Neuromodulation in Neuropsychiatric Disorders

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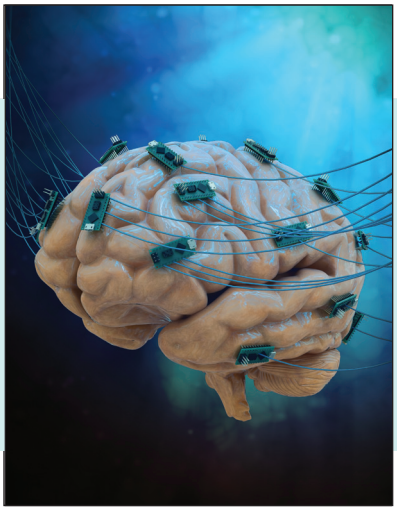
Guest Editor



Neuropsychiatric disorders are significant public health problems. These disorders, including major depressive disorder (MDD), obsessive-compulsive disorder (OCD), Parkinson's disease, and epilepsy, are a major cause of disability in the United States; they constitute 18.7% of the total number of years lost to disability.[1] Prototypical of these disorders, MDD affects about 10% of the population, and is underdiagnosed and undertreated.[2] Existing treatment modalities do not always result in remission of this disorder and may cause significant side effects. Medication-based treatments result in improved symptoms only 40% of the time according to the STAR*D (Sequenced Treatment Alternatives to Relieve Depression) Study.[2]

Treatment-resistant depression (TRD) is a significant clinical problem found in 29% to 46% of depressed patients treated with standard-dose antidepressants for at least 6 weeks.[2] There is a need to explore and implement newer and more effective treatments for MDD. Current treatment options for TRD include changing prescribed antidepressants, augmentation, and implementing neuromodulation techniques, such as electroconvulsive therapy (ECT). Various brain stimulation therapies, other than ECT, including transcranial magnetic stimulation (TMS), vagal nerve stimulation (VNS), and deep brain stimulation (DBS), have been shown to be effective in clinical trials. In my view, current medication and nonpharmacological treatments for neuropsychiatric disorders are suboptimal due to problems of tolerability, inadequate resolution of symptoms, and lack of specificity. Neuromodulation techniques may fill in some of these treatment gaps.

THERAPEUTIC NEUROMODULATION MODELS

The brain is a highly specialized organ with electrochemical activity and connectivity. Brain function can be altered in disease states due to a disturbed neural function or faulty conduction or function of brain network areas. Neuromodulation is defined as the therapeutic modification of brain activity by altering neurotransmission using magnetic or electrical energy, which can be achieved by invasive and noninvasive techniques.

Invasive techniques include VNS, DBS, and epidural prefrontal cortical stimulation. Noninvasive techniques include TMS, transcranial direct current stimulation (tDCS), cranial electrotherapy stimulation (CES), ECT, magnetic seizure therapy (MST), and focal electrically administered seizure therapy (FEAST).[3]

Vagal Nerve Stimulation

VNS works by sending pulses of electrical activity to the brain via the left vagus nerve. These pulses are generated by a device implanted surgically under the skin in the patient's upper chest. This causes afferent stimulation of median raphe nucleus and locus coeruleus, leading to increased central serotonergic and nonadrenergic activity that imparts an antidepressant effect. The stimulating parameters can be adjusted by using a computer and a noninvasive handheld device. In addition to refractory epilepsy, VNS has also been shown to treat chronic depression.[4] VNS is a costly, irreversible procedure with delayed efficacy. VNS has not gained a significant position in the treatment algorithm of chronic depression.

Deep Brain Stimulation

DBS introduces small currents directly into mood-regulating areas in the brain, such as the anterior cingulate cortex. DBS is an invasive investigational treatment.

In the article "Overview of the Current Use of Deep Brain Stimula-

tion in Psychiatric Disorders," Drs. Daniel P. Witter and Herbert E. Ward review the role of DBS in psychiatric disorders. They conclude that DBS possesses a reasonably favorable side-effect profile, and its reversible and adjustable quality offers an advantage over lesioning procedures.

Epidural Prefrontal Cortical Stimulation

This treatment option uses implantable stimulating paddles that do not come in contact with the brain and target the anterior frontal poles and the lateral prefrontal cortex. More research is needed to explore its role in treatment.

Transcranial Magnetic Stimulation

TMS involves electromagnetic fields to create electrical alterations in mood-regulating areas in the prefrontal cortex. High-frequency repetitive transcranial magnetic stimulation (rTMS) applied to the left dorsolateral prefrontal cortex has been shown to relieve depression.[5] rTMS causes focal neuronal changes and is reported to have cognitive side effects. TMS has also been shown to beneficially alter neurotransmission in other brain areas involved in several disorders, including OCD, anxiety, and insomnia. In the article "Update on Transcranial Magnetic Stimulation for Depression and Other Neuropsychiatric Illnesses," Dr. Jonathan E. Becker and colleagues review the role of TMS in various neuropsychiatric disorders.

Transcranial Direct Current Stimulation

tDCS is a noninvasive brain stimulation technique that applies a small (1-2 mA), direct current via the scalp to enhance or diminish neuronal excitability in a specific brain area. tDCS has been shown to be effective in alleviating depressive symptoms.[6] tDCS can be a safe, easy to administer, office-based, inexpensive, and effective treatment option for depression. In the article "Transcranial Direct Current Stimulation Use in the Treatment of Neuropsychiatric Disorders: A Brief Review," Sarah M. Szymkowicz and colleagues provide a brief review of the role of tDCS in neuropsychiatric disorders.

Cranial Electrotherapy Stimulation

This treatment uses small pulses of electrical current delivered across the head and is focused on the hypothalamic region, with electrodes usually placed on the ear at the mastoid. CES has been shown to have some role in depression, anxiety, and sleep disorders in preliminary studies.[7]

Electroconvulsive Therapy

Electroconvulsive therapy is the most effective treatment for severe depression.[8,9] It may also benefit patients with bipolar disorder and acute psychosis. ECT is not a popular treatment due to stigmas associated with it, and it may also cause cognitive side effects.

Focal Electrically Administered Seizure Therapy

This is an alternate form of ECT that involves passage of electrical current unidirectionally from a small anode to a larger cathode electrode. This technique delivers a focal current to the target areas of the brain involved in depression. MST and FEAST show fewer cognitive side effects in a preliminary study.[10] In the article "Charting the Course of Electroconvulsive Therapy: Where Have We Been and Where Are We Headed?," Drs. Peter B. Rosenquist, W. Vaughn McCall, and Nagy Youssef review ECT, its current state, and future directions.

Magnetic Seizure Therapy

In MST, intense, high-frequency, magnetic pulses sufficient to induce a seizure are used. These magnetic pulses are not affected by scalp/skull resistance. The electrical fields generated in the brain are more focal. MST is shown to have no cognitive side effects in a preliminary study.[11] More research is needed to explore the clinical use of MST in psychiatric disorders.

FUTURE DIRECTIVES

Although ECT has demonstrated superior efficacy in treating depression, it has undesirable cognitive side effects. The role of TMS is emerging as it is shown to be effective in treating depression, but can be costly. Its role in other disorders is being evaluated. MST and FEAST are attempts to provide the efficacy of ECT with fewer cognitive side effects.

There is rapid advancement in neuromodulation in the way of techniques and applications. These techniques can be used in conjunction with medication treatments for various neuropsychiatric disorders. There is a need to explore and understand the role of these treatment techniques, as well as to improve the techniques themselves. These techniques can also be chosen based on diagnostic tests that could serve as

biomarkers in choosing a treatment modality that best fits the individual patient.

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He received his Doctorate of Medicine in Psychiatry from All Institute of Medical Sciences (New Delhi, India), and completed his residency training in Internal Medicine and Psychiatry at Southern Illinois University School of Medicine (Springfield, IL). Dr. Khurshid then completed a Fellowship in Sleep Medicine and Circadian Rhythm Disorders at The University of Chicago.

Dr. Khurshid has positively contributed to the discipline of psychiatry and sleep medicine in the state of Florida as well as on a national level. He is a Fellow member of the American Academy of Sleep Medicine and a former chair of its Insomnia section.

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