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ORIGINAL ARTICLE

Evaluating gait and postural responses to subthalamic stimulation and levodopa: A prospective study using wearable technology

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Abstract

Background: The efficacy of subthalamic stimulation on axial signs of Parkinson's disease (PD) is debated in the literature. This study delves into the dynamic interplay of gait and posture, specifically probing their nuanced response to subthalamic stimulation and levodopa.

Methods: We used wearable sensor technology to examine alterations in the spatiotemporal parameters of gait and posture in individuals with PD before and 6 months after subthalamic deep brain stimulation (STN-DBS) surgery. Thirty-three subjects with PD were evaluated in two pre-operative and four post-operative conditions comprising OFF/ON medication and stimulation states. Standardized response mean (SRM) values were calculated to assess treatment responsiveness.

Results: Significant improvements in spatiotemporal gait parameters, including speed, stride length, cadence, and turning, were observed following STN-DBS surgery. Quantitatively, stimulation outperformed levodopa in enhancing gait speed, stride length, and turning, as indicated by SRM. Levodopa moderately improved stride time variability and asymmetry, while stimulation alone demonstrated limited efficacy. Postural parameters exhibited minimal change following STN-DBS, although stimulation showed a slight benefit in certain postural aspects.

Conclusion: Our findings suggest positive effects of stimulation and levodopa on gait and postural parameters, with STN-DBS demonstrating superior efficacy in enhancing

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gait speed, stride length, and turning. However, gait variability remains unaddressed by current therapies, highlighting the need for novel treatments targeting regions beyond the basal ganglia.

KEYWORDS
deep brain stimulation, inertial measurement units, kinematic analysis, neuromodulation, Parkinson's disease

INTRODUCTION

Deep brain stimulation of the subthalamic nucleus (STN-DBS) is a well-established surgical treatment for managing motor symptoms in Parkinson's disease (PD) [1].

Since the first clinical trials, the efficacy of STN-DBS has been primarily assessed using clinical scales, especially the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) [2]. While MDS-UPDRS scores resulted significant lower during stimulation ON periods [3, 4], the scale lacks the sensitivity needed to detect changes in specific motor functions, particularly in axial features such as gait and posture [5]. This limitation highlights the ongoing debate regarding the responsiveness of axial signs to subthalamic stimulation [6]. Few small-sample studies have evaluated the efficacy of STN-DBS on gait and posture using kinematic measures, but variability in design, methods, and follow-up duration has led to inconclusive results [7–11]. Nevertheless, these aspects hold significant clinical importance in advanced stages of PD. Balance is compromised by postural instability, while gait is primarily affected by hypokinesia (reduced gait speed), narrow shuffling steps (short stride lengths, increased step number), start hesitation, and freezing of gait (FOG) [12, 13].

Levodopa therapy can ameliorate specific gait parameters, such as gait speed and stride length; however, literature suggests the existence of levodopa-resistant features (step initiation, cadence, gait variability, turning, balance), pointing toward the involvement of multiple neural circuits in parkinsonian gait and postural disturbances [14, 15].

In this study, we implemented a standardized analysis protocol using wearable sensors in individuals with PD eligible for STN-DBS surgery to obtain quantitative measurements of gait and posture.

We first aimed to evaluate kinematic changes after STN-DBS surgery by comparing pre- and post-operative measurements in ON- and OFF-medication states. Secondly, we estimated the distinct effect of stimulation and levodopa on specific gait and postural parameters, considering that the control of locomotion involves a multimodal network where stimulation and levodopa may affect specific axial features in different ways [16].

Hence, understanding how stimulation and levodopa impact distinct locomotion features is crucial to optimizing therapeutic approaches and improving individual outcomes [17].

MATERIALS AND METHODS

In this prospective study, we consecutively enrolled subjects with PD eligible for bilateral STN-DBS surgery at the Movement Disorder Center of the IRCCS Istituto delle Scienze Neurologiche di Bologna from December 2021 to February 2024.

Inclusion criteria for STN-DBS surgery according to CAPSIT-PD protocol [18] were established clinical diagnosis of PD [19] with disabling motor fluctuations and/or dyskinesias and good response to levodopa defined as improvement rate > 30% on the MDS-UPDRS III at the levodopa challenge test. Exclusion criteria included dementia or ongoing psychiatric disorders assessed through specific cognitive-behavioral assessment; evidence of severe atrophy, diffuse cerebral lesions, high risk of bleeding on brain MRI; systemic comorbidities interfering with surgery.

The electrode lead position was verified through microelectrode recording and imaging obtained by Nexframe™ frameless technique and intraoperative O-arm™, as well as post-operative T1-weighted imaging or CT scan [20]. All implanted electrodes were localized in the subthalamic region.

A monopolar review was conducted 1 month after surgery to assess the amplitude threshold for clinical benefits and side effects for each electrode contact and select the best therapeutic option. Subsequently, stimulation parameters were clinically optimized. Monopolar stimulation parameters were used for all subjects, with a median amplitude of 2.1(1.3)mA and 2.1(1.0)mA for the left and right side, respectively. The frequency was set at 125-130 Hz, and the pulse width was 60 microseconds for all subjects except two, one had a frequency of 210 Hz and another had a pulse width of 90 microseconds.

Clinical motor assessment

Subjects were evaluated before (pre-DBS) and 6 months after surgery (post-DBS) after achieving an optimal motor outcome with stable stimulation parameters and dopaminergic medication for at least 1 month.

Pre-DBS evaluations were performed in OFF state (early in the morning, after withdrawal of 12 hours of levodopa and 24 hours of long-acting antiparkinsonian drugs, med-OFF) and in ON state (the

best subjective motor state between 45–60 minutes from the assumption of the usual morning dose of levodopa, med-ON).

After surgery, subjects were also assessed 60 minutes after switching off (stim-OFF) and 30 minutes after switching on (stim-ON) the stimulator. They were thus sequentially evaluated in the following four conditions: med-OFF/stim-ON, med-OFF/stim-OFF, med-ON/stim-OFF, and med-ON/stim-ON. Pre-DBS and post-DBS monitoring took approximately 2 and 4 hours, respectively.

Each evaluation included 1) motor clinical examination based on MDS-UPDRS III total score and compound postural instability and gait difficulty subscore (PIGD subscore) calculated as the sum of the items 3.10, 3.11, and 3.12 of MDS-UPDRS III [21]; 2) recording of FOG episodes during the standardized motor protocol visually scored by the clinician and defined as brief, episodic absence or marked reduction in forward foot progression despite the intention to walk [22]; 3) levodopa kinetic-dynamic test [23]; 4) kinematic analysis of gait and posture; and 5) computerized alternate index finger tapping test [24].

Clinical information including disease duration, motor phenotype, disease severity, cognitive and behavioral performances including Mini-Mental State Examination(MMSE) [25], post-operative motor improvement calculated as MDS-UPDRSIII score [(pre-DBS med-OFF– post-DBS med-OFF/stim-ON)/pre-DBS med-OFF] × 100, levodopa equivalent daily dose(LEDD) [26] and variations in dopaminergic treatment(Supplementary Figure 1) was systematically collected during pre- and post-operative assessment.

Instrumental motor assessment

Gait and posture were monitored using the mTest3 system (mHealth Technologies srl, Bologna, Italy), comprising three wearable inertial sensors. Two sensors were worn on the shoes using Velcro straps, and one was placed on the lower back using an elastic belt. Wearable sensors were synchronized and connected via Bluetooth to a smartphone with a dedicated app. The instrumental motor assessment was video-recorded for clinical review.

Objective measures of motor performance were chosen based on their test–retest reliability and validity [27]. The standardized motor protocol included

1. Timed Up and Go test (TUG): rise from a chair, walk 3 meters, turn in place, and return to sitting.
2. Quiet standing test (SWAY): maintain their standing position for 30 seconds with their arms placed alongside, looking straight ahead at a fixed point on the wall.
3. Full 360° turns in place: perform two full 360° turns in place, alternately turning clockwise and counterclockwise.
4. 18-m walking test (GAIT): walk straight in a corridor for a fixed distance of 18 meters.
5. Complex task: walk 2 meters, open a door, pass the doorway, walk 3 m, turn in place, and return to the starting position without closing the door [28]. The pivot turn in place was executed in a confined area to enhance the likelihood of experiencing FOG.

All locomotor tasks were performed in consecutive order on the same morning. TUG, GAIT, Full 360° turns, and complex task were completed in both single (ST) and dual-task conditions (DT, serial-3 subtractions). TUG and GAIT single tasks were performed three times to filter out the effects due to habituation or lack of attention [29], whereas the remaining tasks were performed twice. SWAY was repeated twice with open eyes (EO) and twice with closed eyes (EC). Resting periods with subjects sitting in an armchair were incorporated between evaluations to mitigate potential fatigue effects during the protocol.

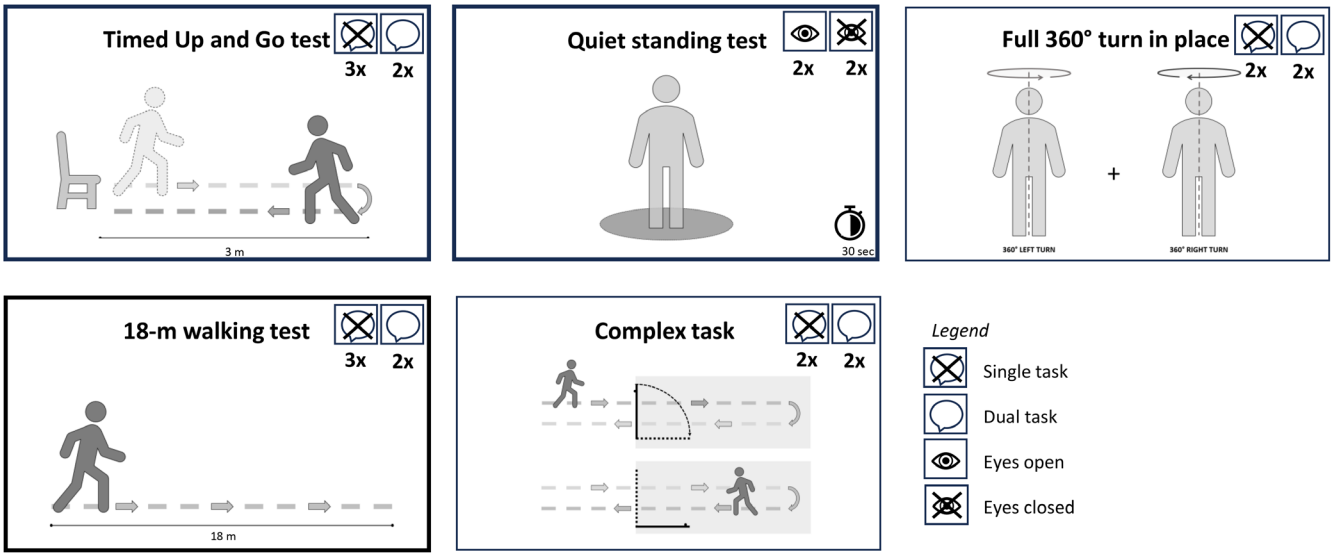

FIGURE 1 Motor tasks included in the DBS monitoring protocol. Tasks analyzed in this study Timed Up and Go test—TUG, 18-m walking test—GAIT, Quiet standing test—SWAY) are outlined in bold.

In the present study, we analyzed the kinematic parameters of TUG, GAIT, and SWAY (Figure 1).

The Ethics Committee of the Local Health Service of Bologna approved this study (CE21156, 21/10/2021), and the research was conducted according to the Declaration of Helsinki. All participants signed an informed consent form before testing.

Data analysis

The following gait and postural parameters were analyzed:

- TUG: time spent to complete the test (*Total duration*); total number of steps during the test (*Total steps*); mean angular velocity of the 180° turn (*180° turn velocity*), number of steps for turning 180° (*180° turn steps*); time to stand up from the chair (*Sit-to-walk duration*); root mean square of the vertical acceleration during sit-to-walk transition (*RMS acc V sit to walk*).
- GAIT: mean gait speed (*Gait speed*); total number of strides during the test (*Total strides*); mean value of strides length (*Stride length*); speed difference between right and left steps (*Asymmetry*); standard deviation of stride time (*Stride time variability*); mean number of steps per minute (*Cadence*).
- SWAY: length of the trajectory covered by the center of mass during postural oscillation on the horizontal plane (*Sway path*); 95% confidence interval ellipse area that incapsulates trajectory points on the horizontal plane (*Ellipse area*); mean sway velocity along anteroposterior (AP) and mediolateral (ML) axes (*Mean AP velocity*, *Mean ML velocity)*; 95% power frequency of the acceleration along the AP and ML axes *(Power frequency acc AP*, *Power frequency acc ML).*

For each subject, motor parameter values obtained from wearable inertial sensors were averaged over the different repetitions to minimize performance differences across trials.

Data were available for 30 subjects at pre-DBS evaluation since three subjects could not perform the gait protocol in med-OFF condition and were excluded from the pre-operative analysis. Post-operative data were available for all the subjects, except for one and three subjects who could not walk independently in the stim-OFF condition of TUG and GAIT, respectively.

Statistical analysis

Continuous variables were presented as median values and interquartile range(IQR), while categorical variables were represented as frequencies and percentages. The Kolmogorov–Smirnov test was conducted to evaluate the normality. A p-value<0.05 was considered statistically significant.

Pre- and post-DBS comparison and comparison across the four post-operative conditions (one factor built considering both medication and stimulation) were performed using repeated measure Wilcoxon and Friedman tests, as appropriate due to ANOVA assumptions not being met for the measured features. Each Friedman test was performed feature-by-feature, using a complete-cases-only approach in each instance. When the Friedman test indicated significance, paired Wilcoxon tests were used to compare each variable against the baseline condition med-OFF/stim-OFF. All p-values obtained in the post hoc multiple comparisons of baseline versus the three other conditions were adjusted by using the Benjamini–Hochberg procedure.

Standardized response mean (SRM) values were computed to assess the responsiveness of sensor-based parameters after surgery [15]. Med-OFF/stim-ON and med-ON/stim-OFF were analyzed against baseline condition to assess responsiveness to stimulation and medication, respectively, while med-ON/stim-ON described their combined effect. SRM values of 0.20–0.50 indicate a small response, 0.50–0.80 a moderate response and above 0.80 a large response to the treatment.

The comparison of ST versus DT performance was achieved by calculating dual-task cost [30]. Positive dual-task cost describes worse performance under DT than under ST, while negative dual-task cost describes better performance under DT than under ST.

Test–retest reliability was estimated using the intraclass correlation coefficients ICC(2,k) [31] of the instrumental variables in all the conditions performed in pre-DBS and post-DBS, considering the subjects who performed all the scheduled trials. Most instrumental variables showed excellent reliability (ICC>0.90) both in pre-DBS and post-DBS conditions (**Supplementary Table 1**) [32].

RESULTS

We enrolled 33 consecutive PD subjects who performed clinical assessments and instrumented gait and posture analysis before and after bilateral STN-DBS. Demographic and clinical features are shown in Table 1.

Clinical and instrumental motor outcomes before and after STN-DBS

Table 2 compares the values of clinical and instrumental outcomes before and after STN-DBS. Subthalamic stimulation induced a significant reduction of MDS-UPDRS III score in med-OFF/stim-ON condition compared to pre-operative med-OFF. Similarly, the PIGD subscore and the number of patients experiencing FOG were reduced following STN-DBS. Furthermore, a significant reduction in LEDD was observed after surgery (levodopa: 800[567] vs. 400[295] mg; dopamine agonists: 105[210] vs. 26[120]mg).

Several quantitative motor parameters of TUG, GAIT, and SWAY extracted through the wearable sensors also changed post-operatively.

Most of the TUG parameters (total duration, total steps, turning phase, sit-to-walk acceleration), as well as GAIT parameters (gait

TABLE 1 Subjects' demographic and clinical features.

Demographic/clinical features	Median (IQR)	
Number, n	33	
Sex, M/F, n	24/9	
Age at DBS, y	62.0 (10.0)	
Disease duration at DBS, y	11.0 (7.0)	
PD subtype, n (%)		
- tremor dominant	12 (36.5%)	
- akinetic-rigid dominant	15 (45.5%)	
- mixed	6 (18.0%)	
Post-DBS motor improvement (%)	49.4% (31.5%)	
	pre-DBS	**post-DBS**
MDS-UPDRS I	8.0 (8.0)	5.0 (5.0) *
MDS-UPDRS II	11.0 (6.0)	5.0 (4.0) *
MDS-UPDRS IV	8.0 (6.0)	1.0 (3.0) *
H&Y	2.0 (0.5)	2.0 (0)
MMSE	30.0 (1.0)	29.5 (2.0)
LD test dose, mg	175 (50)	100 (13) *
LEDD, mg/die	1005 (737)	463 (402) *

Abbreviations: DBS, deep brain stimulation; H&Y, Hoehn and Yahr scale; LD, levodopa; LEDD, Levodopa Equivalent Daily Dose; MDS-UPDRS, Movement Disorder's Unified Parkinson's Disease Rating Scale; MMSE, Mini-Mental State Examination; PD, Parkinson's Disease.

Data are presented as median (IQR).

*: Statistically significant p-value between the pre-DBS and post-DBS evaluation according to paired data Wilcoxon test (p-value <0.05).

speed, total strides, stride length, asymmetry, cadence), significantly improved in the med-OFF condition after STN-DBS.

SWAY parameters did not significantly vary between pre-DBS and post-DBS.

Dual-task gait performance while executing serial-3 subtractions during TUG and GAIT improved post-DBS similarly to the single-task performance. Additionally, we observed a significant reduction of stride time variability in post-DBS assessment compared to pre-DBS (Figure 2, **Supplementary Table 2**).

Gait and postural performances in post-operative conditions

Clinical scales, number of patients experiencing FOG, and kinematic parameters showed improvement with medication and/or stimulation compared to baseline (med-OFF/stim-OFF) (Table 3).

During the TUG, we observed a significant reduction in the overall duration, fewer steps, and an increase in turning velocity in all the treatment conditions compared to the baseline.

Considering the GAIT test, we documented increased stride length and improved cadence with medication and/or stimulation ON compared to the baseline (med-OFF/stim-OFF). Gait speed and number of steps were significantly enhanced in stim-ON conditions (med-OFF/stim-ON, med-ON/stim-ON). Meanwhile, asymmetry and stride time variability significantly improved only in med-ON conditions (med-ON/stim-OFF, med-ON/stim-ON).

SWAY parameters, including sway path, ellipse area and mean AP sway velocity, were smaller in med-OFF/stim-ON condition and larger in med-ON conditions compared to baseline. Additionally, the power frequency of mediolateral postural acceleration was significantly reduced in med-ON conditions (med-ON/stim-OFF, med-ON/stim-ON).

Most of the TUG DT and GAIT DT parameters improved with medication and/or stimulation ON compared to the baseline, similarly to ST (Figure 3, **Supplementary Table 3**).

Stimulation and levodopa responsiveness of kinematic parameters

The responsiveness of kinematic parameters of TUG, GAIT, and SWAY tasks are reported in Figure 4. All the treatments determined a low (SRM:0.2–0.5) to moderate (SRM:0.5–0.8) improvement of TUG total duration and number of steps. Stimulation brought a large improvement (SRM >0.8) in the velocity during the turning phase of TUG compared to a moderate effect of levodopa.

GAIT parameters, including speed and total strides, demonstrated a small improvement with levodopa and a moderate improvement with stimulation or the combination of the two treatments.

Stride length and cadence were largely improved by stimulation and combined treatments.

Stimulation showed a small effect on stride time variability and no effect on asymmetry. However, these parameters were moderately enhanced by levodopa treatment and the combination of levodopa and stimulation.

Postural SWAY parameters slightly improved with stimulation but worsened with levodopa, except for the power frequency of acceleration, which slightly improved in all the treatment conditions.

During DT evaluations, the responsiveness of gait and postural parameters was qualitatively similar to ST, although levodopa produced only a tiny improvement in asymmetry and stride time variability.

DISCUSSION

In this study, we integrated instrumental measures into our clinical protocol for evaluating the motor performances of individuals with PD before and after STN-DBS surgery. This approach allows a deeper exploration of certain motor aspects, particularly gait and posture, that are challenging to characterize through conventional clinical scales.

Using wearable sensor technology, we replicated and extensively characterized previously reported improvements in gait following STN-DBS, drawing from two smaller preliminary studies based on computer-assisted gait analysis systems [7, 11]. Our analysis demonstrated significant improvements in the MDS-UPDRS PIGD subscore, the number of patients experiencing FOG and,

TABLE 2 Clinical scores and sensor-based motor parameters in pre-DBS and post-DBS monitoring performed in single-task mode. Data are presented as median (IQR).

Variable [unit of measurement]	pre-DBS (med-OFF)	post-DBS (med-OFF/ stim-ON)	p-value
Clinical features			
MDS-UDPRS III total score	41.50(17.00)	22.00 (14.25)	**<0.001**
MDS-UPDRS PIGD	2.00(4.00)	1.00(1.00)	**<0.001**
FOG, [n patients (%)]	14 (42.4%)	10 (30.3%)	**<0.001**
Finger tapping score	100.00(38.25)	154.00(69.00)	**<0.001**
Instrumented quantitative motor performances			
TUG ST			
Total duration [s]	13.35(5.98)	9.64(2.40)	**<0.001**
Total steps [#]	15.17(7.00)	12.00(2.67)	**<0.001**
180° turn velocity [°/s]	72.29(23.16)	87.92(20.51)	**<0.001**
180° turn steps [#]	4.00(1.50)	3.33(1.17)	**0.018**
Sit-to-walk duration [s]	1.43(0.44)	1.45(0.29)	0.101
RMS acc V sit to walk [m/s]	1.01(0.51)	1.35(0.67)	**0.011**
GAIT ST			
Gait speed [m/s]	1.24(0.58)	1.55(0.32)	**0.028**
Total strides [#]	28.33(13.16)	24.25(4.34)	**0.002**
Stride length [m]	1.22(0.47)	1.45(0.30)	**0.039**
Asymmetry	3.17(4.06)	1.50(2.17)	**0.038**
Stride time variability	0.07(0.05)	0.04(0.05)	0.324
Cadence [strides/min]	54.33(8.00)	58.33(6.38)	**0.019**
SWAY EO			
Sway path [cm]	135.77(48.38)	149.19(59.07)	0.261
Ellipse area [cm^2]	283.50(596.36)	378.68(422.84)	0.198
Mean AP velocity [cm/s]	0.38(0.20)	0.42(0.14)	0.177
Mean ML velocity [cm/s]	0.15(0.12)	0.16(0.10)	0.877
Power frequency acc AP [Hz]	1.28(1.03)	0.99(0.48)	0.083
Power frequency acc ML [Hz]	2.94(1.03)	2.74(1.23)	0.130

Abbreviations: EO = eyes open, FOG = freezing of gait; GAIT = 18-m walking test, ST = single task, SWAY = quiet standing, TUG = Timed Up and Go.

*: statistically significant differences between the analyzed conditions according to paired data Wilcoxon test (p-value <0.05).

notably, across multiple gait parameters, including gait speed, stride length, cadence, step number, and turning (steps and angular velocity). These improvements are likely to enhance gait stability and reduce the risk of falls during daily activities [33, 34]. Overall, our findings highlight the positive impact of STN-DBS surgery on motor outcomes, with a particular emphasis on its beneficial effects on gait and axial features.

We further explored the potential distinctive effect of levodopa and stimulation on gait parameters by evaluating the four post-operative conditions, as existing literature data on this topic is inconclusive. Some studies reported a similar of stimulation and levodopa, characterized by improvements in gait speed and stride length [9, 35–38], while others suggested a more significant impact of levodopa over stimulation [30, 38]. The heterogeneity of results primarily stems from small exploratory studies with inconsistencies in methodology, type of instrumental approaches for gait analysis, and treatment conditions evaluated (med-ON vs. med-OFF) [7, 9–11].

In our study, both stimulation and levodopa improved gait speed, stride length, and cadence, with stimulation also enhancing turning parameters of TUG. However, stimulation had limited effects on gait variability measures such as stride time variability and asymmetry. Quantitatively, based on the results of SRM, stimulation proved to be more effective than levodopa in enhancing gait speed, stride length, and turning. Stride time variability and asymmetry showed minimal to moderate improvement with levodopa or combined treatment, but poor response with stimulation alone.

This study also investigated the impact of dual tasks on kinematic performances, crucial for a comprehensive gait assessment and insights into real-life challenges faced by PD subjects. Dual task indeed requires additional cognitive functions, exacerbating gait disturbances such as gait variability and FOG, thereby

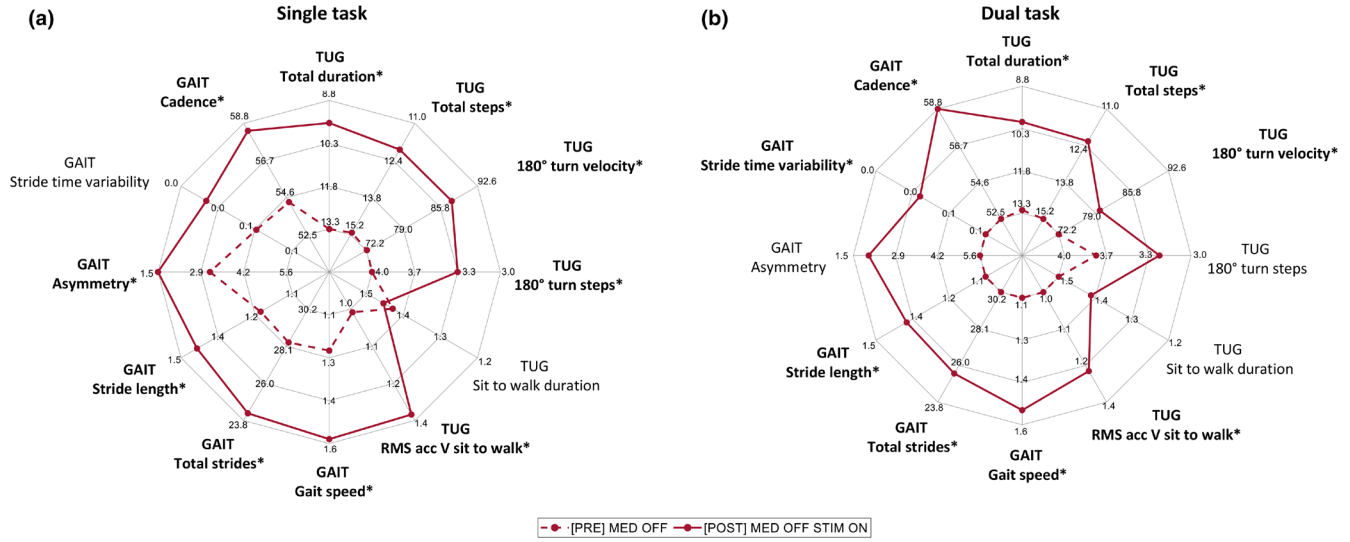

FIGURE 2 Radar plot of sensor-based locomotor parameters in pre-DBS (med-OFF, dashed line) and post-DBS (med-OFF/stim-ON, solid line) evaluations, both in single (2a) and dual (2b) task mode. Outer values represent better motor performance, with a larger area indicating improved gait functionality.

*: Statistically significant differences between pre-DBS and post-DBS conditions according to paired data Wilcoxon test (p-value <0.05).

increasing fall risk [39]. Our results suggest substantial responsiveness of dual-task gait parameters to both stimulation and levodopa, which is quantitatively similar to the single task, except for a smaller effect of levodopa on gait variability. Notably, a recent study compared the efficacy of levodopa and stimulation on 20-m walking parameters under single and dual tasking, pointing out a greater effect of levodopa than stimulation, particularly in the subtraction task, where levodopa improved cadence, gait speed, and number of steps. In contrast, stimulation positively influenced only gait speed [30]. However, these discrepancies may have been induced by using a different protocol, where authors estimated stimulation and levodopa efficacy compared to ON/ON conditions instead of OFF/OFF.

Concerning postural control, sway parameters showed minimal changes following STN-DBS.

Notably, PD subjects in med-OFF had the smallest displacement and sway areas during quiet stance. These observations align with previous research indicating that levodopa can exacerbate postural sway abnormalities by reducing rigidity and potentially inducing dyskinesias [15, 40, 41].

The isolated effect of stimulation on postural parameters remains debated; some studies suggest an improvement of postural control following STN-DBS [42–41], while others reported an increase in the displacement of sway due to reduced rigidity [44]. In our study, sway parameters, such as sway path, ellipse area, and mean sway velocity, showed slight improvement with stimulation but worsened with levodopa. This suggests that stimulation might enhance postural control, whereas levodopa appears to increase challenges by potentially worsening postural sway [41].

The effect of stimulation on postural control warrants further exploration through additional tests on posture, encompassing assessment of dynamic balance, anticipatory postural adjustments in preparation for voluntary movement, and posture abnormalities. However, some findings related to dynamic balance, including the improved sit-to-walk and turn phases during the TUG test, are additional evidence of a potential effect of stimulation on postural control.

In the present study, we endeavored to design a proper evaluation of changes in gait and posture following STN-DBS surgery in PD subjects, aiming to overcome the methodological limitations observed in previous studies. Our approach involved a prospective cohort study, carefully assessing both pre- and post-operative conditions under medication OFF/ON and stimulation OFF/ON states. The study included a standardized motor protocol with various motor tasks to examine multiple overlapping aspects of gait and posture at the same time.

Various spatiotemporal parameters of posture and gait were evaluated consistently across different tests, time evaluations, and treatment conditions, providing confidence in drawing consistent conclusions.

Nevertheless, it is essential to acknowledge some intrinsic limitations of the study. First, the evaluation of each condition was not randomized but performed in consecutive order on the same morning. This approach aimed to prevent overlapping effects of levodopa treatment or sustained effect of stimulation, along with addressing day-to-day variability that would have occurred by performing assessments on distinct days.

Moreover, the responsiveness of gait parameters to levodopa may have been underestimated in post-operative conditions, as subjects received their usual dose of levodopa, which is generally reduced after STN-DBS surgery. On the other hand, the stimulation effect could also be underestimated since the subjects who could not perform the motor tasks in the med-OFF/stim-OFF condition (1 for TUG and 3 for GAIT) did not participate in the analysis.

TABLE 3 Clinical scores and sensor-based motor parameters in the four conditions performed post-DBS in single-task mode.

	post-DBS				
Variable [unit of measurement]	med-OFF stim-ON	med-OFF stim-OFF	med-ON stim-OFF	med-ON stim-ON	Friedman test p-value
Clinical features					
MDS-UDPRS III total score	22.00 (14.25) *	45.00(15.25)	31.00(16.00) *	13.00(9.50) *	**<0.001**
MDS-UPDRS PIGD	1.00(1.00) *	2.00(3.00)	1.00(1.00) *	1.00(1.00) *	**<0.001**
FOG, [n patients (%)]	10 (30.3%) *	14 (42.4%)	9 (27.3) *	8 (24.2%) *	**0.026**
Finger tapping score	154.00(69.00) *	112.00(49.00)	140.50(92.00) *	161.00(81.00) *	**<0.001**
Instrumented quantitative motor performances					
TUG ST					
Total duration [s]	9.84(3.47) *	10.39(4.73)	9.12(3.50) *	8.90(2.17) *	**<0.00**
Total steps [#]	12.00(3.33) *	12.67(6.00)	11.33(4.17) *	11.00(2.83) *	**<0.001**
180° turn velocity [°/s]	87.31(21.26) *	77.23(19.80)	84.68(19.04) *	92.65(26.14) *	**<0.001**
180° turn steps [#]	3.33(1.00)	3.67(1.67)	3.33(1.00)	3.00(1.17)	**0.004**
Sit-to-walk duration [s]	1.45(0.28)	1.32(0.32)	1.27(0.42)	1.29(0.42)	0.498
RMS acc V sit to walk [m/s]	1.39(0.61)	1.15(0.93)	1.24(0.70)	1.37(0.68)	0.223
GAIT ST					
Gait speed [m/s]	1.55(0.29) *	1.39(0.36)	1.46(0.56)	1.53(0.34) *	**<0.001**
Total strides [#]	25.33(5.33) *	26.67(8.25)	25.33(6.67)	23.83(6.50) *	**<0.001**
Stride length [m]	1.43(0.26) *	1.28(0.33)	1.46(0.34) *	1.50(0.32) *	**<0.001**
Asymmetry	2.00(3.79)	3.33(5.50)	2.00(1.63) *	1.50(1.31) *	**0.001**
Stride time variability	0.05(0.07)	0.07(0.06)	0.05 (0.04) *	0.04(0.03) *	**0.006**
Cadence [strides/min]	59.33(7.13) *	57.00(6.08)	58.333(4.83) *	58.33(6.33) *	**0.002**
SWAY EO					
Sway path [cm]	160.13(62.07)	185.63(151.03)	197.72(269.62)	231.76(185.70)	**0.008**
Ellipse area [cm^2]	391.60(423.44)	576.92(672.31)	849.41(1016.38)	807.41(1205.48)	**0.025**
Mean AP velocity [cm/s]	0.43(0.14)	0.49(0.28)	0.56(0.70)	0.60(0.70)	**0.032**
Mean ML velocity [cm/s]	0.17(0.12)	0.20(0.15)	0.24(0.20)	0.24(0.17)	0.065
Power frequency acc AP [Hz]	0.99(0.50)	1.12(1.21)	0.99(0.69)	1.12(0.65)	0.199
Power frequency acc ML [Hz]	2.56(1.26)	2.72(1.80)	2.36(1.29) *	2.04(0.89) *	**0.027**

Abbreviations: EO = eyes open, FOG = freezing of gait; GAIT = 18-m walking test, ST = single task, SWAY = quiet standing, TUG = Timed Up and Go. Data are presented as median (IQR).

*: Statistically significant differences between the analyzed condition (med-OFF/stim-ON, med-ON/stim-OFF, med-ON/stim-ON) and the baseline (med-OFF/stim-OFF), according to paired data post hoc Wilcoxon test (adjusted p-value <0.05).

Finally, our study focused on spatiotemporal parameters of gait and posture, but further and more complex locomotor disturbances occur in PD, including FOG, postural instability, and falls. Evaluating these aspects is an open challenge, especially using wearable inertial sensors in real-world conditions.

This study represents the first comprehensive evaluation of changes in quantitative parameters of gait and posture during a standardized motor protocol employing wearable sensors within a prospective cohort of PD subjects examined before and 6 months after STN-DBS surgery.

While preliminary studies with a relatively small-sample size have explored gait outcomes following STN-DBS surgery using complex instrumental approaches [7–11], there is an increasing interest in using wearable sensors for objective measurement [12, 45, 46]. Wearable sensors offer a cost-effective and accessible approach to quantifying motor impairment [47–49], providing valuable insight into treatment effectiveness. Unlike traditional methods, wearable sensors enable gait analysis across large cohorts and various clinical settings, including outdoor environments, offering greater flexibility and real-world assessment [50, 51].

In conclusion, our findings support the efficacy of the subthalamic nucleus stimulation in improving spatiotemporal gait parameters. Although similar to levodopa, stimulation provides a greater magnitude and more stable outcome, avoiding the fluctuations

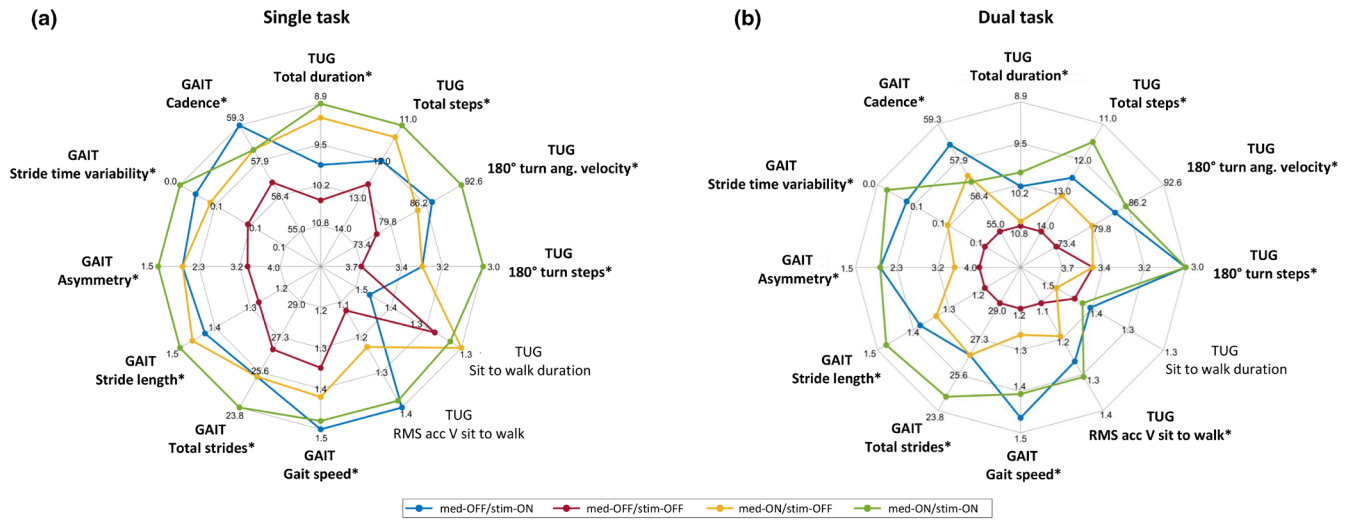

FIGURE 3 Radar plot of sensor-based locomotor parameters post-DBS, both in single (3a) and dual (3b) task mode. Medication and stimulation conditions are distinguished by color. Outer values represent better motor performance, with a larger area indicating improved gait functionality.

*: Statistically significant differences between the four conditions according to Friedman test (p-value <0.05).

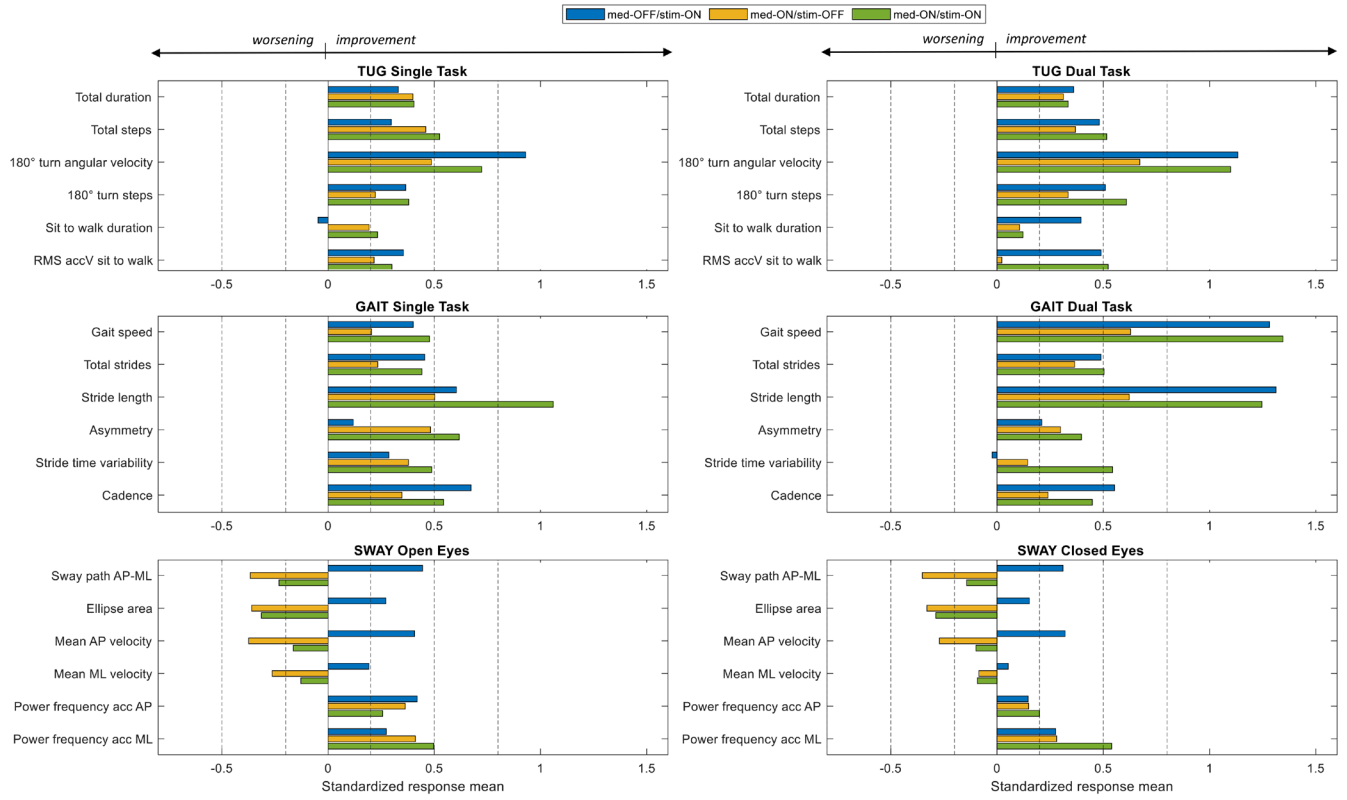

FIGURE 4 Responsiveness of the sensor-based parameters to subthalamic stimulation (med-OFF/stim-ON vs. med-OFF/stim-OFF), to levodopa medication (med-ON/stim-OFF vs. med-OFF/stim-OFF), and their combined effect (med-ON/stim-ON vs. med-OFF/stim-OFF), both in single and dual-task mode.

SRM values 0.20–0.50, 0.51–0.80, and >0.80 indicate small, moderate, and large responsiveness, respectively. Negative values indicate worsening under the respective treatment compared to the baseline condition med-OFF/stim-OFF.

associated with oral therapy. However, stimulation fails to address other parameters, particularly gait variability, echoing the limitation of pharmacotherapy in mitigating specific aspects of locomotor dysfunction in PD.

Indeed, both stimulation and levodopa influence locomotion by targeting the basal ganglia, affecting the selection of motor programs and the intensity of movement. Additionally, dopaminergic projections from the ventral tegmental area to frontal

regions contribute to motivational and reward-related process, which may account for the minor differences observed in gait variability and FOG [52]. Nevertheless, locomotor regulation primarily occurs in the brainstem's mesencephalic locomotor region, which controls movement initiation, speed, termination, and direction [16].

These results emphasize the need to explore therapeutic targets beyond the basal ganglia and dopaminergic system and the necessity to investigate novel strategies to effectively manage gait and postural disturbances resistant to levodopa and subthalamic stimulation, encompassing aspects such as gait variability, FOG, and postural instability [53].

AUTHOR CONTRIBUTIONS

IC, ID, GG, and LP conceived and designed the study; IC, ID, LB, GL, SR, PM, AC, GG, and LP acquired and analyzed data; IC, ID, PC, GCB, LC, GG, and LP interpreted the data; IC and ID wrote the first draft of the manuscript, figures, and table; PC, GCB, LC, GG, and LP contributed to revising the manuscript. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

Luca Palmerini and Lorenzo Chiari are co-founders and own shares of mHealth Technologies. Ilaria Cani, Ilaria D'Ascanio, Luca Baldelli, Giovanna Lopane, Saverio Ranciati, Paolo Mantovani, Alfredo Conti, Pietro Cortelli, Giovanna Calandra-Buonaura, and Giulia Giannini declare no financial or non-financial competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Funding

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Ethical standards

Written informed consent was collected from each patient for the inclusion of deidentified clinical data in a scientific publication, in accordance with the Declaration of Helsinki.

Consent for publication

All authors agreed with this final version.

Availability of data and material

The authors take full responsibility for the data, the analysis and interpretation of the research, and they have full access to all of the data.

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REFERENCES

1. 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
2. Goetz CG, Tilley BC, Shaftman SR, et al. Movement Disorder Society-sponsored revision of the unified Parkinson's disease rating scale (MDS-UPDRS): scale presentation and clinimetric testing results. *Mov Disord*. 2008;23:2129-2170. doi:10.1002/mds.22340
3. Deuschl G, Schade-Brittinger C, Krack P, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. *N Engl J Med*. 2006;355:896-908. doi:10.1056/nejmoa060281
4. Vitek JL, Jain R, Chen L, et al. Subthalamic nucleus deep brain stimulation with a multiple independent constant current-controlled device in Parkinson's disease (INTREPID): a multicentre, double-blind, randomised, sham-controlled study. *The Lancet Neurology*. 2020;19:491-501. doi:10.1016/S1474-4422(20)30108-3
5. Mera TO, Filipkowski DE, Riley DE, et al. Quantitative analysis of gait and balance response to deep brain stimulation in Parkinson's disease. *Gait Posture*. 2013;38:109-114. doi:10.1016/j.gaitpost.2012.10.025
6. Fasano A, Aquino CC, Krauss JK, Honey CR, Bloem BR. Axial disability and deep brain stimulation in patients with Parkinson disease. *Nat Rev Neurol*. 2015;11:98-110. doi:10.1038/nrneurol.2014.252
7. Allert N, Volkmann J, Dotse S, Hefter H, Sturm V, Freund HJ. Effects of bilateral pallidal or subthalamic stimulation on gait in advanced Parkinson's disease. *Mov Disord*. 2001;16:1076-1085. doi:10.1002/mds.1222
8. Cavallieri F, Campanini I, Gessani A, et al. Long-term effects of bilateral subthalamic nucleus deep brain stimulation on gait disorders in Parkinson's disease: a clinical-instrumental study. *J Neurol*. 2023;270:4342-4353. doi:10.1007/s00415-023-11780-5
9. Faist M et al. Effect of bilateral subthalamic nucleus stimulation on gait in Parkinson's disease. *Brain*. 2001;124:1590-1600.
10. Ferrarin M, Rizzone M, Bergamasco B, et al. Effects of bilateral subthalamic stimulation on gait kinematics and kinetics in Parkinson's disease. *Exp Brain Res*. 2005;160:517-527. doi:10.1007/s00221-004-2036-5
11. Krystkowiak P, Blatt JL, Bourriez JL, et al. Effects of subthalamic nucleus stimulation and levodopa treatment on gait abnormalities in Parkinson disease. *Arch Neurol*. 2003;60:80-84. doi:10.1001/archneur.60.1.80
12. di Biase L, Di Santo A, Caminiti ML, et al. Gait analysis in parkinson's disease: an overview of the most accurate markers for diagnosis and symptoms monitoring. *Sensors (Basel)*. 2020;20:3529. doi:10.3390/s20123529
13. Mirelman A, Bonato P, Camicioli R, et al. Gait impairments in Parkinson's disease. *The Lancet Neurology*. 2019;18:697-708. doi:10.1016/S1474-4422(19)30044-4
14. Blin O, Ferrandez AM, Pailhous J, Serratrice G. Dopa-sensitive and Dopa-resistant gait parameters in Parkinson's disease. *J Neurol Sci*. 1991;103:51-54.

15. Curtze C, Nutt JG, Carlson-Kuhta P, Mancini M, Horak FB. Levodopa is a double-edged sword for balance and gait in people with Parkinson's disease. *Mov Disord*. 2015;30:1361-1370. doi:10.1002/mds.26269
16. Leiras R et al. Annual Review of Neuroscience Brainstem Circuits for Locomotion. 2022. doi:10.1146/annurev-neuro-082321
17. Bloem BR, Hausdorff JM, Visser JE, Giladi N. Falls and freezing of gait in Parkinson's disease: a review of two interconnected, episodic phenomena. *Mov Disord*. 2004;19:871-884. doi:10.1002/mds.20115
18. Lang AE, Widner H. Deep brain stimulation for Parkinson's disease: patient selection and evaluation. *Mov Disord*. 2002;17:S94-S101. doi:10.1002/mds.10149
19. Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. *Mov Disord*. 2015;30:1591-1601. doi:10.1002/mds.26424
20. Picciano CP, Mantovani P, Rosetti V, et al. How accurate is frameless fiducial—free deep brain stimulation? *Operative Neurosurgery*. 2024;27:431-439. doi:10.1227/ons.0000000000001151
21. Stebbins GT, Goetz CG, Burn DJ, Jankovic J, Khoo TK, Tilley BC. How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: comparison with the unified Parkinson's disease rating scale. *Mov Disord*. 2013;28:668-670. doi:10.1002/mds.25383
22. Nutt JG, Bloem BR, Giladi N, Hallett M, Horak FB, Nieuwboer A. Freezing of gait: moving forward on a mysterious clinical phenomenon. *Lancet Neurol*. 2011;10:734-744.
23. Contin M, Riva R, Martinelli P, Albani F, Avoni P, Baruzzi A. Levodopa therapy monitoring in patients with Parkinson disease: a kinetic-dynamic approach. *Ther Drug Monit*. 2001;23:621-629. doi:10.1097/00007691-200112000-00005
24. Contin M, Lopane G, Cortelli P, Sambati L, Mohamed S, Calandra-Buonaura G. Quantitative assessment of motor response to a low subacute levodopa dose in the differential diagnosis of Parkinsonisms at disease onset: data from the BoProPark cohort. *J Parkinsons Dis*. 2021;11:811-819. doi:10.3233/JPD-202262
25. Grigoletto F et al. The mini-mental state examination: normative study of an Italian random sample. *Dev Neuropsychol*. 1993;9:77-85. doi:10.1080/87565649109540545
26. Schade S, Mollenhauer B, Trenkwalder C. Levodopa equivalent dose conversion factors: an updated proposal including Opicapone and safinamide. *Movement Disorders Clinical Practice*. 2020;7:343-345. doi:10.1002/mdc3.12921
27. Ferrari A, Milletti D, Palumbo P, et al. Gait apraxia evaluation in normal pressure hydrocephalus using inertial sensors. Clinical correlates, ventriculoperitoneal shunt outcomes, and tap-test predictive capacity. *Fluids and Barriers of the CNS*. 2022;19:51. doi:10.1186/s12987-022-00350-y
28. Zoetewei D, Herman T, Brozgol M, et al. Protocol for the DeFOG trial: a randomized controlled trial on the effects of smartphone-based, on-demand cueing for freezing of gait in Parkinson's disease. *Contemporary Clinical Trials Communications*. 2021;24:100817. doi:10.1016/j.conctc.2021.100817
29. Ferrari A, Milletti D, Giannini G, et al. The effects of cerebrospinal fluid tap-test on idiopathic normal pressure hydrocephalus: an inertial sensors based assessment. *J Neuroeng Rehabil*. 2020;17:7. doi:10.1186/s12984-019-0638-1
30. Langer A, Lucke-Paulig L, Gassner L, et al. Additive effect of dopaminergic medication on gait under single and dual-tasking is greater than of deep brain stimulation in advanced Parkinson disease with long-duration deep brain stimulation. *Neuromodulation*. 2023;26:364-373. doi:10.1016/j.neurom.2022.01.015
31. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull*. 1979;86:420-428. doi:10.1037/0033-2909.86.2.420
32. Fleiss JL. Reliability of measurement. *The Design and Analysis of Clinical Experiments*. *Wiley*; 1986.
33. Fasano A, Canning CG, Hausdorff JM, Lord S, Rochester L. Falls in Parkinson's disease: a complex and evolving picture. *Mov Disord*. 2017;32:1524-1536. doi:10.1002/mds.27195
34. Nemanich ST, Duncan RP, Dibble LE, et al. Predictors of gait speeds and the relationship of gait speeds to falls in men and women with parkinson disease. *Parkinson's Disease*. 2013;2013:1-8. doi:10.1155/2013/141720
35. Lubik S, Fogel W, Tronnier V, Krause M, König J, Jost WH. Gait analysis in patients with advanced Parkinson disease: different or additive effects on gait induced by levodopa and chronic STN stimulation. *J Neural Transm*. 2006;113:163-173. doi:10.1007/s00702-005-0310-8
36. Meka SSL, Kandadai RM, Alugolu R, Haragopal VV, Borgohain R. Effect of medication and deep brain stimulation on gait in Parkinson's disease and its quantitative analysis using Mobishoe - a comparative study. *Ann Indian Acad Neurol*. 2023;26:156-160. doi:10.4103/aian.aian_769_22
37. Stolze H, Klebe S, Poepping M, et al. Effects of bilateral subthalamic nucleus stimulation on parkinsonian gait. *Neurology*. 2001;57:144-146. doi:10.1212/WNL.57.1.144
38. Xie J, Krack P, Benabid AL, Pollak P. ORIGINAL COMMUNICATION effect of bilateral subthalamic nucleus stimulation on parkinsonian gait. *J Neurol*. 2001;248:1068-1072.
39. Amboni M, Barone P, Hausdorff JM. Cognitive contributions to gait and falls: evidence and implications. *Mov Disord*. 2013;28:1520-1533. doi:10.1002/mds.25674
40. Contin M, Riva R, Baruzzi A, Albani F, Macri' S, Martinelli P. 353-8020(95)0ooo&9 postural stability in Parkinson's disease: the effects of disease severity and acute levodopa dosing. *Parkinsonism Relat Disord*. 1996;2:29-33.
41. Rocchi L, Chiari L, Horak FB. Effects of deep brain stimulation and levodopa on postural sway in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2002;73:267-274. doi:10.1136/jnnp.73.3.267
42. Guehl D, Dehail P, de Sèze MP, et al. Evolution of postural stability after subthalamic nucleus stimulation in Parkinson's disease: a combined clinical and posturometric study. *Exp Brain Res*. 2006;170:206-215. doi:10.1007/s00221-005-0202-z
43. Nantel J, McDonald JC, Bronte-Stewart H. Effect of medication and STN-DBS on postural control in subjects with Parkinson's disease. *Parkinsonism Relat Disord*. 2012;18:285-289. doi:10.1016/j.parkreldis.2011.11.005
44. Maurer C, Mergner T, Xie J, Faist M, Pollak P, Lucking CH. Effect of chronic bilateral subthalamic nucleus (STN) stimulation on postural control in Parkinson's disease. *Brain*. 2003;126:1146-1163. doi:10.1093/brain/awg100
45. Maetzler W, Domingos J, Srulijes K, Ferreira JJ, Bloem BR. Quantitative wearable sensors for objective assessment of Parkinson's disease. *Mov Disord*. 2013;28:1628-1637. doi:10.1002/mds.25628
46. Wang X, Yu H, Kold S, Rahbek O, Bai S. Wearable sensors for activity monitoring and motion control: a review. *Biomimetic Intelligence and Robotics*. 2023;3:100089. doi:10.1016/j.birob.2023.100089
47. Palmerini L, Mellone S, Avanzolini G, Valzania F, Chiari L. Quantification of motor impairment in Parkinson's disease using an instrumented timed up and go test. *IEEE Trans Neural Syst Rehabil Eng*. 2013;21:664-673. doi:10.1109/TNSRE.2012.2236577
48. Schlachetzki JCM, Barth J, Marxreiter F, et al. Wearable sensors objectively measure gait parameters in Parkinson's disease. *PLoS One*. 2017;12:e0183989. doi:10.1371/journal.pone.0183989
49. Tsakanikas V, Ntanis A, Rigas G, et al. Evaluating gait impairment in Parkinson's disease from instrumented insole and IMU sensor data. *Sensors (Basel)*. 2023;23:3902. doi:10.3390/s23083902
50. Mancini M, Shah VV, Stuart S, et al. Measuring freezing of gait during daily-life: an open-source, wearable sensors approach. *J Neuroeng Rehabil*. 2021;18:1. doi:10.1186/s12984-020-00774-3
51. Najafi B et al. Laboratory in a box: wearable sensors and its advantages for gait analysis. *Proceedings of the Annual International*

Conference of the IEEE Engineering in Medicine and Biology Society. EMBS; 2011. doi:10.1109/IEMBS.2011.6091605
52. Ferreira-Pinto MJ, Ruder L, Capelli P, Arber S. Connecting circuits for Supraspinal control of locomotion. *Neuron*. 2018;100:361-374. doi:10.1016/j.neuron.2018.09.015
53. Snijders AH, Takakusaki K, Debu B, et al. Physiology of freezing of gait. *Ann Neurol*. 2016;80:644-659. doi:10.1002/ana.24778

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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