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Review Article

Deep Brain Stimulation of the Subthalamic Nucleus in Advanced Parkinson Disease: Long-Term Motor Outcomes

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Abstract

Background: Subthalamic nucleus deep brain stimulation (STN-DBS) is an established surgical treatment for advanced Parkinson disease (PD) with motor fluctuations and dyskinesia refractory to medical therapy.

Objective: To synthesise published evidence on long-term (5-year and, where available, 10- to 20-year) motor outcomes of STN-DBS.

Methods: Narrative review of randomized trials, long-term cohorts, meta-analyses, and consensus literature.

Findings: Randomized trials show sustained gains in off-medication motor score, "on" time without troublesome dyskinesia, and roughly 50% reduction in levodopa-equivalent dose relative to medical therapy. Cohorts extending to 10-20 years confirm durable improvement in tremor, rigidity and dyskinesia, while axial, speech and cognitive domains progressively decline, consistent with disease progression rather than treatment failure. Hardware complications occur in roughly 5-10% of patients, and suicidality, though uncommon, is disproportionately elevated early after surgery.

Conclusions: STN-DBS confers durable, clinically meaningful motor benefit and medication-sparing effects across the long-term literature, with outcome heavily modified by baseline levodopa responsiveness, age, and axial/cognitive status at implantation.

Keywords: Subthalamic nucleus; Deep brain stimulation; Parkinson disease; Long-term outcomes; Levodopa-equivalent dose

Abstract

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Introduction

Parkinson disease (PD) progresses from a levodopa-responsive motor disorder to one complicated, after years of dopaminergic therapy, by disabling motor fluctuations and dyskinesia. High-frequency stimulation of the subthalamic nucleus (STN) was first shown to improve these complications in an open-label series in 1998 [1], and subsequent randomized trials established STN-DBS as superior to best medical therapy alone in

patients with advanced disease [2,3]. STN-DBS has since become one of the most extensively studied interventions in movement-disorder neurosurgery, with a published evidence base spanning double-blind randomized trials, large multicentre cohorts, and prospective single-centre series now followed for up to two decades.

Because PD itself continues to progress after surgery, and because dopaminergic circuitry, axial motor control and cognition are not uniformly rescued by chronic stimulation, the durability of STN-DBS benefit could not be established from the six- to twelve-month horizon of the original registration trials alone. A distinct and substantial literature has therefore accumulated specifically to characterise outcomes at five, ten, fifteen and, in a small number of cohorts, close to twenty years after implantation. This body of evidence is essential to clinical counselling: patients considering STN-DBS, and the clinicians advising them, need to know not only whether motor fluctuations and dyskinesia improve in the short term, but which domains of benefit are sustained, which decline despite continued stimulation, and which patient characteristics at the time of surgery predict a favourable long-term trajectory.

This narrative review synthesises the published randomized-trial, long-term cohort, and meta-analytic literature on long-term motor outcomes of STN-DBS in advanced PD, alongside non-motor, quality-of-life, complication and outcome-predictor data drawn from the same body of evidence. It is intended as an evidence synthesis for clinicians managing patients with advanced PD being considered for, or already treated with, STN-DBS, rather than as a technical or surgical how-to guide.

Patient Selection and Indications

Consensus criteria for STN-DBS candidacy, formalised by a multidisciplinary expert panel of neurologists,

neurosurgeons and neuropsychologists, emphasise idiopathic PD with a robust levodopa response, disabling motor fluctuations or dyskinesia despite optimised medical therapy, absence of significant dementia, and absence of, or well-controlled, psychiatric disease [4]. The magnitude of the preoperative levodopa response is repeatedly identified as the single strongest clinical predictor available to selection teams, because it approximates the ceiling of motor improvement stimulation can be expected to reproduce [4,5]. Age is treated as a continuous rather than a strictly categorical risk factor: younger patients with shorter disease duration and fewer axial, non-levodopa-responsive symptoms such as freezing of gait, falls and dysarthria have historically had the most favourable long-term outcomes, while rigid age cut-offs risk excluding appropriately selected older patients who otherwise meet the remaining criteria [4].

The EARLYSTIM trial extended this framework by showing that STN-DBS improves quality of life and reduces motor complications even in patients with early fluctuations and a mean disease duration of only about 7.5 years, rather than the decade-plus duration typical of earlier trial cohorts, broadening candidacy beyond the traditionally "advanced" phenotype and shifting practice toward earlier referral in appropriately selected patients [6]. Across both the earlier- and later-stage literature, a structured multidisciplinary preoperative work-up — incorporating a formal levodopa challenge, standardised cognitive and psychiatric screening, and shared decision-making about realistic expected benefit — remains the consistent recommendation for maximising the likelihood of a favourable long-term outcome [4,5].

Surgical Technique and Target Selection

Bilateral STN-DBS is implanted stereotactically, typically under multidisciplinary evaluation with imaging- and microelectrode-recording-guided targeting, followed by staged or single-session implantation of the implantable

pulse generator. The STN and the globus pallidus interna (GPi) are the two principal targets; head-to-head randomized and multicentre comparisons (CSP 468 [7,8], NSTAPS [9], a further long-term multicentre STN-versus-GPi comparison [10]) and pooled meta-analyses [11,12] show broadly comparable motor benefit between targets, with STN associated with greater levodopa-equivalent dose (LEDD) reduction and GPi associated with somewhat less cognitive and mood morbidity, informing individualised target selection [12]. LEDD is calculated throughout this literature using a standardised conversion methodology that allows medication burden to be compared across studies and drug regimens [13].

Long-Term Motor Outcomes

Randomized evidence anchors the acute-to-medium-term benefit: the German-French trial found STN-DBS superior to medical management on quality of life and UPDRS motor score at six months in patients under 75 with severe motor complications [2], and the US VA/NINDS CSP 468 trial confirmed superiority of bilateral DBS over best medical therapy, with roughly 4.6 hours per day of additional good "on" time without troublesome dyskinesia [3]. Extension of that cohort to 36 months showed motor scores stable between STN and GPi targets, with sustained "on"-time gains of 4.1-4.6 hours/day [8]. The recent sham-controlled INTREPID trial demonstrated 51% improvement in off-medication UPDRS-III at one year, attenuating modestly but remaining at 36% improvement at five years, with dyskinesia reduced roughly 70-75% and LEDD reduced approximately 28% throughout [14].

Longer, uncontrolled prospective cohorts extend this picture. At five years, the original Grenoble series reported 54% improvement in off-medication motor score and 49% improvement in activities of daily living compared with baseline, with dyskinesia severity and duration markedly

reduced, although speech, postural stability, freezing of gait and akinesia in the on-medication state worsened between years one and five [15]. At eight years the same cohort's successor series confirmed sustained motor benefit alongside continuing decline in axial, speech and some cognitive domains [16], and a ten-year blinded evaluation confirmed a persistent stimulation effect on off-medication UPDRS motor score, again with no comparable benefit for axial symptoms [17]. A cohort followed beyond nine years similarly documented durable improvement in tremor, rigidity and bradykinesia with progressive axial decline [18]. At the extreme of follow-up, a fifteen-year (median 16-year) Grenoble cohort found dyskinesia time reduced 75%, off-time reduced 58.7%, and LEDD reduced 50.6% compared with baseline, with quality-of-life measures also improved despite the natural progression of levodopa-resistant symptoms [19]; a companion analysis of the same programme, following patients to a mean of 12.5 years, confirmed sustained independence in activities of daily living alongside continued quality-of-life benefit [20]. Pooled meta-analytic estimates corroborate these individual cohorts: STN-DBS reduces UPDRS-III motor score by approximately 50% and dyskinesia by 64-69% relative to the preoperative off-medication state across studies with six-to-twelve-month follow-up [12,21,11], while LEDD reduction of roughly 50% is consistently reported from the earliest randomized trials through the longest cohorts [15,19,12]. Taken together, the trajectory that emerges across this literature is remarkably consistent: appendicular symptoms most responsive to levodopa at baseline — tremor, rigidity, bradykinesia and levodopa-induced dyskinesia — remain substantially improved by stimulation for as long as patients have been followed, whereas axial features with limited levodopa responsiveness before surgery, such as postural instability, freezing of gait and hypophonic speech, tend to re-emerge and progress over the second postoperative

decade in step with the underlying neurodegenerative course of PD rather than as a failure of the device or a loss of stimulation efficacy [15,17,16,18,19].

Table 1: Landmark randomized trials and long-term follow-up cohorts of STN-DBS in advanced Parkinson disease reviewed here [1,2,3,7,6,9,15,17,19,14].				
Study	Design	N	Follow-up	Key motor finding
Limousin 1998	Open-label series	24	3-12 months	First demonstration of STN-DBS motor benefit
Deuschl 2006 (German-French)	RCT vs medical therapy	156	6 months	STN-DBS superior on UPDRS motor and quality of life
Weaver 2009 (CSP 468)	RCT vs best medical therapy	255	6 months	+4.6 h/day good "on" time without dyskinesia vs 0 h with medical therapy
Follett 2010 (CSP 468)	RCT, STN vs GPi	299	24 months	Similar motor improvement between targets
Schuepbach 2013 (EARLYSTIM)	RCT, early motor complications	251	24 months	STN-DBS superior on quality of life and motor complications
Odekerken 2013 (NSTAPS)	RCT, STN vs GPi	128	12 months	Comparable functional improvement between targets
Krack 2003	Prospective cohort	49	5 years	54% improvement in off-medication motor score
Castrioto 2011	Blinded evaluation cohort	37	10 years	Persistent stimulation effect on off-medication UPDRS motor score
Bove 2021	Prospective cohort	51	15-24 years (median 16)	Dyskinesia -75%, off-time -58.7%, LEDD -50.6%
Starr 2025 (INTREPID)	Sham-controlled RCT, open-label extension	191 (137 completers)	5 years	UPDRS-III improved 51% (1 yr) and 36% (5 yr)

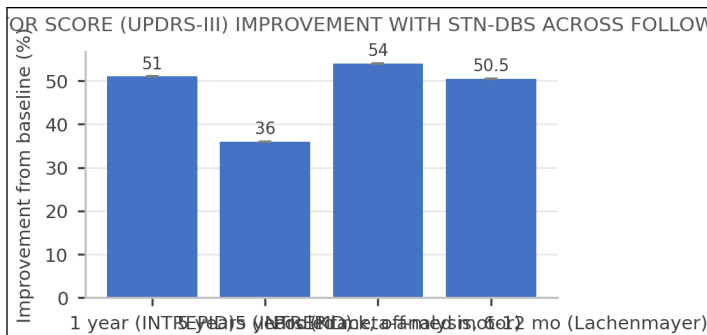


Figure 1: Off-medication motor score (UPDRS-III) improvement with STN-DBS across follow-up duration: 51% at 1 year and 36% at 5 years in the sham-controlled INTREPID trial [14]; 54% at 5 years in the original Grenoble cohort [15]; 50.5% pooled across studies with 6-12 month follow-up in meta-analysis [12].

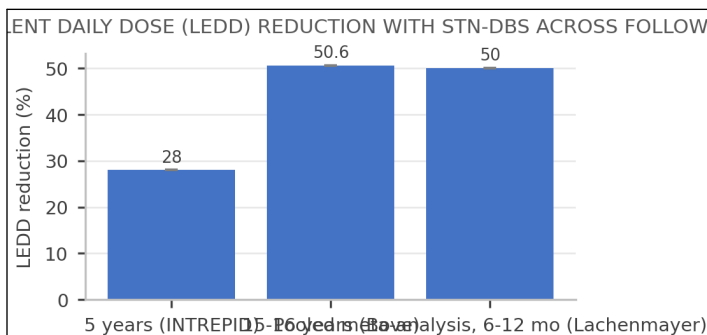


Figure 2: Levodopa-equivalent daily dose (LEDD) reduction with STN-DBS across follow-up duration: 28% at 5 years in INTREPID [14]; 50.6% at 15-16 years in the Grenoble long-term cohort [19]; 50% pooled in meta-analysis [12].

Non-Motor and Quality-of-Life Outcomes

Quality-of-life gains, though generally smaller in magnitude than motor gains and prone to attenuation over time, are reported across the long-term literature: the fifteen-year Grenoble cohort found overall PDQ-39 improvement of 13.8%, with emotional and social functioning domains improved 13.6% and 29.9% respectively [19], and the companion independence/quality-of-life analysis of the same programme confirmed sustained gains in activities-of-daily-living independence beyond ten years despite progressive non-motor symptom burden [20]. Meta-analytic pooling likewise shows PDQ-39 summary index improvement of approximately 22% with STN-DBS

[12]. Cognitive outcomes are less favourable: several long-term cohorts document a gradual decline in processing speed, verbal fluency and, in a minority, incident dementia over years of follow-up, a pattern attributed to underlying disease progression rather than a specific surgical or stimulation effect [16,17,8].

Complications and Adverse Events

A systematic review and meta-analysis of DBS complications in PD reported pooled rates of surgical revision 4.9%, infection 4.2%, lead malposition 3.3%, surgical-site complications 2.8%, intracranial haemorrhage 2.4%, other hardware-related complications (lead fracture, generator malfunction, skin erosion) 2.4%, and seizure 1.9%, with haemorrhage risk rising non-linearly as the number of intraoperative microelectrode recording tracks increased [22]. These figures are broadly consistent with the adverse-event profiles reported in the earliest randomized trials, where surgical and device-related complications occurred in a minority of patients and were weighed against a much larger proportion achieving clinically meaningful "on"-time gains [3,2].

Neuropsychiatric adverse events, including apathy, depression, anxiety and impulse-control or behavioural change, are recognised across the trial and long-term cohort literature and are a principal reason multidisciplinary preoperative psychiatric screening is recommended [4,3]. Suicidality warrants particular attention: a systematic review and meta-analysis found a relatively elevated rate of suicide and suicide attempts after STN-DBS compared with the general PD population, concentrated disproportionately in the early postoperative period, and postulated mechanisms spanning acute psychosocial adjustment, rapid medication reduction unmasking latent depression, and possible direct neuromodulatory effects on limbic circuitry adjacent to the STN [23]. This finding reinforces

consensus recommendations for structured psychiatric screening and closer postoperative follow-up in the first year after implantation [4].

Table 2: Pooled complication rates of STN-DBS for Parkinson disease from systematic review and meta-analysis [22], and suicidality risk from a separate systematic review and meta-analysis [23].

Complication	Pooled rate	Source
Surgical revision	4.9%	rasiah2023
Infection	4.2%	rasiah2023
Lead malposition	3.3%	rasiah2023
Surgical-site complications	2.8%	rasiah2023
Intracranial haemorrhage	2.4%	rasiah2023
Other hardware-related complications	2.4%	rasiah2023
Seizure	1.9%	rasiah2023
Suicide/suicide attempt	Elevated vs general PD population, concentrated early postoperatively	xu2021

Predictors of Outcome

Across randomized and cohort studies, preoperative levodopa responsiveness is the single most consistent predictor of long-term motor benefit, correlating strongly with postoperative UPDRS-III improvement in pooled meta-analytic data [12]. A large single-centre analysis identifying preoperative predictors of long-term outcome confirmed that levodopa response, younger age, and absence of significant axial or cognitive impairment at baseline predicted better sustained motor outcome, while older age and greater baseline axial burden predicted earlier decline in gait and postural stability despite continued stimulation benefit for tremor and rigidity [24]. These findings are consistent with the patient-selection criteria proposed by expert consensus [4] and with the differential trajectories reported across the long-term cohorts summarised above [15,17,16,19].

Conclusion

The cumulative published evidence — from the founding randomized trials [1,2,3,7,6,9,25], through cohorts

followed for a decade or more [15,16,17,18,26,19,20], to contemporary sham-controlled five-year data [14] and pooled meta-analyses [21,11,12] — converges on a consistent picture: STN-DBS produces durable improvement in tremor, rigidity, dyskinesia and levodopa-equivalent dose that persists for at least fifteen years in well-selected patients, even as axial, speech and cognitive domains decline in parallel with underlying disease progression. Complication and suicidality data are now well characterised [22,23], and baseline levodopa responsiveness, age and axial status remain the principal determinants of individual long-term trajectory [24,4].

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