Deep brain stimulation for obsessive compulsive disorder: a crisis of access

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Deep brain stimulation is an approved therapy for obsessive compulsive disorder, but is rarely used despite its efficacy, depriving people from effective treatment.

Obsessive-compulsive disorder (OCD) is characterized by distressing thoughts (obsessions) and repetitive mental or behavioral acts (compulsions). OCD affects 2-3% of the general population and may cause significant disability and impact on quality of life. First line treatment consists of exposure and response prevention via cognitive-behavioral therapy (CBT) and pharmacotherapy, most commonly serotonin-reuptake inhibitors. OCD tends to be chronic and persistent, and impairment is common, despite best medical therapy. Indeed, a

significant number of patients with severe OCD symptoms will not respond to these conventional therapies (1).

Treatment-refractory patients may be candidates for lesional brain surgery or deep brain stimulation (DBS). DBS involves the bilateral placement of electrodes into a specific brain region. The electrodes are connected to a subcutaneously placed pulse generator. Since 1987, DBS has treated more than 200,000 patients worldwide, mostly for movement disorders such as Parkinson's disease, with a proven safety record (2). In the realm of psychiatric diseases, DBS has received regulatory approval in many jurisdictions for treating selected cases of refractory OCD, but access to this therapy is restricted for many patients.

DBS, whether for OCD or for movement or psychiatric disorders, evolved from stereotactic brain lesioning procedures. The first lesioning method for OCD was the anterior capsulotomy, which was developed in the 1940s and 1950s by Jean Talairach and Lars Leksell. The procedure consisted of using stereotactic methods to create thermal lesions in the anterior limb of the internal capsule (ALIC) to selectively dampen pathologically overactive fronto-thalamic circuits (3). Due to its success in treating movement disorders, DBS was introduced to the field of psychiatry decades later, when Bart Nuttin and colleagues treated refractory OCD patients with DBS, also targeting the ALIC to offer an adjustable, programmable alternative to lesion procedures (4). Based on several subsequent DBS trials from various centers around the world, the appreciation of the brain circuitries relevant to OCD has improved substantially. The various anatomically adjacent areas of white matter (ventral capsule, VC) and gray matter (nucleus accumbens, NAc; bed nucleus of the stria terminalis, BNST) that comprise this DBS target are broadly referred to as the ventral capsule/ventral striatum (VC/VS) (5).

Approved for use

In 2009, the U.S Food and Drug Administration (FDA) approved OCD DBS that targets the VC/VS under a humanitarian device exemption (HDE H050003). This approval allows any U.S. center to perform these procedures provided that they obtain local institutional review board (IRB) approval and monitor outcomes (6). In the same year, a Conformité Européenne (CE mark) was also granted for OCD DBS in Europe. Both the US and European approvals cited safety and the demonstration that 'the probable benefit to health from use of the device outweighs the risk of injury or illness from its use... '. This degree of evidence-backed confidence stands in explicit contrast to the agnosticism regarding safety and efficacy characteristic of experimental or investigational therapies, which are regulated by Investigational Device Exemptions (IDEs), rather than HDEs (7).

In 2014, an international group of experts in the field, including neurosurgeons, psychiatrists, neurologists, neuroethicists, and philosophers, and gathered by the World Society for Stereotactic and Functional Neurosurgery (WSSFN) published consensus guidelines for stereotactic neurosurgery for psychiatric disorders (8). The group adopted a definition for 'approved' therapy akin to what is expected for other neurosurgical procedures: "At least two blinded (if possible) randomized controlled clinical trials from two different groups of researchers need to be published, both showing an acceptable risk-benefit ratio, at least comparable with other existing therapies.". The group also adopted a definition of intractable OCD as agreed by psychiatrists as an indication for DBS.

Treatment refractoriness was defined by insufficient response to at least: two trials of selective serotonin reuptake inhibitors at a maximum tolerated dose for at least 12 weeks; one trial of clomipramine at a maximum tolerated dosage for at least 12 weeks; one augmentation trial with an antipsychotic for at least eight weeks in combination with one of the aforementioned drugs; and one complete trial of exposure-based CBT confirmed by a psychotherapist. To date, several OCD DBS trials meeting these criteria have been published.

Evidence of efficacy

In 2010, Denys et al. in the Netherlands published the results of a randomized trial of OCD DBS targeting the ALIC/NAc area of the brain using a delayed randomization design (9). Following 8 months of optimization of DBS therapy, 16 patients were randomized into a two-week crossover period. Nine out of 16 patients were full responders, with a mean decrease of 46% in Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) scores. During the crossover phase, the mean Y-BOCS score difference was 8.3 points (p=.004), that is, a 25% improvement.

Six years later, Luyten et al. (10) from Belgium reported the results of a double-blinded randomized cross-over study of DBS targeting the ALIC/BNST in 17 patients out of 24 total in the cohort. They observed a response rate of 53% and a median 37% improvement in Y-BOCS scores when comparing the double-blinded ON- vs. OFF-DBS phases, each of which lasted three months to allow stabilization between phases. During the subsequent open label phase, 67% of the patients exhibited full response, and the median decrease in Y-BOCS score was 58%.

Mosley et al. further increased the evidence base of ALIC/BNST DBS with their randomized, double-blind trial in nine patients in Australia, in early 2021 (11). Following surgery, participants entered a three-month randomized, double blinded, sham-controlled phase prior to a twelve-month period of open-label stimulation incorporating a course of CBT. In the blinded phase, stimulation provided significant benefit over sham (p =0.025, mean Y-BOCS difference 4.9 points). In the subsequent open phase, Y-BOCS scores decreased by a mean of 50% (17 points), with seven of the nine (78%) participants classified as responders. Importantly, their results also highlighted the synergistic effect of CBT, which further reduced scores by 4.8 points (p = 0.011) when added to DBS.

Most recently, Provenza et al. adopted a design of open-label DBS optimization with CBT boost followed by double-blinded discontinuation in the US (12). All five of five subjects (100%) were full responders during open-label optimization, with a mean Y-BOCS reduction of 55%. All five deteriorated during the double-blinded discontinuation to the point of meeting preset escape criteria and then subsequently improved with DBS re-initiation, demonstrating that the DBS response was true, not sham or due to placebo. This trial was the fourth to show a significant effect of DBS that was robust to double-blinded assessments.

These trials from diverse centers, all incorporating rigorous, blinded designs, demonstrate that DBS can be successfully used in otherwise severely affected, treatment-resistant individuals around the world. Long term follow-up studies have also documented the durability of response over several years (13,14). Other brain targets for DBS have also been investigated, with three trials of DBS applied to the limbic, anteromedial region of the

subthalamic nucleus (amSTN) now meeting criteria for Level 1 evidence (15,16,17). All above-mentioned trials demonstrated a significant effect of DBS relative to sham stimulation.

The emerging reports of an additive effect of CBT when combined with DBS is worthy of mention (9,11,12). By inclusion criteria definition, all these individuals had previously failed CBT and so its beneficial effect, following months of DBS therapy, is not only encouraging from a therapy point of view, but also provides hints of mechanistic synergy: DBS may open the door to the beneficial effects of CBT, which before surgery could not be realized. DBS should not be considered a therapy of last resort within the therapeutic armamentarium, but rather as part of a sequential synergistic approach to complement the effects of conventional treatments (18).

Restricted access DBS as a treatment for refractory OCD is supported by regulatory approvals and robust evidence based on several blinded, randomized-controlled trials. But patients with severe OCD are being denied access to this potentially life-saving therapy, in part because of denial of insurance coverage, which makes the therapy financially infeasible for almost all patients.

DBS for OCD is routinely denied by commercial insurance providers in the U.S, despite this denial violating mental health parity laws enacted in 2008, which prevent discrimination against individuals suffering from disorders of mental health (7). Patient referrals to specialized multidisciplinary centers with DBS expertise remain infrequent, not only because of the unwillingness for insurers to pay, , but also due to the relative paucity of psychiatrists and behavioral therapists who are expert in the most difficult-to-treat forms of OCD. Many psychiatrists and psychologists are perhaps unaware of the potential of DBS to treat OCD, or are believe that such surgery is ineffective or unsafe, based on the enduring legacy of the lobotomy era (19,20). DBS for OCD is safe and effective and carries regulatory approval, but despite this, the vast majority of intractable OCD patients are not treated.

The conditional approval by FDA, CE or other respective national regulatory bodies requires a minimum protocol for quality assurance and long-term standard outcomes, collected as part of a registry. However, the manufacturers of DBS hardware decide which centers to include in this registry. Data from such a registry is also unlikely to persuade insurance companies to reimburse a procedure that can amount to tens of thousands of dollars in expenses.

In addition, anticipated legal restrictions will likely result in a new application process from FDA and CE. . Such a re-application process will likely result in a steep financial burden for the manufacturers of DBS hardware, who may choose to prioritize high volume indications for DBS such as Parkinson´s disease, over severe, but less common, OCD.

Reasons for denial	Potential solutions
Insurance companies refuse to pay	?
Lack of DBS-trained psychiatrists and psychologists	?
Biases against DBS from the lobotomy era	?

Table 2. Reasons why DBS is not used to treat OCD.

DBS for OCD is an FDA- and CE-approved procedure that fulfills scientific and clinical criteria as an effective and safe therapy for patients suffering from severe intractable OCD. Failures of the healthcare system imperil people with this mental health condition, who are unable to receive this potentially life-saving therapy.

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Author contributions

Competing interests

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