

Subthalamic Nucleus Deep Brain Stimulation in a Patient with Severe Axial Symptoms and Suboptimal Levodopa Responsive Parkinson's Disease

Behrad NASSEHI¹, Taha ASSADNEJAD¹, Onur YILDIZ^{1,2}, Dursun AYGUN^{1,3}, Ersoy KOCABICAK^{1,4}

¹Ondokuz Mayıs University, School of Medicine, Neuromodulation Center, Samsun, Turkey

²Erzurum Regional Health Application and Research Hospital, Department of Neurology, Erzurum, Turkey

³Ondokuz Mayıs University, School of Medicine, Department of Neurology, Samsun, Turkey

⁴Ondokuz Mayıs University, School of Medicine, Department of Neurosurgery, Samsun, Turkey

Corresponding author: Ersoy KOCABICAK ✉ ersoykocabicak@gmail.com



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ABSTRACT

AIM: Deep brain stimulation (DBS) is a well-established treatment option for improving function and quality of life (QoL) in carefully selected patients with Parkinson's disease (PD). Patient selection is a crucial step that should be performed by an experienced multidisciplinary team according to the proposed inclusion and exclusion criteria to increase the QoL of patients.

CASE REPORT: A 47-year-old bedridden woman with a 20-year history of PD presented with levodopa-unresponsive tremor and severe axial symptoms. Despite various antiparkinsonian medications, a suboptimal improvement was observed with the levodopa challenge test. After detailed evaluations, she underwent bilateral subthalamic nucleus DBS. During the 2-year follow-up, her axial symptoms improved significantly leading to a better QoL.

CONCLUSION: Although levodopa-resistant axial symptoms are considered a relative contraindication to DBS surgery, this case report demonstrates that with an interdisciplinary approach and an accurate assessment of symptoms, even bedridden and late-stage selected PD cases may benefit from DBS.

KEYWORDS: Axial symptoms, Deep brain stimulation, Parkinson's disease, Subthalamic nucleus

INTRODUCTION

Motor manifestations of Parkinson's disease (PD) play a major role in the challenges with the quality of life (QoL), including bradykinesia, rigidity, tremor, and postural instability. The subthalamic nucleus deep brain stimulation (STN-DBS), which requires proper screening and selection of candidates, is a highly effective treatment for Parkinsonism symptoms (2). The eligibility for DBS is usually

determined according to the core assessment program for surgical interventional therapies in PD (CAPSIT-PD) criteria by evaluating factors such as age, disease duration, levodopa (L-dopa) responsiveness, type and severity of L-dopa-unresponsive symptoms, psychiatric problems, and brain magnetic resonance imaging findings (1). Frizon et al. reported that the PD-related QoL was improved greatly after STN-DBS (4). Recent developments in the diagnosis and advanced management of PD have increased the patient's

life expectancy almost similar to that of healthy individuals (12,13). Therefore, QoL improvement is a significant part of therapeutic plans.

Herein, we present a tremor-dominant patient with L-dopa-resistant axial symptoms who benefited from bilateral STN-DBS and whose life was changed from a bedridden to an independent one.

■ CASE REPORT

A 47-year-old woman with a 20-year history of young-onset PD with L-dopa-resistant severe tremor, worsening axial symptoms, and motor fluctuations presented to our center for DBS evaluation. Her initial sign was jaw tremor, which over time spread to the left and then right extremities during resting, along with bradykinesia and rigidity. She also developed axial symptoms such as gait difficulties and stooped posture. Postural instability and falls began unexpectedly in a few months and gradually increased to an extent that made her bedridden. This significantly reduced her QoL, as she was dependent on assistance for all activities during the last 4 years. Furthermore, her body mass index (BMI) reduced to 17.6 kg/m², due to extreme weight loss during the late disease stage. After primary evaluations, she was referred to our clinic for further investigations. Additional tests and investigations were performed to rule out secondary causes. The results were unremarkable, and she was diagnosed with idiopathic PD. She had no family history for PD. Her unified Parkinson's disease rating scale (UPDRS)-III motor score, "off/on" medication, was 111/94 prior to DBS. She demonstrated a suboptimal improvement in UPDRS-III with the suprathreshold dose of dopaminergic medication. Trials and combinations of various antiparkinsonian medications such as L-dopa/carbidopa, entacapone, amantadine, rasagiline, biperiden, and apomorphine with the maximum L-dopa equivalent daily dose (LEDD) of 1500 mg failed to improve symptoms (Table I). Our interdisciplinary DBS team consisting of a neurosurgeon, movement disorder specialist, neuroradiologist, psychiatrist, and neuropsychologist deemed this patient suitable for STN-DBS for idiopathic PD due to severe tremor despite resistant axial symptoms.

Table I: Pre-Operative Test Results

	Pre-operation
UPDRS-III Med-Off	111
UPDRS-III Med-On	94
PDQ 39	130
LEDD (mg)	1500
MMSE	26
BMI	17.6

Med: Medication, **UPDRS:** Unified Parkinson's Disease Rating Scale, **PDQ-39:** Parkinson's Disease Questionnaire, **LEDD:** L-dopa Equivalent Daily Dose, **MMSE:** Mini-Mental State Exam, **BMI:** Body Mass Index.

After thorough discussions with the patient, detailing the associated risks, potential benefits, side effects, and complications of bilateral STN-DBS, the patient asked to proceed with surgery. The patient and her family provided their signed consent to surgery. The patient underwent bilateral STN-DBS surgery under local anesthesia with microelectrode recording and test stimulation. The detailed surgical procedure can be viewed from our previous publication (7).

After 1 week of post-operative follow-up, the patient was discharged without any complications. At 1 month after the surgery, the patient was admitted for initial adjustment of stimulation parameters. The stimulation parameters were also optimized in the 3rd and 24th months postoperatively, according to the patient's complaints and side effects of stimulation. Bilateral STN-DBS significantly improved her symptoms; in particular, her axial symptoms improved to the point that she was able to walk unassisted for the first time in years. Postoperatively, her on-medication/off-stimulation UPDRS-III score was 82 at the 3rd month compared with the on-medication/on-stimulation score of 44 and 42 in 3rd and 24th month, respectively. At the patient's request, the on-medication/off-stimulation test was not conducted at 24th month postoperatively. However, mild tremor and rigidity of left extremities persisted. Surgery had a noticeable effect on the patient's QoL, and a significant improvement was observed in the Parkinson's disease questionnaire (PDQ-39). Additionally, the LEDD reduction rate was 55% at the 3rd month and 50% at 24th month follow-up visit, compared with baseline. The UPDRS scores and stimulation parameters are summarized in Table II.

■ DISCUSSION

The emergence of axial symptoms, such as freezing of gait, postural instability, and postural anomalies, consequent to the progression of PD reduces the survival and QoL and significantly contributes to disability due to diminished mobility, loss of independence, and repeated falls. The knowledge about the effect of STN-DBS on axial symptoms is still controversial (1,8). However, patient age and L-dopa response to axial symptoms are predictors of DBS outcomes (3,9). Although the mechanism of STN-DBS on axial symptoms may remain unclear in the literature, the effects of STN-DBS on other appendicular motor manifestations can help improve axial features indirectly as well (5). Although studies have suggested that low-frequency STN stimulation is a better option for improving axial symptoms (3,6), the finding that our patient's axial symptoms improved with high-frequency stimulation supports the hypothesis that improvement in severe tremor could have been an underlying cause of the gait improvement. The lack of multifactorial gait analysis system to track gait movements and posture was a limitation in this case. Such a system could have helped in measuring parameters to assess the direct effect of subthalamic stimulation on gait and postural instability.

By contrast, the L-dopa challenge test (LCT) with a minimum improvement of 30% is a key tool for proper patient selection and the possibility of improvement after DBS (11).

Table II: Postoperative 3rd-month and 24th-month Stimulation Settings and Test Results

	Post-operative 3 rd month		Post-operative 24 th month	
	Right STN	Left STN	Right STN	Left STN
Frequency (Hz)	130	130	110	110
Pulse Width (µs)	100	60	110	90
Amplitude (mA)	3.1	2.3	4.5	3.6
Stim On / Med-On - UPDRS-III	44		42	
PDQ 39	50		52	
LEDD (mg)	665		750	
BMI	20.7		22.8	

STN: Subthalamic nucleus, **Stim:** Stimulation, **Med:** Medication, **UPDRS:** Unified Parkinson's Disease Rating Scale, **PDQ-39:** Parkinson's Disease Questionnaire, **BMI:** Body Mass Index.

Therefore, L-dopa-resistant axial symptoms and suboptimal LCT are considered relative contraindications for DBS (1). In the literature, patients with severe dyskinesia, "on/off" fluctuations, and/or medication-resistant tremor are possible DBS candidates, even if they do not benefit by 30% with dopaminergic drugs (11,14). Furthermore, postural instability and gait disturbance, which also respond poorly to L-dopa, may be negative predictors of STN-DBS (15).

By contrast, we reported a severe tremor-dominant patient who underwent STN-DBS. Although our patient had severe axial symptoms and suboptimal LCT, we observed favorable outcomes after STN-DBS. Her preoperative UPDRS-III off/on-medications improvement rate was 15.4%. Moreover, there was a 55% improvement in the UPDRS-III score in the on-medication state (on-stimulation: 42) at the 24th-month follow-up, compared with the preoperative best on-medication state, which was 94. In addition, her BMI and PDQ-39 enhanced 29% and 60% compared with preoperative values, respectively.

The effects of DBS on axial disability are likely to be multifactorial, with neurodegenerative progression, stimulus parameters, and comorbidities all playing a role (3). In the present case, being underweight has been linked to disease progression, poor functional outcomes, and a decline in the subjective QoL of people with PD (16). Moreover, the motor and total UPDRS scores are negatively affected by a decline in BMI (16). STN-DBS results in a weight gain, and the hypothesis behind it may be related to modifying the energy expenditure/energy intake balance concerning motor symptoms and drug intake changes (10). However, it is unclear whether weight gain, in patients with low BMI preoperatively, can help in the improvement of axial symptoms and QoL after DBS. In addition, our patient's young age and tremor-dominant symptoms could have a positive effect on the DBS efficacy (9).

CONCLUSION

By selecting the right patient for DBS, the patient's disability may be reduced, and improvements in their daily living activities and independence may be observed. The indications

for DBS should be a tailored approach for each patient. This case suggests that STN-DBS could be considered in selected patients with tremor-dominant symptoms who are immobile due to extreme axial symptoms and have suboptimal L-dopa responsiveness.

AUTHORSHIP CONTRIBUTION

Study conception and design: EK, BN, TA

Data collection: EK, BN, TA, OY

Analysis and interpretation of results: DA, OY, EK

Draft manuscript preparation: BN, TA, OY

Critical revision of the article: EK, DA

All authors (EK, DA, OY, BN, TA) reviewed the results and approved the final version of the manuscript.

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