

Treating Treatment-Resistant Obsessive-Compulsive Disorder (OCD) via Deep Brain Stimulation (DBS)

Wing Hei Wong *

International School, Jinan University, Guangzhou, 510000, China

* Corresponding Author: e0u0bi@gmail.com

Abstract. Obsessive-Compulsive Disorder (OCD) is a prevalent and challenging mental health condition characterized by persistent, unwanted thoughts (obsessions) and repetitive behaviors (compulsions). Traditional treatment modalities, including pharmacotherapy and cognitive-behavioral therapies, fail to alleviate symptoms in around half of the patients, necessitating the exploration of alternative therapeutic options. Deep Brain Stimulation (DBS) has emerged as a promising intervention for treatment-resistant OCD, with recent studies reporting a success rate of about 60%. This innovative treatment involves the precise placement of electrodes in specific brain regions such as the Nucleus Accumbens (NAcc), Bed Nucleus of the Stria Terminalis (BNST), and Subthalamic Nucleus (STN) to modulate dysfunctional neural circuits. This paper reviews the effectiveness of DBS in reducing OCD symptoms, evaluates its safety, and discusses the neurobiological mechanisms underlying its therapeutic effects. It also explores future research directions, including the optimization of electrode placement, the integration of DBS with other treatment modalities, and the development of personalized medicine approaches. Furthermore, the paper addresses ongoing challenges such as the need for a clearer understanding of DBS mechanisms, the refinement of patient selection criteria, and the management of long-term outcomes. By providing a comprehensive overview of current knowledge and potential developments, this study aims to highlight the role of DBS as a transformative tool for managing severe, refractory OCD.

Keywords: Deep brain stimulation; Treatment-resistant obsessive-compulsive disorder; Subthalamic nucleus (STN); Bed nucleus of the stria terminalis (BNST).

1. Introduction

Obsessive-compulsive disorder (OCD) primarily focuses on two domains — obsessions and compulsions. Obsessions are meddling cognitions or mental images that dismay the patient, such as trepidation of contamination or antagonistic thoughts toward others or oneself [1]. Compulsions are redundant behaviors aimed at ameliorating the distress caused by obsessions according to strict rules, or to achieve a sense of ‘completeness’, such as compulsive counting or exaggerated hand washing [1, 2]. Most OCD symptoms are characterized clinically by apprehensions of contamination and exaggerated hand washing; compulsive and demanding checking, counting, or ordering — patients understand that their nervousness is unwarranted and unreasonable but are unable to eradicate those thoughts; unpleasant and interfering thoughts about sex, brutality, and blasphemy; whimsical ideations about abusing oneself or others.

Epidemiological surveys illustrate contemporary and lifetime majority rates of full-blown OCD around 1.2% and 2.3% in the U.S., respectively [3]. OCD symptoms make it overwhelming for patients to conduct daily activities like cooking and going outdoors, especially some patients may become housebound in order to escape from those aggressive ideas and obsessional checking. Also, patient with OCD may feel anguish, fear and a sense of culpable, which they may undergo mental fatigue, suffer despair and other anxiety disorder jointly, which jeopardize the living standard, both mental and physical well-being of the patient.

Traditional OCD treatment methods are typically pharmacotherapy, and Exposure and Response Prevention therapy (ERP). In pharmacotherapy aspect, only selective-serotonin reuptake inhibitors



(SSRIs) and serotonergic tricyclic antidepressant clomipramine are extensively more effective than placebo in the treatment of OCD [4]. SSRIs treat depression and other mental disorders by heightening the levels in serotonin in the brain. Clomipramine, a tricyclic antidepressant that inhibits serotonin reuptake and attaches several other receptor targets [5]. However, SSRIs compounded with notable negative outcomes comprising GI upset, nausea and sexual dysfunction, although they are usually satisfactorily endured. Furthermore, around half of patients respond incompletely to SSRIs, and at least eight weeks of maintained treatment are commonly mandated before significant clinical betterment is seen [5]. While Clomipramine has greater burden including anticholinergic effects, antihistaminergic effects, anti-alpha-adrenergic effects, arrhythmogenic potential and reduction of the seizure threshold [5]. Over 10-12 weeks, the deterioration of symptoms by about 40% to 60% of patients, however, no one could predict which patient will respond to which drug [6]. Nevertheless, disappearance of all symptoms rarely occurs [6]. Some patients may need to tolerate on medications indefinitely, since there is data suggest that patients' symptoms will reciprocate within one to two months after medications are halted, even after two years of triumphant pharmacotherapy [6].

ERP is a behavioral therapy that uncovers patient to the crisis they discomforted and encounter to the thoughts that initiate their anxiety, it strives to instruct patients how to negotiate with distress without committing in unnecessary procedure and overcome fear response. However, only about half of the patients who receive ERP is able to reach complete symptom remission. Poor response, including lack of obedience to treatment, poor insight, errors of clinicians, comorbid depression, and OCD severity are factors that deter the successful rate of ERP. Also, due to the challenging and time-consuming nature of the treatment, 20–30% of patients drop out of ERP prematurely [7].

As there are shortcomings and limitations in traditional OCD treatment and still no methods to cure OCD thoroughly, furthermore around 10% of OCD patients are treatment refractory and remain severely impaired [8], however, OCD hinder our wellbeing and daily activities, it is vital to discover a treatment that could treat OCD radically.

Deep Brain Stimulation (DBS) is a neurosurgery that uses implanted electrodes and electrical stimulation into deep brain regions in order to measure pathological brain activity and modulating neural function. DBS is an effective treatment for various neurologic and neuropsychiatric disorders, especially when medications have become less effective or their side effects interfere patients' daily activities. Neurosurgeons will implant wires inside the brain. The wires are connected with an insulated wire extension to a very small neurostimulator implanted under the person's collar bone. From the neurostimulator, a continuous pulse of electric current is pass through the wire and into the brain. Twenty years after its first use in a patient with OCD, the results demonstrate that deep brain stimulation (DBS) is a favorable therapy for patients with intense and unassailable forms of the disorder [9]. DBS for OCD can be carried out successfully in clinical settings and deliver hope for OCD patients.

However, DBS is still not been widely recognized clinically due to invasive nature, unanswered mechanism and unsatisfied success rate. Recent studies mainly focus on the mechanism and the improvement of accuracy by investigate more meticulous technique such as imaging technology and precise electrode. This study aims to investigate the advantages and side effect of DBS in treating OCD patients, and also analysis the potential and obstacles in this aspect.

2. Mechanism of DBS

2.1. Technical Principles of DBS

During Deep Brain Stimulation (DBS) surgery, a diminutive hole is drilled in the skull, and high-frequency electrical stimulation is applied through chronically implanted electrodes to the target brain region. The explicit region for electrode arrangement is identified using MRI or CT scans and further refined via intraoperative electrophysiological mapping. The electrodes are connected to a

pacemaker-like pulse generator implanted under the skin in the upper chest or abdomen. This device generates electrical impulses that modulate neuronal exercise and chemical interchanges within the brain, thereby altering the activity of brain regions involved in various neurological disorders, including OCD.

DBS can instantly affect specific neurons, modulate neurotransmitter release, and transform their networks, including those of dopamine and GABA. This modulation aids in rebalancing excitatory and inhibitory signaling for disorders like OCD. In Parkinson's disease, for instance, DBS helps normalize firing rates, intrude with pathological patterns, and modulate local field potentials. The across-the-board effects of DBS arise at the ionic, protein, cellular, and network levels, ultimately leading to behavioral changes and potentially long-term outcomes through mechanisms including neuroplasticity.

3. Target Brain Regions

In OCD, where up to one-third of patients do not respond to standard treatments effectively, DBS has emerged as a persuasive option [10]. Targeted regions including the Nucleus Accumbens (NAc), the bed nucleus of the stria terminalis (BNST), the anterior limb of the internal capsule (ALIC), ventral capsule/ventral striatal (VC/VS), inferior thalamic peduncle (ITP) and the subthalamic nucleus (STN). These locations are implicated in OCD symptoms due to their roles in stress, anxiety, and behavioral or impulse control.

Specifically, stimulation of the BNST has shown to diminish compulsive behaviors significantly. This region coordinates stress and anxiety responses, making it crucial for addressing the heightened anxiety and fear responses characteristic of OCD. Clinical studies have noted substantial symptom reduction in patients following BNST stimulation [11, 12]. Stimulation of the ALIC region has shown reduction in obsessions, compulsions, associated anxiety and depressive symptoms [13]. This region involved in motor supervision, sensory perception, and cognitive operation. Stimulation of this region is more unassailable and competent to enhance global functioning [13]. Stimulation of VC/VS is authenticated the contraction of OCD symptoms in sundry studies, depression symptoms and global functioning is mightily dwindled [13]. Studies have suggested that the VC/VS dorsal-most electrode contacts is the most cogent and work satisfactorily in mood [13,14].

Furthermore, stimulation of the STN in the basal ganglia system, particularly its associative limbic part, has yielded auspicious results in ameliorating OCD symptoms especially cognitive flexibility and compulsive behavior by influencing the brain's motivational and emotional circuits [13,14]. This region coordinates the control of motor and cognitive, it plays a key role in managing depression and anxiety disorder. Clinical cases have ascertained considerable modifications in OCD symptoms pursuing STN-DBS, affirming its likelihood in modulating neural activity related to OCD [15,16].

Lastly, targeting the ventral striatum, particularly entangling the nucleus accumbens and the ventral pallidum, clinical cases have indicated a durable and progressive intervention in OCD symptoms after DBS in ventral striatum [17]. The strategic application of DBS across these essential brain regions highlights its prospect as a transformative treatment for intense, treatment-resistant OCD, enhancing both symptom surveillance and overall quality of life.

4. Application of DBS in OCD Treatment

4.1. Current Clinical Applications

Traditional treatments for OCD, including pharmacological alternatives such as sertraline and clomipramine, and also psychological therapies like Cognitive Behavioral Therapy (CBT) and Exposure and Response Prevention (ERP), are typically first-line interventions. However, up to 60% of OCD patients do not acquire thoroughly consolation from this standard approach [18]. For those unresponsive to conventional treatments, more intensive options such as DBS, ablation surgery,

Transcranial Magnetic Stimulation (TMS), and Transcranial Direct Current Stimulation (tDCS) may be contemplated.

The application of DBS varies by country; in the United States, it is authorized under a Humanitarian Device Exemption (HDE) for treatment-resistant OCD cases, though not for general OCD treatment. In contrast, Australia's Therapeutic Goods Administration (TGA) approves DBS devices, limiting its use to specific research settings [19]. China recently conducted its DBS surgery on a severe OCD patient, targeting the septum nucleus and the forelimb of the inner capsule, with no related adverse effects.

For DBS to be evaluated, patients generally must have exhausted multiple treatment avenues, including several selective serotonin reuptake inhibitors (SSRIs), clomipramine, and ERP sessions, and must fulfill specific severity criteria for OCD symptoms and functional impairment. Treatment appropriateness and persistent management involve a collaborative approach among neurologists, psychiatrists, and surgeons, with regular follow-ups including brain scans and psychological appraisals are fundamental for monitoring patient progress.

4.2. Surgical Procedure and Risks

The surgical procedure for DBS concerns stereotactic brain surgery, which requires the patient to be awake and under local anesthesia to guarantee authentic electrode placement. This is critical as the patient's ability to obey commands permits real-time feedback that aids in meticulous detection and positioning. Initially, a metal head frame is fixed to the patient's skull to facilitate accurate targeting through magnetic resonance imaging (MRI). After determining the valid coordinates, the surgical team makes a small incision in the skull to implant the electrode wire. During this phase, brain mapping is utilized via an electrode needle to document brain activity and ascertain the optimal arrangement of the electrode based on the brain's electrical responses.

The procedural interaction requires the patient's coalition to adapt the electrode placement based on the observed brain activity, which is through sounds and waves yielded by the brain. Once the ideal site is corroborated, the permanent DBS electrode is inserted, and functionality examinations are conducted. These tests, lasting about 20 minutes, are essential for identifying any instantaneous adverse effects such as numbness or visual disturbances when the current is activated. After victorious testing, the electrode wire is embedded under the scalp, and the frame is removed. Subsequently, the pulse generator, which controls the stimulation, is entrenched under the skin near the clavicle, with a channel running internally under the neck and scalp to connect the system. Postoperative adjustments are vital to assure the system's operational effectiveness and patient safeness.

Regarding risks, DBS surgery carries a general complication rate of approximately 2-3% across both mental health and neurological applications [20]. The most typical surgical complications include depression and anxiety rebound, which can transpire if the neurostimulator turns off abruptly, often due to battery failure. Battery replacements are necessary for 6-16 months initially and an overall lifespan for 3-5 years on average, involve a simple outpatient procedure.

Moreover, the procedure may lead to serious side effects such as intracranial hemorrhage with a miniature chance of resulting in stroke, potentially leading to temporary or permanent neurological deficits depending on the severity of the bleed. The risk of infection stands at about 4%, which, if it occurs, requires the removal and possible reinstallation of the DBS system once the infection is controlled [21]. Temporary tissue swelling or edema near the electrode site is another potential postoperative complication. From a patient illness perspective, postoperative challenges may include insomnia, and personality or mood changes, normally resolving within 1-2 weeks. Other inordinary but noteworthy effects include weight gain, plight in finding words, and slurred speech. Notably, there is an elevated risk of suicide post-DBS surgery, accentuating the necessity for prudent monitoring and support [22].

5. Efficacy and Side Effects of DBS

5.1. Efficacy Evaluation

The success rate of Deep Brain Stimulation (DBS) in treating obsessive-compulsive disorder (OCD) around 60%, varies from different studies, as gauged by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). On average, patients experience a 53% reduction in Y-BOCS scores, decreasing from 28.3 at baseline to 13.3 at the last follow-up, demonstrating notable improvements in depressive symptoms, global functioning, and living standard [23]. Investigation from the University of Amsterdam signifies that brain stimulation also immensely reduces OCD-related depression and anxiety, with obsessions improving over days, and compulsions over weeks to months [24].

5.2. Side Effects and Long-Term Outcomes

DBS involves drilling a small hole in the skull to implant an electrode and a gadget under the upper chest, assuming conceivable risks and side effects. Surgical risks incorporate the possibility of puncturing a blood vessel, leading to hemorrhage in the brain and resulting in stroke or stroke-like symptoms such as sensory loss and muscle difficulties. Anesthesia may compel reactions such as breathing hardships and nausea. Hardware-related complications are also typical, comprising wound infection (1.7%), loss of effect (2.6%), lead malposition and/or migration (1.7%), component fracture (1.4%), and component malfunction (0.5%) [25].

Postoperative issues can include headaches, confusion, predicament in concentrating, temporary pain and swelling at the implantation site, and also hypotension (0.3%) [25]. DBS also carries a potential risk for intracerebral hemorrhage (ICH) (0.5%), asymptomatic intraventricular hemorrhage (3.4%), cerebral ischemia, seizures (0.3%), and infections, with most hemorrhages arise immediately postoperatively [25]; delayed hemorrhages are extraordinarily occasional. Long-term side effects include hardware discomfort (1.1%) and loss of desired effect (1.4%) [25]. After stimulation, patients may undergo numbness, tingling, muscle tightness, involuntary muscle contractions, and temporary worsening in speech and balance, alongside personality and mood changes.

One-year post-DBS, a significantly deduction in OCD symptoms is typically observed, with long-term follow-ups illustrating a sustained 39% reduction. Anxiety and depression decline by 48%-50% after one year. The World Health Organization Quality of Life Scale-Brief Version (WHOQOL-BREF) general score also shows striking advancement [26]. Unemployment rates ameliorate from 78% at baseline to 58% at the last follow-up, implying that DBS can enhance daily functioning and overall mental well-being, as a result, patient are able to improve their living standard after performing DBS surgery [26].

However, severe adverse events noted include one suicide attempt, which was associated to comorbid depression [26]. The battery life of the DBS system ranges from 3 to 5 years, requiring surgical replacement. While the DBS device can last several years and may improve symptoms for up to 10 years, comprehensive data on the longevity of the stimulator remains limited.

6. Comparison of DBS with Other Treatment Methods

6.1. Comparison with Pharmacotherapy

Selective serotonin reuptake inhibitors (SSRIs) and behavior therapy are suggested as first-line treatments for OCD. However, meta-analyses reveal that 40%–60% of patients do not respond effectively to these treatments [18]. Notably, around 10% of OCD patients are treatment refractory and remain severely impaired [8]. For those who respond to medication, common SSRIs like fluvoxamine (Luvox), paroxetine (Paxil), escitalopram (Lexapro), and venlafaxine (Effexor) can induce unfavorable effects such as insomnia, restlessness, and nausea. Clomipramine, a tricyclic antidepressant, may induce sedation, blood pressure issues, and irregular heartbeats, mandating supplementary monitoring in children and patients with heart disorders. DBS, contrariwise, can be

beneficial for patients resistant to both CBT and medication, potentially diminishing the demand for high doses of medication, minimizing side effects in medications, and enhancing mobility and independence, thus improving quality of life.

6.2. Comparison with Other Neuromodulation Techniques

Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Current Stimulation (tDCS) are non-invasive neuromodulation treatments. TMS, which uses a helmet with electromagnetic coils to stimulate the brain through the scalp, is FDA-approved for depression and OCD. TMS targets areas such as the dorsolateral prefrontal cortex, which are implicated in mood regulation and memory formation. Despite its benefits, TMS can cause headaches, facial twitching, scalp irritation, and, rarely, seizures. A significant drawback is its time-intensive nature, requiring nearly daily sessions over several weeks, with only about 30% of patient achieved remission [27].

tDCS involves passing feeble electrical currents through electrodes on the scalp to induce modifications in cortical activity. While tDCS has shown promise in reducing OCD symptoms, its overall efficacy remains inconclusive, and like TMS, it is time-consuming to achieve meaningful outcomes.

Ablation surgery, a more invasive and irreversible procedure compared to DBS, uses heat from lasers to disrupt electrical signals causing abnormal symptoms or seizures. It is effective in 60-70% of cases, achieving at least a 35% reduction in disease severity. However, potential complications include headaches (14.9%), cognitive deficit (9.1%), and brain edema or cysts (1.5%) [28].

Each treatment illustrates distinct advantages and limitations. While TMS offers a non-invasive approach with minimal threats, it requires extensive time commitment and targets only specific brain regions with a milder outcome. tDCS, though non-pharmacological, has not proven significantly effective for OCD. Ablation surgery and DBS show comparable mechanism and efficacy in treating refractory OCD, but the irreversible nature of ablation surgery necessitates attentive consideration of risks and benefits. Ultimately, patients must mull over these factors to select the most appropriate treatment option.

7. Challenges and Future Directions

7.1. Challenges in Research

A primary challenge in DBS research is the target of brain regions such as the Bed Nucleus of the Stria Terminalis (BNST) and Subthalamic Nucleus (STN). The mechanisms by which DBS of the BNST and STN alleviates OCD symptoms are not wholly comprehended. Additionally, patient selection criteria are stringent, requiring a history of failure with various types of antipsychotic drugs and numerous sessions of Exposure and Response Prevention (ERPs) without improvement. This restricts the potential patient pool significantly. Furthermore, DBS requires highly specialized skills and is performed in specific centers by multidisciplinary teams, including neurosurgeons additionally trained in functional neurosurgery, neurologists, and psychiatrists to assess patient suitability for DBS.

7.2. Future Development Directions

Future research should explore the mechanisms by which electrode implantation in targeted regions alleviates OCD symptoms, understand the side effects during treatment, and develop methods to mitigate them. Enhancing the success rate of DBS, currently at around 60%, is crucial [23]. Innovations could include the development of new electrode materials, such as conductive hydrogel coatings (CHs), or more precise imaging techniques like Electrode Shaft Modeling in CT images to better target brain regions.

The potential for combining DBS with other treatment methods offers promising avenues for research. Integrating DBS with behavioral therapies like Cognitive Behavioral Therapy (CBT) could enhance outcomes by addressing both neurophysiological and cognitive aspects of OCD. Although DBS can reduce brain overactivity, behavioral therapies help patients change their mindset and manage symptoms. Recent study has shown that adding CBT to DBS significantly reduces OCD symptoms, suggesting that a combined approach could be optimal for treating refractory OCD [29]. Further exploration is also warranted into combining DBS with medications to manage both chemical and electrical brain functions, potentially reducing the dosages required.

Moreover, DBS has shown varying effectiveness depending on the type of OCD symptoms. While effective for sexual/religious obsessions and compulsions, DBS might be less effective for symptoms related to perfectionism, symmetry, and ordering behaviors. Additional studies are needed to evaluate DBS's efficacy across these different symptom dimensions and potentially adjust targeting strategies accordingly.

8. Conclusion

DBS has emerged as a vital intervention for approximately one-third of OCD patients who do not respond effectively to standard treatments. This advanced therapeutic option directly influences neuronal activity, suppresses brain overactivity, and modulates neurotransmitter dysfunctions. According to recent research, DBS has demonstrated the capacity to significantly alleviate OCD-related depression and anxiety, achieving a success rate of around 60% as measured by reductions in the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS).

Internationally, countries like Austria and Canada are intensifying efforts to research and potentially integrate DBS into clinical practice for OCD, aiming to develop the therapeutic possibilities for manipulating this demanding ailment. In China, the implementation of DBS in clinical settings has been documented with a case involving a severe OCD patient who, after a decade of unsuccessful drug and psychological treatments, underwent DBS surgery showing only mild adverse effects.

DBS presents a promising treatment alternative for patients who have exhausted traditional therapeutic avenues. By targeting specific brain regions such as the NAcc, BNST, and STN, DBS modulates overactivity and mitigates symptoms effectively. However, despite its successes, DBS faces ongoing challenges and unanswered questions. The precise mechanisms by which DBS achieves its effects remain partially understood, and there is a continual need to enhance the accuracy of targeting through advanced imaging techniques. Furthermore, there is a pressing need for long-term studies to better understand the durability of DBS effects and to manage potential side effects more effectively.

As research progresses, future directions include the integration of DBS with behavioral therapies such as Cognitive Behavioral Therapy (CBT) and the exploration of new electrode materials and designs to improve outcomes and diminish side effects. The interdisciplinary approach, combining neurosurgical innovations with pharmacological and psychological therapies, holds the commitment of providing more comprehensive and permanent solutions for those suffering from refractory OCD.

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