What Psychiatrists Need to Know About Transcranial Direct Current Stimulation

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Transcranial direct current stimulation is a battery-powered noninvasive device used to treat a range of neuropsychiatric disorders. Details here.

Transcranial direct current stimulation (tDCS) is a low-intensity, noninvasive form of brain stimulation delivered by a small battery-powered portable machine. Conventionally, 2 disposable electrodes are positioned on the head, and a small current is passed between these electrodes to stimulate the brain "transcranially." A typical session uses a low-intensity current of 1 to 2 mA (ECT by comparison is 800 mA), which is given continuously for about 30 minutes. Also in contrast to ECT, the tDCS current is continuous (not pulsed) and flows in one direction from the anode electrode to the cathode electrode ("direct current").

Only a fraction of the current reaches the brain —it passes through the skin, skull, and cerebrospinal fluid —but the excitative qualities of the brain and its plasticity make it sensitive to even a low level of direct current stimulation. The injected electric current does not generate action potentials per se, but modulates ongoing brain activity and influences synaptic transmission, with effects on brain function that outlast the stimulation session. The potential to produce lasting changes in brain function with tDCS, especially after repeated sessions of stimulation, has encouraged clinical trials for the treatment of psychiatric and neurological disorders.
Initial tDCS protocols suggest that the anode and cathode electrodes can induce excitatory or inhibitory effects, respectively, in the underlying cortex. More recently, it was found that the direction of the effects also depends on other parameters, such as current intensity, session duration, brain state, and any concurrent pharmacology.[1] Other distinct forms of low-intensity transcranial electric stimulation also exist, such as alternating, pulsed, or random noise ("tRNS") electric stimulation. However, clinical research is currently most advanced with direct current.
The regulatory status of tDCS in the US is as an investigational device. In the European Union, Canada, Brazil, Australia, and Singapore, specific tDCS products have been approved for the treatment of various neuropsychiatric disorders.

Adverse effects

Mild adverse effects during the stimulation session, such as skin redness, itching, and burning sensation are common, although these effects are generally well tolerated and limited to the duration of the sessions. There are case reports of tDCS-induced induction of manic and hypomanic episodes in patients with mood disorders. A recent meta-analysis found that the risk of manic switch is not statistically higher in patients receiving active (3.5%) compared with sham (0.5%) stimulation, although this analysis is limited by the low number of reports.
Currently, more than 50,000 sessions of tDCS have been used to treat more than 5000 participants in clinical studies. There have been no reports of serious adverse events (ie, hospitalization, seizures, cardiac arrest, death) associated with tDCS.[1] Animal safety studies have shown that the clinical dose is over an order of magnitude lower than the minimum dose required to induce brain injury. Studies in humans showed that tDCS does not increase blood enolase (a marker of brain injury) levels. Several recent meta-analyses have concluded tDCS is well tolerated.[2] The balance of evidence, therefore, shows that tDCS is a safe technique, within the parameters currently used.

Mechanisms of tDCS

The mechanisms and rationale for tDCS have been characterized over several decades. The passage of direct current through electrodes on the scalp generates a standing electric field in the brain, which in turn produces a sustained polarization of the membranes of neurons. Neuronal functions, including information processing and plasticity, are highly sensitive to changes in membrane polarization. By influencing ongoing brain activity and facilitating long-term changes, there is an established pathway for tDCS to influence cognition and behavior. Enhancement and restoration of

neuroplasticity in depressed patients was demonstrated after a 4-week treatment course of tDCS.[3] Evidently, as with any neuropsychiatric intervention, questions remain about mechanism as it related to disease etiology. Nonetheless, changes in brain function following tDCS are not surprising given the wealth of data from animal models and clinical imaging/neurophysiology.

Dose decisions

The key decisions in application of tDCS are: stimulation dose that includes electrode position, stimulation current, and duration[4]; subject state during stimulation including use of any adjunct acute interventions (eg, cognitive behavioral therapy); and subject inclusion/exclusion along with adjunct chronic therapies (eg, pharmacotherapy).

Stimulation dose matters in that the polarity and position of the electrodes determine which brain regions are influenced by tDCS. For example, in the treatment of depression the positive electrode (anode) is positioned over the left dorsolateral prefrontal cortex. However, conventional tDCS using 2 electrodes can also stimulate additional brain regions between electrodes. High-definition tDCS uses arrays of smaller electrodes to focus current to targeted brain regions.

Current intensity and duration are important to set the degree of neuromodulation produced. Subject state, including any concurrent therapy with tDCS, is considered important, since the effects of tDCS on the brain depend on the state of the brain.[5] For example, animal studies show that when synaptic plasticity is initiated (by training), concurrent stimulation boosts the plasticity (more effective training). Subject condition also matters for similar reasons. For example, the use of pharmaceuticals may influence the effects of tDCS.

tDCS in depression

The life prevalence of MDD is between 6% and 12% and yearly between 3% and 11% worldwide. Approximately 80% of patients have a recrudescence of depressive symptoms after 1 year of treatment with antidepressant drugs, and up to 33% do not achieve complete remission after 2 or 3 medication trials. In view of the complexity and heterogeneity of MDD —with variations in its etiology, symptoms, course, and response to the treatment —further investigation that aims to refine the knowledge of underlying neurobiology is needed, with the goal to identify circuits and brain areas connected with this pathology.

There is increasing evidence regarding the efficacy of tDCS for the treatment of depression. The latest CANMAT (Canadian Network for Mood and Anxiety Treatments) edition and a European consensus of experts graded tDCS as a probably effective technique in the treatment of depression. The first pilot studies of tDCS in depression were conducted over 10 years ago and showed promising results; however, the samples were small.6 More recently, 2 large, placebo-controlled studies (N = 120; N = 245 patients) explored the role of tDCS in the context of pharmacological therapies. Findings from the first study indicate that tDCS combined with sertraline is more effective than tDCS or sertraline alone.[7]

The second was a non-inferiority trial that compared tDCS (2 mA prefrontal stimulation sessions for 15 consecutive weekdays, followed by 7 weekly treatments) with full-dose escitalopram (10 mg/d for 3 weeks, 20 mg/d thereafter).[8] The main findings showed that escitalopram was superior to tDCS, and tDCS was superior to placebo. This suggests that tDCS is less effective on average as a monotherapy than escitalopram and therefore should not be considered a replacement for antidepressant medication. However, tDCS had minimal adverse effects and was more effective than placebo, which allows it to be considered as a treatment in settings where escitalopram or other pharmacological interventions are not recommended, or where there is a patient preference for non-pharmacological treatments.

Novel tDCS protocols should investigate how to optimize parameters to further enhance patient outcomes. Home-based tDCS where the patient (or carer) is trained to administer tDCS at home, under the remote supervision of clinicians, is currently being developed and has the potential to greatly increase the feasibility and convenience of tDCS treatment. This procedure requires special equipment certified for remote use and protocols for monitoring progress.[9]

Bilateral prefrontal stimulation has been shown to be effective in the treatment of depression.[6] The left anode was placed over the dorsolateral prefrontal cortex, and the right cathode was placed in the prefrontal area. The current was 2 mA, and session duration was 30 minutes. Increasing efficacy was noted as the number of sessions increased. Other protocols have been tested, but all used anodal stimulation over the dorsolateral prefrontal cortex.

tDCS in schizophrenia

Schizophrenia occurs in 0.5% to 1.5% of the population. The clinical symptoms of the disorder can be divided in 3 groups: positive, negative, and cognitive. Positive symptoms are characterized by hallucinations, delusions, thought disorders, and movement disorders. Negative symptoms involve

blunted affect, lethargy, and social withdrawal. Traditional antipsychotic medications have limited efficacy in treating these chronic, often refractory, symptoms.

The effects of tDCS have been investigated with 3 main outcomes:

1) Auditory verbal hallucinations using a fronto-temporal tDCS montage (the anode is placed over the left dorsolateral prefrontal cortex coupled with the cathode over the left temporoparietal junction)[10]

2) Negative symptoms using a frontal montage (the anode placed over the left dorsolateral prefrontal cortex coupled with the cathode placed over the right dorsolateral prefrontal cortex, the right supraorbital region, or extra-cephalically)

3) Enhancement of cognitive functions, using different tDCS montages[11]

Promising results have been reported for these 3 outcomes. tDCS can decrease the severity of symptoms by about 30% and enhance a wide range of cognitive functions (eg, working memory, self-monitoring, facial emotion recognition). However, most studies to date are case reports or open-label studies with small samples. Thus, large randomized controlled studies are needed to confirm the usefulness of tDCS in schizophrenia.

tDCS in other disorders

tDCS has also been investigated in a range of other psychiatric conditions, such as obsessive-compulsive disorder, addiction, and neurodegenerative disorders.[12] Results have been mixed, and to date no randomized controlled trials have investigated efficacy outcomes for these disorders. There is also considerable interest in the use of tDCS combined with cognitive training to enhance cognitive functioning, with potential application to a number of neuropsychiatric disorders.[13]

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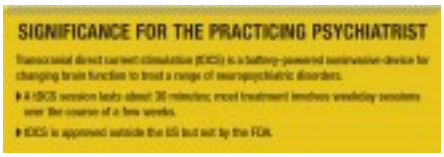

SIGNIFICANCE FOR THE PRACTICING PSYCHIATRIST

Disclosures:

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Dr. Bikson reports that Soterix Medical Inc produces tDCS and high definition tDCS devices and he is the founder and has shares in the company. Ms. Unal and Dr. Brunoni report no conflicts of interest concerning the subject matter of this article. Dr. Loo reports that she has received equipment support from Soterix Medical Inc.

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