofrontal cortex in a patient with treatment-resistant obsessive-compulsive disorder. The Journal of ECT, 31(4), 271-2. [DOI:10.1097/YCT.0000000000000218]

Najafi, K., Najafi, T., Fakour, Y., Zarrabi, H., Heidarzadeh, A., & Kahlkhali, M., et al. (2017). Efficacy of transcranial direct current stimulation in the treatment-resistant patients who suffer from severe obsessive-compulsive disorder. Brain Stimulation, 10(2), 367. [DOI:10.1016/j.brs.2017.01.081]

Öst, L. G., Rüse, E. N., Wergeland, G. J., Hansen, B., & Kvale, G. (2016). Cognitive behavioral and pharmacological treatments of OCD in children: A systematic review and meta-analysis. Journal of Anxiety Disorders, 43, 58-69. [DOI:10.1016/j.janxdis.2016.08.003]

Palm, U., Leitner, B., Kirsch, B., Behler, N., Kumpf, U., & Wulf, L., et al. (2017). Prefrontal tDCS and sertraline in obsessive compulsive disorder: A case report and review of the litera-
ture. *Neurocase*, 23(2), 173-7. [DOI:10.1080/13554794.2017.1319492]

Rapp, A. M., Bergman, R. L., Piacentini, J., & McGuire, J. F. (2016). Evidence-based assessment of obsessive-compulsive disorder. *Journal of Central Nervous System Disease, 8*. [DOI:10.4137/jcnisd.s38359]

Schruers, K., Koning, K., Luermans, J., Haack, M. J., & Griez, E. (2005). Obsessive-compulsive disorder: A critical review of therapeutic perspectives. *Acta Psychiatrica Scandinavica, 111*(4), 261-71. [DOI:10.1111/j.1600-0447.2004.00502.x]

Senço, N. M., Huang, Y., D’Urso, G., Parra, L. C., Bikson, M., & Mantovani, A., et al. (2015). Transcranial direct current stimulation in obsessive-compulsive disorder: Emerging clinical evidence and considerations for optimal montage of electrodes. *Expert Review of Medical Devices, 12*(4), 381-91. [DOI:10.1586/17434440.2015.1037832]

Stagg, C. J., Antal, A., & Nitsche, M. A. (2018). Physiology of transcranial direct current stimulation. *The Journal of ECT, 34*(3), 144-52. [DOI:10.1097/YCT.0000000000000510]