

UNIVERSITÀ POLITECNICA DELLE MARCHE

FACOLTÀ DI MEDICINA E CHIRURGIA

Corso di Laurea Magistrale in

Scienze Riabilitative delle Professioni Sanitarie

TESI DI LAUREA

Comparing turning kinematics between Parkinson's disease individuals with and without deep brain stimulation: An exploratory retrospective analysis

Confronto della cinematica di rotazione in individui con malattia di Parkinson con e senza deep brain stimulation: Un'analisi retrospettiva esplorativa

Relatrice *Prof.ssa Maria Gabriella Ceravolo*

Candidata *Lucia Borghi*

Correlatore *Prof. Moran Gilat*

Matricola *1126024*

A.A. 2025/2026

Abstract

Background: La rotazione è un compito motorio complesso, frequentemente compromesso nella malattia di Parkinson (MP), che può innescare il freezing (freezing of gait, FOG) e aumentare il rischio di caduta. Sebbene la deep brain stimulation (DBS) possa migliorare la velocità e l'ampiezza del movimento, la sua influenza sul controllo motorio assiale e sulla fluidità del movimento durante i cambiamenti di direzione rimane poco chiara. Questo studio retrospettivo esplorativo ha confrontato i parametri cinematici oggettivi del cambiamento di direzione tra persone con MP con e senza DBS.

Metodi: I dati sono stati aggregati a partire da tre studi precedenti condotti presso il Parkinson Rehabilitation Research Lab della KU Leuven. L'analisi primaria ha incluso 62 partecipanti valutati in fase ON farmacologica, di cui 10 portatori di DBS con stimolazione attiva e 52 trattati esclusivamente con terapia dopaminergica. I partecipanti hanno eseguito per un minuto giri continui di 360° in condizioni di compito singolo e di doppio compito. La jerkiness media rappresentava l'outcome primario, mentre l'angolo di rotazione, la durata della rotazione, la velocità media di rotazione e il FOG ratio costituivano gli outcome secondari. I parametri relativi al cambiamento di direzione sono stati analizzati mediante un'ANOVA a modello misto, considerando lo stato DBS come fattore tra soggetti, la condizione di compito come fattore entro soggetti e la durata della malattia, espressa in anni, e il punteggio MDS-UPDRS III come covariate. L'analisi del FOG ratio ha incluso 59 partecipanti. In un sottogruppo dello studio FOG-IT, sono stati utilizzati modelli lineari misti per esplorare gli effetti dello stato farmacologico, dello stato DBS e della condizione di compito.

Risultati: Contrariamente all'ipotesi iniziale, la jerkiness media non differiva significativamente tra i partecipanti con e senza DBS. Non sono state rilevate differenze significative associate alla DBS nell'angolo di rotazione, nella durata della rotazione, nella velocità media di rotazione o nel FOG ratio. I partecipanti effettuavano i cambiamenti di direzione più lentamente nella condizione di doppio compito, sebbene la dimensione dell'effetto fosse ridotta. La durata della malattia era significativamente associata alla jerkiness media e la relazione tra durata della malattia e jerkiness differiva in base allo stato DBS. Nell'analisi esplorativa relativa allo stato farmacologico, i partecipanti mostravano una jerkiness inferiore e una maggiore velocità di rotazione in

fase ON farmacologica. In questo sottogruppo, i partecipanti con DBS presentavano inoltre una maggiore durata della rotazione, ma tale risultato deve essere interpretato con cautela.

Conclusioni: Lo stato DBS non era associato a differenze significative nella fluidità del cambiamento di direzione o negli altri outcome analizzati nelle condizioni esaminate. La durata della malattia e la terapia dopaminergica sembravano contribuire in modo più evidente alla prestazione durante i cambiamenti di direzione, con la terapia farmacologica associata a rotazioni più fluide e più veloci. Questi risultati devono essere interpretati con cautela a causa delle dimensioni ridotte e dello sbilanciamento del campione, della disponibilità limitata di informazioni cliniche specifiche relative alla DBS e della natura esplorativa della misura di jerkiness. Sono necessari studi prospettici più ampi, basati su misure validate della fluidità del movimento, come la Spectral Arc Length (SPARC), per chiarire la relazione tra DBS e qualità del cambiamento di direzione nella MP.

Abstract

Background: Turning is a complex motor task that is frequently impaired in Parkinson's disease (PD), triggers freezing of gait (FOG), and increases fall risk. Although deep brain stimulation (DBS) may improve movement speed and amplitude, its influence on axial motor control and movement smoothness during turning remains unclear. This exploratory retrospective study compared objective turning kinematics between individuals with PD with and without DBS.

Methods: Data were pooled from three previous studies conducted at the Parkinson Rehabilitation Research Lab at KU Leuven. The primary analysis included 62 participants assessed in the ON-medication state, of whom 10 had DBS with stimulation active, and 52 were managed with dopaminergic medication alone. Participants completed a one-minute continuous 360° turning task under single-task and dual-task conditions. Average jerkiness was the primary outcome, while turn angle, turn duration, mean turning speed, and the FOG ratio were secondary outcomes. Turning metrics were examined using mixed-model ANOVA, with DBS status as a between-subject factor, task condition as a within-subject factor, and disease duration (years) and MDS-UPDRS III score as covariates. The FOG ratio analysis included 59 participants. In a subset from the FOG-IT study, linear mixed models were used to explore the effects of medication state, DBS status, and task condition.

Results: Contrary to the initial hypothesis, average jerkiness did not differ significantly between participants with and without DBS. No significant DBS-related differences were detected in turn angle, turn duration, mean turning speed, or FOG ratio. Participants turned more slowly during the dual-task condition, although the effect size was small. Disease duration was significantly associated with average jerkiness, and its relationship with jerkiness differed according to DBS status. In the exploratory medication analysis, participants demonstrated lower jerkiness and higher turning speed in the ON-medication state. Participants with DBS also showed longer turn durations in this subset, but this finding should be interpreted cautiously.

Conclusions: DBS status was not associated with significant differences in turning smoothness or other turning outcomes under the conditions examined. Disease duration and dopaminergic medication appeared to contribute more clearly to turning

performance, with medication associated with smoother and faster turning. These findings require cautious interpretation because of the small, unbalanced sample, limited DBS-specific clinical information, and the exploratory jerkiness measure. Larger prospective studies using validated smoothness measures, such as Spectral Arc Length (SPARC), are needed to clarify the relationship between DBS and turning quality in PD.

Table of Contents

Introduction 1

Materials and Methods 6

Participants 6

Inclusion and exclusion criteria 7

Ethics 8

Study protocol 8

Instrumented Measures of Turning Metrics and FOG 10

Study outcomes 11

Statistical Analysis and Analytic Sample 11

Results 17

Turning metrics in ON-state medication during different tasks 17

Primary Outcome - average jerkiness 17

Secondary Outcomes - average angle, duration and mean speed 19

FOG Ratio 20

Effect of medication state between groups, within task, for turning metrics 22

Primary Outcome - average jerkiness 22

Secondary outcomes - average angle, duration and mean speed 23

Discussion 26

Average jerkiness 27

Secondary turning outcomes 27

FOG Ratio 28

Effect of medication 28

Limits 29

Conclusion 30

Supplementary Materials 32

Bibliography 35

Introduction

Parkinson disease (PD) is the second most common neurodegenerative disorder (1). The prevalence of PD continues to rise globally, with recent projections estimating that 17.5 million people will be living with PD by 2040, more than doubling the number of cases observed in 2015 (1). This growth has led researchers to describe an emerging "Parkinson's disease pandemic". PD is an age-related disorder with incidence and prevalence increasing with age, affecting both sexes. Both genetic and environmental factors influence its development (2). In particular, exposure to pesticides and other toxic compounds is involved in disease development, which may explain why PD is more prevalent in industrialized countries (3).

The pathophysiology of PD is characterized by the progressive loss of dopaminergic neurons in substantia nigra pars compacta (SNpc) (3,4). Another hallmark of PD is Lewy pathology, which results from the aggregation of misfolded proteins. In PD, these aggregates are primarily composed of α-synuclein (5). The loss of dopaminergic neurons and protein aggregation impair both automatic and voluntary movements. PD is primarily characterized by motor cardinal symptoms, including bradykinesia, muscular rigidity, and resting tremor (3,4), and the clinical diagnosis of PD is based on the presence of parkinsonian motor features, namely bradykinesia plus rigidity and/or resting tremor (3). As the disease progresses, more complex impairments emerge, such as postural instability, gait disturbances, and freezing of gait (FOG) (4,6). Non-motor symptoms including cognitive decline, depression and pain are common and contribute substantially to overall disability (4,6,7).

With advancing disease severity, patients enter the advanced stage of PD. Common clinical changes include motor fluctuations, dyskinesia, and the presence of significant daily "off" periods (8). Axial features, such as gait and postural stability, deteriorate markedly in this phase (9). While various non-motor symptoms are present at all stages of PD, emergence of neurobehavioral and cognitive issues is often considered a hallmark of advancing disease (7). Among the axial features of advanced PD, FOG is one of the most disabling (10).

FOG is defined as “a period of paroxysmal inability to take an effective step towards the direction of attempted travel, which does not resemble the typical or quasi-normal step performance exhibited in the same individual when performing a similar gait task under similar conditions” (11). It has a high impact on the quality of life and is associated with a higher risk of falls (13). FOG is well known to be especially elicited in difficult gait situations such as turning, initiating gait, negotiating narrow doorways or constrained spaces, and dividing attention while walking, as well as in anxiety-provoking or threatening contexts (10,14).

Turning is one of the most frequent of these triggers. It is a complex movement that requires substantial control and coordination (15). Difficulties in turning are often present in PD even in the early stages (16), possibly reflecting the compromised ability to change motor patterns from walking straight to turning (17). The 360° turn in particular is a sensitive task for provoking FOG episodes (18), especially under dual task conditions (19).

Pharmacological dopamine replacement therapies remain the most used treatment in the early and mid-stages of PD, focusing on alleviating the cardinal symptoms of the disease. There are currently no disease-modifying treatments for PD (20). In advanced PD, axial motor signs such as gait impairment, postural instability and postural abnormalities are common and disabling, and dopamine replacement therapy provides at best only partial relief from them (21). Long-term use of these medications is associated with side effects, particularly motor complications such as fluctuations between “on” and “off” states and dyskinesia. Evidence suggests that up to 50% of patients treated with levodopa develop these complications within five years (22). At this stage, and for many individuals, deep brain stimulation (DBS) is considered an effective additive treatment. DBS is a well-established surgical treatment for managing motor symptoms in PD. It involves the implantation of electrodes that deliver precisely targeted electrical impulses to modulate abnormal neural activity (23). The most common stimulation target is the subthalamic nucleus (STN), although stimulation of the globus pallidus internus (GPi) is also used, with broad effects on cardinal motor symptoms and significantly reducing dyskinesia and motor fluctuations, thereby improving quality of life for most patients with DBS (23).

These benefits, however, are not distributed uniformly across the motor spectrum. Appendicular signs, such as limb tremor, bradykinesia and rigidity respond well and durably, whereas the response of gait and postural function is considerably more heterogeneous, and tends to decline as the disease advances, so that disease duration is itself an important determinant of long-term outcome (24,25). Gait and turning outcomes under stimulation are consequently variable across individuals (24), which makes it important to characterise them with measures capable of detecting more than aggregate improvement.

Turning is a particularly informative window onto this purpose. It accounts for a substantial proportion of steps taken in daily life (26), and it imposes demands that straight-line walking does not: asymmetric step generation, interlimb coordination, and the sequential craniocaudal reorientation of eyes, head, trunk, pelvis and feet (27). Despite this, turning has received considerably less attention in the DBS literature than straight-line gait. The continuous 360° turning task concentrates these demands into a short, standardised and self-paced protocol, and reliably elicits FOG in susceptible individuals, especially when associate to dual-task condition (19), which makes it well suited to probing the limits of stimulation-related benefit.

The studies that have examined turning under stimulation converge on a consistent picture. Cani and colleagues followed patients with wearable sensors before and six months after STN-DBS surgery and reported postoperative improvements in gait speed, stride length, cadence, and turning parameters, while gait variability remained unaddressed by either stimulation or levodopa (28). Kroneberg and colleagues, evaluating combined subthalamic and nigral stimulation, similarly relied on duration- and speed-based metrics derived from the Timed Up and Go test (29). Taken together, these findings indicate that stimulation makes turning faster and more efficient in aggregate terms.

What these outcomes have in common is that they are essentially spatiotemporal descriptors: how long a turn takes, how many steps it requires, how fast the body rotates. They quantify how much and how fast a patient moves and say less about how the movement is executed. Faster turning is not a measure of the quality of the turn performance: a movement can be executed more rapidly while being assembled from a

greater number of corrective adjustments. A patient may therefore complete a turn more quickly while still producing a fragmented trajectory. This distinction between the quantity and the quality of movement is what measures of movement smoothness are designed to capture.

Smoothness reflects how continuously and fluidly a movement is performed, rather than being interrupted by multiple small corrective adjustments and without acceleration control. It is commonly quantified through jerk, the time derivative of acceleration, on the rationale that planned voluntary movement minimises fast and irregular changes in acceleration. Since inertial sensors directly record acceleration, jerk-based metrics can be obtained from a single sensor placed on the lower back. Previous studies have used these measures to assess gait and postural control in people with PD (12).

During turning, smoothness is particularly relevant because the task requires coordinated control of body reorientation and lateral weight shifting (30). Difficulties in mediolateral trunk control have been associated with postural instability and increased fall risk in PD (27). From a physiological perspective, smoothness is closely related to the role of the basal ganglia in planning and coordinating movement (31). Parkinsonian turning is often characterised by fragmented and hesitant movement patterns that are not fully captured by temporal measures alone. Consequently, improvements in turning speed following treatment or DBS do not necessarily imply a corresponding improvement in the smooth and continuous execution of the movement.

To our knowledge, movement smoothness during turning has not been compared between people with PD who have and have not received DBS. Existing work on turning and stimulation has been limited by small samples and has prioritised spatiotemporal outcomes. This exploratory retrospective study aims to address this gap by systematically comparing objective turning kinematics between individuals with PD with and without DBS using previously collected data from a total of 70 people with PD. Data were collected in previous studies conducted in the Parkinson Rehabilitation Research Lab at KU Leuven. This approach will provide much-needed insight into whether DBS has measurable beneficial effects on turning performance in PD.

Its primary outcome was average jerkiness during a one-minute continuous 360° turning task. We compared participants implanted with DBS (DBS), tested with stimulation active, to participants managed with dopaminergic medication alone (non-DBS), in the ON-medication state and under single- and dual-task conditions (ST, DT), with disease duration (years) and MDS-UPDRS III score entered as covariates. Because stimulation reliably increases movement speed and amplitude while its effect on axial control remains partial, and because it remains unclear whether the increased motor output induced by DBS translates into equally smooth and well-coordinated movement patterns, we hypothesised that participants with DBS would show higher average jerkiness, that is less smooth turning, than participants without DBS.

Additional turning metrics, including average turn angle, turn duration, and mean turning speed, will also be analysed. Further analyses will examine the FOG ratio by comparing the DBS and non-DBS groups in the ON-medication state. Secondary analyses will be conducted in a subset of participants assessed in both the ON- and OFF-medication states to investigate the influence of medication status on turning metrics and the FOG ratio.

Materials and Methods

This exploratory retrospective study includes data from four separate studies conducted at the Parkinson Rehabilitation Research Lab (PRO-Labo) at KU Leuven between June 2019 and October 2025.

Participants

A total of 112 participants were screened from the following studies: FOG-IT (N = 40), DeFOG (N = 25), SBT Training (N = 26), and SBT-RCT (N = 21) (32,33). Due to overlap in study participants between studies, the first step consisted of identifying duplicate cases and selecting them using pre-set selection criteria. To resolve duplicate entries, we applied a hierarchical selection rule in which datasets containing both ON- and OFF-medication assessments were prioritized. Participants were then selected in the following order: FOG-IT and DeFOG, followed by SBT Training, and finally SBT-RCT. After resolving duplicates based on this criterion, the final cohort comprised 88 unique participants, of whom 18 had DBS, and 70 did not.

The final 88 participants were included from: FOG-IT (N = 40), DeFOG (N = 18), SBT Training (N = 14), and SBT-RCT (N = 16).

Regarding medication status, 30 participants were assessed exclusively in the ON state (participants included in SBT-RCT and SBT-training), while 58 participants had assessments in both ON and OFF states (participants included in DeFOG and FOG-IT studies). In terms of FOG, 64 participants were classified as freezers and 24 as non-freezers, using NFOGQ.

Participants were initially screened across four studies. Following the identification of the eligible cohort, participants from the DeFOG study were excluded due to the unavailability of the turning metrics required for the present analyses. Therefore, the final analytical sample was derived from the remaining three studies. The final sample included a total of 70 participants with PD, of whom 12 had DBS, and 58 did not. Participant selection is described in the following flowchart (Figure 1).

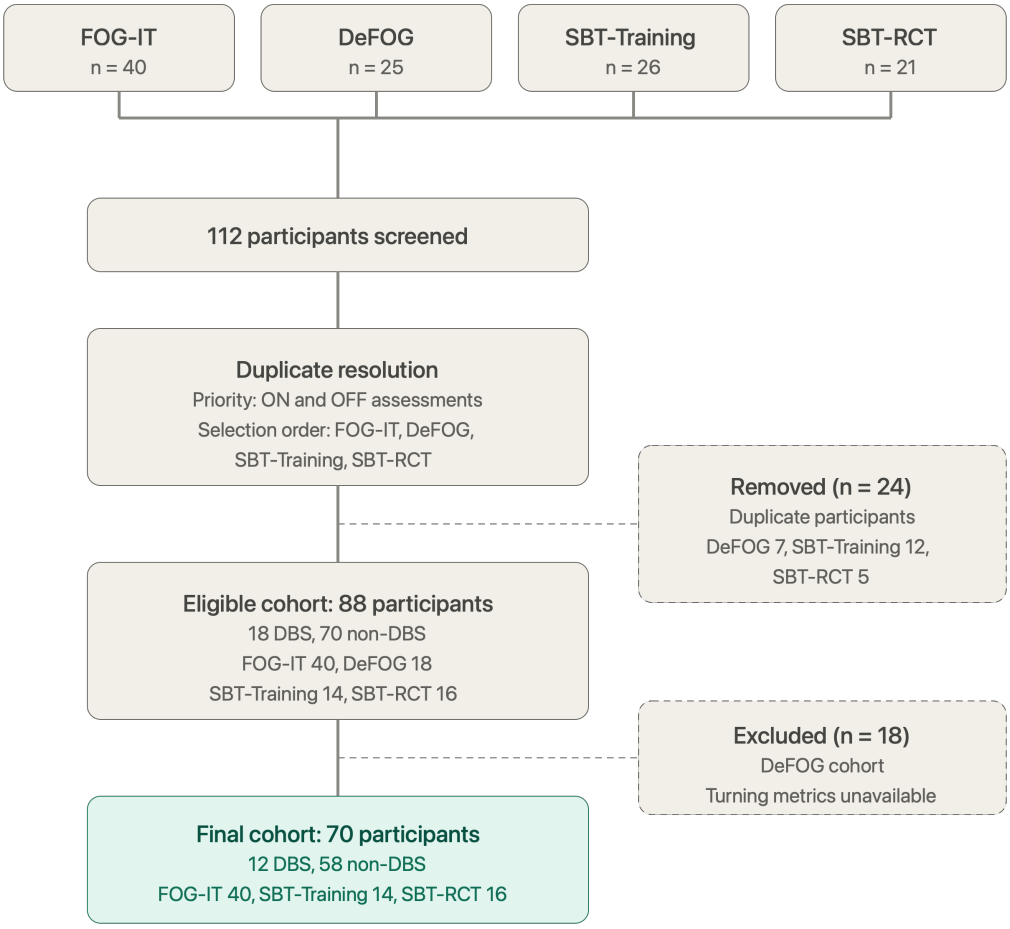


Figure 1 Flowchart study selection

Inclusion and exclusion criteria

The inclusion and exclusion criteria were created by merging the criteria from the four previous studies. Participants eligible for inclusion in this study must meet all the following criteria:

1. Clinical diagnosis of PD made by a neurologist according to the diagnostic criteria of the Movement Disorder Society (SBT-RCT, FOG-IT, SBT-training) (34) or UK Brain Bank (DeFOG) (35)
2. Modified Hoehn & Yahr Stage I to IV in the ON medication state
3. Ability to walk 10 meters independently with or without the use of a walking aid
4. Able to understand and follow study instructions

5. Stable PD medication and DBS settings in the week before and during the assessment

Participants eligible for this study must not meet any of the following criteria:

1. Presence of (acute) musculoskeletal or other neurological or cardiovascular conditions during data collection that affected gait or any other medical condition which, in the opinion of the investigator, might have prevented the participant from completing the protocol in full.
2. Occurrence of any of the following events within 3 months before informed consent for the original study: orthopaedic surgery of the lower extremity, myocardial infarction, hospitalization for unstable angina, coronary artery bypass graft, percutaneous coronary intervention, implantation of a cardiac resynchronization therapy device.

Ethics

This study was approved by the Medical Ethical Committee Research of KU Leuven-UZ Leuven (S71599). The study was performed in accordance with the protocol, current ICH and ICH-GCP guidelines, and applicable regulatory and country-specific requirements. An information letter will be shared with all participants included in this exploratory study.

Study protocol

All participants underwent screening of their demographic information PD related characteristics, including disease duration (years), levodopa equivalent daily dosage (LEDD), motor symptom severity (assessed using the MDS-UPDRS Part III and the Hoehn & Yahr stage), and the presence of deep brain stimulation (DBS; yes/no). Self-reported FOG was further quantified using the New Freezing of Gait Questionnaire (NFOG-Q). Additional clinical assessments included the Montreal Cognitive Assessment (MoCA) to evaluate cognitive function.

For each study, participants completed either a laboratory-based assessment (SBT-RCT) or a home-based assessment (DeFOG, SBT-training, FOG-IT). When home-based

assessments were unavailable, laboratory assessments were used instead. This applied to four participants from the FOG-IT study. All assessments included a one-minute alternating 360° turning-in-place task.

During the 360° turning tasks, participants performed alternating turns in place for one minute. The direction of the first turn was chosen freely by the participant; if needed, the assessor provided verbal instructions to ensure correct alternation. Participants were instructed to turn as fast as possible while remaining safe throughout the task. The 360 turning task was performed in a single-task (ST) and a cognitive dual-task (DT).

For the FOG-IT and DeFOG studies, the protocol was first administered in the participants' practical OFF-medication state (approximately 12 hours after their last intake of antiparkinsonian medication). The entire protocol was then repeated in their ON-medication state, approximately one hour after medication intake. For the SBT-RCT and SBT-training studies, all assessments were conducted exclusively in the ON-medication state.

The FOG-IT study evaluated a personalized, AI-driven platform for measuring FOG and included a standardized FOG-provoking protocol with TUG and 360° turns performed in both directions within a defined rectangular walkway. Assessments were conducted in both ON and OFF medication states.

SBT-training included two study designs: a prospective short-term study to collect fNIRS data from 40 PD patients and 20 healthy controls at the movement analysis laboratory to investigate short-term responses to split-belt perturbations, and a prospective longer-term interventional study to collect fNIRS data from 30 PD freezers over 4 months to investigate long-term responses to repeated split-belt training.

Split-belt investigated the effects of repeated SBT versus tied-belt treadmill (TBT) training on retention and automaticity of gait adaptation and its transfer to overground walking and turning (33).

DeFOG investigated the effectiveness of DeFOG, a smartphone- and sensor-based on-demand cueing solution for FOG (32).

Instrumented Measures of Turning Metrics and FOG

Participants wore inertial measurement units (IMUs) during the assessment. Different types of sensors were used across studies: SB-training used APDM Opal sensors using 5 sensors, one on the lumbar, two on the shins and feet, which recorded at 128 Hz. SBT-RCT used 3 APDM Mobility Lab (Portland, USA) sensors on the lumbar and shins. Data were processed with MATLAB software using custom scripts. Shimmer3 sensors were used in the FOG-IT study. Seven sensors were placed on lumbar, upper legs, shins, and feet, and recorded at 64 Hz. For DeFOG an Axivity sensor present in the DeFOG system was used, placed on the lower back.

To ensure comparability across studies, raw sensor data were converted into a common format and processed using the same analysis pipeline implemented in MATLAB; specifically, Shimmers data from FOG-IT study were processed with a custom script. Several turning metrics were extracted from the identified turns. Turn duration (s) was defined as the time elapsed between turn onset and turn completion. Mean turn speed (°/s) was calculated as the average absolute angular velocity during each turn, whereas peak turn speed (°/s) corresponded to the maximum absolute angular velocity reached during the turn. Turn angle (°) was computed by integrating pelvic angular velocity over time, providing the total angular displacement achieved during the turn. Movement smoothness was quantified using average jerk, derived from the mediolateral acceleration signal of the pelvis sensor as the square root of the integrated squared derivative of acceleration, higher jerk values reflect less smooth and more abrupt turning movements.

Freezing severity was quantified using the Freezing of Gait Ratio (FOGRatio_A_mean), calculated from the anteroposterior acceleration signals recorded at the right and left shanks during the turning task. Following power spectral density analysis, the accelerometer signal was normalized and decomposed into frequency bands. The FOG Ratio was calculated as the squared power in the freeze band (3-8 Hz) divided by the squared power in the locomotor band (0.5-3 Hz), with higher values indicating a greater predominance of movement patterns characteristic of FOG. Separate ratios were obtained for each shank and subsequently averaged to generate a single outcome

measure for statistical analyses. This approach is consistent with previous studies using instrumented turning tasks to quantify freezing severity in PD (12,36).

Study outcomes

The primary outcome of this study is the difference in the average turning jerkiness during the 360° turn-in-place task, comparing individuals with PD with and without DBS in the ON medication state, within ST and DT. Performance will be averaged across left and right turning directions. Secondary analyses explore the other turning metrics, including average angular velocity, duration, and turning speed, comparing individuals with PD, with and without DBS in the ON-medication state, within ST and DT. In the same conditions, FOG Ratio between the DBS and non-DBS groups is analysed.

Additional analyses will evaluate the effect of medication state (ON vs. OFF) on turning kinematics and FOG Ratio.

Statistical Analysis and Analytic Sample

Descriptive statistics were reported as means and standard deviations for normally distributed continuous variables and as medians and quartiles for non-normally distributed variables. Categorical variables were summarized as frequencies and percentages. Normality and homogeneity of variance were assessed using Shapiro–Wilk tests and looking at Kurtosis and Skewness. For normally distributed variables, independent t-tests were used, Maan-Witney U tests were used for non-normally distributed variables. Differences in categorical variables were assessed using chi-square tests.

Turning metrics and FOG Ratio were analysed in the ON-medication state across all three included studies. Comparison between ON- and OFF-medication states was performed only for participants from the FOG-IT study. All analyses were performed in JASP 0.97.1, with statistical significance set at $\alpha = .05$.

The primary analysis was restricted to the ON-medication state and examined differences between participants with and without DBS, with group (DBS vs. non-DBS)

included as a between-subject factor and task condition (single-task vs. dual-task) included as a within-subject factor, using a mixed model ANOVA. For each trial, the metric was averaged across left and right turns. The following turning metrics were analysed: average jerkiness, average angle, average duration, and average mean speed. FOG ratio was analysed as a further secondary outcome. Effect sizes were reported as eta squared (η^2). P-values for post hoc comparisons were adjusted using the Holm correction for multiple testing. Bootstrapped estimated marginal means and their 95% confidence intervals were calculated to aid interpretation of significant effects.

Disease duration and disease severity using MDS-UPDRS III scale, were included as covariates in all analyses. LEDD was excluded from the models because of missing data and its association with disease duration. Although the correlation between LEDD and disease duration was statistically significant, it was of moderate strength (Spearman's $\rho = 0.40$) and remained below commonly accepted thresholds considered indicative of strong collinearity (≥ 0.70).

Data were pooled from three studies. Two of these assessed participants exclusively in the ON state and contributed 14 (SBT-training) and 16 (SBT-RCT) participants, respectively. The third study (FOGIT) assessed participants in both medication states and enrolled 40 participants, 4 of whom were excluded from the present analysis because no ON-state measurement was available, leaving 36 eligible participants.

The pooled sample therefore comprised 66 participants, 11 with DBS and 55 without DBS. As each participant was expected to contribute two observations, one per task condition, 132 observations were expected overall: 22 in the DBS group (11 ST, 11 DT) and 110 in the non-DBS group (55 ST, 55 DT).

A total of 128 observations (97.0% of those expected) were available. In the DBS group, 21 of 22 expected observations were collected (95.5%): 11 ST (100%) and 10 DT (90.9%). In the non-DBS group, 107 of 110 expected observations were collected (97.3%): 53 ST (96.4%) and 54 DT (98.2%). The 4 missing observations (3.0%) all originated from the FOGIT cohort and were attributable to missing data from the study or inability to perform a complete turn. Given their small number and even distribution

across groups and task conditions, missingness was summarised descriptively rather than tested inferentially.

Because the analysis was based on a mixed-model ANOVA, which requires complete data on all within-subject levels, only participants with valid observations in both task conditions could be included. Participants contributing a single task condition were therefore excluded listwise from the corresponding analysis.

For the turning metrics, the 4 participants lacking one of the two task conditions were excluded (1 DBS, 3 non-DBS), leaving 62 participants (10 DBS, 52 non-DBS) and 124 observations (93.9% of the 132 initially expected).

For the FOG ratio, further observations were lost because the processing script did not return a valid value. This occurred in both task conditions for 2 participants and in the dual-task condition only for 1 further participant (1 DBS, 2 non-DBS overall); the cause could not be established, and no systematic pattern was identified across groups or task conditions. The FOG ratio analysis was therefore based on 59 participants (9 DBS, 50 non-DBS) and 118 observations (89.4% of those initially expected). The derivation of the analytical samples is summarised in Figure 2; the specific missing observations are listed in Supplementary Table S1 for metrics analysis and Table S2 for FOG ratio analysis. The DBS group was reduced to 9 participants for the FOG ratio analysis, which markedly limits the precision of any between-group comparison for this outcome.

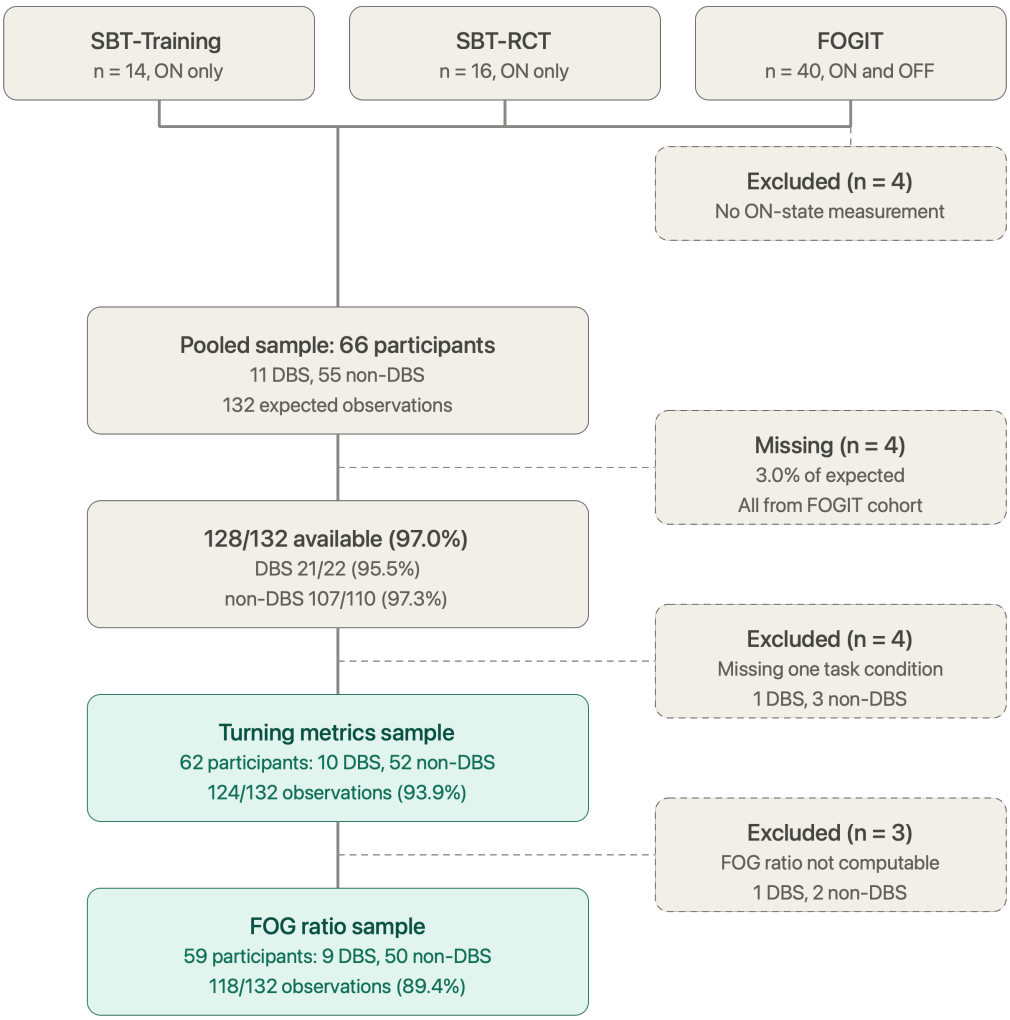


Figure 2 Participant flow from the three studies to the analytical samples. Values are reported as available/expected observations and percentage. Exclusion was applied because the mixed-model ANOVA requires complete data on all within-subject levels.

A secondary analysis was conducted using data from the FOG-IT study to investigate the effect of medication. A linear mixed model was used to evaluate the effect of medication status, DBS status, and task conditions on turning metrics and FOG Ratio. The following turning metrics were analysed: average jerkiness, average angle, average duration, and average mean speed. The experimental design required four observations from each participant, corresponding to the combination of medication state (ON, OFF) and task condition (ST, DT): ON–ST, ON–DT, OFF–ST, OFF–DT. A total of 160 observations were therefore expected across the 40 recruited participants. The sample

comprised 9 patients with DBS and 31 without DBS, corresponding to 36 and 124 expected observations, respectively.

A total of 135 observations (84.4% of those expected) were acquired. In the DBS group, 29 of 36 expected observations were collected (80.6%), comprising 15 in the ON state (8 ST, 7 DT) and 14 in the OFF state (8 ST, 6 DT). In the non-DBS group, 106 of 124 expected observations were collected (85.5%), evenly distributed across the two medication states: 53 in ON (26 ST, 27 DT) and 53 in OFF (27 ST, 26 DT). The analytic sample is summarized in the following flowchart (Figure 3).

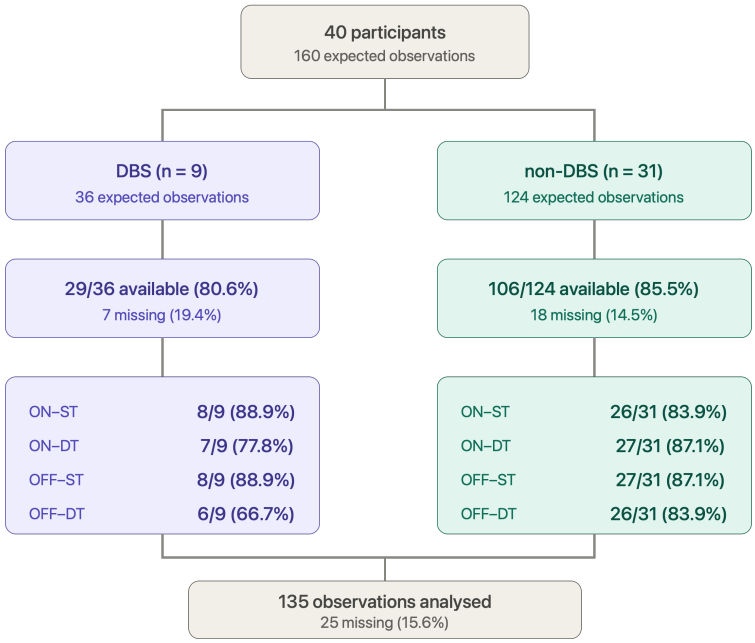


Figure 3 Flow chart of expected, available and missing observations. Values are reported as available/expected observations, with the corresponding percentage in parentheses.

Overall, 25 observations were missing (15.6% of those expected), 7 in the DBS group and 18 in the non-DBS group. Data completeness was comparable across groups (80.6% in the DBS group and 85.5% in the non-DBS group), with the lowest value observed for the OFF–DT condition in the DBS group (6 of 9 expected observations, 66.7%). Missing observations were attributable to missing data from the study or

inability of the participant to perform a full turn. Details of the missing observations for each individual participant are reported in Supplementary Table S3.

Results

A total of 70 participants with PD were included, of whom 12 had DBS, and 58 did not. Demographic and clinical characteristics of the participants are presented in Table 1. No significant differences were found between groups, except for the percentage of patients who experienced FOG (p = 0.037), with a higher number of freezers in the DBS group (91.67% freezers) versus the non-DBS group (60.34% freezers)

Table 1: Demographic and clinical statistics

Variable	non-DBS (n = 58)	DBS (n=12)	Statistics	p-value
Age (years)	67.31 ± 8.135	66.58 ± 7.115	U = 384	.580
Sex (Male%)	63.79%	83.33%	χ^2 =1.721	.190
PD diagnosis (years)	9.621 ± 4.937	10.92 ± 5.265	t = -0.8187	.416
Baseline LEDD	705.0 ± 408.1	574.8 ± 314.4	t = 8090	.422
MDS-UPDRS III (ON)	33.60 ± 12.69	36.83 ± 12.68	U = 315.5	.618
MoCA	25.95 ± 2.812	26.58 ± 1.881	U = 329	.841
FOG (Freezers%)	60.34%	91.67%	χ^2 = 4.329	.037
NFOGQ	12.40 ± 10.06	16.75 ± 8.792	U = 264.5	.189

LEDD: levodopa equivalent daily dose (mg/day)
MDS-UPDRS III (ON): Movement Disorder Society–Unified Parkinson's Disease Rating Scale Part III, motor examination in the ON-medication state
MoCa: Montreal Cognitive Assessment
FOG: freezing of gait
NFOGQ: New Freezing of Gait Questionnaire

Values are presented as mean ± standard deviation, median (interquartile range), or frequency (%), as appropriate. Between-group comparisons were conducted using independent-samples t-tests, Mann–Whitney U tests, or χ^2 tests depending on the distribution.

Turning metrics in ON-state medication during different tasks

Primary Outcome - average jerkiness

This analysis was performed on a sample of 62 participants, including 10 individuals with implanted DBS and 52 individuals without DBS.

No significant differences in the primary outcome, average jerkiness, were observed between participants with and without DBS (F (1,58) = 0.349, p = .557, η^2 = 0.005). Among the covariates, disease duration showed a significant effect (F (1,58) = 8.559, p

= .005, η^2 = 0.121), and MDS-UPDRS III did not reach statistical significance (F (1, 58) = 1.259, p = .266, η^2 = 0.018).

The main effect of task did not reach statistical significance (F (1, 58) = 3.899, p = .053, η^2 = 0.002). No significant interaction between groups and task was observed (F (1, 58) = 0.059, p = .808, $\eta^2 = 3.151 \times 10^{-5}$). Among the covariates, disease duration showed a significant association across task conditions (F (1,58) = 4.373, p=.041, η^2 = 0.002), whereas no significant effect of MDS-UPDRS III was detected (F (1, 58) = 3.043, p = .086, η^2 = 0.002) (Table 2).

Table 2: ANOVA results for average jerkiness

Effect	F	p	η^2
Groups	0.3492	.557	0.0049
Disease duration	8.559	.005	0.121
Task	3.899	.053	0.002
Group * Task	0.059	.808	3.151×10^{-5}
Group * Disease duration	4.373	.041	0.002
Group * UPDRS III	3.043	.086	0.002

Group comparisons under single-task and dual-task conditions, ANOVA outcomes for average jerkiness

Bootstrapped estimated marginal means (1,000 resamples) indicated numerically higher average jerkiness values in the DBS group across both task conditions. In both groups average jerk increased during the dual-task condition compared to the single-task condition. Specifically, average jerkiness increased from 2.069 to 2.204 in the non-DBS group and from 2.519 to 2.709 in the DBS group, with the highest values observed in the DBS group during the DT condition (Table 3).

Table 3: Bootstrapped Marginal Means - DBS ✻ Task

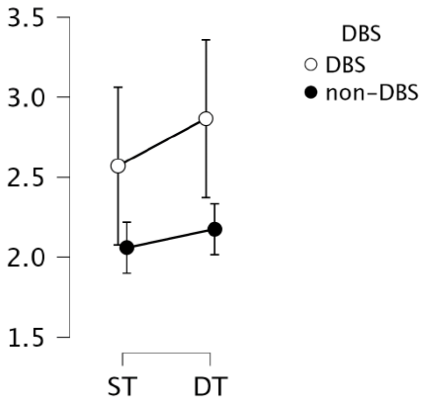
				95% bca† CI				
DBS	Trial	Marginal Mean	bias	Lower	Upper	SE	t	df
0	ST	2.069	-1.648×10^{-4}	1.561	2.729	0.2938	7.442	58.00
1		2.519	0.05505	1.107	3.840	0.6761	3.851	58.00
0	DT	2.204	0.002236	1.620	2.954	0.3303	7.260	58.00
1		2.709	0.04574	1.363	4.052	0.6689	3.819	58.00

† Bias corrected accelerated.
Note. Bootstrapping based on 1000 successful replicates.
Note. Marginal Means estimate is based on the median of the bootstrap distribution.
0 (non-DBS group), 1 (DBS group); ST (single task), DT (dual task).

Descriptive plots showed numerically higher average jerkiness values in the DBS group across task conditions; however, the effect of DBS status was not statistically significant (Figure 1).

Holm-corrected pairwise comparisons showed no statistically significant difference between DBS and non-DBS participants (pHolm = .557) and no statistically significant DBS × task interaction (pHolm = 1.000).

Figure 1: Descriptive plot average jerkiness



Descriptive plots of average jerkiness for the DBS and non-DBS groups under single-task (ST) and dual-task (DT) conditions. Data are shown as mean ± SD, with error bars representing standard deviations.

Secondary Outcomes - average angle, duration and mean speed

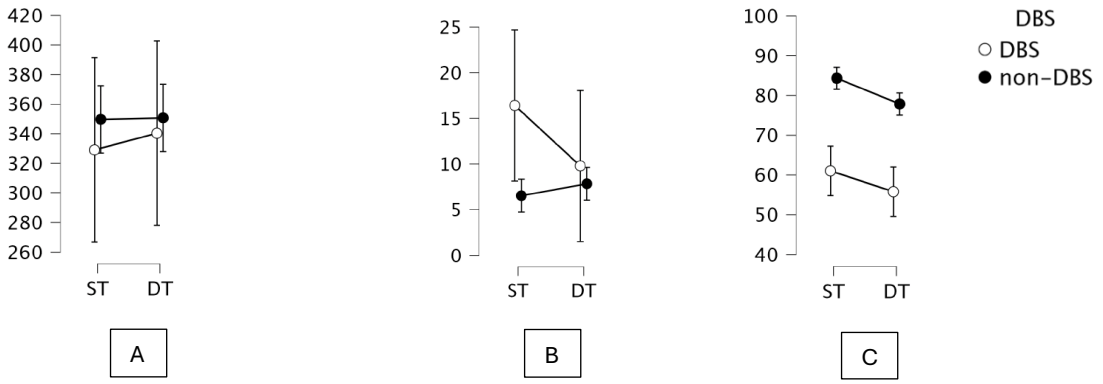
Consistent with the primary outcome analysis, this analysis was conducted on the analytical sample of 62 participants, comprising 10 participants with DBS and 52 participants without DBS.

For average angle, duration, and mean speed no significant effect of group was found. Among the covariates, none of them showed an effect on the variable. A significant effect of task was found for mean speed of turn ($F(1, 58) = 6.129$, $p = 0.016$, $\eta^2 = 0.003$), but not for the other variables. The interaction between DBS status and task was

not significant for the three variables, and covariates did not show interference. After adjusting for MDS-UPDRS III scores, a significant effect was observed for average mean speed ($F(1, 58) = 4.410$, $p = 0.046$, $\eta^2 = 0.002$).

Bootstrapped estimated marginal means are presented for descriptive purposes. Participants with DBS exhibited longer turning durations, with mean values of 11.60 s compared with 7.309 s in the non-DBS group.
In contrast, average turning speed was lower in the DBS group (62.08°/s) than in the non-DBS group (80.24°/s) and decreased from ST to DT in both groups. However, these descriptive differences should be interpreted considering the absence of statistically significant group effects.

Figure 2: Descriptive plots of average angle (A), duration (B), and mean speed (C)



Descriptive plots of average angle (A), duration (B) and mean speed (C) for the DBS and non-DBS groups under ST and DT conditions. Data are shown as mean ± SD, with error bars representing standard deviations.

FOG Ratio

The sample for the FOG ratio consisted of 59 participants, including 9 participants with DBS and 50 participants without DBS.
No main effect of the groups was found ($F(1, 55) = 0.8321$, $p = .707$, $\eta^2 = 0.002334$). After adjustment for covariates, no significant main or interaction effects were observed. The effect of task and the effect of task on groups were not significant (Table 4).

Table 4: ANOVA results for FOG Ratio

Effect	F	p	η^2
Group	0.142	.707	0.002
Task	0.008	.930	$9.347x10^{-6}$
Group * Task	0.895	.348	0.001

Group comparisons under ST and DT conditions, ANOVA outcomes for FOG Ratio

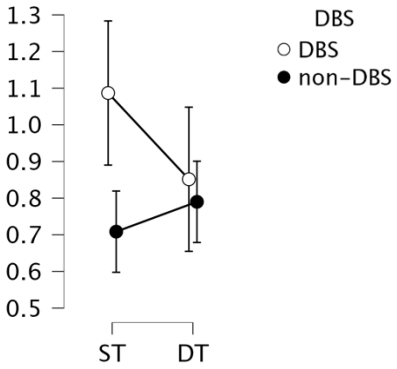
Bootstrapped estimated marginal means indicated a higher FOG ratio in the non-DBS group compared to the DBS group (non-DBS MM = 0.9638, SE = 0.245, DBS MM = 0.6886, SE = 0.4892). While the non-DBS group showed a decrease in FOG ratio from the ST to the DT condition, FOG ratio remained relatively stable across task conditions in the DBS group (see Table 5 and descriptive plot Figure 3).

Table 5: Bootstrapped Marginal Means - DBS ✻ Task

				95% bca† CI				
DBS	Trial	Marginal Mean	bias	Lower	Upper	SE	t	df
0	ST	1.057	-0.0073	0.7024	1.784	0.2731	4.036	55.00
1		0.6565	0.0020	0.0927	2.256	0.4671	1.095	55.00
0	DT	0.8179	-0.0069	0.5409	1.603	0.2263	3.724	55.00
1		0.7533	-0.0045	0.1001	2.350	0.4989	1.441	55.00

† Bias corrected accelerated.
Note. Bootstrapping based on 1000 successful replicates.
Note. Marginal Means estimate is based on the median of the bootstrap distribution.
0 (non-DBS group), 1 (DBS group); ST (single task), DT (dual task).

Figure 3: Descriptive plot of FOG Ratio



Descriptive plots of mean FOG Ratio for the DBS and non-DBS groups under single-task (ST) and dual-task (DT) conditions. Data are shown as mean ± SD, with error bars representing standard deviations.

Effect of medication state between groups, within task, for turning metrics

A linear mixed model was used to analyse the effect of medication state for each turning metric, between groups, within task conditions. The sample consisted of 40 participants, including 9 participants with DBS and 31 participants without DBS.

Primary Outcome - average jerkiness

For average jerkiness, the linear mixed model revealed no significant main effect of group (DBS vs non-DBS) and no significant main effect of task condition. However, a significant main effect of medication state was observed ($F(1, 97.47) = 16.54$, $p < .001$) (Table 6).

Table 6: ANOVA Summary average jerkiness

Effect	df	F	p
DBS	1, 39.98	0.01694	.897
MED_state	1, 99.11	16.54	< .001
Task	1, 97.47	2.057	.155

Note. Model terms tested with Satterthwaite method.

Note. The following variable is used as a random effects grouping factor: 'DBS_turn_code'.

Note. Type III Sum of Squares

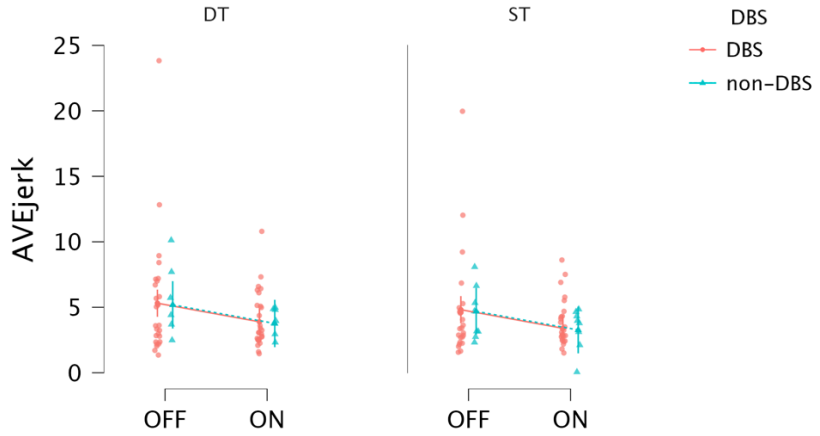
Looking at estimated marginal means (EMM), both groups exhibited a small reduction in average jerkiness when transitioning from the OFF to the ON medication state. EMM between the groups (DBS vs non-DBS) in the different medication conditions (ON vs OFF) are described in Table 7 and the visual representation in Figure 4.

Table 7: EMM for average jerkiness

				95% CI		
DBS	MED_state	Estimate	SE	Lower	Upper	z
0	OFF	5.063	0.4885	4.106	6.021	10.36
1	OFF	4.937	0.8741	3.224	6.650	5.648
0	ON	3.642	0.4896	2.683	4.602	7.440
1	ON	3.516	0.8743	1.803	5.230	4.022

Note. Results are averaged over the levels of trial.
0 (non-DBS group), 1 (DBS group); ST (single task), DT (dual task).

Figure 4: Descriptive plot of average jerkiness in groups for different medication state



Descriptive plots illustrating the effects of medication state (ON vs OFF) and task condition (single task [ST] vs dual task [DT]) on the average jerkiness in the DBS group and the non-DBS group.

Secondary outcomes - average angle, duration and mean speed

Average angle and average mean speed did not show significant effects between the two groups (DBS vs no DBS) (Table 8, 10). Only average duration showed a difference between the two groups ($F(1, 38.72) = 5.297$, $p = .027$), with longer turning durations in participants with DBS than in participants without DBS. For average duration, the main effect of medication state approached significance ($F(1, 98.12) = 3.865$, $p = .052$), with shorter turning durations in the ON compared to the OFF-medication state; values are described in Table 9. For average mean speed, significant effects of medication state ($F(1, 95.11) = 29.61$, $p < .001$) and task condition ($F(1, 94.50) = 9.076$, $p = .003$) were found, with higher turning speeds in the ON medication state.

Table 8: Average angle

Effect	df	F	p
DBS	1, 41.76	0.03983	.843
MED_state	1, 103.00	0.8382	.362
Task	1, 100.75	0.7009	.404

Note. Model terms tested with Satterthwaite method.

Note. The following variable is used as a random effects grouping factor: 'DBS_turn_code'.

Note. Type III Sum of Squares

*Table 9: A*verage duration

Effect	df	F	p
DBS	1, 38.72	5.297	.027
MED_state	1, 98.12	3.865	.052
Task	1, 96.41	1.422	.236

Note. Model terms tested with Satterthwaite method.

Note. The following variable is used as a random effects grouping factor: 'DBS_turn_code'.

Note. Type III Sum of Squares

Table 10: Average mean speed

Effect	df	F	p
DBS	1, 38.71	2.976	.093
MED_state	1, 95.11	29.61	< .001
Task	1, 94.50	9.076	.003

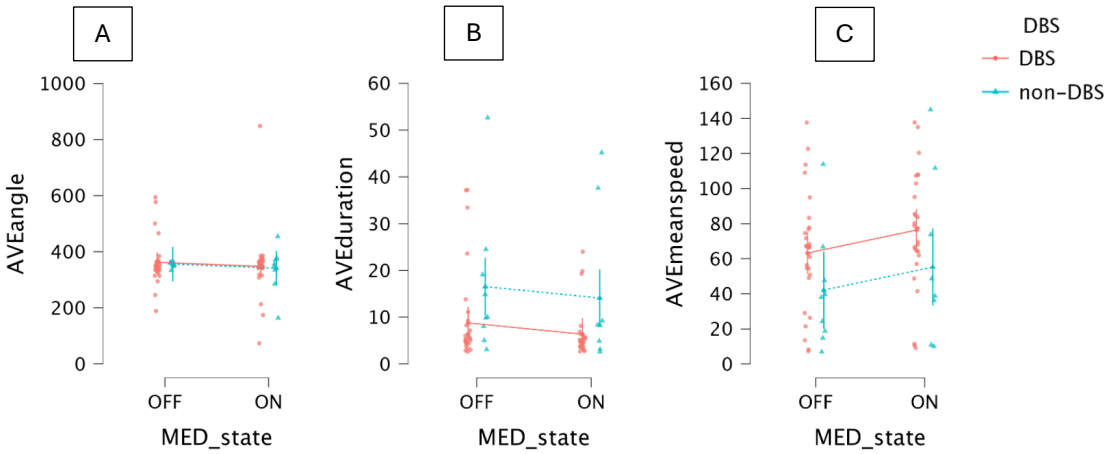
Note. Model terms tested with Satterthwaite method.

Note. The following variable is used as a random effects grouping factor: 'DBS_turn_code'.

Note. Type III Sum of Squares

No different pattern was observed across ST and DT conditions for the three variables. Average angle in the two groups, DBS and non-DBS, in both medical conditions, looked quite similar (Figure 5A). The average duration of turn looks higher in the DBS group and stayed similar in the two medical conditions (Figure 5B). The average mean speed is higher in the non-DBS group and increases in the ON-medication state (Figure 5C). Estimated marginal means are reported in supplementary material (Table S4).

Figure 5: Turning outcomes across medication states (ON vs OFF) in participants with and without DBS



Estimated marginal means derived from the linear mixed-effects models for average angle (A), average turn duration (B), and average mean turning speed (C). Results are shown for participants with DBS and without DBS in the ON and OFF med state.

Discussion

The present study investigated whether DBS is associated with a difference in turning metrics in people with PD, particularly during the 360° turning. Turning was selected as the target task because it represents one of the most challenging motor activities in daily life, requiring an integration of postural control, balance, anticipatory motor planning, and cognitive resources (15). Moreover, turning is particularly relevant in PD, as it frequently triggers FOG episodes and is associated with a high risk of falls (18).

Beyond the successful completion of the movement itself, turning quality is also an important aspect of motor performance. One characteristic often used to describe movement quality is smoothness, which reflects the ability to produce coordinated and continuous motion while minimizing unnecessary fluctuations or corrective adjustments (37). Reduced smoothness may indicate impaired motor control and poorer coordination, even when traditional measures such as speed or duration remain unchanged (38).

Jerk, defined as the time derivative of acceleration, has been used as an empirical indicator of movement smoothness. In individuals with PD, the integral of square trunk jerk has previously been applied to accelerometric data as a measure of postural changes (39), with higher values indicating less smooth movements. While previous studies (28) have primarily focused on conventional turning metrics such as turn duration, angular velocity, and number of steps, little attention has been paid to smoothness-related measures. Because movement smoothness might not be fully reflected by temporal-spatial outcomes, average jerkiness was selected as the primary outcome of the present study.

Contrary to our initial hypothesis, no significant differences in average jerkiness were observed between participants with and without DBS. However, disease duration emerged as a significant predictor of turning smoothness, while medication state significantly influenced both average jerkiness and turning speed. Taken together, these findings suggest that disease progression and dopaminergic therapy may have a greater influence on turning than the presence of DBS alone under the condition examined.

An important methodological consideration when interpreting these findings concerns the jerkiness metric itself. Jerk-based measures are strongly influenced by movement duration and amplitude unless appropriately normalised. Therefore, although jerkiness was selected as an indicator of movement smoothness, the metric employed in the present study may also partially reflect differences in movement execution characteristics rather than smoothness alone. This issue is further discussed in the limitations section.

Average jerkiness

Contrary to the initial hypothesis, no significant differences in average jerkiness were observed between participants with and without DBS. Average jerkiness did not differ between groups [$F(1, 58) = 0.349$, $p = .557$, $\eta^2 = 0.005$], and the result remained unchanged after correction for multiple comparisons ($pHolm = .557$). Neither the main of task not the group x task interaction reached statistical significance [$F(1,58) = 3.899$, $p = 0.53$, $\eta^2 = 0.002$); $F(1,58) = 0.059$, $p = .808$, $\eta^2 = 3.151x10^{-5}$].

Disease duration reached statistical significance in two different interactions: task x disease duration [$F(1,58) = 4.373$, $p = 0.041$, $\eta^2 = 0.002$] and presence of DBS × disease duration [$F(1,58) = 8.559$, $p = .005$, $\eta^2 = 0.121$]. The task x disease duration explained only a small portion of variance, and it does not have clinical meaning. In contrast, the DBS presence x disease duration interaction accounted for 12.1% of the variance in average jerkiness, representing a moderate effect size. This suggests that the relationship between disease duration and turning smoothness differed between participants with and without DBS. The relatively small sample size further limited statistical power and reduced the ability to detect small between-group differences.

Secondary turning outcomes

Average turn angle was included as a control measure to verify successful task execution and establish whether participants in both groups performed turns of comparable amplitude. Participants were instructed to perform a complete 360° turn, and the value observed was closed around the target. For this reason, this outcome provides limited information regarding the tuning characteristic itself. No significant difference was found between DBS groups or task conditions, and no interactions were observed. This suggests

that participants in both groups performed turns of similar angular range, but the absence of a statistically significant difference should not be interpreted as evidence of equivalence between groups.

Turn duration showed no significant effect of groups, task condition, or their interaction. Mean turning speed was significant for the task condition [$F(1,58) = 6.129$, $p = .016$, $\eta^2 = .003$], with participants turning more slowly during the DT condition. This is consistent with the expected interference produced by the increased cognitive demands during a complex motor task (19). A significant task x MDS-UPDRS III interaction was observed [$F(1,58) = 4.410$, $p = .040$, $\eta^2 = 0.002$], indicating that the cost of the task varied according to the motor symptom severity. Both effects explained only a very small proportion of variance.

FOG Ratio

The FOG ratio was analysed using the same mixed-model approach adopted for the primary outcome. No significant main effect of DBS, task condition, or their interaction was identified, and these findings remained unchanged after adjustment for covariates.

Effect of medication

A subset of participants completed assessments both ON and OFF dopaminergic medication. Medication state was investigated as a within-subject factor, within task condition and between groups (DBS vs non-DBS). Because this analysis involved a smaller subset of participants than the primary analysis, funding should be considered exploratory.

Average jerkiness showed a significant effect of medication state [$F(1, 99.11) = 16.54$, $p < .001$], with lower jerkiness values observed in the ON-medication condition, indicating a smoother turning performance. Similarly, mean turning speed was significantly influenced by medication state [$F(1,95.11) = 29.61$, $p < .001$] and task condition [$F(1,94.50) = 9.076$, $p = .003$], with participants turning faster when assessed ON medication. Turn duration differed significantly between groups [$F(1, 38.72) = 5.297$, $p = .027$], with longer turn duration in participants treated with DBS. Observations related

to these findings are that turning smoothness improved in the ON-medication condition; a significant difference between participants with and without DBS emerged only in the average duration of turn. The magnitude of the effect cannot be directly compared, and this funding not necessarily indicate that medication is better than DBS, considering the small sample. The effect of medication on turning speed and smoothness is consistent with the reduction of bradykinesia associate to dopaminergic treatment (20). This finding supports the idea that turning performance remains responsive to dopaminergic modulation even during a complex task. Participants with DBS showed longer turn durations than those without DBS. Although this observation is consistent with the descriptive values observed in the primary analyses, where the DBS group also tended to turn more slowly, the difference was not significant in the larger sample. Because the present analysis was conducted on a smaller and differently selected subgroup, this finding should not be interpreted as confirmation of a true DBS-related effect but rather as evidence that results may vary across subsamples and analytical approaches.

Limits

Several limitations should be considered when interpreting the findings of the present study. First, although no statistically significant baseline differences were observed between participants with and without DBS, the relatively small and highly unbalanced sample limits statistical power and reduces the ability to exclude residual confounding. Consequently, differences related to disease characteristics, treatment history, such as level of physical exercise, or other unmeasured clinical factors may have influenced the observed outcomes. Furthermore, detailed DBS-related information, including stimulation parameters, electrode location, target nucleus, and time since implantation, was not available for all participants. This reflects the retrospective nature of data collection, which was conducted within a university research setting and combined participants recruited from different studies. The absence of these variables prevented a more detailed exploration of potential sources of variability within the DBS group. Second, the FOG ratio analysis was conducted on an even smaller sample, with only 9 participants in the DBS group, substantially limiting the precision of between-group comparisons and requiring these findings to be considered exploratory. Another important methodological limitation concerns the assessment of movement smoothness.

Although jerkiness has previously been used to quantify motor smoothness in PD, the metric employed in the present study is not dimensionless and may therefore be influenced by movement duration and amplitude. More recently, alternative measures such as the Spectral Arc Length (SPARC) have been proposed as more robust and sensitive indicators of movement smoothness. To date, however, investigations of smoothness in PD have focused primarily on gait, whereas turning quality in individuals with DBS has received little attention. Therefore, the present study should be viewed as an exploratory first step aimed at examining whether turning smoothness may be affected by DBS.

Conclusion

In conclusion, this study did not identify significant differences in turning smoothness or other turning outcomes between participants with and without DBS. Disease duration emerged as a significant factor associated with turning smoothness, while dopaminergic medication was associated with improvements in both movement smoothness and turning speed. These findings highlight the potential contribution of disease progression and medication state to turning performance in people with PD and suggest that their influence may be more readily detectable than the effect of DBS status alone under the conditions examined in the present study.

However, these results should be interpreted with caution given the relatively small and unbalanced sample and the limited availability of DBS-specific clinical information. In addition, the smoothness metric adopted in the present study was exploratory and may be influenced by movement characteristics such as duration and amplitude.

Despite these limitations, this study represents one of the first attempts to investigate turning smoothness during turning in people with PD with and without DBS. Future studies should include larger and more balanced samples and systematically collect DBS-specific clinical variables, including stimulation settings, electrode placement, target nucleus, and time since implantation. The use of more advanced and validated measures of smoothness, such as the Spectral Arc Length (SPARC), may further improve the

sensitivity of turning assessments and help clarify whether specific DBS characteristics are associated with turning performance and quality in PD.

Supplementary Materials

Table S1: Participants excluded from the DBS * task analysis due to missing data for at least one trial

DBS_turn_code	Reason
DBS_34	Missing trial ST
DBS_39	Missing trial DT
DBS_42	Missing trial DT
DBS_48	Missing trial ST

Table S2: Participants excluded from the FOG ratio analysis due to failure of FOG ratio calculation by the processing script

DBS_turn_code	Reason
DBS_16	Missing ST and DT
DBS_18	Missing ST and DT
DBS_25	Missing DT

Table S3: Reasons for missing trial in the FOG-IT secondary study included in the DBS*medication state*task condition linear mixed model

DBS_turn_code	Missing trials	Reason
DBS_24	OFF - ST	Less than one turn
DBS_26	OFF - DT	Missing data
DBS_33	ON – ST/DT OFF - DT	Missing data
DBS_34	ON -ST	Missing data
DBS_36	OFF - ST	Less than 1 turn
DBS_38	OFF – ST	Less than 1 turn
DBS_39	OFF – ST/DT ON - DT	Missing
DBS_40	ON – ST/DT OFF - ST	Missing
DBS_41	OFF - DT	Missing
DBS_42	ON – DT	Less than one turn

	OFF - DT	
DBS_44	OFF – ST/DT	Missing
DBS_45	ON – ST/DT	Missing
DBS_48	ON - ST	Missing
DBS_50	OFF - DT	Missing
DBS_54	ON -ST/DT	Missing

Table S4: Estimated marginal means derived from the DBS status*medication state *task condition linear mixed model

***EMM* – Average angle**

					95% CI		
DBS	MED_state	trial	Estimate	SE	Lower	Upper	z
0	OFF	DT	369.0	19.12	331.5	406.4	19.29
1	OFF	DT	362.3	31.75	300.1	424.6	11.41
0	ON	DT	354.4	19.07	317.0	391.8	18.58
1	ON	DT	347.8	31.65	285.7	409.8	10.99
0	OFF	ST	355.7	19.17	318.2	393.3	18.56
1	OFF	ST	349.1	31.05	288.2	410.0	11.24
0	ON	ST	341.2	19.30	303.3	379.0	17.68
1	ON	ST	334.5	31.06	273.6	395.4	10.77

0 (non-DBS group), 1 (DBS group); ST (single task), DT (dual task); ON and OFF indicate the medication state.

***EMM* – Average duration**

					95% CI		
DBS	MED_state	trial	Estimate	SE	Lower	Upper	z
0	OFF	DT	9.507	1.803	5.972	13.04	5.271
1	OFF	DT	17.26	3.119	11.15	23.37	5.533
0	ON	DT	7.083	1.800	3.555	10.61	3.935
1	ON	DT	14.83	3.116	8.728	20.94	4.761
0	OFF	ST	8.052	1.805	4.513	11.59	4.460
1	OFF	ST	15.80	3.071	9.784	21.82	5.146
0	ON	ST	5.628	1.816	2.070	9.187	3.100
1	ON	ST	13.38	3.076	7.352	19.41	4.350

0 (non-DBS group), 1 (DBS group); ST (single task), DT (dual task); ON and OFF indicate the medication state.

***EMM* - Average mean speed**

DBS	MED_state	trial	Estimate	SE	95% CI		z
					Lower	Upper	
0	OFF	DT	59.63	6.029	47.81	71.45	9.891
1	OFF	DT	38.52	10.94	17.07	59.96	3.520
0	ON	DT	72.75	6.025	60.94	84.56	12.08
1	ON	DT	51.64	10.94	30.19	73.08	4.719
0	OFF	ST	66.79	6.030	54.97	78.61	11.08
1	OFF	ST	45.68	10.88	24.35	67.01	4.197
0	ON	ST	79.91	6.044	68.06	91.76	13.22
1	ON	ST	58.80	10.89	37.45	80.15	5.397

0 (non-DBS group), 1 (DBS group); ST (single task), DT (dual task); ON and OFF indicate the medication state.

Bibliography

1. Dorsey ER, Sherer T, Okun MS, Bloem BR. The Emerging Evidence of the Parkinson Pandemic. J Park Dis. 18 dicembre 2018;8(s1):S3–8. doi:10.3233/JPD-181474

2. Pringsheim T, Jette N, Frolkis A, Steeves TDL. The prevalence of Parkinson's disease: a systematic review and meta-analysis. Mov Disord Off J Mov Disord Soc. novembre 2014;29(13):1583–90. doi:10.1002/mds.25945 PubMed PMID: 24976103.

3. Kalia LV, Lang AE. Parkinson's disease. Lancet Lond Engl. 29 agosto 2015;386(9996):896–912. doi:10.1016/S0140-6736(14)61393-3 PubMed PMID: 25904081.

4. Bloem BR, Okun MS, Klein C. Parkinson's disease. Lancet Lond Engl. 12 giugno 2021;397(10291):2284–303. doi:10.1016/S0140-6736(21)00218-X PubMed PMID: 33848468.

5. Dickson DW, Braak H, Duda JE, Duyckaerts C, Gasser T, Halliday GM, et al. Neuropathological assessment of Parkinson's disease: refining the diagnostic criteria. Lancet Neurol. 1 dicembre 2009;8(12):1150–7. doi:10.1016/S1474-4422(09)70238-8

6. Balestrino R, Schapira AHV. Parkinson disease. Eur J Neurol. gennaio 2020;27(1):27–42. doi:10.1111/ene.14108 PubMed PMID: 31631455.

7. Riedel O, Klotsche J, Spottke A, Deuschl G, Förstl H, Henn F, et al. Frequency of dementia, depression, and other neuropsychiatric symptoms in 1,449 outpatients with Parkinson's disease. J Neurol. 1 luglio 2010;257(7):1073–82. doi:10.1007/s00415-010-5465-z

8. Aslam S, Manfredsson F, Stokes A, Shill H. «Advanced» Parkinson's disease: A review. Parkinsonism Relat Disord. giugno 2024;123:106065. doi:10.1016/j.parkreldis.2024.106065 PubMed PMID: 38418318.

9. Becker D, Maric A, Schreiner SJ, Büchele F, Baumann CR, Waldvogel D. Onset of Postural Instability in Parkinson's Disease Depends on Age rather than Disease Duration. Park Dis. 2022;2022:6233835. doi:10.1155/2022/6233835 PubMed PMID: 36506486; PubMed Central PMCID: PMC9734006.

10. Nutt JG, Bloem BR, Giladi N, Hallett M, Horak FB, Nieuwboer A. Freezing of gait: moving forward on a mysterious clinical phenomenon. Lancet Neurol. agosto 2011;10(8):734–44. doi:10.1016/S1474-4422(11)70143-0 PubMed PMID: 21777828; PubMed Central PMCID: PMC7293393.

11. Gilat M, Nonnekes J, Factor SA, Bloem BR, Nutt JG, Giladi N, et al. An updated definition of freezing of gait. Nat Rev Neurol. marzo 2026;22(3):172–81. doi:10.1038/s41582-025-01179-3

12. Mancini M, Smulders K, Cohen RG, Horak FB, Giladi N, Nutt JG. The clinical significance of freezing while turning in Parkinson's disease. Neuroscience. 20

febbraio 2017;343:222–8. doi:10.1016/j.neuroscience.2016.11.045 PubMed PMID: 27956066; PubMed Central PMCID: PMC5289743.

13. 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(8):871–84. doi:10.1002/mds.20115

14. Ehgoetz Martens KA, Hall JM, Georgiades MJ, Gilat M, Walton CC, Matar E, et al. The functional network signature of heterogeneity in freezing of gait. Brain. 1 aprile 2018;141(4):1145–60. doi:10.1093/brain/awy019

15. Stack E, Ashburn A. Dysfunctional turning in Parkinson's disease. Disabil Rehabil. 2008;30(16):1222–9. doi:10.1080/09638280701829938 PubMed PMID: 18608364.

16. Zampieri C, Salarian A, Carlson-Kuhta P, Aminian K, Nutt JG, Horak FB. The instrumented Timed Up and Go test: Potential outcome measure for disease modifying therapies in Parkinson's disease. J Neurol Neurosurg Psychiatry. febbraio 2010;81(2):171–6. doi:10.1136/jnnp.2009.173740 PubMed PMID: 19726406; PubMed Central PMCID: PMC3065923.

17. Earhart GM. Dynamic Control of Posture Across Locomotor Tasks. Mov Disord Off J Mov Disord Soc. 15 settembre 2013;28(11):1501–8. doi:10.1002/mds.25592 PubMed PMID: 24132838; PubMed Central PMCID: PMC3801425.

18. Conde CI, Lang C, Baumann CR, Easthope CA, Taylor WR, Ravi DK. Triggers for freezing of gait in individuals with Parkinson's disease: a systematic review. Front Neurol. 21 dicembre 2023;14:1326300. doi:10.3389/fneur.2023.1326300 PubMed PMID: 38187152; PubMed Central PMCID: PMC10771308.

19. Spildooren J, Vercruysse S, Desloovere K, Vandenberghe W, Kerckhofs E, Nieuwboer A. Freezing of gait in Parkinson's disease: the impact of dual-tasking and turning. Mov Disord Off J Mov Disord Soc. 15 novembre 2010;25(15):2563–70. doi:10.1002/mds.23327 PubMed PMID: 20632376.

20. Fox SH, Katzenschlager R, Lim SY, Ravina B, Seppi K, Coelho M, et al. The Movement Disorder Society Evidence-Based Medicine Review Update: Treatments for the motor symptoms of Parkinson's disease. Mov Disord Off J Mov Disord Soc. ottobre 2011;26 Suppl 3:S2-41. doi:10.1002/mds.23829 PubMed PMID: 22021173.

21. Fasano A, Aquino CC, Krauss JK, Honey CR, Bloem BR. Axial disability and deep brain stimulation in patients with Parkinson disease. Nat Rev Neurol. febbraio 2015;11(2):98–110. doi:10.1038/nrneurol.2014.252

22. Kwon DK, Kwatra M, Wang J, Ko HS. Levodopa-Induced Dyskinesia in Parkinson's Disease: Pathogenesis and Emerging Treatment Strategies. Cells. 23 novembre 2022;11(23):3736. doi:10.3390/cells11233736 PubMed PMID: 36496996; PubMed Central PMCID: PMC9736114.

23. Groiss SJ, Wojtecki L, Südmeyer M, Schnitzler A. Deep brain stimulation in Parkinson's disease. Ther Adv Neurol Disord. novembre 2009;2(6):20–8. doi:10.1177/1756285609339382 PubMed PMID: 21180627; PubMed Central PMCID: PMC3002606.

24. Fasano A, Aquino CC, Krauss JK, Honey CR, Bloem BR. Axial disability and deep brain stimulation in patients with Parkinson disease. Nat Rev Neurol. febbraio 2015;11(2):98–110. doi:10.1038/nrneurol.2014.252 PubMed PMID: 25582445.

25. Limousin P, Foltynie T. Long-term outcomes of deep brain stimulation in Parkinson disease. Nat Rev Neurol. aprile 2019;15(4):234–42. doi:10.1038/s41582-019-0145-9

26. Mancini M, Weiss A, Herman T, Hausdorff JM. Turn Around Freezing: Community-Living Turning Behavior in People with Parkinson's Disease. Front Neurol. 26 gennaio 2018;9:18. doi:10.3389/fneur.2018.00018 PubMed PMID: 29434567; PubMed Central PMCID: PMC5790768.

27. Mellone S, Mancini M, King LA, Horak FB, Chiari L. The quality of turning in Parkinson's disease: a compensatory strategy to prevent postural instability? J NeuroEngineering Rehabil. 19 aprile 2016;13(1):39. doi:10.1186/s12984-016-0147-4

28. Cani I, D'Ascanio I, Baldelli L, Lopane G, Ranciati S, Mantovani P, et al. Evaluating gait and postural responses to subthalamic stimulation and levodopa: A prospective study using wearable technology. Eur J Neurol. gennaio 2025;32(1):e16580. doi:10.1111/ene.16580 PubMed PMID: 39702816; PubMed Central PMCID: PMC11658965.

29. Kroneberg D, Al-Fatly B, Morkos C, Steiner LA, Schneider GH, Kühn A. Kinematic Effects of Combined Subthalamic and Dorsolateral Nigral Deep Brain Stimulation in Parkinson's Disease. J Park Dis. 2024;14(2):269–82. doi:10.3233/JPD-230181 PubMed PMID: 38363617; PubMed Central PMCID: PMC10977420.

30. Mancini M, Weiss A, Herman T, Hausdorff JM. Turn Around Freezing: Community-Living Turning Behavior in People with Parkinson's Disease. Front Neurol. 2018;9:18. doi:10.3389/fneur.2018.00018 PubMed PMID: 29434567; PubMed Central PMCID: PMC5790768.

31. Wu T, Wang J, Wang C, Hallett M, Zang Y, Wu X, et al. Basal ganglia circuits changes in Parkinson's disease patients. Neurosci Lett. 22 agosto 2012;524(1):55–9. doi:10.1016/j.neulet.2012.07.012 PubMed PMID: 22813979; PubMed Central PMCID: PMC4163196.

32. Zoetewei D, Herman T, Brozgol M, Ginis P, Thumm PC, Ceulemans E, 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. Contemp Clin Trials Commun. 29 giugno 2021;24:100817.

doi:10.1016/j.conctc.2021.100817 PubMed PMID: 34816053; PubMed Central PMCID: PMC8591418.

33. Hulzinga F, Seuthe J, D'Cruz N, Ginis P, Nieuwboer A, Schlenstedt C. Split-Belt Treadmill Training to Improve Gait Adaptation in Parkinson's Disease. Mov Disord. 2023;38(1):92–103. doi:10.1002/mds.29238

34. MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) [Internet]. [citato 17 marzo 2026]. Disponibile su: https://www.movementdisorders.org/MDS/MDS-Rating-Scales/MDS-Unified-Parkinsons-Disease-Rating-Scale-MDS-UPDRS.htm

35. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry. marzo 1992;55(3):181–4. doi:10.1136/jnnp.55.3.181 PubMed PMID: 1564476; PubMed Central PMCID: PMC1014720.

36. D'Cruz N, Seuthe J, De Somer C, Hulzinga F, Ginis P, Schlenstedt C, et al. Dual Task Turning in Place: A Reliable, Valid, and Responsive Outcome Measure of Freezing of Gait. Mov Disord Off J Mov Disord Soc. febbraio 2022;37(2):269–78. doi:10.1002/mds.28887 PubMed PMID: 34939224.

37. On the analysis of movement smoothness | Journal of NeuroEngineering and Rehabilitation | Springer Nature Link [Internet]. [citato 2 settembre 2026]. Disponibile su: https://link.springer.com/article/10.1186/s12984-015-0090-9

38. Pinto C, Schuch CP, Balbinot G, Salazar AP, Hennig EM, Kleiner AFR, et al. Movement smoothness during a functional mobility task in subjects with Parkinson's disease and freezing of gait – an analysis using inertial measurement units. J NeuroEngineering Rehabil. 5 settembre 2019;16:110. doi:10.1186/s12984-019-0579-8 PubMed PMID: 31488184; PubMed Central PMCID: PMC6729092.

39. Mancini M, Horak FB, Zampieri C, Carlson-Kuhta P, Nutt JG, Chiari L. Trunk Accelerometry Reveals Postural Instability in Untreated Parkinson's Disease. Parkinsonism Relat Disord. agosto 2011;17(7):557–62. doi:10.1016/j.parkreldis.2011.05.010 PubMed PMID: 21641263; PubMed Central PMCID: PMC5327861.