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Transcranial Direct Current Stimulation Use in the Treatment of Neuropsychiatric Disorders: A Brief Review

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Abstract

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that has grown in popularity over the past two decades as an alternative treatment option for various neuropsychiatric disorders. tDCS modulates cortical excitability through the application of a weak direct current to the scalp via electrodes placed over cortical regions of interest. It has been shown to be a promising and relatively safe treatment tool with few adverse events. In this article, we will briefly review the efficacy of tDCS in depression, bipolar disorder, schizophrenia, and obsessive-compulsive disorder. We will also discuss biomarkers of tDCS efficacy in depression, as it is the most studied neuropsychiatric disorder using tDCS application. We will then offer suggestions for future directions. Although efficacy results show promise, more studies with larger samples and longer treatment periods are needed to better understand the benefits of using tDCS as an alternative treatment option for neuropsychiatric disorders.

Transcranial direct current stimulation (tDCS) was re-introduced as a non-invasive brain stimulation technique applicable in humans at the turn of the millennium. tDCS involves the application of a weak electrical current through two or more electrodes placed on the scalp, with the goal of stimulating underlying brain tissue. The principal mechanism of action in tDCS is a subthreshold modulation of neuronal membrane potentials, which alters cortical excitability and activity dependent on the current flow direction through the target neurons[1]. Other biological effects of the electric field are also likely relevant (i.e., changes in neurotransmitters, effects on glial cells and on microvessels, modulation of inflammatory processes). Similar to pharmacological neuromodulators, tDCS does not induce activity in

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resting neuronal networks, but modulates spontaneous neuronal activity. Consequently, the amount and direction of effects critically depend on the previous physiological state of the target neural structures. In this sense, tDCS represents a neuromodulatory technique. This neuromodulatory technique has been applied as both a neuroenhancer, a method for adjunctively enhancing treatment outcome, and as a primary intervention in various brain-related disorders. Neuropsychiatric disorders represent a major area of investigation for tDCS as both a primary treatment and adjunctive treatment strategy for symptom management. This brief review will describe the current state of tDCS as a treatment in neuropsychiatric disorders.

Acute Depressive Episodes

Fregni and colleagues[2] reported on one of the first randomized, controlled, and double-blind trials of tDCS versus sham in 10 depressed patients using a current of 1 mA for 20 minutes per day over five alternated days. Results indicated that four of the five depressed patients in the active group showed significant decreases in their depression scores, while this was not the case for those in the sham condition. Since then, several randomized controlled trials with various stimulation protocols (i.e., different current intensity, duration of stimulation, and number and frequency of sessions) have been described in the literature[3-5].

The most common electrode montage for tDCS in depression involves placing the anode electrode at F3 (International 10-20 Electrode Placement System) over the left dorsolateral prefrontal cortex (DLPFC) and the cathode electrode over the contralateral supraorbital area. Studies suggest that tDCS is a generally effective treatment option for acute major depressive episodes with minimal side effects[6]. Compared to sham and/or active control treatments, tDCS exerts acute antidepressant effects[3,4] that can last for up to 30 days after treatment[3]. However, one study failed to find a statistically significant difference between the active and sham groups over 5 treatment sessions – both groups appeared to improve in their depressive symptoms over time[5].

Treatment-Resistant Depression

Open-label trials of tDCS in treatment-resistant depression (TRD) suggest there is an antidepressant response. In 14 unipolar TRD patients, Ferrucci and colleagues[7] found that depression scores decreased after 10 sessions of tDCS. In 23 TRD outpatients (15 unipolar, 8 bipolar), Dell'Osso and team[8] reported a significant reduction in depression scores over 5 days that was extended over the first week of follow-up. In a follow-up study[9], these patients were observed for an additional 3 months and results indicated that the antidepressants effects of the acute trial was maintained throughout subsequent time points in half of the sample. However, several placebo-controlled trials in TRD outpatients indicated no significant differences in depression scores between active and sham treatments – both groups equally improved[10-12]. A recent meta-analysis also suggests that tDCS for TRD may not be efficacious[6]. Potential reasons for this include under-powering of studies with small sample sizes, varying levels of treatment-resistance between studies, different study requirements for antidepressant washouts (or lack thereof), and different stimulation parameters.

To date, tDCS appears to be most efficacious for individuals with mild-to-severe levels of depression who do not fit criteria for TRD. More research is needed to better understand the effectiveness of tDCS for both acute depressive episodes and TRD.

Biomarkers of Transcranial Direct Current Stimulation Treatment in Depression

Although tDCS has been shown to be effective in treating acute depressive symptoms, the mechanism of this improvement is still relatively unknown. Multiple biomarkers have been examined as potential predictors for treatment response in tDCS or as a physiological marker of improvement following treatment. To date, brain-derived neurotrophic factor (BDNF), neurotrophins 3 and 4, nerve growth factor, glial cell line-derived neurotropic factor, and cytokine levels have failed to show either a predictive property in determining response to tDCS or a marker of change following treatment[13-15]. BDNF polymorphisms have also failed to show any connection in predicting treatment response to tDCS[16]. However, people with the long/long allele of the functional 44-bp insertion/deletion polymorphism (5-HTTLPR) have had significant improvement after active tDCS compared to sham tDCS, whereas those with short/short 5-HTTLPR have a similar response to active and sham tDCS[16]. This suggests the possibility that tDCS may be affecting the serotonergic system in depression. Mechanistic studies are needed to further elucidate both the mechanism of action in tDCS treatment for depression, as well as to identify potential biological predictors of effectiveness.

Bipolar Disorder

Research on tDCS treatments for bipolar disorder is limited. While multiple studies[4,8,12,17,18] of the effects of tDCS in depression include bipolar patients, few researchers separate out bipolar and unipolar depression to assess the efficacy of tDCS on these different groups. One study to date has examined the impact of bifrontal tDCS treatment (anode placed over the left DLPFC at F3, cathode placed over the right DLPFC at F4) on 14 subjects with bipolar disorder and found a significant reduction in depressive symptom both immediately following treatment and at a one-month follow up[19]. Additionally, when compared to a unipolar depression group, those with bipolar depression appeared to have a larger benefit from tDCS treatment; however this result is difficult to interpret due to baseline differences in depression severity and different medication usage between the two groups.

One case study[20] has reported tDCS as a potential treatment for manic symptoms in bipolar disorder. A patient received stimulation over the right DLPFC (anode placed at F4, cathode placed over contralateral supraorbital region) after 7 days of mania. Following tDCS, the patient demonstrated reduced manic symptoms for 2 days followed by hypomanic symptoms. The report indicated tDCS may have reduced the patient's manic symptoms; however, the patient was experiencing multiple medication changes at the time of treatment, so it is difficult to determine the cause of symptom improvement[20]. Research studies examining the impact of tDCS on mania in bipolar depression have yet to be conducted.

In regards to safety, hypomania has been reported in one individual following stimulation over the left dorsolateral prefrontal cortex (anode at F3) with the cathode electrode placed on the contralateral arm[21]. Of note, this patient had previously undergone bifrontal tDCS stimulation with no adverse events reported. Overall, limited data suggest tDCS may be a promising treatment for depressive symptoms in bipolar disorder; however double-blind, placebo controlled trials need to be implemented to determine tDCS's efficacy in this group. Additionally, research needs to examine the potential impact of tDCS treatments on mania and hypomania in bipolar disorder.

Schizophrenia

Schizophrenia is a brain disorder that affects thought processes and perception. Auditory hallucinations and delusions are the predominant positive symptoms of schizophrenia and the negative symptoms may range from blunted affect and poverty of speech to decreased interests. There have been multiple studies and case reports conducted[22-24] evaluating the efficacy of tDCS for different symptoms in schizophrenia and using different stimulation protocols. Most studies[25-27] have examined the effects of tDCS on the reduction of positive symptoms, especially hallucinations. The most common electrode montage in schizophrenia consists of anodal placement over the right DLPFC (at F4) and cathodal placement over the left temporoparietal junction (midway between T3 and P3). Both open-label and randomized controlled trials have shown significant reduction in treatment resistant auditory hallucinations in patients with schizophrenia using tDCS[25-27]. One study did not see any improvement in positive symptoms of schizophrenia when the electrodes were placed over the left DLPFC (at F3) and the contralateral supraorbital area[28], although another study[18] noticed an improvement in symptoms with similar electrode placement. Other studies[29,30] noticed a significant improvement in the negative symptoms of schizophrenia, with anode placement over the left DLPFC (at F3) and cathode placement over the contralateral supraorbital area[30] or contralateral arm[29].

It is important to note that most of the studies in schizophrenia are preliminary and have limitations. Small samples sizes, variations in medication use and baseline symptoms, and differences in stimulation protocols and treatment duration makes it difficult to elucidate the impact of tDCS on schizophrenic symptoms. Follow-up periods in most studies are also relatively short, so long-term effects of treatment are unknown. Though positive effects of tDCS in alleviating symptoms of schizophrenia have been observed, given the limitations, large scale controlled randomized double blind studies with longer follow up are needed.

Obsessive-Compulsive Disorder

To date, few studies have examined the potential therapeutic effects of tDCS in patients with obsessive-compulsive disorder (OCD). A pilot study[31] examining the effects of stimulation over the left orbitofrontal cortex (at FP1, cathode; anode place over the right cerebellum) in treatment-resistant patients found a significant reduction in OCD symptoms both at the end of a 10-day trial (mean reduction of symptoms 26.4%) and at the 3-month follow-up visit. Case studies[32,33] of the effects of tDCS have primarily focused on treatment resistant patients. Sites of stimulation, number of stimulation sessions and length of time between

stimulation sessions have varied between studies. Results from these case control studies have also varied. One study found that tDCS effects were polarity dependent: stimulation over the pre-supplementary motor area (pre-SMA; anode) and right arm (cathode) caused worsening in OCD symptoms; however, after inverting the polarity of the electrodes, there was a reduction of OCD symptoms of over 30 percent[32]. Another case-control study reported significant symptom improvement after stimulation over the left pre-SMA (anode, with cathode placed over the right supraorbital area) in two patients with treatment-resistant OCD[33].

Overall, studies examining the potential therapeutic effects of tDCS in OCD have been promising, however, significantly more research is needed to determine the treatment efficacy and mechanism of action in patients with OCD. Limitations of research to date include the case-study format, a wide range of stimulation sites, and variability in length of treatments and follow-up periods. Larger, placebo controlled studies examining the potential positive impact tDCS may have on treating OCD symptoms are needed.

Future Directions and Conclusions

A number of avenues have been outlined for research using tDCS in neuropsychiatric disorders. The use of tDCS has been studied in patients with depression, bipolar disorder, schizophrenia, and OCD. However, considerably more research is needed to fully understand both the efficacy and mechanism of tDCS treatments in these populations. Consistent methodology across tDCS studies is an important future step, but first, dose-response relationship between treatment and effect need to be established for various neuropsychiatric disorders. Currently, there are inconsistencies regarding the efficacy of tDCS in treating almost all neuropsychiatric disorders, which may be due, in part, to differences in methodology, including electrode placement, stimulation length and intensity, and length of intervention and follow-up, as well as differences within and across patient populations. The parameter space of tDCS is highly complex and small shifts in the location of an electrode can alter where current flows in the brain[1,34], which suggests that the application of tDCS is anything but simple. Both methodological and individual factors that may affect treatment efficacy need to be elucidated and studied further.

In addition, long-term outcomes and safety within neuropsychiatric populations must undergo further investigation, though a recent study indicates that tDCS has not been associated with any serious adverse events across various populations[35]. Randomized, double-blind, placebo-controlled trials examining the impact of tDCS using various stimulation methodologies are needed to help determine the overall effectiveness of tDCS in various groups. Additional future research should also focus on the potential additive benefits of tDCS treatments when coupled with medication or other treatment modalities. Another important concern is the regulation of the device. As tDCS represents a clinical research tool that is currently available in various unregulated and uncertified forms on the world market, a growing number of people outside of clinical or research settings have self-administered tDCS. Until the above issues are addressed, long-term consequences are established, and long-term randomized trials are completed, self-administration/treatment is ill advised.

In summary, tDCS is a method that has shown promise as a treatment method in a number of neuropsychiatric disorders. Although future research is required to fully understand the extent of its utility in neuropsychiatric disorders, the method has the potential to become a powerful clinical tool.

References

1. Woods AJ, Antal A, Bikson M, et al. A technical guide to tDCS, and related non-invasive brain stimulation tools. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology. 2016; 127(2):1031–1048. [PubMed: 26652115]
2. Fregni F, Boggio PS, Nitsche MA, Marcolin MA, Rigonatti SP, Pascual-Leone A. Treatment of major depression with transcranial direct current stimulation. Bipolar Disord. 2006; 8(2):203–204. [PubMed: 16542193]
3. Boggio PS, Rigonatti SP, Ribeiro RB, et al. A randomized, double-blind clinical trial on the efficacy of cortical direct current stimulation for the treatment of major depression. The international journal of neuropsychopharmacology / official scientific journal of the Collegium Internationale Neuropsychopharmacologicum. 2008; 11(2):249–254.
4. Loo CK, Alonzo A, Martin D, Mitchell PB, Galvez V, Sachdev P. Transcranial direct current stimulation for depression: 3-week, randomised, sham-controlled trial. The British journal of psychiatry : the journal of mental science. 2012; 200(1):52–59. [PubMed: 22215866]
5. Loo CK, Sachdev P, Martin D, et al. A double-blind, sham-controlled trial of transcranial direct current stimulation for the treatment of depression. The international journal of neuropsychopharmacology / official scientific journal of the Collegium Internationale Neuropsychopharmacologicum. 2010; 13(1):61–69.
6. Meron D, Hedger N, Garner M, Baldwin DS. Transcranial direct current stimulation (tDCS) in the treatment of depression: Systematic review and meta-analysis of efficacy and tolerability. Neuroscience and biobehavioral reviews. 2015; 57:46–62. [PubMed: 26232699]
7. Ferrucci R, Bortolomasi M, Vergari M, et al. Transcranial direct current stimulation in severe, drug-resistant major depression. Journal of affective disorders. 2009; 118(1-3):215–219. [PubMed: 19286265]
8. Dell'Osso B, Zanoni S, Ferrucci R, et al. Transcranial direct current stimulation for the outpatient treatment of poor-responder depressed patients. European psychiatry : the journal of the Association of European Psychiatrists. 2012; 27(7):513–517. [PubMed: 21621982]
9. Dell'Osso B, Dobrea C, Arici C, et al. Augmentative transcranial direct current stimulation (tDCS) in poor responder depressed patients: a follow-up study. CNS spectrums. 2014; 19(4):347–354. [PubMed: 23962405]
10. Bennabi D, Nicolier M, Monnin J, et al. Pilot study of feasibility of the effect of treatment with tDCS in patients suffering from treatment-resistant depression treated with escitalopram. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology. 2015; 126(6):1185–1189. [PubMed: 25454337]
11. Blumberger DM, Tran LC, Fitzgerald PB, Hoy KE, Daskalakis ZJ. A randomized double-blind sham-controlled study of transcranial direct current stimulation for treatment-resistant major depression. Frontiers in psychiatry. 2012; 3:74. [PubMed: 22912618]
12. Palm U, Schiller C, Fintescu Z, et al. Transcranial direct current stimulation in treatment resistant depression: a randomized double-blind, placebo-controlled study. Brain stimulation. 2012; 5(3): 242–251. [PubMed: 21962978]
13. Brunoni AR, Machado-Vieira R, Zarate CA, et al. Cytokines plasma levels during antidepressant treatment with sertraline and transcranial direct current stimulation (tDCS): results from a factorial, randomized, controlled trial. Psychopharmacology. 2014; 231(7):1315–1323. [PubMed: 24150249]
14. Brunoni AR, Machado-Vieira R, Zarate CA Jr. et al. Assessment of non-BDNF neurotrophins and GDNF levels after depression treatment with sertraline and transcranial direct current stimulation in a factorial, randomized, sham-controlled trial (SELECT-TDCS): an exploratory analysis.

Progress in neuro-psychopharmacology & biological psychiatry. 2015; 56:91–96. [PubMed: 25172025]

15. Brunoni AR, Machado-Vieira R, Zarate CA Jr. et al. BDNF plasma levels after antidepressant treatment with sertraline and transcranial direct current stimulation: results from a factorial, randomized, sham-controlled trial. European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology. 2014; 24(7):1144–1151. [PubMed: 24702987]
16. Brunoni AR, Kemp AH, Shiozawa P, et al. Impact of 5-HTTLPR and BDNF polymorphisms on response to sertraline versus transcranial direct current stimulation: implications for the serotonergic system. European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology. 2013; 23(11):1530–1540. [PubMed: 23615118]
17. Martin DM, Alonzo A, Mitchell PB, Sachdev P, Galvez V, Loo CK. Fronto-extracephalic transcranial direct current stimulation as a treatment for major depression: an open-label pilot study. Journal of affective disorders. 2011; 134(1-3):459–463. [PubMed: 21641047]
18. Palm U, Keeser D, Blautzik J, et al. Prefrontal transcranial direct current stimulation (tDCS) changes negative symptoms and functional connectivity MRI (fcMRI) in a single case of treatment-resistant schizophrenia. Schizophrenia research. 2013; 150(2-3):583–585. [PubMed: 24060570]
19. Brunoni AR, Ferrucci R, Bortolomasi M, et al. Transcranial direct current stimulation (tDCS) in unipolar vs. bipolar depressive disorder. Progress in neuropsychopharmacology & biological psychiatry. 2011; 35(1):96–101.
20. Schestatsky P, Janovik N, Lobato MI, et al. Rapid therapeutic response to anodal tDCS of right dorsolateral prefrontal cortex in acute mania. Brain stimulation. 2013; 6(4):701–703. [PubMed: 23158877]
21. Galvez V, Alonzo A, Martin D, Mitchell PB, Sachdev P, Loo CK. Hypomania induction in a patient with bipolar II disorder by transcranial direct current stimulation (tDCS). The journal of ECT. 2011; 27(3):256–258. [PubMed: 21206371]
22. Agarwal SM, Shivakumar V, Bose A, et al. Transcranial direct current stimulation in schizophrenia. Clinical psychopharmacology and neuroscience : the official scientific journal of the Korean College of Neuropsychopharmacology. 2013; 11(3):118–125. [PubMed: 24465247]
23. Koops S, van den Brink H, Sommer IE. Transcranial direct current stimulation as a treatment for auditory hallucinations. Frontiers in psychology. 2015; 6:244. [PubMed: 25798123]
24. Nieuwdorp W, Koops S, Somers M, Sommer IE. Transcranial magnetic stimulation, transcranial direct current stimulation and electroconvulsive therapy for medication-resistant psychosis of schizophrenia. Current opinion in psychiatry. 2015; 28(3):222–228. [PubMed: 25768083]
25. Brunelin J, Mondino M, Gassab L, et al. Examining transcranial direct-current stimulation (tDCS) as a treatment for hallucinations in schizophrenia. The American journal of psychiatry. 2012; 169(7):719–724. [PubMed: 22581236]
26. Mondino M, Haesebaert F, Poulet E, Suaud-Chagny MF, Brunelin J. Fronto-temporal transcranial Direct Current Stimulation (tDCS) reduces source-monitoring deficits and auditory hallucinations in patients with schizophrenia. Schizophrenia research. 2015; 161(2-3):515–516. [PubMed: 25468175]
27. Shivakumar V, Chhabra H, Subbanna M, et al. Effect of tDCS on auditory hallucinations in schizophrenia: Influence of catechol-O-methyltransferase (COMT) Val158Met polymorphism. Asian journal of psychiatry. 2015; 16:75–77. [PubMed: 26070413]
28. Smith RC, Boules S, Mattiuz S, et al. Effects of transcranial direct current stimulation (tDCS) on cognition, symptoms, and smoking in schizophrenia: A randomized controlled study. Schizophrenia research. 2015; 168(1-2):260–266. [PubMed: 26190299]
29. Kurimori M, Shiozawa P, Bikson M, Aboseria M, Cordeiro Q. Targeting negative symptoms in schizophrenia: results from a proof-of-concept trial assessing prefrontal anodic tDCS protocol. Schizophrenia research. 2015; 166(1-3):362–363. [PubMed: 26032568]
30. Palm U, Keeser D, Hasan A, et al. Prefrontal Transcranial Direct Current Stimulation for Treatment of Schizophrenia With Predominant Negative Symptoms: A Double-Blind, Sham-Controlled Proof-of-Concept Study. Schizophrenia bulletin. 2016

31. Bation R, Poulet E, Haesebaert F, Saoud M, Brunelin J. Transcranial direct current stimulation in treatment-resistant obsessive-compulsive disorder: An open-label pilot study. Progress in neuro-psychopharmacology & biological psychiatry. 2016; 65:153–157. [PubMed: 26439873]

32. D'Urso G, Brunoni AR, Anastasia A, Micillo M, de Bartolomeis A, Mantovani A. Polarity-dependent effects of transcranial direct current stimulation in obsessive-compulsive disorder. Neurocase. 2016; 22(1):60–64. [PubMed: 25971992]

33. Narayanaswamy JC, Jose D, Chhabra H, et al. Successful Application of Add-on Transcranial Direct Current Stimulation (tDCS) for Treatment of SSRI Resistant OCD. Brain stimulation. 2015; 8(3):655–657. [PubMed: 25583654]

34. Woods AJ, Bryant V, Sacchetti D, Gervits F, Hamilton R. Effects of Electrode Drift in Transcranial Direct Current Stimulation. Brain stimulation. 2015; 8(3):515–519. [PubMed: 25583653]

35. Bikson M, Grossman P, Thomas C, et al. Safety of Transcranial Direct Current Stimulation: Evidence Based Update 2016. Brain stimulation. 2016; 9(5):641–661. [PubMed: 27372845]