Deep brain stimulation (DBS) is an effective surgical treatment for medication-refractory hypokinetic and hyperkinetic movement disorders, and it is being explored for a variety of other neurological and psychiatric movement diseases. Deep brain stimulation has been Food and Drug Administration–approved for essential tremor and Parkinson disease and has a humanitarian device exemption for dystonia and obsessive-compulsive disorder. Neurostimulation is the fruit of decades of both technical and scientific advances in the field of basic neuroscience and functional neurosurgery. Despite the clinical success of DBS, the therapeutic mechanism of DBS remains under debate. Our objective is to provide a comprehensive review of DBS focusing on movement disorders, including the historical evolution of the technique, applications and outcomes with an overview of the most pertinent literature, current views on mechanisms of stimulation, and description of hardware and programming techniques. We conclude with a discussion of future developments in neurostimulation.

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Deep brain stimulation (DBS) has evolved as an important therapy for the treatment of essential tremor, Parkinson disease (PD), and dystonia, and it is also emerging for the treatment of medication-refractory psychiatric disease. Food and Drug Administration approval was granted in 1997 for thalamic DBS for essential tremor and PD-related tremor, followed in 2003 by approval for subthalamic nucleus (STN) and globus pallidus internus (GPI) DBS for PD. A humanitarian device exemption for STN DBS and GPI DBS for primary generalized and segmental dystonia was granted in 2003 and for obsessive-compulsive disorder, in 2009. Deep brain stimulation has also been used successfully in the treatment of Tourette syndrome, depression, and epilepsy, and there are case reports of using DBS for the treatment of headache, pain, vegetative state, addiction, obesity, dementia, and stroke recovery. New applications continue to emerge, encouraged by past successes and the fact that DBS effects are reversible allowing exploration of new targets and applications not previously possible with lesion surgery. The history of DBS is a fascinating example of the interplay between basic and clinical research. It is the coming together of these 2 arenas that has led to the evolution of DBS for the treatment of disease as it is used today and will be used tomorrow. Table 1 summarizes milestones in the evolution of surgical therapy for movement disorders.

CURRENT APPLICATIONS AND OUTCOMES

Tremor

Deep brain stimulation is an attractive alternative to surgery for the management of tremor. Surgical ablation of the ventral intermediate nucleus of the thalamus has been used as a therapy for tremor since the 1950s. However, bilateral thalamotomy is not well tolerated because of the risk of...
speech and swallowing deficits. Thalamic DBS has been shown to be efficacious in the treatment of essential and parkinsonian tremor, with excellent long-term outcomes and an acceptable adverse effect profile (Table 2). The main adverse effects of the stimulation are paresthesias, headache, dysthria, paresis, gait disturbance, and ataxia.40 Adverse effects are usually mild and effectively managed by stimulation parameter adjustment. Deep brain stimulation and thalamotomy have also been used with less success in the treatment of action tremor. This type of tremor typically occurs in patients with multiple sclerosis, trauma, or stroke that leads to interruption of cerebellar outflow pathways and has a more complex pathophysiology.31 Clinical improvement in these patients is often short lived and, in the case of multiple sclerosis, complicated by disease progression.42,43 Although treatment for tremor targets the ventral intermediate nucleus, several studies have suggested that the posterior subthalamic area is a better location and that patients may be incidentally benefiting from electrode contacts located outside of the thalamus.44 Overall, DBS for essential and parkinsonian tremor has been successful, while treatment of other causes of tremor has been more limited.

Table 1. Evolution of Surgical Therapy for Movement Disorders

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
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<tbody>
<tr>
<td>1890</td>
<td>Horsley6 performed extirpation of the motor cortex for treatment of athetosis.</td>
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<tr>
<td>1947</td>
<td>Spiegel et al8 described a stereotactic frame.</td>
</tr>
<tr>
<td>1950</td>
<td>Spiegel et al8 made lesions in patients with PD to interrupt pallidofugal fibers causing improvement in bradykinesia, rigidity, and tremor.</td>
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<tr>
<td>1950s</td>
<td>Hassler and Riechter4 and Talairach et al39 treated parkinsonism with lesions in the VL thalamic nucleus.</td>
</tr>
<tr>
<td>1963</td>
<td>Albe Fessard et al11 reported that stimulation in the area of the ventromedial nucleus of the thalamus at frequencies of 100-200 Hz improved tremor in patients with parkinsonism.</td>
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<tr>
<td>1969</td>
<td>Levodopa was introduced, parkinsonian symptoms were improved, and stereotactic surgery fell out of favor.12</td>
</tr>
<tr>
<td>1989-1990</td>
<td>Albin et al14 and DeLong15 introduced a model of basal ganglia function based on the hypothesis that there were segregated circuits within the basal ganglia, functional motor and sensory function.</td>
</tr>
<tr>
<td>1992</td>
<td>Laitinen and colleagues16 reintroduced the Leksell pallidotomy technique for patients with advanced PD along with severe adverse effects from levodopa therapy.</td>
</tr>
<tr>
<td>1998</td>
<td>Documentation of safety and efficacy of bilateral STN DBS by Limousin et al17, including its potential for reducing the dose of dopaminergic medications in patients with advanced PD.</td>
</tr>
<tr>
<td>2000</td>
<td>Coubes et al18 presented data for GPi DBS in treatment of dystonia.</td>
</tr>
</tbody>
</table>

Abbreviations: DBS, deep brain stimulation; GPi, globus pallidus internus; PD, Parkinson disease; STN, subthalamic nucleus; VL, ventrolateral.

Parkinson Disease

One of the primary clinical uses of DBS is for the treatment of PD. A robust motor response to levodopa is generally considered a prerequisite for successful DBS outcome in PD (except for tremor-predominant PD), and stimulation may be considered once patients develop disabling motor fluctuations and dyskinesias while receiving medical therapy. Although thalamic stimulation has been effective in controlling parkinsonian tremor, the lack of a reliable effect on other motor symptoms has limited thalamic DBS for the treatment of PD.33,40 Today, the STN and GPi are the most commonly used targets in PD.20,21 Electrode placement in the STN was initially favored because of reports that it yielded greater improvement in motor scores and a greater reduction in antiparkinsonian medications compared with placement in the GPi.27,47 Additional studies have shown that GPi DBS also significantly improved the cardinal motor symptoms, drug-induced dyskinesia, and motor fluctuations.32,44,46,48 Although STN remains the preferred target, GPi can be considered in patients who have speech, cognitive, and mood disturbances, as STN DBS can sometimes worsen these symptoms.32,39 Studies of DBS for PD have reported significant improvement in cardinal motor signs, including tremor, bradykinesia, and rigidity, with variable response in medication-refractory gait freezing, postural instability, and gait mechanics (Table 2). Marked benefits in improvement of levodopa-related complications such as drug-induced dyskinesia, motor fluctuations, and off-period dystonia have also been demonstrated.29 Adverse effects are typically transient and reversible.17,39 Additional limitations of DBS therapy that need to be considered prior to surgery include risk of hemorrhage or infection, risk of mechanical failure (now much less common as both physicians and manufacturers develop more familiarity with the device), frequent follow-up visits, and cost of the device and battery replacements.

Dystonia

Deep brain stimulation has also been useful for treatment of primary dystonia. Renewed interest in pallidotomy for PD in the early 1990s and the observation that it improved dystonic symptoms in PD led to the proposal of using pallidotomy for patients with primary generalized dystonia.46,49 Given concerns about bilateral GPi lesions causing speech and cognitive deficits as seen in PD, it was not long before GPi DBS was being explored for the treatment of primary generalized dystonia, sometimes with remarkable outcomes.18,25,50,51 Unlike tremor and PD, there is typically a gradually increasing clinical response to stimulation over weeks to months of therapy. Efficacy of DBS in primary generalized and segmental dystonia has been well documented39 (Table 2). There has been no difference in outcomes based on DYT1 gene status,31 but shorter disease duration has been reported to lead to better results.22,23 Intractable cervical dystonia has also shown improvement in several smaller case series.27 Secondary dystonia is a set of heterogeneous disorders, and their response to stimulation is more vari-
Tardive dyskinesias typically respond well, whereas dystonias due to encephalitis and birth injury fare worse.

### MECHANISMS OF DBS

Although an effective surgical therapy for medication-refractory hypokinetic and hyperkinetic movement disorders, the mechanism of action underlying the therapeutic effectiveness of DBS continues to be debated.

The earliest hypotheses on DBS mechanisms attempted to reconcile the similarity in clinical outcome after a lesion and during DBS by proposing that high-frequency stimulation inhibited neurons and decreased output from the stimulated site. Inhibition of activity was initially observed in rat STN DBS, and similar findings

<table>
<thead>
<tr>
<th>Year</th>
<th>Tremor</th>
<th>PD</th>
<th>Dystonia</th>
</tr>
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<tbody>
<tr>
<td>1987</td>
<td>Vim DBS decreased tremor almost as well as thalamotomy. Optimal stimulation frequency was about 200 Hz but stimulator capabilities were limited to 130 Hz at the time.</td>
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<tr>
<td>1991</td>
<td>Bilateral Vim stimulation was well tolerated and resulted in complete or almost complete tremor suppression in PD and ET.</td>
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<td>1993</td>
<td>First report of STN DBS in a patient with PD.</td>
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<tr>
<td>1994</td>
<td>First use of GPi DBS in PD.</td>
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<tr>
<td>1998</td>
<td>First open-label trial of bilateral STN DBS showing about 60% improvements in motor scores and dyskinesias.</td>
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<tr>
<td>1999</td>
<td>Randomized comparison of STN and GPi DBS showed similar improvement in both groups.</td>
<td></td>
<td>First case report of GPi DBS for dystonia resulting in a dramatic improvement.</td>
</tr>
<tr>
<td>2000</td>
<td>Vim DBS provided long-term efficacy in ET, but device-related complications were common.</td>
<td>In a large prospective, double-blind study, STN DBS was associated with greater benefit compared with GPi DBS (49% vs 37% motor score reduction); however, target sites were not randomized.</td>
<td>GPi DBS was effective in treating DYT1 primary generalized dystonia.</td>
</tr>
<tr>
<td>2001</td>
<td>Multicenter trial showing persistent suppression (approximately 50%) at 6 y in patients with essential tremor with Vim DBS.</td>
<td>First long-term follow-up study of STN DBS showing about 50% improvement in motor and activities of daily living scores at 5 y.</td>
<td>First blinded evaluation of STN DBS yielded similar results.</td>
</tr>
<tr>
<td>2003</td>
<td>In a large prospective, double-blind study, STN DBS was associated with greater benefit compared with GPi DBS (49% vs 37% motor score reduction); however, target sites were not randomized.</td>
<td>In a small study, GPi DBS effectively treated generalized non-DYT1 dystonia.</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>Efficacy of GPi DBS was equal in DYT1-positive and DYT1-negative patients, but improvement was greater in children than adults.</td>
<td>Randomized, blinded study showed both STN and GPi DBS provided similar motor improvement, but cognitive and behavioral complications were seen only in STN DBS.</td>
<td>Double-blinded evaluation of GPi DBS resulted in about 50% improvement in dystonia score.</td>
</tr>
<tr>
<td>2006</td>
<td>First randomized comparison demonstrating superiority of STN DBS over medical management in patients with advanced PD and levodopa-related motor complications.</td>
<td>First randomized, double-blind, sham-controlled trial of GPi DBS in primary segmental or generalized dystonia.</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>Single-blind study of GPi DBS in cervical dystonia resulted in about 40% improvement.</td>
<td>Randomized trial showing no major differences in mood and cognition between STN and GPi DBS.</td>
<td>GPI DBS had variable effect on dystonia-choreoathetosis in cerebral palsy.</td>
</tr>
<tr>
<td>2009</td>
<td>Large randomized study of STN vs GPi DBS showed both targets provided similar improvement in motor function (25% and 28%, respectively), but smaller than seen in other studies.</td>
<td></td>
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<tr>
<td>2010</td>
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</table>

Abbreviations: DBS, deep brain stimulation; ET, essential tremor; GPi, globus pallidus internus; PD, Parkinson disease; STN, subthalamic nucleus; Vim, ventral intermediate nucleus.
were replicated in humans and monkeys with either STN or GPi stimulation. Activation of presynaptic inhibitory afferents to the stimulated site was hypothesized to be the underlying mechanism for the observed inhibition. One study on thalamic DBS has shown that thalamic neurons that receive predominantly excitatory afferents can be excited by stimulation.

At the same time, studies that recorded neuronal activity in the downstream nuclei showed an increase in overall firing, suggesting that output from the stimulated nucleus was, in fact, increased. Hashimoto et al. applied STN DBS in parkinsonian monkeys and recorded increased activity in the GPi and external globus pallidus, both of which receive excitatory glutamatergic afferents from the STN. Similar findings were seen with inhibitory efferents; GPi stimulation inhibited thalamic neurons in normal monkeys and patients with dystonia, and external globus pallidus stimulation inhibited SNc neurons. In addition, human positron emission tomography studies showed an increase in blood flow in the region of the GPi during STN DBS and an increase in cortical blood flow during thalamic DBS, both consistent with activation of output from the stimulated site. Similarly, a functional magnetic resonance imaging study found an increase in blood oxygen level–dependent signal in the GPi of patients undergoing STN DBS.

Inhibition of firing in the stimulated nucleus with a simultaneous increase in activity in the downstream structures presented an apparent paradox. Modeling studies suggested that extracellular electrical stimulation directly activated the axons while suppressing the cell bodies through activation of the inhibitory synaptic terminals, and this effect was dependent on the distance from the electrode. When a neuron is exposed to extracellular stimulation, the stimulation-induced action potential initiates in the axon rather than the cell body, in which case inhibition of the cell body can occur coincident with axonal activation. Experimental and modeling studies noted that axonal response was time-locked to the stimulus leading to a regularization of neuronal activity.

These data led to the hypothesis that DBS exerts its therapeutic effects by overriding the irregular, pathological activity from the stimulation target and replacing it with a stimulus-induced regular pattern. This effect spreads downstream through the entire basal ganglia thalamocortical network. For example, STN DBS affects not only pallidal activity but also causes neurons in the pallidal- and cerebellar-receiving areas in the thalamus to become more periodic and regular. In the same way, GPi DBS induces changes in the firing pattern of the motor cortex. Parkinson disease is also characterized by the development of rhythmic, oscillatory activity within the basal ganglia predominantly in the 15- to 30-Hz (beta) range. Treatment with levodopa attenuates these low-frequency oscillations. Similarly, STN DBS shifts pallidal and thalamic oscillatory activity from low to high frequencies.

The stimulus-induced tonic high-frequency firing pattern was hypothesized to be devoid of informational content and results in an “informational lesion,” preventing the pathological activity from being transmitted within the basal ganglia. More recent studies, however, suggest that information processing is enhanced and DBS is associated with improved information content in the network. Modeling studies have shown that DBS-induced regularization of basal ganglia input into the thalamus restores the responsiveness of thalamocortical cells to the incoming sensorimotor information, resulting in improved motor function. While this theory provides a framework to begin understanding the mechanisms of DBS, PD symptoms respond to stimulation at different latencies so more than 1 mechanism is likely responsible for the overall therapeutic benefit.

Although the initial focus had been on the direct effects on the stimulated target, more recent work has suggested that activation of adjacent fiber tracts surrounding or running through the stimulated site may also contribute to the observed clinical effects. Stimulation of the STN can activate nigrostriatal (increasing release of dopamine), pallidothalamic, cerebellothalamic, and pallidonigral fiber tracts, all of which could contribute to the therapeutic effects of DBS. One example is the reported beneficial effect of STN DBS on essential tremor as a result of activation of cerebellothalamic fiber pathways that pass just posterior and ventral to the STN. This also explains why cerebellar-receiving areas of the thalamus can be modulated by STN stimulation.

In summary, DBS increases output from the stimulated nucleus and activates surrounding fiber pathways resulting in a complex pattern of excitatory and inhibitory activity.
inhibitory effects that modulate the entire basal ganglia thalamocortical network. The stimulation-induced regularization of neuronal patterns prevents transmission of pathologic bursting and oscillatory activity within the network, resulting in improved processing of sensorimotor information and reduction of disease symptoms.

**DBS HARDWARE AND PROGRAMMING**

**Electrodes and Pulse Generators**

A DBS system is composed of 1 or more electrode leads implanted in the brain parenchyma and extension wires tunneled underneath the skin to an implanted pulse generator (IPG) positioned below the collar bone. The Medtronic Inc electrode is a flexible urethane 1.27-mm-diameter cylinder with 4 platinum/iridium contacts at the distal end. The IPG is a battery-powered device, about the size of a half a deck of cards, that sends a continuous electric signal to the brain at a set amplitude, pulse width, and frequency. Traditional IPGs were voltage controlled, meaning the stimulation amplitude was set in volts and the amount of current delivered to the brain tissue would depend on electrode impedance, which can vary because of electrochemical changes occurring at the electrode-brain interface. Since the amount of current delivered determines the volume of brain tissue stimulated, the clinical effects of stimulation could theoretically be variable when using voltage-controlled stimulation. The latest IPG from Medtronic (Activa PC) offers a current-controlled stimulation. Various combinations of active contacts can be used to direct current flow through desired target areas.88 Additionally, novel electrode designs can be used to steer the flow of current in a desired direction to achieve the optimal stimulation. At present, this goal is most commonly achieved by choosing either monopolar or bipolar stimulation and using various combinations of active contacts.87 In monopolar stimulation, the active contact is set as the negative pole, or cathode, and the IPG case is set as the positive pole, or anode. This creates a wide electric field with relatively equal spread of stimulation in all directions. In bipolar stimulation, another electrode contact serves as the anode, minimizing the spread of current and yielding a narrower area of stimulation. Various combinations of active contacts can be used to direct current flow through desired target areas.89 Additionally, novel electrode designs can provide more freedom in sculpting the area of activation. Compared with circumferential cylindrical contacts, segmented electrode arrays can be used to steer current and preferentially activate tissue along only 1 side of the DBS lead (Figure 3). This feature would be especially useful in cases of suboptimal electrode placement. Another stimulation technique that is already available in clinically approved IPGs is pulse interleaving, which allows rapid switching between 2 sets of parameters and electrode contacts. This can be particularly useful in cases where stimulation at 1 contact cannot alleviate all symptoms and simultaneous stimulation with equal amplitudes at multiple contacts induces adverse effects.80,81

**Programming Parameters**

Selecting appropriate patients and implanting hardware are only first steps toward successful DBS therapy. Programming refers to the process of selecting the most appropriate stimulation parameters to provide the patient with maximum therapeutic benefit while minimizing adverse effects. Finding the optimal electrode contact, stimulus amplitude, pulse width, and frequency has traditionally been a process of trial and error. After withholding the patient’s medication, the medical provider goes through the arduous process of trying out each electrode contact and various combinations of stimulation parameters while subjectively assessing the clinical benefit and degree of adverse effects.

Novel computational techniques can make programming a more efficient process. Computer models have been used to determine optimal stimulation parameters based on the precise electrode location, the desired stimulation target, and the estimated spread of current through the brain tissue.70 The electrode location can be determined with postoperative magnetic resonance imaging, which has shown to be safe when performed with certain precautions, or alternatively, preoperative magnetic resonance imaging can be fused with postoperative computed tomography.82 Stimulation targets have been derived from prior clinical experience, which incorporates evolving understanding of the DBS mechanisms. For example, in the case of STN stimulation for PD, the optimal stimulation target is thought to be the dorsal area of the STN that borders the lenticular fasciculus carrying pallidothalamic and nigrostriatal efferent fibers.83,84 Detailed biophysical computational models can then be used to calculate the electric field induced by the DBS electrode and predict its effect on the surrounding neurons. These predictions can subsequently be used to derive stimulation parameters that will provide maximum activation of the target area while minimizing spread of stimulation to the surrounding areas.85 Even though computationally intensive, model-derived parameters have shown to be superior to traditionally derived parameters and would presumably minimize the amount of patient time spent in programming sessions (Figure 2).

When therapeutic target sites are near areas causing adverse effects, it is necessary to sculpt the electric field or steer the flow of current in a desired direction to achieve the optimal stimulation. At present, this goal is most commonly achieved by choosing either monopolar or bipolar stimulation and using various combinations of active contacts.86 In monopolar stimulation, the active contact is set as the negative pole, or cathode, and the IPG case is set as the positive pole, or anode. This creates a wide electric field with relatively equal spread of stimulation in all directions. In bipolar stimulation, another electrode contact serves as the anode, minimizing the spread of current and yielding a narrower area of stimulation. Various combinations of active contacts can be used to direct current flow through desired target areas.89 Additionally, novel electrode designs can provide more freedom in sculpting the area of activation. Compared with circumferential cylindrical contacts, segmented electrode arrays can be used to steer current and preferentially activate tissue along only 1 side of the DBS lead.89 This feature would be especially useful in cases of suboptimal electrode placement. Another stimulation technique that is already available in clinically approved IPGs is pulse interleaving, which allows rapid switching between 2 sets of parameters and electrode contacts. This can be particularly useful in cases where stimulation at 1 contact cannot alleviate all symptoms and simultaneous stimulation with equal amplitudes at multiple contacts induces adverse effects.80,81

**FUTURE DEVELOPMENTS**

**Programming**

Deep brain stimulation programming, whether done as a trial-and-error procedure or computer model targeting of predefined therapeutic volumes, relies on a subjective evaluation of clinical benefit during programming sessions. A more objective approach to parameter selection could be achieved through closed-loop pro-
gramming, which is defined as a dynamic adjustment of stimulation parameters based on a patient’s current clinical status. This concept has been applied to neurostimulation in epilepsy treatment, where detection of abnormal cortical activity turns on the stimulator to abort an impending seizure.92

Various patient responses can be used to provide feedback to the stimulator, such as kinematics of movement, electrical neural activity, or neurotransmitter concentration in a target nucleus. Kinematic data acquired using motion sensors to quantify the degree of impairment during patient test movements can be used to systematically find the optimal stimulation settings.93 Neural activity can be determined by local field potentials, which can be measured through the unused contacts of the DBS electrode. Local field potential characteristics, which define the disease state, such as excessive oscillations in the beta frequency range, could then trigger the appropriate stimulation response.94 Electrical discharge is not the only measure of neuronal activity, and micro measurements of neurotransmitter levels have also been proposed as an input variable for the closed-loop system.95

This approach to treating PD is complicated by the fact that the disease has many different symptoms that can have varying pathological signatures that may respond to different stimulation settings. Similarly, stimulation of distinct regions within the target nucleus may preferentially affect various symptoms.75 Stimulation using sequential high-frequency pulse trains at different contacts within the target region has been shown, theoretically and in animal studies, to prolong the therapeutic benefits beyond the period of active stimulation. This concept of coordinated reset stimulation was developed using techniques from nonlinear dynamics and was designed specifically to counteract pathological synchronization processes by providing an antikindling effect and retraining the neural network.96 These approaches potentially increase the complexity of upcoming closed-loop stimulation systems but also represent a groundbreaking development in DBS therapy.

Figure 2. Patient-specific computational deep brain stimulation (DBS) model. A, Electrode location shown with respect to the subthalamic nucleus (green), thalamus (yellow), and desired stimulation target (gray). B and C, Computational estimate of volume of tissue activated (red) using model-defined (B) and clinically defined (C) stimulation parameters. D, The patient’s ability to maintain uniform finger motor force (y-axis) during an increasingly difficult cognitive task (x-axis) is optimal when using model-defined parameters.86 *P < .05. Image courtesy of Cameron McIntyre, PhD (Cleveland Clinic).
Optogenetic Techniques

The electric field generated by DBS is applied indiscriminately to all the neural elements surrounding the electrode. This can sometimes result in stimulation of areas that cause undesirable adverse effects (eg, corticospinal axons in the internal capsule). Optogenetics is a powerful and promising technique that allows selective activation of neurons using light, rather than electricity. A viral vector targeted to select neural populations can be used to carry genes for light-sensitive excitatory or inhibitory ion channels, which can then be triggered by light. Although clinical applications of this technology are still remote, it has been used to further elucidate the mechanisms of DBS in animal models.

CONCLUSIONS

Deep brain stimulation therapy has revolutionized treatment of movement disorders such as tremor, Parkinson disease, and dystonia, and it has shown promise in other neuropsychiatric disorders, eg, depression, epilepsy, and obsessive-compulsive disorder. Additional applications continue to be explored including Tourette syndrome, headache, vegetative state, stroke recovery, dementia, and addiction. Mechanisms of DBS are being actively investigated. Current understanding is that DBS activates neurons and regularizes pathologic activity and oscillations within the basal ganglia thalamocortical network, which in turn improves sensorimotor processing and alleviates disease symptoms. Better understanding of basic science concepts has encouraged development of new techniques that are permeating into the clinical practice, such as current-controlled stimulators, novel electrode designs, and optimization of stimulation parameters. More exciting developments on the horizon, including closed-loop stimulators and optogenetic applications, will make DBS a more versatile and successful treatment strategy.


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Author Contributions: Drs Miocinovic and Somayajula had full access to all of the data in the study and take full responsibility for the integrity of the data and accuracy of the data analysis.

Study concept and design: Miocinovic, Somayajula, Chitnis, and Vitek. Acquisition of data: Miocinovic and Vitek. Analysis and interpretation of data: Miocinovic, Somayajula, and Vitek. Drafting of the manuscript: Miocinovic and Vitek. Analysis and interpretation of data: Miocinovic, Somayajula, and Vitek. Drafting of the manuscript: Miocinovic, Somayajula, and Vitek. Critical revision of the manuscript for important intellectual content: Miocinovic and Vitek. Administrative, technical, and material support: Miocinovic, Somayajula, Chitnis, and Vitek. Study supervision: Chitnis and Vitek.

Conflict of Interest Disclosures: None reported.

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