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Deep brain stimulation for obsessive-compulsive disorder: past, present, and future

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Obsessive-compulsive disorder (OCD) is a psychiatric illness that can lead to chronic functional impairment. Some patients with severe, chronic OCD have been treated with ablative neurosurgical techniques over the past 4 decades. More recently, deep brain stimulation (DBS) has been investigated as a therapy for refractory OCD, and the procedure was granted a limited humanitarian device exemption by the FDA in 2009. In this article, the authors review the development of DBS for OCD, describe the current understanding of the pathophysiological mechanisms of the disorder and how the underlying neural circuits might be modulated by DBS, and discuss the clinical studies that provide evidence for the use of this evolving therapy. The authors conclude with suggestions for how a combined basic science and translational research approach could drive the understanding of the neural mechanisms underlying OCD as well as the clinical effectiveness of DBS in the setting of recalcitrant disease.
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Key Words • **deep brain stimulation** • **obsessive-compulsive disorder** • **psychiatric neurosurgery** • **ventral striatum** • **subthalamic nucleus**

Obsessive-compulsive disorder is a psychiatric illness in which intrusive thoughts or impulses (obsessions) generate anxiety that is relieved through the engagement in ritualistic or repetitive behaviors (compulsions). Obsessive-compulsive disorder is relatively common, with a lifetime prevalence of 2%–3% in the US.[63] Standard therapeutic options consist of selective serotonin reuptake inhibitors and cognitive behavioral therapy;[32] despite these interventions, however, 20%–40% of patients with OCD have persistent symptoms leading to chronic functional impairment.[58,64]

Over the past 4 decades, some patients with severe, refractory OCD have been treated with ablative neurosurgical techniques, including anterior capsulotomy[26] and cingulotomy.[15] Although the outcomes of these lesioning procedures have been variable,[42] most reports reflect a meaningful improvement in 30%–70% of patients,[26,51] thereby offering a valuable option to debilitated patients with OCD who have exhausted less invasive therapeutic measures.

For the past 2 decades, DBS has been validated as an alternative to lesional neurosurgery for movement disorders such as PD, dystonia, and essential tremor. Since the first report in 1999 by Nuttin and colleagues,[56] DBS has also been investigated in the treatment of refractory OCD. Deep brain stimulation has certain advantages over lesional surgery, offering an adjustable, nondestructive (and reversible) means for neuromodulation. In addition, clinical studies in which DBS is used can include "on" and "off" phases, facilitating blinding and crossover designs.

Clinical studies targeting a variety of neural structures in patients with OCD have suggested that DBS may yield a therapeutic benefit comparable to that derived from ablative techniques.[43,56] In 2009, the FDA granted a limited humanitarian device exemption for using DBS in the setting of intractable OCD. This was the first such approval for a psychiatric disorder. Although the precise role that DBS will play in treating OCD has yet to be established, 4 centers—including our own—are now collaborating in a National Institute of Mental Health–supported trial to explore this issue (see www.ClinicalTrials.gov: NCT00640133). The following review offers a brief summary of the current state of DBS for OCD as well as perspective on the scientific and clinical frontiers of this evolving therapy.

Abbreviations used in this paper: ACC = anterior cingulate cortex; ALIC = anterior limb of the internal capsule; CSTC = cortical-striato-thalamo-cortical; DBS = deep brain stimulation; ITP = inferior thalamic peduncle; NAc = nucleus accumbens; OCD = obsessive-compulsive disorder; OFC = orbitofrontal cortex; PD = Parkinson disease; PFC = prefrontal cortex; STN = subthalamic nucleus; VC = ventral capsule; VS = ventral striatum; Y-BOCS = Yale-Brown Obsessive-Compulsive Scale.

Historical Perspective

The use of chronic electrical stimulation as a treatment for psychiatric disorders mainly developed as an extension of ablative procedures, although brain stimulation has been used in neurosurgery for some time. In the 1930s and 1940s, Wilder Penfield and Herbert Jasper developed the Montreal procedure, a technique in which they applied acute electrical stimulation to the brains of patients with epilepsy to map the functions of regions in the neighborhood of planned resections.[59] Pool[62] may have been the first to use chronic stimulation for the treatment of a psychiatric condition when he stimulated the caudate nucleus in an attempt to cure depression and anorexia. Modern DBS, however, is rooted in ablative procedures. The transition from ablative procedures to DBS has been possible because the effects of chronic stimulation can be similar to those of ablation in certain cases.[48]

Egas Moniz was an early pioneer of ablative psychiatric neurosurgery, earning the 1949 Nobel Prize in Physiology or Medicine for the development of the prefrontal leukotomy. Walter Freeman, who was not a neurosurgeon, popularized a crude version of the technique, performing more than 3000 lobotomies during the 1940s and early 1950s. Lobotomies severed the connections of the frontal cortex, rendering many patients apathetic and abulic. The typical outcome was that the illness became easier to manage in patients with problematic mental health issues, but concerns grew over the ethical implications of indiscriminate application of a crude surgical procedure to the mentally ill. Lobotomies ultimately fell into disfavor after the introduction of effective oral medications such as chlorprozamine. The creation of an unfortunate group of lobotomy patients with severe and irreversible lesions led to a backlash against surgical interventions for psychiatric disorders.

Subsequent development of ablative neurosurgical procedures attempted to limit side effects by reducing lesion size. The anterior capsulotomy was introduced by Talairach and Leksell in 1949 to disrupt fibers linking the PFC and ACC to the thalamus.[40] Disruption of these cortical-thalamic connections at a different location was the goal of the subcaudate tractotomy, first performed by Knight[38] in the mid-1960s. Around the same time, the cingulotomy procedure was developed to target the ACC and underlying cingulum bundle.[8] The limbic leukotomy, a combination of both the cingulotomy and subcaudate tractotomy, was introduced in the early 1970s for patients who failed to respond to cingulotomy alone.[37] These lesioning procedures have provided significant benefit to thousands of treatment-resistant OCD patients over 4 decades, and are still in use today.[15,27]

The success of modern DBS for movement disorders and the demonstrated efficacy of lesional surgery for OCD paved the way for the extension of DBS to psychiatric disorders. The current era of using DBS in the setting of psychiatric illness began in 1999 when Nuttin and colleagues[56] used DBS to treat intractable OCD, with targeting informed by experience with the anterior capsulotomy. By that time, however, there were already indications that DBS could have psychiatric effects, including numerous reports of psychiatric effects among DBS-treated patients with PD. Deep brain stimulation held appeal for several reasons, one of which was that its theoretical reversibility offered to mitigate the risks associated with permanent lesions. Despite such advantages and an apparent efficacy comparable to ablative techniques, DBS for OCD has yet to be adopted widely, and there remain relatively few published cases in the literature more than a decade after its first introduction.

Ongoing studies of DBS for OCD focus on both patient selection and the refinement of stimulation sites to target specific dimensions of this complex disorder. Focal stimulation is expected to modulate some, but not all, disease elements. Current research is guided by the premise that the coupling of a thorough understanding of the brain circuitry underlying a psychiatric disease such as OCD with a deconstruction of the illness into clusters of pathological components will yield more effective and targeted interventions.[12,13] If patients are selected according to their unique clusters of symptoms (which presumably correspond to homogeneous pathophysiological patterns), then stimulation perhaps could be tailored for specific disease manifestations, thereby improving the probability of achieving meaningful clinical benefit.

Mechanisms of OCD

The pathophysiological basis of OCD appears to involve abnormal functioning in CSTC brain circuits that involve ventral-mesial PFC, dorsal ACC, OFC, and their associated basal ganglia and thalamic connections.[12] Looped CSTC circuits subserve a diversity of physiological functions,[3] and pathological activity in these loops might form the basis for OCD.[53] Frontal lobe and basal ganglia abnormalities have been observed among OCD patients,[25,66] and the fibers linking these regions traverse the ALIC, which is the site of anterior capsulotomy lesions. Dysregulation of neurotransmitters, including dopamine[76] and serotonin,[30,57,79] may also play an important role.

Neuroimaging has provided a revealing window into the neural circuitry underlying OCD. Hyperactivity is frequently observed in CSTC circuits (especially in the OFC and caudate nucleus) in OCD patients, and this hyperactivity can be magnified by provocation of OCD symptoms.[49,66,71] Some studies point to differences in the volumes of CSTC structures between patients with OCD and control volunteers.[33,68] Additionally, the white matter tracts linking putative CSTC nodes may be abnormal; a diffusion tensor imaging study found differences in the cingulum bundles and ALICs of patients with OCD compared with non-OCD controls.[11]

Nonhuman primate studies can tell us a great deal about fine-grained mechanisms of decision-making and reward processing, which could in turn help us understand the pathophysiological origins of OCD. Animal research suggests, for example, that the OFC manages satiety mechanisms.[69] These mechanisms dictate that rewarding actions are performed until a feeling of "fullness" is achieved. This basic process appears to be disrupted in some OCD subtypes,[60] possibly explaining why such patients develop compulsions.

The mechanisms by which DBS relieves OCD symptoms are largely unknown. Complicating the issue, distinct DBS-mediated effects evolve on different time scales, and patients have dynamic clinical trajectories. Comorbid depressive symptoms, for instance, appear to improve relatively quickly,[73] whereas the OCD symptoms themselves tend to lessen over weeks or months.[23] Everitt and Robbins[17] recently proposed a neural mechanism for drug addiction in which the transition from voluntary to habitual and compulsive drug use involves a transfer of control from PFC to striatal regions as well as a progression from ventral to more dorsal domains of the striatum. One possible mechanism of action of DBS may be to perturb the balance between cortical and subcortical influences on behavior.[28] In this scenario, exogenous stimulation may reverse the established pathological balance, ultimately leading to a transfer of behavioral control from the striatum back to PFC regions. This putative mechanism generates hypotheses that can be tested with functional neuroimaging or animal studies. Such a mechanism would agree with the known time course of the effects of DBS on OCD symptoms. It would also support the observation that patients who are treated with DBS become more receptive to standard behavioral therapies, having a heightened ability to choose new courses of action in familiar situations.[50]

Patient Considerations

Ethical objections have been raised regarding the application of neurosurgery to psychiatric illnesses, with critics often citing the notorious legacy of indiscriminate psychosurgery prior to the stereotactic era, as well as the concern over inappropriate behavioral modification or control. Although modern psychiatric neurosurgery in no way resembles the transorbital lobotomies of yesteryear, these concerns nonetheless merit cautious consideration.

Currently adopted standards for patient selection for psychiatric surgery originate from interactions between physicians and the US Congress in the late 1970s. To allay fears about the inappropriate use of psychiatric surgery, a congressional commission was formed to evaluate the indications for surgery and the criteria for patient selection. Their report[54] was the basis for guidelines surrounding the practice of psychiatric surgery that were adopted by centers performing such procedures, including ours.[16] These guidelines are summarized in Table 1, and are reflected in the inclusion and exclusion criteria of recent clinical trials. Paramount among these is involvement of a multidisciplinary team consisting of psychiatrists, neurologists, psychologists, and neurosurgeons.[14] Participation of such a team increases the likelihood that the often complicated psychiatric and medical histories of candidate patients are properly considered. The expertise of these specialists is also essential in the postoperative period as the patient is adjusting to unaccustomed changes in mood and behavior.

With respect to outcome measures, the most commonly invoked metric of efficacy is a reduction in the Y-BOCS[21] score. The Y-BOCS is a 10-item scale in which higher scores reflect more intense symptoms, and a score

TABLE 1: Guidelines for psychiatric neurosurgery based on the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Patient Selection	Evidence for OCD Intractability	Exclusion Criteria
patient should be referred to the psychiatric neurosurgery team by his/her primary psychiatrist, who should also be willing to resume psychiatric care of the patient postop	pharmacotherapy evidence for reasonable exhaustion of drugs & drug combinations acceptable doses checked by plasma levels where indicated	personality disorder, especially antisocial or borderline behavior primary substance abuse evidence of lack of reliability or compliance
decision for candidacy should be made by a multidisciplinary team composed of: qualified psychiatrist, neurologist, & neurosurgeon for patient evaluation qualified psychologist for psychometric testing	reasons for failure include lack of response, intolerance, or severe side effects individual psychotherapy group, couples, & family psychotherapy cognitive & behavioral therapy electroconvulsive therapy	unwillingness to continue medications or psychiatric evaluation postop lack of personal support systems, including family or friends
the psychiatrist & neurologist should not be primarily involved in the care of patient being evaluated	chronicity & disability illness should be of sufficient duration to permit spontaneous remission & completion of the above treatment protocols	
unanimous approval should be obtained before proceeding w/ op		

of 24 or more (of a possible 40) is considered "severe" illness. Most studies designate a therapeutic response as a Y-BOCS reduction of 35% or more from the pretreatment baseline. Some studies also report reductions of 25% or more (partial responses), which indeed can represent meaningful improvements in certain patients.

Current Targets

After a decade of small studies and case series, the application of DBS to treatment-resistant OCD remains investigational. Clinicians have used a wide variety of paradigms for selecting DBS in the treatment of OCD, giving rise to heterogeneities in patient selection, neural targeting, and stimulation protocols that preclude a rigorous meta-analysis. The following material outlines the theoretical basis and clinical outcomes for 3 DBS target regions. Table 2 offers a summary of the outcome studies published to date.

Target 1: the ALIC and VC/VS

In the first cases of DBS for OCD,[56] the site of lead implantation was based on experience with the anterior capsulotomy, a lesioning technique shown to be successful in reducing symptom severity in roughly one-half of cases.[52] In subsequent years, DBS has been applied at several loci along the rostral-caudal dimension of the ALIC. Studies have been performed to interrogate the effects of stimulating not only this VC territory but also the adjacent VS, which in turn contains the NAc. This region is often referred to as the VC/VS.

Greenberg and colleagues[23] recently reviewed outcomes from 4 centers in which the VC/VS target is used. As had been previously suggested with thermocapsulotomies and Gamma Knife capsulotomies, response rates improved as the target was shifted posteriorly, to within a millimeter of the posterior border of the anterior commissure.[41] This migration of the target site reduced the stimulation energies required for eliciting a clinical response, possibly because the fiber bundle being targeted grows more compact as it courses posteriorly.[65] The refinement in target selection was attended by an increase in the percentage of patients manifesting ≥ 35% reductions in Y-BOCS scores (from 33% to 75%). In the dorsal-ventral dimension, the most distal of the 4 contacts (contact 0) was in the VS, 3–4 mm ventral to the anterior commissure-posterior commissure line, and the next most distal contact (Contact 1) was in the VC, just dorsal to the anterior commissure–posterior commissure line. Contacts 2 and 3 were in the middle and dorsal aspect of the capsule, respectively. The observation that the 2 ventral-most contacts were chosen most often for chronic stimulation[20] further suggests that the optimal location spans the most ventral region of the capsule and the VS itself, which animal model data[77] and neuroimaging studies[74] have also suggested might hold therapeutic potential. We and others are currently involved in a clinical trial in which we are using an electrode with more compactly spaced contacts, all within this more ventral region (Fig. 1).

Citing the role of the NAc in modulating the neural circuit presumed to be dysfunctional in OCD (as reviewed by Nicola[55]), Sturm and colleagues[74] advocated stimulation of the NAc shell in OCD. They conducted a small pilot study showing that DBS of the right NAc yielded

TABLE 2: Literature review of outcomes studies after DBS for OCD*

Authors & Year	No. of Patients	Target	% Responders (ΔY-BOCS Score) ≥35%	% Responders (ΔY-BOCS Score) ≥25%	FU (mos)
Mallet et al., 2002	2	STN	100	100	6
Anderson & Ahmed, 2003	1	ALIC	+	+	3
Sturm et al., 2003	4	rt NAc	75	NA	30–34
Aouizerate et al., 2004	1	ventral Cd	+	+	15
Fontaine et al., 2004	1	STN	+	+	6
Abelson et al., 2005†	4	ALIC	50	50	10
Jiménez et al., 2007†	1	ITP	+	+	18
Mallet et al., 2008†	16	STN	NA	75	3
Plewnia et al., 2008	1	rt ALIC/NAc	–	+	24
Aouizerate et al., 2009	2	VS	100	100	15
Jiménez-Ponce et al., 2009	5	ITP	100	100	12
Huff et al., 2010†	10	rt NAc	10	50	12
Goodman et al., 2010†	6	VC/VS	67	67	12
Greenberg et al., 2010‡	26	VC/VS	62	73	3–36

* The outcomes of single case reports are indicated with either a "+" for positive response or "–" for lack thereof. A therapeutic response is represented by a score of ≥ 35%; partial response by a score of ≥ 25%. Abbreviations: Cd = caudate; FU = follow-up; NA = not applicable; Δ = change.

† Study invoked a double-blind sham-stimulation crossover design.

‡ See reference 23. Reflects results compiled for patients from other studies (Nuttin et al., 1999; Goodman et al., 2010; Cosyns et al., 2003; Nuttin et al., 2003; and Gabriels et al., 2003).

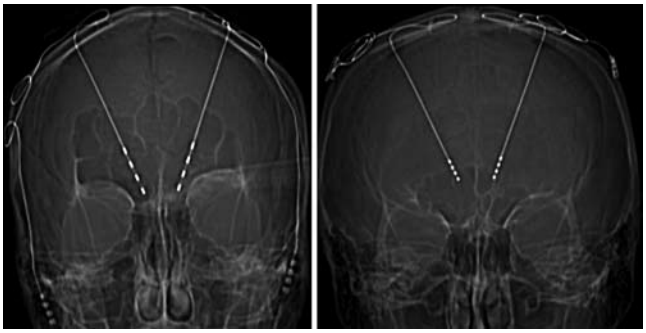

Fig. 1. Neuroimages demonstrating evolution in targeting of the VC/VS target. **Left:** In recent studies an electrode design with 3-mm leads spaced 4 mm apart (Medtronic model 3391; previously referred to as model 3387IES in 2010 articles by Goodman et al. and Greenberg et al.) was used to span the entirety of the ALIC and VS, paralleling the targeted region in the capsulotomy experience. **Right:** In the current study of the VC/VS target, an electrode with 1.5-mm contacts spaced 1.5 mm apart (Medtronic model 3387) was used. This more compact design places all the contacts within the VS and ventral-most region of the capsule.

clinical improvement and that bilateral stimulation offered no additional benefit. One precedent for this laterality of responsiveness was a previous report that right-sided lesions in the midsection of the ALIC were critical to therapeutic outcome in patients who underwent thermocapsulotomy.[41] Of 4 patients who received DBS of the shell of the right NAc, 3 achieved near complete recoveries over 2 years. However, this efficacy was not borne out subsequently in a larger series of patients;[31] in this recent study, only 1 of 10 patients manifested a Y-BOCS score reduction of 35% or more. Thus, the evidence at present favors a bilateral VC/VS implantation.

The most worrisome stimulation-associated adverse events in the preceding studies were hypomania and suicidal ideation. Hypomania has generally been transient and reversible; it also appears to be dependent on stimulation intensity.[22] Suicidal ideation has also been observed among patients with OCD who are receiving DBS, and 1 patient in a series reported by Abelson et al.[1] committed suicide during the open stimulation period (although she left a note absolving her study participation and response to DBS as motivating factors). It is important to note that the suicide rate among patients with severe depression, which frequently accompanies intractable OCD, is as high as 15%. These sobering findings underscore the importance of careful screening of DBS candidates by a multidisciplinary team.

Target 2: the STN

The STN has emerged as a possible node for modulating OCD circuitry following observations that DBS of the STN in patients with PD ameliorates obsessive-compulsive traits[2] and also reduces Y-BOCS scores in those with OCD.[18,43] Additional studies have demonstrated the capacity of STN stimulation to attenuate repetitive behaviors[7] and anxiety[29] as well as to interfere with decision-deferring processes.[19] Anatomically, the ventral anteromedial STN receives limbic and associative cortical input via CSTC circuits originating in the OFC.[36] These lines of evidence point to a role for the STN in behavioral integration.[45] Given the neurosurgical community's extensive experience with DBS of the STN for PD, this structure would thus seem to be an appealing target for OCD neuromodulation.

In 2008, Mallet et al.[44] reported the results of a crossover, double-blinded trial of STN DBS in 18 patients with OCD. These investigators targeted the anteromedial STN at the boundary of the limbic and associative territories; the center of this region lies approximately 2 mm anterior and 1 mm medial to the target used for patients with PD.[10] Stimulation resulted in Y-BOCS score reductions of 25% or more in 75% of study subjects, but there were several serious adverse events, including 1 intracerebral hemorrhage, 2 infections requiring electrode removal, and 3 cases of transient, stimulation-induced hypomania. The authors point out, however, that the number of surgery-related complications was similar to rates previously reported,[39,67] and that the stimulation-associated adverse events largely consisted of motor or psychiatric symptoms that resolved either spontaneously or promptly with adjustment of stimulator settings.

Target 3: the ITP

The ITP is a white matter bundle that has been evaluated for DBS implantation in OCD. This structure links the OFC and thalamus, and it also corresponds to part of the territory targeted by the subcaudate tractotomy.[72] Electrical stimulation of the ITP could mitigate OCD symptoms via effects propagated along the swath of OFC and ventromedial striatum projections entering the thalamus. In addition, the relative compactness of the ITP offers the theoretical advantage of reducing the charge density needed to mediate a clinical response, which could lengthen battery life.

Clinical investigation of DBS of the ITP has been reported by only one group. Jiménez-Ponce and colleagues[35] stimulated the ITP bilaterally, noting Y-BOCS score reductions of at least 35% as well as dramatic global assessment of function increases in 5 of 5 patients with OCD. This was an open series, however, and the inclusion criteria were not as stringent as in other studies (1 patient had a schizoid personality disorder and 3 were illicit drug abusers). The effects of these factors on the reported outcomes are unclear.

The potential utility of stimulating the ITP remains unsettled. The trajectories of all DBS leads in the Jiménez-Ponce[35] study traversed the anterior horn of the lateral ventricle. Recent reports have suggested that a transventricular trajectory incurs increased risk of hemorrhage[9] and reduces targeting accuracy.[81] The ITP trajectories avoiding the ventricles, if feasible, would be preferred. Also, although the authors describe and reference a method for identifying the ITP by using electrocortical recruiting responses,[78] the ITP is a small target not commonly localized by using standard microelectrode recordings. Larger series and additional experience will perhaps shed light on these issues.

Future Directions

Deep brain stimulation for psychiatric disorders is

in its infancy, especially when compared with its use for movement disorders. The nearly routine use of DBS for PD ensures that the coming generation of neurosurgeons will be well versed in the technique, most metropolitan areas will have the capability, and a rapidly growing proportion of the American public will be intimately familiar with the ameliorative effects of well-placed high-frequency stimulators within the brain for certain disorders.

As with PD, we predict that the use of DBS for OCD will contribute greatly to the scientific understanding of complex brain disorders. Our understanding of OCD is likely to benefit even more from experience with patients receiving DBS than has our understanding of PD, because there is currently no standard animal model of OCD, making the observational data obtained in patients with this disease especially valuable. Obsessive-compulsive disorder might prove to be a uniquely human condition, involving an imbalance in an elaborate human ability to assess uncertainty and to predict negative outcomes that is beyond the capacity of our nearest evolutionary relatives. It is our belief, however, that animal studies—particularly studies of awake, behaving nonhuman primates engaged in cognitively demanding tasks—will figure prominently in the near-term growth of understanding of psychiatric disorders and will set the stage for optimally targeted, effective, and individualized treatment of human patients with specific subtypes of OCD.

One experimental approach would be to begin by identifying differences between patients with OCD and healthy volunteers in their performance of various decision-making tasks. Primates could then be trained to perform similar tasks, while physiological recordings interrogate the role of various regions in the circuit implicated in OCD.[12] In our current research, we are exploring the abnormally high sensitivity to potentially aversive outcomes in OCD by training animals to perform a task in which they must weigh combined aversive and rewarding stimuli. Knowledge of the neural circuitry of OCD suggests that the OFC, basal ganglia, and thalamic targets might mediate this decision-conflict paradigm, because patients with OCD perform this task abnormally.

Once the relevant dimensions of OCD's pathological features can be identified and instantiated into a task suitable to nonhuman primates, one could then systematically explore both the parameter space and the effects of stimulation in ways that are impractical with human subjects. For example, in recent DBS studies investigators have observed improvements in patient outcomes with posterior migration of the stimulation site.[20,23] Nonhuman primate research could more quickly ascertain the effects of small, systematic refinements in the location of DBS leads.

We predict that the next major advancement in the field will result from research on how target selection could differentially mitigate symptoms of different OCD subtypes. Evidence suggests that such subtypes have origins in distinct neural circuits.[47,70] Furthermore, stimulation of individual circuits yields distinct patterns of clinical effects. For example, Aouizerate and colleagues[5] reported that caudate nucleus stimulation preferentially alleviates OCD manifestations, whereas NAc stimulation tends to improve depressive symptoms. It has also been suggested that VC/VS DBS preferentially benefits patients in whom OCD symptoms are motivated principally by a feared consequence rather than a feeling of incompleteness.[24] If the effects of stimulating different targets can be well characterized, DBS lead placement might someday be personalized based on an individual's disease manifestations.

An interesting possibility is that DBS may indirectly benefit patients with OCD by reducing symptom severity sufficiently to allow engagement in other forms of therapy. This phenomenon has been described after capsulotomy.[50] For clinical research purposes, we must first clarify the impact of DBS on OCD in isolation, but in the near future it will be important to integrate DBS treatments successfully with both cognitive behavioral therapy and modifications in pharmacotherapy.

Conclusions

Deep brain stimulation is a promising therapy for intractable OCD. Future refinements may include the development of a demand-controlled rather than an open loop stimulator.[75] This type of device could responsively apply stimulation when necessary, potentially providing greater behavioral control, reducing side effects, and extending battery life. Indeed, our understanding of the underlying mechanisms obtained through experience with DBS may even lead to completely novel and individualized approaches. Light-activated manipulation of neural circuits may allow specific activation or suppression of certain cell types.[80] Genetic material introduced into specific dysfunctional targets may permit beneficial modification of their function.[46] Harnessing emerging technologies such as optogenetics, gene therapy, and others will probably revolutionize the treatment of neurological and psychiatric disease, so that DBS might prove to be a stepping-stone to even more precise treatments in the future. Regardless of the device or technology used to treat patients with intractable OCD, however, it is important to note that these are highly complex and fragile patients. To ensure that past mistakes are not repeated, the care of these patients should be managed by a multidisciplinary team, adhering to accepted guidelines.

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