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Article

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Article.

Foot-Floor Contact Sequences: A Metric for Gait Assessment in Parkinson's disease after Deep Brain Stimulation

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Abstract: Digital gait monitoring is increasingly used to assess locomotion and fall risk. The aim of this work is analyzing the changes in the foot-floor contact sequences of Parkinson's Disease (PD) patients in the year following the implant for deep brain stimulation (DBS). During their best-ON condition, 30 PD patients underwent gait analysis at baseline (T_0), at 3 months (T_1), and 12 months (T_2) after the DBS neurosurgery for bilateral high-frequency subthalamic nucleus stimulation. Thirty age-matched controls underwent gait analysis once. Each subject was equipped with bilateral foot-switches and a 5-minute walk was recorded, including both straight-line and turnings. The walking speed, turning time, stride time variability, percentage of atypical gait cycles, stance, swing, and double support duration were estimated. Overall, the gait performance of PD patients improved after DBS, as also confirmed by the decrease in the UPDRS-III score from 19.4±1.8 to 10.2±1.0 points (T_0 vs. T_2) ($p < 0.001$). In particular, the percentage change of atypical gait cycles of PD more affected side decreased at T_1 (Straigh-line: -72%; Turnings: -43%) and at T_2 (Straigh-line: -54%; Turnings: -20%). The percentage of atypical gait cycles proved an informative digital biomarker for quantifying PD gait changes after DBS, both in straight-line paths and turnings.

Keywords: DBS; foot-floor contact; gait analysis; locomotion; PD; UPDRS

1. Introduction

Gait alterations are frequent and disabling in Parkinson's Disease (PD) patients, leading to an increased falling risk [1]. High-frequency Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) is a neurosurgical therapy that has proved successful in alleviating motor symptoms of patients suffering from advanced PD [2–8]. The efficacy of DBS for improving motor symptoms is clinically assessed through the Unified Parkinson's Disease Rating III Scale (UPDRS-III) [9].

Gait analysis can be used to objectively quantify abnormalities in locomotion patterns of PD patients [10–12] and their modifications after DBS. To monitor gait, previous studies have employed Inertial Measurement Units (IMU) [13,14], walking mats [15], or foot-worn sensors like foot-pressure insoles and footswitches [16]. To classify motor anomalies in PD, the foot movement is very informative compared to the study of other body segments [14], and investigating the foot-floor contact quality during locomotion can provide unique information about fall risk.

A reliable detection of the gait events for timing the gait cycle, and the detailed study of the foot-floor contact sequence of gait phases, can be obtained through a direct-measurement system based

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on foot-switches [16–18]. PD patients showed an increased percentage of gait cycles with an irregular pattern of foot-floor contact with respect to controls and these "atypical" gait cycles (e.g., forefoot and flatfoot initial-contact gait cycles) were suggested to be tightly related with an increased fall risk [19].

Independently from the technique used to perform gait analysis and the gait parameters considered, the great majority of studies focuses solely on straight-line walking [10,11,15,20,21], neglecting turnings and curved trajectories. This is done because straight-line walking is more repeatable than curved trajectories. Nevertheless, walking patterns collected during turnings can be altered even in early PD stages [22,23]. Furthermore, curved walking and turnings induce more gait instabilities and variability compared to straight walking [24] and hence are more challenging for patients.

This study aims to fill in the gaps in existing research by assessing gait performance in PD patients before, at 3 months, and at 12 months after DBS neurosurgery, by monitoring foot-floor contact sequences during a 5-minute walk that includes both straight-line paths and turnings. We hypothesized that motor symptom improvements in PD patients could be quantitatively assessed by evaluating the foot-floor contact sequences, specifically through the analysis of the percentage of "atypical" gait cycles. An improvement in PD motor performance is expected to result in a reduction in the percentage of gait cycles characterized by irregular patterns.

2. Materials and Methods

2.1. Participants

A total of 60 subjects voluntarily participated in this study. Thirty patients suffering from PD were enrolled at the Stereotactic and Functional Neurosurgery Unit of the University of Turin (Turin, Italy) among those patients eligible for high-frequency (130 Hz) bilateral DBS neurosurgery.

Inclusion criteria were: (*i*) diagnosis of PD, according to the UK Brain Bank principles; (*ii*) good response to levodopa; (*iii*) medication-resistant motor fluctuation and dyskinesia; (*iv*) age at neurosurgery under 70 years; (*v*) absence of freezing of gait and postural instability unresponsive to pharmacological therapy; (*vi*) absence of dementia or severe cognitive impairment, psychiatric or behavioral disturbances as tested through a standardized battery of cognitive tests, assessing reasoning, memory, language, and frontal executive functions [19]; (*vii*) absence of abnormalities at cerebral MRI or relevant condition that increase surgical risk; (*viii*) the ability to walk independently for a few minutes without walking aids or external support during the pharmacological best-ON time window. The only exclusion criterion was the presence of co-morbidities potentially affecting gait performances, such as knee or hip prostheses. Thirty healthy adults were enrolled among the patients' caregivers as a control group, excluding those reporting neurological or musculoskeletal disorders potentially affecting gait performance.

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of A.O.U. Città della Salute e della Scienza di Torino - A.O. Ordine Mauriziano - A.S.L. "Città di Torino" (No. 0092029 approved on 11 September 2018). Written informed consent was obtained from all subjects involved in the study before data acquisition.

2.2. Experimental Protocol and Data Acquisitions

PD patients were tested always during their optimal pharmacological condition (T_0: medication ON; T_1: medication ON + DBS ON; T_2: medication ON + DBS ON). Participants performed a 5-minute walk at self-selected speed, moving back and forth on a 9-meter straight line path. **Figure 1A** shows a schematic representation of the walking path. PD patients performed the overground walking task three times: (*i*) before DBS neurosurgery (baseline, T_0), (*ii*) 3 months after DBS neurosurgery (T_1), and (*iii*) 12 months after DBS neurosurgery (T_2), to study both short- (T_1) and long-

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term (T_2) effects of DBS on walking performance. Healthy controls performed the walking task only once.

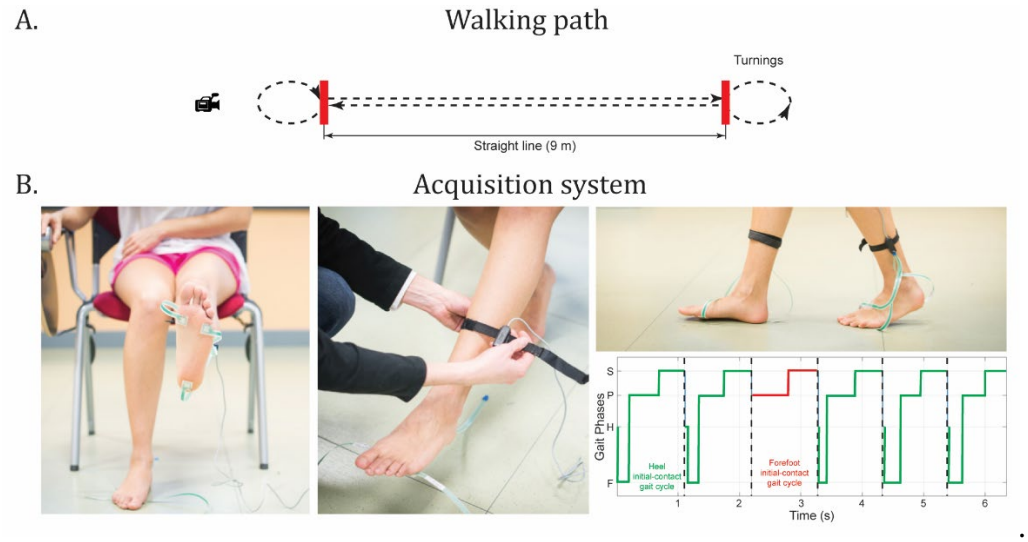

Figure 1. Schematic representation of the walking path and acquisition system. Examples of heel and forefoot initial-contact gait cycles are provided for a representative subject of the sample population.

PD patients were clinically assessed at the Stereotactic Functional Neurosurgery Unit of the University of Turin (Turin, Italy) at baseline (T_0) and at 12 months after DBS (T_2). Assessments included the Unified Parkinson's Disease Rating Scale – Part III (UPDRS-III), the Hoehn and Yahr scale (H&Y), and the Levodopa Equivalent Daily Dose (LEDD).

All participants were instructed by experimenters to walk along the 9-meter straight line path and then perform a 180-degree turn.

Foot-floor contact sequences were recorded through the STEP32 acquisition system (Medical Technology, Turin, Italy). Volunteers were equipped, bilaterally, with 3 footswitches (size: 10 mm × 10 mm × 0.5 mm; activation force: 3 N), fixed beneath the heel, the first, and the fifth metatarsal heads of each foot through double-sided adhesive tape. For PD patients, the more affected side was identified based on the side where the disease first manifested, whereas for healthy controls, the dominant side was determined according to the preferred foot to start walking. **Figure 1B** shows the placement of the footswitches and an example of a footswitch signal acquired during locomotion (sampling rate: 2 kHz) to detect the foot-floor contact sequences. Walking tasks were also simultaneously video-recorded through the STEP32 high-resolution camera.

All data acquisitions were performed at the Motion Analysis Laboratory of the PolitoBIOMed Lab of Politecnico di Torino (Turin, Italy).

2.3. Gait Analysis

After the acquisition of the digital signals during walking, the gait performance was quantitatively assessed in terms of: (*a*) walking speed, (*b*) turning time, (*c*) stride time variability, (*d*) percentage of forefoot and flatfoot initial-contact gait cycles, (*e-f*) stance and swing phase duration, and (*g*) double support.

The straight-path time and the turning time were manually estimated by synchronously analyzing gait signals and video recordings and using a stopwatch. Walking speed (v) was defined as the total distance walked along the straight path (i.e., 9 meters) divided by the total time required to go through it. Turning time (T_{turn}) was defined as the overall time required by the subject to perform the turnings.

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Gait cycles were automatically segmented and classified into typical (i.e., heel initial-contact gait cycles) and forefoot and flatfoot initial-contact gait cycles based on the foot-floor contact sequences detected from the foot-switch signal [16]. Briefly, gait cycles showing the physiological sequence of phases (i.e., Heel contact, Flat foot contact, Push off, and Swing ("HFPS")) were classified as "heel initial contact" or "standard" gait cycles. By contrast, gait cycles characterized by the foot-floor sequence "PFPS" (i.e., push off, flat foot contact, push off, and swing) or "PS" (i.e., push off and swing) and "FPS" (i.e., flat foot contact, push off, and swing) were classified as "forefoot initial-contact" and "flatfoot initial-contact" gait cycles, respectively [16]. The percentage of forefoot and flatfoot initial-contact gait cycles was defined as the percentage of gait cycles showing "PFPS", "PS", and "FPS" foot-floor sequences compared to the total number of gait cycles segmented.

Stride time variability (CoV_{Stride}) was defined as the coefficient of variation ($CoV = standard\ deviation\ /\ mean \times 100$) of the stride durations. From the foot-switch signal, the stance phase duration, the swing phase duration, and the double-support duration were also computed, expressed as a percentage of the Gait Cycle (GC).

Stride time variability (CoV_{Stride}), percentage of forefoot and flatfoot initial-contact gait cycles, stance, swing, and double support were computed for each side (i.e., more-/less-affected side for PD patients and dominant/non-dominant side for healthy controls), separately for straight-line and curvilinear walking.

2.4. Statistical Analysis

Differences in anthropometric characteristics between groups (PD patients - at T_0 and T_2 - and healthy controls) were assessed through the two-tailed Student's *t*-test. One-way multivariate analysis of variance (*1-way* MANOVA) for repeated measures followed by *post-hoc* analysis with Bonferroni adjustment for multiple comparisons was conducted to determine whether there are differences in gait data between groups. The *1-way* MANOVA was conducted considering Group (PD patients and controls) as the between-subjects factor, Body Mass Index (BMI) as the covariate, and all the computed gait parameters (i.e., v, T_{turn}, CoV_{Stride}, percentage of forefoot and flatfoot initial-contact gait cycles, stance, swing, and double support) as the within-subjects variables. In all the analyses, the significance level (α) was set equal to 0.05.

To further evaluate any side-based difference in gait performance, the *1-way* repeated measures MANOVA was performed twice. The first time, only the gait parameters extracted from the more affected side of PD patients (dominant side for controls) were considered. The second time, only the gait parameters extracted from the less affected side of PD patients (non-dominant side for controls) were considered. For each population, all estimated parameters were expressed as mean values and standard errors across the population.

The statistical analysis was carried out using SPSS Statistical Software, version 27.0 (SPSS Inc., Chicago, IL).

3. Results

Three out of thirty PD patients who underwent the gait examinations were then excluded from the final data analysis since they had orthopedic surgery during the follow-up (between T_1 and T_2). Therefore, 27 PD patients (at three time points) and 30 controls were further analyzed. The anthropometric characteristics of PD patients (before DBS, and at 12 months after DBS) and healthy controls enrolled in the study are detailed in **Table I**.

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Table 1. Anthropometric characteristics of PD patients and healthy controls.

		Sex	Age ($years$)	Weight (kg)	Height (m)	UPDRS-III (Best-On condition)	H&R (Best-On condition)	Disease duration ($years$)	LEDD (mg)
PD (n=27)	Before DBS	8 F, 19 M	57.4 ± 1.5	74.4 ± 2.7	1.72 ± 0.02	**19.4 ± 1.8†**	I - III	11.2 ± 0.6	**1354.5 ± 79.9†**
	12-mo after DBS		58.6 ± 1.5			**10.2 ± 1.0†**	I - III	12.3 ± 0.6	**669.4 ± 65.0†**
Controls (n=30)		18 F, 12 M	55.0 ± 1.6	74.1 ± 3.4	1.68 ± 0.01	N/A	N/A	N/A	N/A

Parameters' values are reported as mean ± standard error over the sample population. M: males; F: females; UPDRS-III: Unified Parkinson's Disease Rating Motor Subscale; H&Y: Hoehn and Yahr scale; N/A: Not assessed; LEDD: Levodopa Equivalent Daily Dose. Statistically significant differences are represented through daggers († p <0.001).

No statistically significant differences were detected between PD patients (before DBS) and healthy controls for age, weight, and height. A statistically significant reduction in the UPDRS-III motor scale at 12 months after DBS (T_0: 19.4 ± 1.8; T_2: 10.2 ± 1.0; p < 0.001) was observed, revealing that PD patients clinically improved their motor performance after DBS neurosurgery. Moreover, a statistically significant decrease in LEDD at 12 months after DBS (T_0: 1354.5 ± 79.9 mg; T_2: 669.4 ± 65.0 mg; p < 0.0005) was found, showing a reduction in the levodopa equivalent daily dose after DBS surgery.

To evaluate the gait performance, walking speed, turning time, stride time variability, percentage of forefoot and flatfoot initial-contact gait cycles, stance, swing, and double support duration were assessed during both straight-line walk and turnings. Average gait performance of PD patients (at T_0, T_1, and T_2) and healthy controls are represented in **Table II** with the indication of the statistically significant differences between groups as assessed through the Bonferroni post-hoc analysis (indicated by asterisks, daggers, and double daggers).

After adjusting for BMI, there was a statistically significant difference in gait performance based on Group, $F(66, 203) = 1.63$, $p = 0.007$, Wilk's $\Lambda = 0.28$, partial $\eta^2 = 0.34$. More specifically, groups have a statistically significant effect on turning time ($F(3, 89) = 8.27$, $p < 0.0005$, partial $\eta^2 = 0.22$), percentage of forefoot and flatfoot initial-contact gait cycles considering both the more affected side (straight-line walk: $F(3, 89) = 6.57$, $p < 0.0005$, partial $\eta^2 = 0.18$; turnings: $F(3, 89) = 6.24$, $p = 0.001$, partial $\eta^2 = 0.17$) and the less affected side (turnings: $F(3, 89) = 3.63$, $p = 0.016$, partial $\eta^2 = 0.11$), stance phase duration of the more affected side (straight-line walk: $F(3, 89) = 3.25$, $p = 0.026$, partial $\eta^2 = 0.10$; turnings: $F(3, 89) = 4.56$, $p = 0.005$, partial $\eta^2 = 0.13$), and swing phase duration of the more affected side (straight-line walk: $F(3, 89) = 3.57$, $p = 0.017$, partial $\eta^2 = 0.10$; turnings: $F(3, 89) = 4.62$, $p = 0.005$, partial $\eta^2 = 0.14$). There was no significant effect on walking speed, stride time variability, and double support based on Group.

Table 2. Gait performance o PD patients (at T_0, T_1, and T_2) and healthy controls.

	PD patients			Controls	*1-way* MANOVA Group (*p*-value)
	Before DBS	3-mo after DBS	12-mo after DBS		
Walking speed (m/s)	1.05 ± 0.04	1.03 ± 0.04	0.99 ± 0.06	1.11 ± 0.03	0.25

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TURNING TIME (s)		2.77 ± 0.13*	2.68 ± 0.13†	2.81 ± 0.20‡	2.05 ± 0.11*,†,‡	**< 0.0005**
STRIDE TIME VARIABILITY (%)						
Straight-line	More affected	8.48 ± 1.53	4.95 ± 1.53	5.88 ± 2.39	3.89 ± 1.35	0.16
	Less affected	9.92 ± 1.97	9.50 ± 1.97	5.99 ± 3.08	5.62 ± 1.74	0.30
Turnings	More affected	16.74 ± 1.73	14.73 ± 1.73	16.79 ± 2.70	12.65 ± 1.53	0.29
	Less affected	18.75 ± 1.82	17.63 ± 1.82	16.19 ± 2.85	14.05 ± 1.61	0.25
ATYPICAL GAIT CYCLES (FOREFOOT AND FLATFOOT IC) (%)						
Straight-line	More affected	11.07 ± 1.51*,†	3.06 ± 1.51*	5.09 ± 2.36	3.07 ± 1.33†	**< 0.0005**
	Less affected	10.53 ± 2.62	8.74 ± 2.62	4.18 ± 4.11	5.42 ± 2.32	0.40
Turnings	More affected	13.69 ± 1.12*,†	7.80 ± 1.12*	10.91 ± 1.76	8.05 ± 0.99†	**0.001**
	Less affected	13.25 ± 1.22*	12.28 ± 1.22	9.59 ± 1.90	8.36 ± 1.08*	**0.016**
STANCE (%GC)						
Straight-line	More affected	54.41 ± 0.84*	57.35 ± 0.84*	58.52 ± 1.31	56.76 ± 0.74	**0.026**
	Less affected	57.36 ± 1.06	55.62 ± 1.06	58.65 ± 1.66	57.61 ± 0.94	0.38
Turnings	More affected	59.37 ± 1.21*	62.93 ± 1.21	67.03 ± 1.90*,†	60.56 ± 1.08†	**0.005**
	Less affected	61.89 ± 1.55	61.12 ± 1.56	66.56 ± 2.42	61.67 ± 1.37	0.28
SWING (%GC)						
Straight-line	More affected	45.70 ± 0.85*	42.44 ± 0.85*	41.47 ± 1.33	43.26 ± 0.75	**0.017**
	Less affected	42.51 ± 1.07	44.41 ± 1.07	41.14 ± 1.68	42.34 ± 0.95	0.32
Turnings	More affected	40.62 ± 1.21*	37.12 ± 1.21	32.91 ± 1.89*,†	39.42 ± 1.07†	**0.005**
	Less affected	38.09 ± 1.53	38.85 ± 1.53	33.27 ± 2.40	38.28 ± 1.36	0.25
DOUBLE SUPPORT (%GC)						
Straight-line	More affected	13.98 ± 1.22	14.91 ± 1.22	17.77 ± 1.92	14.62 ± 1.08	0.42
	Less affected	14.28 ± 1.42	15.34 ± 1.42	17.83 ± 2.22	14.63 ± 1.26	0.57
Turnings	More affected	22.75 ± 1.77	23.44 ± 1.77	29.19 ± 2.78	21.62 ± 1.57	0.13
	Less affected	23.86 ± 1.92	24.14 ± 1.92	29.17 ± 3.00	21.98 ± 1.70	0.23

Parameters' values are reported as mean ± standard error over the sample population (after adjusting for BMI). In PD patients, the more and less affected sides are considered as indicated (in controls, the dominant and non-dominant sides are considered in the correspondent rows). DBS=Deep Brain Stimulation; GC=Gait Cycle. Asterisks; IC = Initial Contact. (*), daggers (†), and double daggers (‡) represent statistically significant differences between groups.

Figure 2 shows the gait parameters averaged across each sample population with the indication of the statistically significant differences among groups as assessed through the Bonferroni *post-hoc* analysis (indicated by asterisks). For each sample population, **Figure 2** shows a standard visualization of central tendency through a boxplot (representing minimum, 25th percentile, median, mean, 75th percentile, and maximum) and raw jittered data points of each specific individual (scatter plot).

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Considering only the more affected (or dominant) side, a statistically significant difference in gait performance ($F(36, 243) = 1.99$, $p = 0.001$, Wilk's $\Lambda = 0.47$, partial $\eta^2 = 0.23$) was detected between groups. More specifically, gait performance of PD patients increased at T_1 and T_2, becoming not different from that of healthy controls. No statistically significant group-based differences were detected considering only the less affected (or non-dominant) side.

4. Discussion

This study aimed at assessing gait performance in PD patients before, at 3 months, and at 12 months after DBS neurosurgery, by monitoring gait during a 5-minute walk that included both straight-line gait and turnings.

PD gait performance increased at 3 months (T_1) and at 12 months (T_2) after DBS surgery, becoming not different from that of healthy controls, when considering altogether the tested gait parameters (i.e., velocity, turning duration, stride time variability, percentage of forefoot and flatfoot initial-contact gait cycles, stance/swing duration, and double support) and walking conditions (i.e., straight-line and curvilinear paths). More specifically, a statistically significant improvement in PD gait performance after DBS was found when considering the percentage of forefoot and flatfoot initial-contact gait cycles of the more affected side during both straight-line walk (decreasing from 11.1 ± 1.5% at T_0 to 3.1 ± 1.5% at T_1 and 5.1 ± 2.4% at T_2) and turnings (decreasing from 13.7 ± 1.1% at T_0 to 7.8 ± 1.1% at T_1 and 10.9 ± 1.8% at T_2). In other words, foot-floor contact sequences of PD at 3 months and at 12 months after DBS became comparable to those of healthy controls (straight-line: 3.07 ± 1.33%; turnings: 8.05 ± 0.99%), suggesting improvements in motor performance and a potential reduction in fall risk. These improvements align with the overall clinical enhancement observed in PD patients, as suggested by the UPDRS-III scores (decreasing from an average baseline value of 19.4 ± 1.8 points to 10.2 ± 1.0 points at 12 months after DBS).

Considering the percentage change of forefoot and flatfoot initial-contact gait cycles ($Follow\ up\ time\ point - Baseline\ value / Baseline\ value \times 100$), an improvement in PD gait performance is evident. A higher percentage decrease was found at 3 months after DBS with respect to baseline (-72% during straight line and -43% during turnings) than at 12 months after DBS with respect to baseline (-54% during straight line and -20% during turnings). In other words, a higher decrease in the percentage of forefoot and flatfoot initial-contact gait cycles was observed at 3 months after DBS compared to 12 months after DBS. Results demonstrated that PD patients still face difficulties in performing curvilinear trajectories, as suggested by the smaller decrease in the percentage of atypical gait cycles observed during turnings after DBS with respect to baseline.

In a previous study by Ghislieri *et al.* [19], the percentage of forefoot and flatfoot initial-contact gait cycles was demonstrated to be a valuable biomarker for assessing gait performance in individuals with Parkinson's disease. This measure revealed a moderate-to-strong correlation (r = 0.91, p = 0.002, 95% CI: [0.59, 0.98]) with the UPDRS-III score, highlighting its potential for providing insights into the severity of motor impairments. The present study further emphasizes the usefulness of this parameter for quantifying gait improvements and evaluate the effectiveness of subthalamic nucleus DBS in advanced PD patients. Notably, the improvement in gait performance was aligned with the clinical enhancement observed following DBS surgery.

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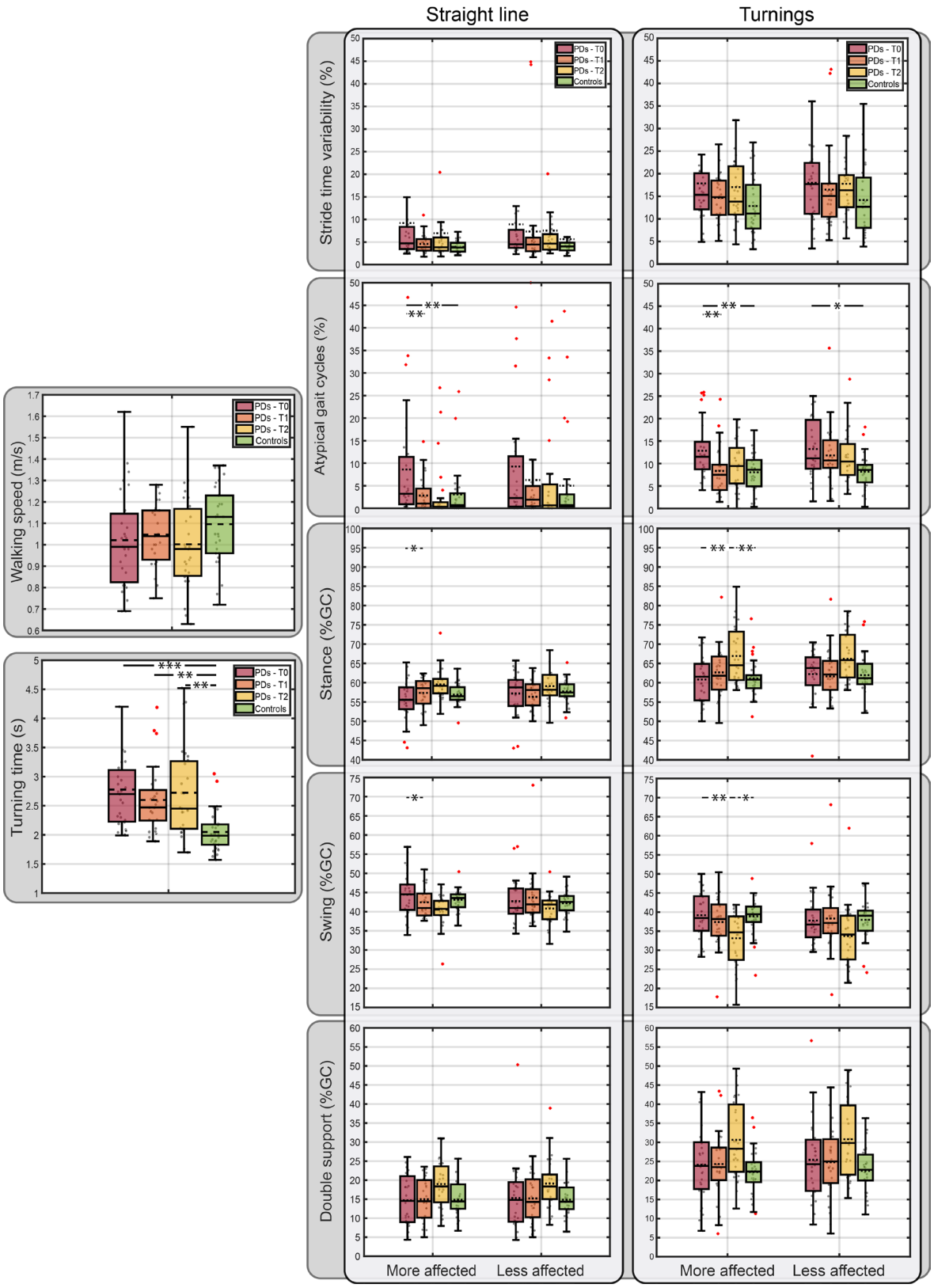

Figure 2. Gait parameters of PD patients (at T_0, T_1, and T_2) and healthy controls. Statistically significant differences ($p < 0.05$) between group mean values are represented by asterisks. Data distributions are shown through boxplots representing minimum, 25th percentile, median, mean, 75th percentile, and maximum. Horizontal dotted lines represent mean values.

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The authors focused their attention on the forefoot and flatfoot initial-contact gait cycles since they hypothesize that the presence of forefoot-strike cycles, and in particular, "PS" cycles (where the heel never touches the ground during the entire stride), can be related to an increase in fall risk. Depending on the way the turning is approached by the subject (e.g., pivoting on the forefoot or executing a broader curve trajectory), the forefoot and flatfoot initial-contact gait cycles can become more frequent during turnings, even in control subjects. Despite this caveat, the findings of this study emphasize the usefulness of foot-switch recordings, through the estimation of the percentage of forefoot and flatfoot initial-contact gait cycles, to detect changes in PD locomotor control during rectilinear and curvilinear paths, providing valuable insights into the effectiveness of DBS surgery in mitigating motor impairments. In addition, in a previous study, forefoot and flatfoot initial-contact gait cycles were found to be strongly correlated with the Unified Parkinson's Disease Rating III Scale (UPDRS-III) [9], indicating its potential for clinical management of PD patients [19].

Despite DBS intervention, PD patients revealed higher turning durations (T_0: 2.8 ± 0.1 s, T_1: 2.7 ± 0.1 s, T_2: 2.8 ± 0.2 s) compared to healthy controls (2.1 ± 0.1 s), indicating persistent difficulty in direction changes during walking even after DBS surgery.

In accordance with the previous observation, a longitudinal trend was also observed, in the PD more affected side, toward increased stance and decreased swing phase duration, during the turnings. This can be hypothesized to be related to the augmented turning time shown by PD patients, even after DBS.

Previous literature has already established that most PD patients have difficulty in turning, even in the early stages of the disease [25], likely because of the complex interaction of gait with dynamic balance during turning. More specifically, it was reported that turning in PD is characterized by long turning duration (and, consequently, slow speed), a large number of steps [26–28], impaired segmental coordination of rotation ("en-bloc"), a narrow base of support and decreased postural stability [29–33]. Not surprisingly, PD patients fall five times more than age-matched older adults and they often fall while turning [34].

Based on the results of this study, the assessment of gait performance during turnings, a more task-demanding activity than straight-line walking, proved highly informative given the gait instabilities and alterations induced by curved trajectories in PD patients both before and after DBS surgery. This emphasizes the significance of broadening the scope of experimental protocol designs to encompass curvilinear trajectories, ensuring a more comprehensive and ecological understanding of gait performance.

Some limitations of the study should be acknowledged. The evaluation of gait performance was only conducted during the best-ON pharmacological time window, which may limit the generalizability of the findings to other phases of medication response. Including different pharmacological phases could provide a more comprehensive understanding of the impact of DBS neurosurgery on gait performance in PD patients. Moreover, while foot-floor contact sequences provide a detailed description of the timing of foot strikes, they do not capture a comprehensive analysis of overall body movements. Future studies could incorporate the assessment of overall body movements, including trunk and upper limb movements, to gain a more comprehensive understanding of how DBS impacts gait performance in Parkinson's disease.

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Data Availability Statement: Data and algorithms presented in this study are available from the corresponding author upon reasonable request.

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References

1. Mirelman, A.; Bonato, P.; Camicioli, R.; Ellis, T.D.; Giladi, N.; Hamilton, J.L.; Hass, C.J.; Hausdorff, J.M.; Pelosin, E.; Almeida, Q.J. Gait Impairments in Parkinson's Disease. *Lancet Neurol* 2019, *18*, 697–708.
2. Dharnipragada, R.; Denduluri, L.S.; Naik, A.; Bertogliat, M.; Awad, M.; Ikramuddin, S.; Park, M.C. Frequency Settings of Subthalamic Nucleus DBS for Parkinson's Disease: A Systematic Review and Network Meta-Analysis. *Parkinsonism Relat Disord* 2023, *116*, 105809, doi:10.1016/j.parkreldis.2023.105809.
3. Vercruysse, S.; Vandenberghe, W.; Munks, L.; Nuttin, B.; Devos, H.; Nieuwboer, A. Effects of Deep Brain Stimulation of the Subthalamic Nucleus on Freezing of Gait in Parkinson's Disease: A Prospective Controlled Study. *J Neurol Neurosurg Psychiatry* 2014, *85*, 871–877, doi:10.1136/jnnp-2013-306336.
4. Cavallieri, F.; Campanini, I.; Gessani, A.; Budriesi, C.; Fioravanti, V.; Di Rauso, G.; Feletti, A.; Damiano, B.; Scaltriti, S.; Guagnano, N. Long-Term Effects of Bilateral Subthalamic Nucleus Deep Brain Stimulation on Gait Disorders in Parkinson's Disease: A Clinical-Instrumental Study. *J Neurol* 2023, 1–12.
5. Hausdorff, J.M.; Gruendlinger, L.; Scollins, L.; O'Herron, S.; Tarsy, D. Deep Brain Stimulation Effects on Gait Variability in Parkinson's Disease. *Movement Disorders* 2009, *24*, 1688–1692, doi:10.1002/mds.22554.
6. Limousin, P.; Foltynie, T. Long-Term Outcomes of Deep Brain Stimulation in Parkinson Disease. *Nat Rev Neurol* 2019, *15*, 234–242, doi:10.1038/s41582-019-0145-9.
7. Zibetti, M.; Merola, A.; Rizzi, L.; Ricchi, V.; Angrisano, S.; Azzaro, C.; Artusi, C.A.; Arduino, N.; Marchisio, A.; Lanotte, M.; et al. Beyond Nine Years of Continuous Subthalamic Nucleus Deep Brain Stimulation in Parkinson's Disease. *Movement Disorders* 2011, *26*, 2327–2334, doi:10.1002/mds.23903.
8. Schlenstedt, C.; Shalash, A.; Muthuraman, M.; Falk, D.; Witt, K.; Deuschl, G. Effect of High-Frequency Subthalamic Neurostimulation on Gait and Freezing of Gait in Parkinson's Disease: A Systematic Review and Meta-Analysis. *Eur J Neurol* 2017, *24*, 18–26, doi:10.1111/ENE.13167.
9. Goetz, C.G.; Tilley, B.C.; Shaftman, S.R.; Stebbins, G.T.; Fahn, S.; Martinez-Martin, P.; Poewe, W.; Sampaio, C.; Stern, M.B.; Dodel, R.; et al. Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale Presentation and Clinimetric Testing Results. *Movement Disorders* 2008, *23*, 2129–2170, doi:10.1002/mds.22340.
10. Di Biase, L.; Di Santo, A.; Caminiti, M.L.; De Liso, A.; Shah, S.A.; Ricci, L.; Di Lazzaro, V. Gait Analysis in Parkinson's Disease: An Overview of the Most Accurate Markers for Diagnosis and Symptoms Monitoring. *Sensors 2020, Vol. 20, Page 3529* 2020, *20*, 3529, doi:10.3390/S20123529.
11. Zanardi, A.P.J.; da Silva, E.S.; Costa, R.R.; Passos-Monteiro, E.; dos Santos, I.O.; Kruel, L.F.M.; Peyré-Tartaruga, L.A. Gait Parameters of Parkinson's Disease Compared with Healthy Controls: A Systematic Review and Meta-Analysis. *Scientific Reports 2021 11:1* 2021, *11*, 1–13, doi:10.1038/s41598-020-80768-2.
12. Horak, F.B.; Mancini, M. Objective Biomarkers of Balance and Gait for Parkinson's Disease Using Body-Worn Sensors. *Movement Disorders* 2013, *28*, 1544–1551, doi:10.1002/MDS.25684.
13. Lee, M.; Youm, C.; Jeon, J.; Cheon, S.M.; Park, H. Validity of Shoe-Type Inertial Measurement Units for Parkinson's Disease Patients during Treadmill Walking. *J Neuroeng Rehabil* 2018, *15*, 1–12, doi:10.1186/S12984-018-0384-9/TABLES/5.
14. Caramia, C.; Torricelli, D.; Schmid, M.; Munoz-Gonzalez, A.; Gonzalez-Vargas, J.; Grandas, F.; Pons, J.L. IMU-Based Classification of Parkinson's Disease from Gait: A Sensitivity Analysis on Sensor Location and Feature Selection. *IEEE J Biomed Health Inform* 2018, *22*, 1765–1774, doi:10.1109/JBHI.2018.2865218.
15. Galna, B.; Lord, S.; Rochester, L. Is Gait Variability Reliable in Older Adults and Parkinson's Disease? Towards an Optimal Testing Protocol. *Gait Posture* 2013, *37*, 580–585, doi:10.1016/j.gaitpost.2012.09.025.

16. Agostini, V.; Balestra, G.; Knaflitz, M.; Agostini V.; Balestra G.; Knaflitz M.; Agostini, V.; Balestra, G.; Knaflitz, M. Segmentation and Classification of Gait Cycles. *IEEE Transactions on Neural Systems and Rehabilitation Engineering* 2014, *22*, 946–952, doi:10.1109/TNSRE.2013.2291907.
17. Di Nardo, F.; Strazza, A.; Mengarelli, A.; Cardarelli, S.; Tigrini, A.; Verdini, F.; Nascimbeni, A.; Agostini, V.; Knaflitz, M.; Fioretti, S. EMG-Based Characterization of Walking Asymmetry in Children with Mild Hemiplegic Cerebral Palsy. *Biosensors (Basel)* 2019, *9*, 82, doi:10.3390/bios9030082.
18. Agostini, V.; Ganio, D.; Facchin, K.; Cane, L.; Moreira Carneiro, S.; Knaflitz, M. Gait Parameters and Muscle Activation Patterns at 3, 6 and 12 Months After Total Hip Arthroplasty. *J Arthroplasty* 2014, *29*, 1265–1272, doi:10.1016/j.arth.2013.12.018.
19. Ghislieri, M.; Agostini, V.; Rizzi, L.; Knaflitz, M.; Lanotte, M. Atypical Gait Cycles in Parkinson's Disease. *Sensors* 2021, *21*, 5079, doi:10.3390/s21155079.
20. E, B.; D, B.; Elumalai, V.K.; K, U. Data-Driven Gait Analysis for Diagnosis and Severity Rating of Parkinson's Disease. *Med Eng Phys* 2021, *91*, 54–64, doi:10.1016/j.medengphy.2021.03.005.
21. Schlachetzki, J.C.M.; Barth, J.; Marxreiter, F.; Gossler, J.; Kohl, Z.; Reinfelder, S.; Gassner, H.; Aminian, K.; Eskofier, B.M.; Winkler, J.; et al. Wearable Sensors Objectively Measure Gait Parameters in Parkinson's Disease. *PLoS One* 2017, *12*, e0183989, doi:10.1371/journal.pone.0183989.
22. Song, J.; Sigward, S.; Fisher, B.; Salem, G.J. Altered Dynamic Postural Control during Step Turning in Persons with Early-Stage Parkinson's Disease. *Parkinsons Dis* 2012, doi:10.1155/2012/386962.
23. Turcato, A.M.; Godi, M.; Giardini, M.; Arcolin, I.; Nardone, A.; Giordano, A.; Schieppati, M. Abnormal Gait Pattern Emerges during Curved Trajectories in High-Functioning Parkinsonian Patients Walking in Line at Normal Speed. *PLoS One* 2018, *13*, doi:10.1371/journal.pone.0197264.
24. Yang, W.C.; Hsu, W.L.; Wu, R.M.; Lu, T.W.; Lin, K.H. Motion Analysis of Axial Rotation and Gait Stability during Turning in People with Parkinson's Disease. *Gait Posture* 2016, *44*, 83–88, doi:10.1016/j.gaitpost.2015.10.023.
25. Zampieri, C.; Salarian, A.; Carlson-Kuhta, P.; Aminian, K.; Nutt, J.G.; Horak, F.B. The Instrumented Timed up and Go Test: Potential Outcome Measure for Disease Modifying Therapies in Parkinson's Disease. *J Neurol Neurosurg Psychiatry* 2010, *81*, 171–176, doi:10.1136/JNNP.2009.173740.
26. Stack, E.; Ashburn, A. Dysfunctional Turning in Parkinson's Disease. *Disabil Rehabil* 2008, *30*, 1222–1229, doi:10.1080/09638280701829938.
27. Hulbert, S.; Ashburn, A.; Robert, L.; Verheyden, G. A Narrative Review of Turning Deficits in People with Parkinson's Disease. *Disabil Rehabil* 2015, *37*, 1382–1389, doi:10.3109/09638288.2014.961661.
28. Hong, M.; Perlmutter, J.S.; Earhart, G.M. A Kinematic and Electromyographic Analysis of Turning in People With Parkinson Disease. *http://dx.doi.org/10.1177/1545968308320639* 2008, *23*, 166–176, doi:10.1177/1545968308320639.
29. Mancini, M.; Weiss, A.; Herman, T.; Hausdorff, J.M. Turn Around Freezing: Community-Living Turning Behavior in People with Parkinson's Disease. *Front Neurol* 2018, *9*, doi:10.3389/fneur.2018.00018.
30. Mak, M.K.Y.; Patla, A.; Hui-Chan, C. Sudden Turn during Walking Is Impaired in People with Parkinson's Disease. *Exp Brain Res* 2008, *190*, 43–51, doi:10.1007/S00221-008-1446-1/FIGURES/3.
31. Crenna, P.; Carpinella, I.; Rabuffetti, M.; Calabrese, E.; Mazzoleni, P.; Nemni, R.; Ferrarin, M. The Association between Impaired Turning and Normal Straight Walking in Parkinson's Disease. *Gait Posture* 2007, *26*, 172–178, doi:10.1016/J.GAITPOST.2007.04.010.
32. Huxham, F.; Baker, R.; Morris, M.E.; Iansek, R. Head and Trunk Rotation during Walking Turns in Parkinson's Disease. *Movement Disorders* 2008, *23*, 1391–1397, doi:10.1002/MDS.21943.
33. Visser, J.E.; Voermans, N.C.; Nijhuis, L.B.O.; van der Eijk, M.; Nijk, R.; Munneke, M.; Bloem, B.R. Quantification of Trunk Rotations during Turning and Walking in Parkinson's Disease. *Clinical Neurophysiology* 2007, *118*, 1602–1606, doi:10.1016/J.CLINPH.2007.03.010.
34. Weaver, T.B.; Robinovitch, S.N.; Laing, A.C.; Yang, Y. Falls and Parkinson's Disease: Evidence from Video Recordings of Actual Fall Events. *J Am Geriatr Soc* 2016, *64*, 96–101, doi:10.1111/JGS.13878.