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## EFFECTS OF BILATERAL DEEP BRAIN STIMULATION IN THE SUBTHALAMIC NUCLEUS AND LEVODOPA ON GAIT IN PARKINSON'S DISEASE

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### SUMMARY

The goal of the present study was to compare the gait parameters of Parkinson's Disease (PD) patients under the influence of dopaminergic medication and/or high frequency deep brain stimulation (DBS) using the Gait Deviation Index (GDI) and the Gait Profile Score (GPS). The gait assessment was conducted using three-dimensional kinematics. Statistically significant differences ( $P < 0.05$ ) were found for the variables GDI, GPS and GVS (Gait Variable Score) (Hip Flexion / Extension; Knee Flexion / Extension) between the treatment with medication and without stimulation and the other two treatment conditions. In the comparison between treatment without medication and with stimulation and the other two treatment methods, or isolated medication compared to the other two treatment methods together, a high magnitude of effect was observed for the variables GPS and GVS (Hip and Knee), whereas a medium magnitude was found for GDI bilaterally. The results demonstrated that PD patients recorded greater scores in the GDI and GPS/MAP when the two treatments were applied together.

### INTRODUCTION

Levodopa has been shown to be efficient in treating PD in its initial phase. However, as the disease progresses, motor complications, such as abnormalities of the gait, are common [1,2]. High frequency DBS of the subthalamic nucleus (STN) is one of the surgical treatment methods recommended for advanced cases [3,4].

Three-dimensional gait analysis has been used to improve the characterization of specific alterations in the movement patterns of these individuals, thereby allowing a quantitative assessment of pharmacological and/or surgical interventions. However, due to the large quantity of information generated by this analysis, certain indices, such as the GDI and the GPS/MAP were created to condense the complex kinematic parameters of the gait, thus providing simple and easy to interpret measurements for clinical practice [5,6].

The goal of the present study was to analyze and compare the gait parameters of PD patients under the influence of

dopaminergic medication and/or high frequency DBS using the GDI and the GPS.

### METHODS

After approval by the local ethics committee, we selected sixteen patients with PD (11 male and 5 female) who were submitted to bilateral high frequency DBS of the STN, classified between level 1 and 3 on the Hoehn-Yahr modified scale; score  $\geq 24$  points on the Mini Mental State Examination; able to walk independently without the use of antiparkinsonian medication and with the deep brain stimulator switched off.

The gait assessment was conducted using three-dimensional kinematics (SMART-D<sup>®</sup> BTS) in three conditions: without medication and with stimulation (OFF med / ON DBS); with medication and stimulation (ON med / ON DBS); with medication and without stimulation (ON med / OFF DBS). The label of the markers and the processing of the biomechanical model to obtain kinematic data were performed using Vicon Nexus<sup>®</sup> software and the Plug in Gait<sup>®</sup> model.

The kinematic data were imported into a spreadsheet, where a mathematical routine was used to calculate the GDI and GPS/MAP in different conditions. The Unified Parkinson's Disease Rating Scale (UPDRS) part III also was applied during the three conditions.

The data were analyzed using the variance for repeated measures test (ANOVA), with the level of statistical significance set at  $p < 0.05$ . Tukey's multiple comparison test was used when differences were found. Interactions between the variables and treatment were also analyzed. Cohen's  $d$  was used to measure the effect size for treatments for power analysis purposes.

### RESULTS AND DISCUSSION

The results for variables in each treatment are represented as mean and standard deviation in the table 1. A difference was found between the treatment OFF Med / ON DBS compared to ON Med / OFF DBS and ON Med / ON DBS compared to ON Med / OFF DBS for the variables UPDRS,

GDI, GPS and GVS (Hip Flexion/ Extension, Knee Flexion/ Extension). This demonstrated that the condition involving medication and DBS performed better than the other two conditions for these variables.

A difference between the sides was found for the variables GDI, GPS sides and GVS (Hip and Foot Internal / External). The effect size observed between treatments (ON Med / ON DBS versus ON Med / OFF DBS and ON Med / OFF DBS versus OFF Med / ON DBS) was high for both treatment comparisons for the variables UPDRS, GPS overall, GPS side and GVS (Hip Flexion / Extension and Knee Flexion/ Extension). The effect size for GDI was medium for ON med / ON DBS versus ON Med / OFF DBS and high for the ON Med / OFF DBS versus OFF Med / ON DBS comparison (Cohen's  $d = 0.45$ ).

There is evidence that the symptoms that are most responsive to dopamine are also those that provide improved results under the influence of stimulation [7]. However, it is believed that a combination of DBS of the STN and medication reduces motor fluctuations and dyskinesias, as well as reducing tremors, muscle stiffness and bradykinesia.

The exact mechanisms of stimulation are still unknown. The effect of DBS on the STN during walking can be partially measured by the interaction of pedunculopontine nucleus (PPN) and STN. It is believed that the effects of treatment with levodopa were potentiated by the addition of stimulation, suggesting a synergistic effect of the two treatments by different routes [8].

## CONCLUSIONS

We observed that the best scores in UPDRS, GDI and GPS / MAP were obtained when patients were under the effect of two treatments together.

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**Table 1:** Variables UPDRS, GDI and GPS / MAP during gait in patients with Parkinson's disease under treatment effects OFF Med / ON DBS, ON Med / ON DBS and ON Med / OFF DBS.

	OFF Med / ON DBS		ON Med / ON DBS		ON Med / OFF DBS	
	Right	Left	Right	Left	Right	Left
UPDRS <sup>a†</sup>	19.44 (5.86)		13.81 (4.42)		28.56 (9.85)	
GPS Overall <sup>a†</sup>	8.21 (1.89)		7.86 (1.80)		9.47 (2.60)	
GDI <sup>a§, b§</sup>	75.39 (10.47)	79.01 (12.01)	76.83 (10.38)	81.42 (14.01)	69.63 (12.70)	73.23 (13.20)
GPS <sup>a§, b§</sup>	7.88 (1.87)	7.41 (1.87)	7.69 (1.86)	7.12 (2.03)	9.17 (2.69)	8.55 (2.50)
Hip Flx / Ext <sup>a†, c†</sup>	9.97 (4.10)	8.64 (4.74)	9.03 (4.21)	8.10 (5.46)	12.49 (5.79)	11.50 (6.32)
Hip Int /Ext <sup>b†</sup>	7.72 (4.17)	6.30 (3.47)	7.68 (3.78)	6.42 (4.17)	9.54 (4.47)	7.61 (3.78)
Knee Flx/ Ext <sup>a†</sup>	9.33 (2.88)	8.95 (2.28)	8.87 (2.64)	7.59 (1.75)	12.30 (4.48)	11.15 (4.21)
Foot Int / Ext <sup>b†</sup>	9.34 (5.62)	8.31 (5.42)	9.87 (5.11)	7.73 (4.14)	9.45 (5.11)	8.30 (4.43)

<sup>a</sup> Mean difference between treatments. <sup>b</sup> mean difference between sides. <sup>c</sup> interference effect between treatment and side.

† Mean difference is significant at the .050 level. § Mean difference is significant at the .001 level.