



## GUEST EDITORIAL

# Interventional psychiatry for schizophrenia: The role of transcranial direct current stimulation

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Schizophrenia (SZ) is among the most disabling psychiatric disorders. Recent estimates based on Global Burden of Disease has shown increasing burden due to schizophrenia. Psychopharmacological, psychological, and social interventions, especially focusing on the early stage of SZ, have the potential to decrease the disability due to SZ (1). Antipsychotic medications, the mainstay treatment for SZ, have been effective in treating the acute symptoms as well as preventing the relapse of symptoms to a considerable extent. Nonetheless, these medications have not substantially improved the outcome of SZ. Furthermore, about one-third of SZ patients show little or no clinical response to treatment of non-clozapine antipsychotic. Treatment resistance is an important contributor to disease burden (2).

Efforts to identify newer therapeutic targets for psychopharmacological intervention development of novel molecules, perhaps, in the long term may lead to a path-breaking impact in treating SZ. It has been proposed that focus on disease modification and prevention (albeit an ambitious goal) needs to drive these research efforts. Such futuristic studies need to be anchored on the development of valid biomarkers that can objectively (a) detect subjects at risk for conversion to psychosis, (b) identify prodrome, and (c) predict patients who are likely to become treatment-resistant. The potential avenues for these biomarkers involve brain imaging, electrophysiology, blood-based, and other similar parameters (3).

In this context, it is important to note that given the view of the brain as an “electrochemical soup,” SZ, too,

has been shown to have electrophysiological and neurochemical (neurotransmitter) aberrations. Nonetheless, harnessing the potential of therapeutic avenues that modulate the “electro” component has not been extensively pursued as much as that of the psychopharmacological interventions that have anchored their impetus on the “chemical” component. The above-summarized two key directions, i.e., neuroscience-informed biomarkers for diagnostic/prognostic applications and technologies that modulate the electrophysiological aberrations for therapeutic applications, in SZ can be optimally blended within the framework of “interventional psychiatry” (4).

Interventional psychiatry, an emerging subspecialty in psychiatry, encompasses two complementary components: (i) leverage the neurotechnological applications to unravel the circuit level brain dysfunctions that lead to the pathogenesis of psychiatric disorders and (ii) utilizing the spectrum of brain stimulation techniques to adaptive modulate these dysfunctional brain circuits (5). With reference to SZ, interventional psychiatry offers the paradigm to apply neuromodulation techniques with contemporaneous neurotechnology-based investigations to understand the pathogenetic basis [e.g., transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are illustrative neuromodulatory perturbation techniques that can help us to understand the neuroplasticity basis and relevant neural circuitry correlates of SZ, especially when combined with brain imaging/electrophysiology]. Furthermore, such

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translational neuroscience studies combined with neuromodulatory treatment outcome research can pave way for informed clinical practice to optimally harness the potential of such treatments (4).

Among the several different types of neuromodulation treatment approaches, techniques that are based on the application of weak electric current for therapeutic applications have been in vogue for centuries. Nonetheless, a substantial majority of these weak intensity current applications have used pulsed waveforms that did not involve direct current. tDCS is a reemerging neuromodulation technique that utilizes a weak-intensity electric current (6). tDCS refers to the “technique in which the dose is a waveform of single sustained direct current, with the exception of one ramp-up and one ramp-down period, applied to the head using at least one cephalic electrode. tDCS is non-invasive and requires appropriate electrolyte buffer (conductive gel, paste, or saline) between the electrode and the skin” (7).

In contrast to other neuromodulation techniques such as TMS that involve the application of suprathreshold stimulus which subsequently leads to the generation of an action potential, tDCS is implicated to cause subthreshold changes in neuronal membrane potential (without generating action potential) which in turn leads to adaptive modulations in spontaneous brain activity. Repeated sessions of tDCS (typically each session lasting for a duration of 20 min) can cause persisting alterations of cortical excitability (at least for a short term) akin to long-term potentiation or depression (6). It is possible that these potential neuroplasticity modulatory effects of tDCS might underlie its clinical benefits in SZ.

An attractive aspect of tDCS is that this neuromodulation technique is simple and can be administered with ease. Furthermore, tDCS is cost-effective and much more economical compared with other neuromodulation techniques such as electroconvulsive therapy and TMS. Most importantly, numerous studies have established the safety and tolerance of tDCS (6). A recent meta-analysis proposing evidence-based recommendations observed that, with regard to the utility of tDCS to treat auditory verbal hallucinations in SZ, the findings are consistent and indeed promising in support of left prefrontal anodal and left temporoparietal cathodal montage-based therapeutic application (8). The utility of tDCS to treat other symptom domains of SZ, cognitive deficits and negative symptoms, is increasingly being pursued through several ongoing research studies. However, one

needs to be mindful of the fact that the available evidence base for the therapeutic application of tDCS in SZ is still nascent with studies reporting varying findings using heterogeneous methods (8). Future research needs to explore optimized delivery of tDCS (for example high-definition electrodes with better focality), characterize between-individual for inter-individual brain architectural variations, and harness the potential of computational neuromodeling with concurrent neuronavigation techniques to impart individualized treatment approaches using tDCS (9). Given the need for long-term treatment in SZ, tDCS offers the unique option of developing a scalable application in terms of domiciliary tDCS that can be delivered at home with careful remote supervision (10).

In summary, tDCS is an exciting tool within the spectrum of avenues in “interventional psychiatry” that offers novel potential to unravel the neurobiological underpinnings as well as formulate safe, affordable, and effective interventions for SZ.

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