Deep Brain Stimulation
Clinical Applications

Darin D. Dougherty, MD, MMSc

KEYWORDS

• Deep brain stimulation • DBS in Psychiatry • Mechanisms of DBS
• Treatment resistant depression • Treatment-refractory OCD

KEY POINTS

- Deep brain stimulation has a longer history of use in neurology for movement disorders, but work has been performed for psychiatric indications.
- Deep brain stimulation of the ventral/capsule/ventral striatum is approved by the US Food and Drug Administration for the treatment of treatment-refractory obsessive-compulsive disorder.
- Although open-label trials of deep brain stimulation for treatment-resistant depression at multiple targets have been encouraging, controlled trials for approval from the US Food and Drug Administration have been negative.
- Future approaches may include refined targeting using tractography, alternate clinical trial designs, or closed loop approaches.

INTRODUCTION

Deep brain stimulation (DBS) has been used since the 1980s for the treatment of movement disorders. First used for Parkinson's disease, DBS is now approved by the US Food and Drug Administration (FDA) the for treatment of Parkinson's disease, essential tremor, and dystonia, and it is estimated that approximately 150,000 patients with movement disorders have been implanted with DBS devices in the United States

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Division of Neurotherapeutics, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, CNY2612, 149 13th Street, Boston, MA 02129, USA
E-mail address: ddougherty@partners.org

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Abbreviations	
DBS	Deep brain stimulation
FDA	US Food and Drug Administration
HDE	Humanitarian device exemption
HDRS-17	Hamilton Depression Rating Scale
MADRS	Montgomery-Åsberg Rating Scale
OCD	Obsessive-compulsive disorder
sgACC	Subgenual anterior cingulate cortex
slMFB	Superolateral branch of the medial forebrain bundle
STN	Subthalamic nucleus
TRD	Treatment-resistant depression
VC/VS	Ventral capsule/ventral striatum
YBOCS	Yale-Brown Obsessive Compulsive Scale.

alone.[1] DBS works, as the name suggests, via electrodes stereotactically implanted in specific targets within the brain. A subcutaneous wire travels from the electrode to a pacemaker-like device, called an implantable pulse generator that is implanted subcutaneously on the chest wall (usually subclavicular). After DBS implantation, clinicians use a computer that communicates with the implantable pulse generator transcutaneously to set the stimulation parameters. Stimulation parameters include which contacts on the electrode (there are usually 4) deliver stimulation (thus, precisely where in the brain stimulation is delivered), amplitude, frequency, and pulse width. Targets most commonly used for DBS for movement disorders are the subthalamic nucleus (STN) and globus pallidus interna.

The first use of DBS for a psychiatric indication was published by Nuttin and colleagues[2] in 1999. Based on an extant literature suggesting that ablation of the anterior limb of the internal capsule (called an anterior capsulotomy) is an effective treatment for treatment-refractory obsessive-compulsive disorder (OCD), the investigators implanted bilateral DBS electrodes in the anterior limb of the internal capsule in 4 patients with treatment-refractory OCD and reported that 3 of the 4 patients received clinical benefit. Since then, many studies of DBS for treatment-refractory psychiatric illness have been performed. It is essential to note that DBS is only indicated for severe, chronic, treatment-refractory psychiatric illness and that DBS for treatment-refractory psychiatric illness should be overseen by an experienced multidisciplinary team of clinicians. The object of this review is to review the experience of DBS for treatment-refractory psychiatric illness up until now and then to discuss future directions for the field (**Fig. 1**).

OBSESSIVE-COMPULSIVE DISORDER

Ventral Capsule/Ventral Striatum

After the positive results reported by Nuttin and colleagues, multiple groups of investigators began to explore the use of DBS for treatment-refractory OCD. The worldwide experience of DBS for treatment-refractory OCD was described in a landmark paper by Greenberg and colleagues[3] in 2010. Their article describes the results of the use of DBS at the ventral capsule/ventral striatum (VC/VS) target for treatment-refractory OCD from teams in the United States and Europe. In a total of 26 patients with treatment-refractory OCD, the mean baseline Yale-Brown Obsessive Compulsive Scale (YBOCS) score of 34.0 decreased to a mean of 21.0 after 3 months of active DBS treatment.[4] As a categorical measure, a total of 73% of the patients with treatment-refractory OCD experienced at least a 25% improvement on the YBOCS at last follow-up, and 61.5% experienced at least a 35% improvement on the YBOCS