

## Case Report

# Deep brain stimulation for Parkinson's disease prior to L-dopa treatment: A case report

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## Abstract

**Background:** Leva-dopa (L-dopa) is the gold-standard treatment for Parkinson's disease (PD). Deep brain stimulation is generally reserved for patients who become refractory to l-dopa treatment.**Case Description:** We present a male patient with a 9-year course of PD who at 53 years of age preferred deep brain stimulation (DBS) of the subthalamic nucleus over initial l-dopa treatment. The patient argued that he wanted to avoid the serious adverse effects of l-dopa, which would have presented within his time of full professional activity. DBS resulted in significant motor improvement lasting for 6 years without l-dopa treatment.**Conclusion:** Large multicentre-based international trials with long follow-ups are needed to answer the effectiveness of early DBS in PD.**Key Words:** Deep brain stimulation, L-dopa, Parkinson's disease**Access this article online****Website:**[www.surgicalneurologyint.com](http://www.surgicalneurologyint.com)**DOI:**

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## INTRODUCTION

Parkinson's disease (PD) is a progressive, neurodegenerative disorder characterized by resting tremor, rigidity, bradykinesia, and postural instability.<sup>[12]</sup> Initial management of the disease consists of a pharmacological approach with Levo-dopa (L-dopa) as the gold-standard treatment, in attenuating the cardinal debilitating motor symptoms.<sup>[4,8]</sup> However, L-dopa is associated with severe long-term motor and mood side effects, such as hypo-hyperkinetic phenomena and psychosis.<sup>[8,17]</sup> Deep brain stimulation (DBS) for PD is considered, since its renaissance in the 1990s,<sup>[1]</sup> an effective and safe treatment for advanced stages of PD. General inclusion criteria for DBS are (a) idiopathic PD, (b) IV or V Hoehn and Yahr stage, (c) motor fluctuations and L-dopa induced dyskinesias, despite optimal pharmacological management, (d) absence of dementia

or psychiatric disease, (e) a preoperative motor response to L-dopa challenge (at least 30% improvement in UPDRS-III), and (f) preferably, a disease duration of 5 years or more.<sup>[2]</sup> PD patients are not eligible for DBS, if they present (a) an atypical Parkinsonism, (b) current psychiatric history, (c) significant medical or surgical history, and (d) a cardiac pacemaker. In recent times, however, the inclusion criteria of PD patients for DBS have been vividly debated.<sup>[3,5,7,9,11,13,15,16]</sup> Within this context of the current debate on inclusion criteria

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for DBS for PD, we present a case of a patient who underwent DBS prior to L-dopa treatment.

## CASE REPORT

A 53-year-old engineer, who was suffering from PD for 9 years, worked as a manager for an international company and was an avid downhill skier. His initial symptoms of PD were right hemibody rigidity, bradykinesia, and resting tremor without any axial symptoms or freezing of gait. Pre-DBS medical treatment consisted of ropirinole 8 mg/day, rotigotine 8 mg/day, and selegiline 20 mg/day until 2009 when the symptoms became moderately disabling (leading to a decline in work performance and withdrawal from his passion to ski). Considering the worsening of symptoms and long-lasting dopamine-agonists' intake, L-dopa treatment was proposed by his neurologist. As the patient was well-informed about DBS as an alternative option to the pharmacological treatment for PD and also aware of the possible serious side effects of long-lasting L-dopa intake, he was referred to our centre (Galeazzi Institute, Milan, Italy). After an exhaustive discussion with our multidisciplinary movement disorders team and a presurgical evaluation (56% UPDRS-III improvement at L-dopa challenge; average score at cognitive and psychiatric evaluations), we opted for a STN-DBS lead implantation. His preoperative UPDRS was 17. The uneventful procedure was performed in September 2009. Stimulation parameters were monopolar stimulation, pulse width of 60 ms, frequency of 130 Hz, initial amplitude of 2.5 V, which was increased to 3.5 V. The patient's pharmacological therapy was not changed after DBS surgery. The patient was able to return to work, resume skiing, and thus had a significant improvement in quality of life. The postoperative UPDRS dropped to 8. A slight progression of the hypophonia was observed (which could have been or due to natural disease progression or also to DBS); whereas balance, sleep, and salivation remained unremarkable (which could have been also due to a "protective" effect of DBS). In January 2015, the patient returned to our clinic because of a subtle worsening of his resting tremor and rigidity, which were more prominent on the right side. During the internal pulse generator (IPG) interrogation, the battery was found to be almost exhausted, thus necessitating IPG replacement. After IPG replacement, the patient's tremor and rigidity reduced. However, the patient's fatigue and general bradykinesia remained unchanged during the follow-up neurologic visits. In June 2015, the patient was started with L-dopa treatment (400 mg/day) that led to further improvement of his fatigue and motor performance. In January 2016, the neuropsychological tests were normal and in June 2016 at his latest follow-up visit, the UPDRS III was in On Med/On Stim settings 18.

## DISCUSSION

Within the multifaceted treatment of PD, two aspects are of prime importance, the timing of DBS and the timing of L-dopa treatment. DBS is associated with potential surgical risks,<sup>[6,11]</sup> whereas L-dopa with unavoidable long-term adverse effects. After 5 years of L-dopa treatment, nearly 50%, and after 10 years of treatment, 100% of the patients complain of motor complications.<sup>[17]</sup>

Some authors advocate to delay L-dopa treatment in PD in order to postpone the related motor adverse effects.<sup>[12]</sup>

Given that L-dopa is unavoidably associated with long-term side effects at a stage when DBS becomes a potential treatment option, should one consider to reverse the approach anticipating DBS, consequently delaying the use of L-dopa and its side effects?

The EARLYSTIM trial<sup>[15]</sup> focused on DBS feasibility in a young PD population, with shorter disease duration ( $7.3 \pm 3.1$  years) and early motor complications (for 3 years or less). This trial<sup>[15]</sup> showed that earlier DBS is superior to medical treatment alone, resulting in a longer and more stable improvement in Quality of Life (QoL). In addition, the Vanderbilt group<sup>[3]</sup> recently published the results of a pilot subthalamic stimulation (STN-DBS) study conducted among 30 patients, age span of 50–75 years, with a very short duration of idiopathic PD (>6 months <2 years), a Hoehn and Yahr Stage II in off-medication state, and without motor fluctuations or dyskinesias. However, in contrast to the Vanderbilt trial, the patients included in the Schüpbach's trial<sup>[15]</sup> had more than 5 years disease duration and manifested early motor fluctuations in contrast to the Charles *et al.* trial. Including patients with a disease duration of less than 5 years, as the Charles *et al.*<sup>[3]</sup> trial did, harbors the risk of including cases with atypical Parkinsonism, who are contraindicated for DBS. Our case differs in some critical points from the patients' demographics of these two recent trials.<sup>[3,15]</sup> Our patient had a disease duration of 9 years, which is in line with the current average disease duration of PD patients undergoing DBS, and he displayed a good pre-DBS L-dopa sensitivity. However, contrary to the general PD population treated with DBS at this stage, he had no motor fluctuations or dyskinesias because the patient was not (on his explicit wish) on any L-dopa treatment; within this contest the decision to pursue with DBS was that of the patient, in respect of the patient's right to self-determination.

Within this particular clinical and therapeutic constellation, an interesting finding of our case was that DBS had not only a highly beneficial but also a long lasting effect for 6 years without any significant worsening of symptoms (promising results in the Schüpbach *et al.*<sup>[15]</sup> trial were based on a 2 years follow-up). The protective

effect of DBS might be the reason why despite the natural disease course his UPDRS returned only 7 years later to his preoperative UPDRS score.

Our patient was due to DBS able to continue with his work and to return to ski, both events significantly enhancing his QoL.<sup>[10,14]</sup>

## CONCLUSION

The timing of DBS<sup>[3,5,9,15]</sup> as the timing of L-dopa<sup>[12,18]</sup> in the course of PD remain a matter of debate. The current DBS guidelines as to inclusion criteria in PD patients are vividly discussed and we feel they need broadening. The EARLYSTIM trial<sup>[15]</sup> and our case show promising preliminary results in offering to carefully selected PD patients earlier DBS treatment and to delay the severe disabling L-dopa adverse effects.

We propose to consider DBS in patients prior to L-Dopa, however, with at least a 5 years of disease duration. Despite the promising results of the Schüpbach *et al.*, EARLYSTIM Study<sup>[15]</sup> and the interesting results in our patient, definitive conclusions cannot be made at the current stage of research and evidence.

Large multicentre-based international trials with long follow-ups are needed to answer the effectiveness of earlier DBS in PD. Only this data set will allow to refine further the guidelines of DBS for PD.

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## Conflicts of interest

There are no conflicts of interest.

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