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Effect of subthalamic nucleus deep brain stimulation on balance in Parkinson's disease: A static posturographic analysis

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ABSTRACT

Background: The effect of subthalamic deep brain stimulation on balance in Parkinson's disease remains unclear.
Objective: To evaluate the effect of subthalamic nucleus stimulation on balance in Parkinson's disease using posturography.
Methods: 16 patients (9 women) who underwent subthalamic deep brain stimulation [mean age 59.6 years (46–70); mean disease duration 15.6 years (7–25); mean duration of subthalamic stimulation 32.1 months (3.0–69.6)] and 13 healthy age-matched controls were evaluated using a static posturography analysis. Patients were assessed under four conditions: 1) off medication/off stimulation; 2) off medication/on stimulation; 3) on medication/off stimulation and 4) on medication/on stimulation in ten experimental paradigms, some reproducing common situations of daily living. The displacement of the centre of pressure was analyzed using 14 posturographic parameters. The Mann-Whitney test was used to compare patients with controls. The Wilcoxon signed rank test was used to compare patients under different clinical conditions.
Results: Patients off medication/off stimulation showed larger and more rapid displacements of the centre of pressure than controls in most paradigms ($p < 0.05$), particularly when performing a dual task. Subthalamic stimulation alone reduced the lateral excursion and anterior-posterior velocity of the centre of pressure in quite stance paradigms ($p < 0.05$). Subthalamic stimulation combined with antiparkinsonian medication did not induce statistically significant changes in posturagraphic measures in any experimental paradigm.
Conclusions: Although subthalamic stimulation alone may induce some positive effect on balance, subthalamic stimulation in addition to antiparkinsonian medication, which is the usual treatment in clinical practice, did not modify balance as assessed by static posturography in patients with Parkinson's disease.

1. Introduction

Postural instability and gait disorders (PIGD) are a major problem for patients with advanced Parkinson's disease (PD). Impairment of balance and gait is the main cause of falls in PD and, consequently, of diminished quality of life, morbidity, and mortality [1].

Cortical control plays a key role in the balance of PD patients [2], and is particularly important in dual-task situations. For example, when maintaining postural control while simultaneously performing a secondary cognitive or motor task, patients abnormally prioritize the second task, with the consequent risk of imbalance. This is known as a "posture second" strategy [2,3].

Deep brain stimulation of the subthalamic nucleus (STN-DBS) is an effective, established, evidence-based therapy for patients with Parkinson's disease and motor fluctuations [4]. STN-DBS alleviates the cardinal symptoms of the disease, decreases off periods, and reduces levodopa-induced dyskinesias. However, its effects on the axial manifestations of the disease, such as PIGD, are debated [5]: while some authors reported an improvement in postural control in patients with STN-DBS therapy by developing more appropriate sensorimotor strategies when stimulated [6] or by a higher velocity of displacement of the centre of pressure (CoP) in the lateral axis [7], other authors reported a reduced flexibility of the trunk and pelvis to be a cause of postural instability that was

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resistant to STN-DBS [8], or worse automatic postural responses after STN-DBS [9].

Most published studies evaluated balance in PD patients within the first year after surgery, as Bakker et al. *meta*-analysis [10], who did not observe adverse effects on balance in patients who underwent STN-DBS. But the effect of STN-DBS on balance may change over time. In the first *meta*-regression analyzing the long-term effect of DBS on balance and gait in PD [11], patients who underwent STN-DBS experienced an initial improvement in PIGD, probably due to improvement of dopa-responsive symptoms as rigidity and bradykinesia, although after the second year, progressive worsening was observed compared with cardinal symptoms, which continued to improve five years after surgery.

Therefore, it seems necessary to understand and evaluate the effect of STN-DBS on the pathophysiology of balance control disorders in patients with advanced PD. Recent publications show that interest in balance disability after STN-DBS is growing [12,13].

The aim of our study is to evaluate the effect of STN-DBS on balance in PD patients by static posturography. We consider that a posturography assessment could provide insight into this unsolved topic.

2. Methods

2.1. Participants

The study population comprised 16 patients with PD (nine women and seven men) with a mean age of 59.6 years (range 46–70 years) and mean disease duration of 15.6 years (range 7–25 years).

All patients fulfilled the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria [14] and underwent bilateral STN-DBS at Hospital General Universitario Gregorio Marañón (Madrid, Spain). Target localization was supported by intraoperative microrecordings, the clinical effect of intraoperative electrical stimulation and the accuracy of macroelectrode placement using postoperative magnetic resonance imaging. All patients were implanted with constant voltage stimulation devices (Medtronic Inc., Minneapolis, Minnesota, USA). The mean duration of STN-DBS therapy was 32.1 ± 23.8 months. After STN-DBS all patients experienced a reduction in duration of daily off-time duration (mean 80%, range 50–100%) and in duration and severity of dyskinesias (mean 81%, range 50–100%). All patients were clinically stable, and no adjustments of the stimulation parameters were made during the three months preceding the study. Antiparkinsonian medication expressed as levodopa equivalent daily dose (LEDD), stimulation parameters, Hoehn and Yahr stage [15] and history of previous falls were recorded (Tables 1 and 2).

All recruited patients were able to walk and stand without assistance and were in a Hoehn and Yahr stage ≤ 3 in the on medication-on stimulation condition. All enrolled patients were dopa-responsive, with an improvement of motor symptoms of more than 33% in the UPDRS part III previous to surgery in a levodopa test. The exclusion criteria included the presence of moderate to severe dyskinesias under the effect of medication and STN-DBS, severe tremor when STN-DBS was turned off and cognitive impairment measured by a Minimental State Examination [16] score <24 and the existence of any medical condition that could impair balance. In addition, 13 age-matched healthy controls (six women and seven men) with a mean age of 60.9 years (range 47–73 years) were also investigated.

The study was approved by the local ethics committee, and all subjects gave their written informed consent to participate.

2.2. Experimental design

Participants were examined in the Gait Analysis Laboratory of Hospital General Universitario Gregorio Marañon using an AMTI's AccuSway ^{PLUS} force platform (Advanced Mechanical Technology Inc, MA, USA). This force transducing system calculates the CoP from the ground reaction forces and records and displays the anterior-posterior and lateral displacements of the CoP. Data were acquired, recorded and analyzed using Balance Clinic software (Balance software for the AMTI' s AccuSway plus balance platform, version 2.02.01, Advanced Medical Technology, Inc) [7]. The frequency of the signal acquisition was 50 Hz.

The posturographic study was performed in 10 experimental paradigms of static posturography: Eyes open/wide stance base

Table 1
Demographic and clinical characteristics of patients.

Patient	Gender	Age	Disease Duration (years)	LEDD (mg)	Falls	Duration of DBS therapy (months)	Hoehn&Yahr ON therapy	Hoehn&Yahr OFF therapy
1	F	56	16	800	Yes	36	III	III
2	F	56	23	1100	Yes	69.6	II	III
3	F	68	18	600	Yes	3.6	II	III
4	M	62	14	500	No	43.2	II	III
5	F	70	25	1000	No	64	II	III
6	M	56	14	900	No	31	II	III
7	F	63	7	600	Yes	65	II	III
8	F	68	12	500	Yes	6	II	III
9	F	59	20	950	Yes	36	II	III
10	M	46	16	1200	Yes	34.8	III	III
11	M	57	11	650	Yes	12	II	III
12	F	63	18	400	Yes	4.8	III	III
13	M	65	12	1200	No	56.4	II	III
14	M	47	15	1150	Yes	43.2	II	III
15	M	61	20	1100	Yes	3	II	III
16	F	56	8	1100	Yes	6	III	III

LEDD: Levodopa equivalent daily dose.
ON therapy: ON medication/ON STN-DBS.
OFF therapy: OFF medication/OFF STN-DBS.
DBS: Deep brain stimulation.
STN: Subthalamic nucleus.