DEEP BRAIN STIMULATION: PRINCIPLES, CLINICAL APPLICATIONS, OUTCOMES AND EMERGING TECHNOLOGIES

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Abstract

Background: Deep brain stimulation (DBS) delivers chronic electrical stimulation to targeted brain circuits through implanted electrodes and a pulse generator. It is an established treatment for Parkinson disease, essential tremor and dystonia and is being investigated in epilepsy and psychiatric disorders. **Aim:** To review the principles, surgical technique, clinical applications, outcomes, complications and emerging technologies of DBS. **Methods:** Narrative review of landmark randomized trials, meta-analyses and technical reviews. **Results:** Randomized trials show that subthalamic stimulation is superior to best medical therapy in advanced Parkinson disease and in patients with early motor complications, and that stimulation of the anterior thalamic nucleus reduces seizures in refractory focal epilepsy (56% median reduction at two years). In a meta-analysis of 21,261 patients with Parkinson disease, infection (4.2%) and lead malposition (3.3%) were the most frequent complications and hemorrhage occurred in 2.4%. Evidence in psychiatric disorders is mostly open-label, and sham-controlled comparisons in depression have not shown a clear advantage of active stimulation. Adaptive (closed-loop) stimulation received US regulatory approval for Parkinson disease in 2025. **Conclusion:** DBS is a safe and effective circuit-based therapy for selected patients, but better-designed trials are needed outside movement disorders.

Introduction

Deep brain stimulation (DBS) is a neurosurgical procedure that allows targeted, circuit-based neuromodulation. It is a standard of care in Parkinson disease (PD), essential tremor and dystonia, and is under active investigation for other conditions linked to pathological circuitry, including major depressive disorder and Alzheimer disease [1]. Modern systems consist of an intracranial electrode, an extension wire and an implanted pulse generator [1]. Because stimulation can be adjusted after implantation, DBS has also become a tool for studying how circuit malfunction leads to brain disorders [2].

This article reviews the history, technical principles and surgical technique of DBS, summarizes the evidence for its main indications, and discusses complications, emerging technologies and current limitations.

Keywords: deep brain stimulation, neuromodulation, Parkinson disease, subthalamic nucleus, adaptive stimulation, epilepsy, psychiatric neurosurgery.

Literature Review

The evidence base for DBS combines technical reviews, large randomized trials and meta-analyses. Key sources include the comprehensive review of DBS technology by Krauss et al. [1], the randomized trials of subthalamic stimulation in advanced PD [3] and in PD with early motor complications [4], the multicenter SANTE trial of anterior thalamic stimulation in epilepsy [5], a large meta-analysis of complications in PD [6], and the ADAPT-PD trial of adaptive stimulation [7]. Outside movement disorders, most evidence comes from small or open-label studies.

Historical Background

Electrical stimulation of deep brain structures in humans was already being explored between 1947 and 1987, a period that Hariz and colleagues have described as an overlooked part of the field's history [8]. The modern era began in 1987, when Benabid and colleagues combined thalamotomy with stimulation of the ventralis intermedius (VIM) nucleus in patients with bilateral PD [9]. Chronic VIM stimulation as a treatment for movement disorders was described in 1996 [10]. Unlike ablative surgery, stimulation can be adjusted after implantation, which made it an attractive alternative.

System Components and Surgical Technique

A DBS system borrows heavily from cardiac pacemaker technology. Pulse generators have evolved from external devices into small, rechargeable implantable ones, and directional leads now allow the current to be steered toward the intended anatomical structure [1,11].

Surgery is performed with stereotactic guidance. Specialized MRI sequences such as the Fast Gray Matter Acquisition T1 Inversion Recovery (FGATIR) sequence improve visualization of subcortical structures for targeting [12]. Many centers add intraoperative microelectrode recording (MER) to confirm the target, but each additional MER track carries a cost: in a large meta-analysis, hemorrhage did not increase significantly with a single track, whereas it rose non-linearly with each additional one [6]. The choice of target depends on the disease (Table 1).

Table 1. Main indications for DBS and commonly used targets

Indication	Common target(s)	Status of evidence
Parkinson disease	Subthalamic nucleus (STN); globus pallidus internus (GPi)	Randomized trials [3,4,13]; standard of care [1]
Essential tremor	VIM nucleus of the thalamus	Standard of care [1,10]
Dystonia	GPi	Meta-analysis of pallidal stimulation [15]; standard of care [1]

Indication	Common target(s)	Status of evidence
Refractory focal epilepsy	Anterior nucleus of the thalamus	Randomized double-blind trial [5]
Obsessive–compulsive disorder	Ventral capsule/ventral striatum, nucleus accumbens, STN and others	Small controlled and open-label studies [17,18]
Treatment-resistant depression	Medial forebrain bundle, ventral capsule/ventral striatum, subcallosal cingulate and others	Mostly open-label; mixed sham-controlled results [17]

Compiled from the sources cited in the table.

Clinical Applications

Parkinson disease. In a randomized-pairs trial of 156 patients with advanced PD and severe motor complications, STN stimulation plus medication was superior to best medical therapy at six months for both primary outcomes, quality of life (PDQ-39) and motor severity off medication (UPDRS-III). Serious adverse events were more frequent with neurostimulation (13% vs 4%) and included one fatal intracerebral hemorrhage [3]. The EARLYSTIM trial extended these findings to younger patients earlier in the disease. In 251 patients (mean age 52 years, mean disease duration 7.5 years) with early motor complications, PDQ-39 improved by 7.8 points with neurostimulation and worsened by 0.2 points with medical therapy alone (between-group difference 8.0 points, $P = 0.002$), and neurostimulation was also superior for motor disability, activities of daily living and levodopa-induced complications [4].

The choice between STN and GPi has been compared in a large randomized trial [13]. A 2025 meta-analysis reported consistent improvement in tremor, rigidity, bradykinesia and dyskinesia regardless of the stimulation target or medication state, although effects on gait and speech have been less consistent [14].

Table 2. Landmark randomized trials of DBS

Trial	Population and design	Main findings
Deuschl et al., 2006 [3]	156 patients with advanced PD; STN stimulation plus medication vs best medical therapy; 6 months	Superior PDQ-39 and off-medication UPDRS-III; serious adverse events 13% vs 4%

Trial	Population and design	Main findings
Schuepbach et al., 2013 (EARLYSTIM) [4]	251 patients with PD and early motor complications; 2 years	PDQ-39 improved 7.8 points vs worsened 0.2 points (difference 8.0; P = 0.002); implantation- or device-related serious adverse events 17.7%
Fisher et al., 2010 (SANTE) [5]	110 patients with refractory focal epilepsy; anterior thalamic stimulation vs no stimulation for 3 months, then open label	Median seizure reduction 40.4% vs 14.5% at end of blinded phase; 56% at 2 years

PDQ-39, Parkinson's Disease Questionnaire-39; UPDRS-III, Unified Parkinson's Disease Rating Scale, part III.

Essential tremor and dystonia. Thalamic VIM stimulation was the first modern application of DBS [9,10] and remains the standard target for tremor. Pallidal stimulation is effective in isolated dystonia according to a systematic review and meta-analysis [15]. Clinical response nevertheless varies between patients even when surgery is uncomplicated, and structural MRI features are being investigated as predictors of motor outcome [16].

Epilepsy. In the SANTE trial, 110 adults with medically refractory focal seizures received bilateral anterior thalamic electrodes and were randomized to stimulation or no stimulation for three months, after which all received stimulation. At the end of the blinded phase the median seizure reduction was 40.4% in the stimulated group and 14.5% in controls. By two years the median reduction was 56%, 54% of patients had a reduction of at least 50%, and 14 had been seizure-free for at least six months. There was no symptomatic hemorrhage or brain infection, but depression and memory problems were reported more often as adverse events in the stimulated group [5].

Psychiatric disorders. A recent narrative review summarizes the evidence for treatment-resistant psychiatric disorders [17]. In depression, average symptom improvement was about 47% at intermediate to long-term follow-up, with response and remission rates of about 48% and 35%. However, open-label studies reported improvements more than 20 percentage points larger than randomized trials, and the review found no statistically significant difference between active and sham stimulation in randomized comparisons, possibly because of a microlesion-type "implant effect", placebo effects and small sample sizes [17]. In severe obsessive–compulsive disorder, subthalamic stimulation was evaluated in a controlled crossover trial [18], and pooled data show a mean reduction of more than 14 points on the Yale-Brown scale, with about two thirds of patients responding [17]. In severe Tourette

syndrome, more than two thirds of patients achieved a tic reduction above 50% at a median follow-up of 12 months, without significant change in sham conditions [17]. Reported stimulation settings in these disorders are typically 130–180 Hz with pulse widths of 60–120 μs [17]. Most of these indications remain investigational.

Complications and Safety

In a systematic review and meta-analysis of 262 articles covering 21,261 patients with PD, the most frequent complications were revision surgery (4.9%), infection (4.2%) and lead malposition (3.3%), followed by surgical site complications (2.8%), hemorrhage (2.4%), hardware-related complications (2.4%) and seizure (1.9%) [6]. Randomized trials report higher rates of serious adverse events with stimulation than with medical therapy alone: 13% vs 4% in advanced PD [3], and 17.7% of patients with an implantation- or device-related serious adverse event in EARLYSTIM [4]. In epilepsy, the SANTE trial reported no symptomatic hemorrhage or brain infection [5].

Stimulation-related effects depend on the target and the indication. In depression, suicidal behavior is closely monitored; the suicide rate in a pooled analysis (0.87 per 100 person-years) was comparable to that in other neuromodulation studies, and causal attribution to DBS remains uncertain [17]. Device problems can also have clinical consequences: battery depletion was associated with relapse of depressive symptoms in a small subset of patients, which improved after battery replacement [17]. These findings support careful patient selection, multidisciplinary follow-up and regular device checks.

Emerging Technologies

Adaptive (closed-loop) stimulation. Conventional DBS delivers continuous stimulation regardless of the patient's state. Adaptive DBS senses a neural signal and adjusts stimulation accordingly. Early studies in advanced PD used local field potential activity from the implanted electrode as the control signal [19], and candidate biomarkers for closed-loop control have been reviewed [20]. In the ADAPT-PD trial, 45 people with moderate to advanced PD who had been stable on conventional DBS used adaptive stimulation driven by α–β band (8–30 Hz) activity at home; long-term adaptive DBS was tolerable, effective and safe, and total electrical energy delivered was 15% lower with single-threshold adaptive stimulation than with conventional stimulation [7]. On this basis, the US Food and Drug Administration approved an adaptive DBS system for PD in February 2025 [21].

Imaging and connectomics. Postoperative electrode localization combined with normative connectivity data can predict clinical outcome in PD [22], and open-source toolboxes such as Lead-DBS support electrode localization and visualization [23]. These methods are expected to improve target selection and programming.

Connectivity and security. As DBS systems become compatible with wireless networks, remote programming by physicians will become possible, but privacy and security issues, including so-called "brainjacking", must be addressed [1,24].

Limitations and Future Directions

Outside movement disorders and epilepsy, the evidence for DBS is limited by small samples, heterogeneous targets and stimulation settings, short sham-controlled periods and a high proportion of open-label designs [17]. Even in PD, outcomes for gait and speech are inconsistent [14], and a substantial proportion of patients do not reach the expected benefit despite uncomplicated surgery [16]. Future work should focus on larger controlled trials with standardized outcome measures, biomarker-guided adaptive stimulation, and better individual prediction of response.

Conclusion

DBS is an established, adjustable treatment for advanced Parkinson disease, essential tremor and dystonia, and has demonstrated benefit in refractory focal epilepsy. Serious complications are uncommon but not negligible, and most are related to hardware, infection or lead placement. Adaptive stimulation, advanced imaging and connectomic targeting are moving the field toward personalized therapy. In psychiatric disorders, DBS remains investigational, and rigorous randomized trials are needed before it can be recommended more widely.

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