Assessing stability in mild and moderate Parkinson's disease : Can clinical measures provide insight?

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Title: Clinically assessing postural stability in Parkinson's disease: Can mobility measures provide insight?

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Author Roles

- Authors RH and MC were involved with the research project conception, organization and execution, statistical analysis design, execution and review and critique, and the manuscript review and critique. RH was involved with writing the first draft of the manuscript. PS was involved with the organization of the project and the review and critique of the manuscript. GN was involved with the review and critique of the manuscript.

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Abbreviations:

ABC	=	Activities-Specific Balance Confidence scale
ACE	=	Addenbrooke's Cognitive Examination
PD	=	Parkinson's disease
TUG	=	Timed Up and Go test
UPDRS	=	Unified Parkinson's Disease Rating Scale

Abstract

This cross-sectional study aimed to investigate the relationship between accelerometer-derived measures of movement rhythmicity and clinical measures of mobility, balance confidence and gait difficulty in people with Parkinson's disease (PD). Twenty-nine independently-living PD patients (Hoehn & Yahr stages 1-3) with no history of significant injury or orthopaedic/deep brain stimulation surgery were recruited from a database of patients who had expressed an interest to participate in research. Participants completed clinical assessments of mobility, postural stability, balance confidence and symptom severity, while head and trunk rhythmicity was evaluated during gait using accelerometers. Following data collection, patients were stratified based on disease stage into either a Mild (Hoehn & Yahr Stage 1) or Moderate (Hoehn & Yahr Stages 2 to 3) PD group. The results highlighted that the Moderate PD group had poorer quality of life, reduced balance confidence and increased gait and falls difficulty. Furthermore, for these patients, gait disability and the number of previous falls were both negatively correlated with multiple components of head and trunk rhythmicity. For the Mild PD group, six-meter walk time was positively correlated with ML head rhythmicity and linear regression highlighted a significant predictive relationship between these outcomes. For the Mild and Moderate PD groups, balance confidence respectively predicted anterior-posterior trunk rhythmicity and vertical head rhythmicity. While these findings demonstrate that falls history and the Gait and Falls questionnaire provide moderate insight into head and trunk rhythmicity in Moderate PD patients, objective and clinically-feasible measures of postural instability would assist with the management of these symptoms.

Introduction

Postural instability is one of the most disabling symptoms of Parkinson's disease (PD) and significantly increases the risk of falling[1]. The costs of falls and falls-related injuries are not well established for many countries[2], but Australian estimates indicate that approximately AUD$27.5 million was spent on injuries associated with falls and falls-related injuries in 2010[3]. Given the significant physical and financial burden associated with falls in PD, a clear need exists to develop an improved capacity to assess symptoms of postural instability to assist with their early identification and treatment. For people with PD, symptoms of postural instability are often accompanied by a decline in the patient's mobility[4]. Traditionally, clinical tests like the Timed up and Go (TUG)[5] and 10-meter[4] (or 6-meter[6]) walk tests have been used to assess changes in mobility for a range of healthy[7] and pathological[4] populations. Given the ease with which they can be administered and their widespread use in hospitals and other clinical settings, it is not surprising that such tests are often used to assess the efficacy of exercise interventions aimed at improving mobility and/or preventing falls in people with PD[8]. However, despite their widespread use for the assessment of people with PD[9], research suggests that some of these clinical tests are not always able to identify differences in mobility between people with PD and age-matched controls[10, 11]. Therefore, while the TUG and 6-meter walk tests are widely acceptable as clinical tests of mobility, there seems to be a need for further investigations to determine whether such clinical tests have the capacity to identify changes in postural stability in people with PD.

The improved availability and affordability of wearable sensors has now made it feasible to develop and/or enhance clinical assessments to incorporate more objective measures of walking stability. For example, research has shown that by placing a wearable sensor on a

patient's body during the performance of the TUG test, the objectivity of the assessment can be significantly improved[11]. Specifically, research utilising this adaptation of the TUG test has reported differences in the amplitude, rhythmicity and smoothness of segmental motion (as measured using RMS accelerations, harmonic ratios and jerk, respectively) for people with PD compared with age-matched controls[12]. Of the numerous accelerometer-based outcomes reported in the literature, the harmonic ratio (HR) is the most commonly reported for people with PD[13] and provides a measure of gait rhythmicity by assessing the ratio of in-phase accelerations to out-of-phase accelerations within a given gait cycle[14]. Additionally, the HR has been shown to have the capacity to discriminate PD patients with a history of falling from patients who have not previously fallen[15]. Despite its frequent use in the research setting, more traditional tests of mobility continue to prevail in daily clinical practices. As such, this study aimed to determine whether the results of common clinical tests of mobility, balance confidence and gait difficulty correlate with laboratory-based measures of postural stability to determine whether these assessments offer insight into deficits in postural stability for people with PD. It was hypothesised that clinical measures of mobility, gait difficulty, postural stability and balance confidence would not be related to movement rhythmicity and, therefore, offer limited insight into dynamic postural stability.

Methods

Participants

Thirty participants diagnosed with idiopathic PD, based on the UK Brain Bank Criteria were recruited. Patients with a history of two or more near-misses and/or at least one fall in the previous 12 months were contacted via a pre-existing database of people with PD who had expressed an interest to participate in research. Prospective participants received an information letter outlining the study's details and inviting them to contact a member of the

research team if they were interested in volunteering. Participants were excluded if they were; i) unable to stand and walk independently; ii) significantly visually (Bailey-Lovie high contrast visual acuity > 0.30 logMAR) or cognitively impaired (Addenbrooke's cognition examination score <82); iii) known to have uncontrolled hypertension; iv) taking psychotropic medications; v) significantly limited by osteoporosis; vi) a recipient of orthopaedic surgery within the previous year; vii) suffering serious neck, shoulder or back injuries (including spinal fusions); or viii) a recipient of deep brain stimulation surgery to manage their symptoms. Experimental procedures were approved by the University's Human Research Ethics Committee and volunteers provided written informed consent. An a-priori sample size calculation based on a p-value of 0.05, a power of 80% and a large effect size (ρ=0.6) indicated that at least 13 participants were required per group to examine the relationships between the clinical tests and harmonic ratios.

Experimental Protocol

Individuals attended a single testing session during which a battery of tests was performed including clinical assessments of; i) cognition (Addenbrooke's Cognitive Examination (ACE)); ii) visual acuity (Bailey-Lovie high contrast visual acuity); iii) symptom severity (Unified Parkinson's Disease Rating Scale (UPDRS), the modified Hoehn & Yahr (H&Y) scale, the Schwab & England Activities of Daily Living Scale and the PD Gait and Falls questionnaire and the Freezing of Gait (FOG) questionnaire); iv) balance confidence (Activity-specific Balance Confidence (ABC) scale); and v) quality of life (39-item Parkinson's Disease Questionnaire (PDQ-39)). A measure of postural instability and gait disability (PIGD) was also calculated for each participant by summing items 27-30 of the UPDRS motor sub-section[16]. The ACE was used to assess cognition, as it incorporates the Mini Mental State Examination and has high sensitivity and specificity for detecting

dementia (cut-off score of <82 gives 82% sensitivity and 100% specificity). These assessments were selected due to their established reliability, validity[17, 18] and previous use in assessing individuals with PD[19]. In addition to the clinical assessments, participants were also asked to report any falls and/or near misses experienced in the previous year. For this study, a fall was defined as "any coming to the ground or other lower level not as the result of a major intrinsic event or overwhelming hazard[20]". A near miss was defined as "an event on which an individual felt that they were going to fall but did not actually do so[20]".

Following the questionnaire-based assessments, participants completed five barefoot trials of the TUG test. Participants were seated in a 42cm high chair with their feet flat on the floor, their back flat against the backrest and their arms resting on the armrests, which were situated 20 cm above the seat. Upon the word 'GO,' participants were required to stand from the chair and walk at a brisk, but comfortable pace to a line on the floor three meters away, turn around and return to the chair to sit down. The time taken to complete the test was recorded using a stopwatch. Following the TUG test, participants completed 6 barefoot walking trials at a comfortable pace along a 10-meter firm walkway. In accordance with the established procedures of the 6-meter walk test (6MWT), walking speed was assessed over the middle 6-meter distance using a dual beamed timing gait system (SWIFT Performance Equipment, Alstonville, Australia) that was positioned at hip height.

Gait rhythmicity was assessed during the 6MWT using two microelectromechanical (MEMS) three-dimensional accelerometers (1500 Hz; Noraxon Inc., Scottsdale, AZ) to provide insight into the patients' dynamic postural control. Each accelerometer was statically-calibrated prior to attachment by aligning each of its sensing axes perpendicular to a horizontal surface to

establish the exact value of gravitational acceleration (i.e. 1 gravitational unit or 1g)[14]. Following static calibration, one accelerometer was firmly attached to a sport headband and positioned over the occipital protuberance and the second accelerometer was firmly attached using double-sided tape to the skin overlying the spinous process of the 10th thoracic vertebra (T10) and reinforced with Micropore. During the 6MWT trials, 3D head and trunk accelerations were wirelessly telemetered to a Telemyo DTS unit, which was connected to a laptop computer running the MyoResearch XP (v1.08) software.

Data Analysis

Raw accelerations were transformed to represent a horizontal-vertical orthogonal coordinate system[14]. Transformation was necessary, as accelerometers measured data relative to a local (or internal) rather than global coordinate system. As such, positioning sensors on body segments often results in two or more of the sensing axes being influenced by gravitational accelerations, which can make it difficult to identify the proportion of the signal attributable to movement-related accelerations[14]. After data transformation, accelerations were filtered using a bi-directional fourth-order low-pass Butterworth filter with a cut-off frequency of 30 Hz[21]. Given 99% of accelerations during walking occur at or below 15 Hz[22], the cut-off frequency of 30 Hz was sufficient to ensure higher frequencies, unrelated to movement, were attenuated without influencing the gait-related accelerations. Filtered and transformed accelerations for the anteroposterior (AP), mediolateral (ML) and vertical (VT) axes were then used to derive the HRs for head and trunk segments, separately. To calculate the harmonic ratios, the time-series data were divided into individual gait cycles by identifying the positive peaks in the VT trunk accelerations, which coincided with heel contact. Using a custom Matlab program (version R2015), AP, ML and VT harmonic ratios were calculated for four consecutive gait cycles identified in the central portion of each 6MWT trial. As the

HR provides a ratio of the in-phase to out-of-phase accelerations during gait, larger values are considered to represent more regular movement patterns, while lower values represent less regular movements[14].

Statistical Analysis

Following processing, data were sub-divided based on each patient's H&Y stage score. Patients who had mild symptoms affecting one side of the body only (H&Y Stage 1) were combined to form a Mild PD group, while data for patients presenting with Mild (H&Y Stage 2) to Moderate (H&Y Stage 3) bilateral symptoms were combined to form a Moderate PD group. To assess for any significant differences between the groups with respect to the continuous demographic variables and clinical assessments, a one-way analysis of variance (ANOVA) was used, while the Chi-square tests were used to identify any differences in the frequency of categorical data. If the assumptions of normality (Shapiro-Wilks test) and/or homogeneity of variance (Levene's test) were violated, the equivalent non-parametric Mann-Whitney was used for the continuous variables[23].

Bivariate correlations were used to establish the relationship between clinical tests of mobility and stability and laboratory-based measures of dynamic postural control. To determine the appropriateness of the parametric Pearson's correlation coefficient, the normality of the continuous measures was assessed using the Shapiro-Wilk test and where a p-value less than 0.05 was returned, the non-parametric Spearman's Rho test was used. Linear regression analyses examined whether clinical measures of mobility, postural stability, balance confidence and gait difficulty were capable of explaining a significant proportion of the variance in head and trunk rhythmicity during walking. Statistical analyses were performed in SPSS version 22 (New York, USA) with significance set at $p<0.05$.

Results

Of the thirty participants recruited, one was excluded prior to completing the assessments due to deficits in cognitive function (i.e. ACE total score <82). Based on the neurological assessment, the remaining 29 patients had mild to moderate symptoms of PD, were independently living and most (90%) were taking anti-parkinsonian medication. Patients comprising the Moderate PD group were shown to have more severe motor symptoms ($p=0.004$) and reported poorer balance confidence ($p<0.001$), poorer quality of life ($p=0.001$), a greater incidence of freezing of gait ($p=0.040$) and increased postural instability and gait difficulty ($p=0.002$) compared with the Mild PD group (Table 1).

INSERT TABLE 1 ABOUT HERE

Correlation Analyses

Tests of normality indicated that a number of the continuous outcome measures were not normally distributed, hence the non-parametric Spearman's Rho test was used to assess the relationships between the clinical tests and the accelerometer-based measures of walking rhythmicity (Table 2). For the whole PD sample, previous falls were shown to be positively correlated with the gait and falls questionnaire ($\rho=0.508$, $p=0.005$) and negatively correlated with the 6-meter walk time ($\rho=-0.466$, $p=0.011$) and all harmonic ratios for the head ($\rho=-0.448$ to -0.513, $p\leq0.02$) and trunk ($\rho=-0.437$ to -0.623, $p\leq0.02$). The sub-group analyses indicated that these relationships were further strengthened for the Moderate PD patients, when patients with milder symptoms were considered separately. Specifically, the bivariate correlations revealed that previous falls were moderately positively correlated with gait and falls difficulty ($\rho=0.600$, $p=0.014$) and moderately negatively correlated with 6-meter walk time ($\rho=-0.531$, $p=0.034$) and all head ($\rho=-0.537$ to -0.693, $p\leq0.05$) and most trunk ($\rho=-0.595$

to -0.766, $p \leq 0.015$) HRs. In contrast, the number of previous falls was moderately positively correlated with balance confidence ($\rho=0.555$, $p=0.049$) and moderately negatively correlated with AP trunk rhythmicity ($\rho=-0.611$, $p=0.027$) for the Mild PD patients.

Analysis of the two mobility assessments demonstrated that the 6-meter walk time negatively correlated with gait speed ($\rho=-1.000$, $p<0.001$) and positively correlated with TUG total time ($\rho=0.519$, $p=0.004$) and mediolateral head HR ($\rho=0.416$, $p=0.025$). The sub-group analyses showed that the 6-meter walk time was moderately positively correlated with TUG total time ($\rho=0.624$, $p=0.010$) for the Moderate PD group, while ML head rhythmicity was moderately positively correlated with the 6-meter walk time ($\rho=0.573$, $p=0.041$) for the Mild PD group. For the whole PD cohort, TUG total time was negatively correlated with gait speed ($\rho=-0.519$, $p=0.004$) and balance confidence ($\rho=-0.565$, $p=0.001$), but the sub-group analyses revealed that these relationships only remained significant for the Moderate PD group (gait speed: $\rho=-0.624$, $p=0.010$; ABC: $\rho=-0.708$, $p=0.002$).

Similar to clinical tests of mobility, the retropulsion test was negatively correlated with balance confidence ($\rho=-0.595$, $p=0.001$) and positively associated with the Gait and Falls questionnaire ($\rho=0.434$, $p=0.019$). Additionally, the Gait and Falls questionnaire was moderately negatively correlated with balance confidence ($\rho=-0.555$, $p=0.002$) and AP trunk rhythmicity ($\rho=-0.425$, $p=0.022$). The sub-group analyses indicated that the retropulsion test was moderately negatively correlated with balance confidence ($\rho=-0.652$, $p=0.006$) and AP head rhythmicity ($\rho=-0.499$, $p=0.049$) for the Moderate PD group. Furthermore, for the Moderate PD group, the gait and falls questionnaire was moderately negatively correlated with balance confidence ($\rho=-0.521$, $p=0.038$) and most head ($\rho=-0.526$ to -0.538, $p<0.05$) and

all trunk (ρ=-0.510 to -0.642, $p<0.05$) HRs. No other relationships were observed between the questionnaires and the objective measures of walking stability (Table 2).

INSERT TABLE 2 ABOUT HERE

Regression Analysis

The linear regression analyses performed for the entire PD cohort indicated that, of all of the clinical assessments conducted, the 6MWT and ABC scale were the only tests that were able to predict any component of head or trunk rhythmicity. Specifically, the 6MWT predicted ML head HRs (p=0.041) and the ABC scale predicted VT head HRs (p=0.032). Similar results were returned for the regression analyses conducted for the two sub-groups, with the 6MWT predicted ML head HRs (p=0.036) for the Mild PD group and the ABC scale predicted AP trunk HRs (p=0.012) and VT head HRs (p=0.047) for the Mild and Moderate PD groups, respectively (Table 3).

INSERT TABLE 3 ABOUT HERE

Discussion

The purpose of this study was to examine whether common clinical tests of mobility, postural stability, balance confidence and gait difficulty were capable of providing insight into walking stability in people with PD. The results indicated that those with moderate disease severity reported experiencing poorer balance confidence, greater postural instability and gait difficulty and poorer quality of life than patients with milder symptoms. Interestingly, however, the Moderate and Mild PD groups had similar results for the clinically-administered assessments, including the retropulsion test, TUG and 6MWT. Similar findings were evident

for the correlation analyses, which indicated that while the outcomes of the clinically-administered tests were not correlated with the measures of head and trunk rhythmicity, those patients in the Moderate PD group who reported a greater number of previous falls and/or greater difficulties with gait and falls also had poorer head and trunk rhythmicity. These findings were similar to previous research that has shown that PD fallers with moderate symptoms had poorer head and pelvis rhythmicity during gait than patients with milder symptoms who had not previously fallen[15]. Collectively, these findings suggest that clinical measures of balance, mobility, gait difficulty and balance confidence may not provide insight into the walking rhythmicity of those with milder symptoms. However, for patients who have more advanced symptoms, it seems that the assessments that rely more on a patient's self-reported difficulties may provide better insight into the gait rhythmicity of these patients. These findings would appear to have important clinical implications and suggest that objectively evaluating a patient's mobility without considering their perceived difficulties may inadvertently result in important information regarding falls risk being overlooked. Nevertheless, it is widely recognised that self-report assessments can be limited by patients over- or under-reporting their difficulties, hence more objective tests would greatly benefit the clinical assessment of postural stability in people with PD.

The Retropulsion test is one of the most commonly used clinical assessment of postural stability for people with PD and is incorporated into the motor sub-section of the UPDRS[24]. Despite its widespread use and its apparent capacity to assess a patient's stability under static conditions, previous research has highlighted its inability to discriminate PD fallers from non-fallers[25] or single fallers from recurrent fallers in cohorts with and without PD[26]. While our findings largely agreed with these studies, it is important to highlight that the retropulsion test was significantly correlated with AP head rhythmicity in

those with moderate symptom severity. Given that the retropulsion test examines a patient's postural response to a firm backward pull on their shoulders, it is perhaps not surprising that those who scored more poorly on the retropulsion test also demonstrated poorer AP head control during gait (i.e. lower AP head HRs). The poor relationship between the retropulsion test and the continuous measures of head and trunk rhythmicity may be explained, at least in part, by a number of factors. First, the retropulsion test is somewhat limited by its use of a Likert scale that ranges from zero (normal response) to four (unable to stand without assistance). Specifically, for a patient's score to change from a zero to a one for the retropulsion test, they must demonstrate a retropulsive gait pattern and recover without assistance. Given the marked heterogeneity of PD symptoms, it is very likely that some patients will develop difficulties that affect their gait and balance, but do not manifest in the form of a retropulsive gait pattern during the retropulsion test. A second factor that may influence the applicability of the retropulsion test to dynamic situations could be the fact that it assesses postural stability during quiet stance rather than under dynamic conditions. Given that only 32% of falls occur during standing[27], it is possible that the retropulsion test may be limited in its capacity to explain the factors contributing to the 66% of falls that occur during ambulation and transfer events[27].

Another interesting finding of this study was that the number of previous falls experienced by patients in the Mild PD group was significantly positively correlated with balance confidence, suggesting that those who fell more had greater balance confidence. This finding is in contrast with a growing body of literature that supports the use of the ABC scale for assessing balance confidence in people with PD and for identifying patients who are at an increased risk of future recurrent falls[28, 29]. While the uncharacteristically high balance confidence reported for those in the Mild PD group may have been influenced by their higher

level of motor functioning (i.e. lower UPDRS scores) and the improved quality of life reported for these patients, it remains unclear what attributes of the disease most influence one's perceived risk of falling. As such, there is a need for future research to examine how self-reported balance confidence changes with disease progression and to establish what symptoms are most likely to influence one's fear of falling.

As with any study, our results should be considered in the context of a couple of limitations. First, our sample size, particularly once stratified based on disease severity, may be considered quite small from a statistical perspective. While the two groups were at least the size of the minimum group size determined in our a-priori sample size calculation, further research involving larger cohorts would be warranted. Second, the patients involved in this study were typically of mild to moderate disease severity (Hoehn & Yahr stages 1 to 3), hence the transferability of our findings may be limited to similar patient cohorts.

Conclusion

Although existing tests of mobility, postural stability, balance confidence and gait difficulty provide little insight into movement rhythmicity in those with mild symptom severity, this study suggests that falls history and the Gait and Falls questionnaire may provide some insight into head and trunk rhythmicity in those with moderate symptom severity. Nevertheless, given that these measures rely on accurate patient recall, the development and implementation of objective and clinically-feasible measures of postural instability and gait disability would help to improve the management of these symptoms in people with PD.

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Table 1. Demographic information and results for the assessments of mobility, balance confidence, quality of life and symptom severity for the Mild and Moderate PD groups.

	All PD (n = 29)	Mild PD (n = 13)	Moderate PD (n = 16)	Test	p-value
Demographics					
Male	21 (72.4%)	8 (61.5%)	13 (81.3%)	3	0.238
Age (years)	64.7 ± 6.4	62.8 ± 7.1	66.3 ± 5.4	1	0.147
Height (cm)	171.7 ± 8.0	170.6 ± 8.9	172.6 ± 7.3	1	0.504
Mass (kg)	80.4 ± 20.1	78.8 ± 20.2	81.7 ± 20.7	1	0.709
Body Mass Index (kg/m^2)	27.0 ± 5.3	26.8 ± 5.1	27.2 ± 5.6	1	0.853
Cognition and Vision					
Addenbrooke's Cognitive Exam	91.7 ± 6.1	92.5 ± 5.2	91.1 ± 6.8	1	0.527
High Contrast Visual Acuity (LogMAR)	0.0 ± 0.1	0.0 ± 0.1	0.0 ± 0.1	2	0.475
Balance Confidence and Quality of Life					
Previous Fallers	23 (79.3%)	11 (84.6%)	12 (75.0%)	3	0.525
Previous Falls	1.4 ± 2.0	1.2 ± 1.5	1.6 ± 2.4	2	0.846
Activities-specific Balance Confidence (%)	77.8 ± 24.8	93.2 ± 6.6	65.4 ± 27.4	2	**<0.001**
39-Item Parkinson's Disease Questionnaire	23.5 ± 15.3	14.9 ± 6.9	30.4 ± 16.9	2	**0.001**
Mobility					
Timed Up and Go Total Time (s)	9.4 ± 1.5	9.0 ± 1.2	9.8 ± 1.7	1	0.202
6-Meter Walk Test (s)	4.7 ± 0.6	4.8 ± 0.5	4.7 ± 0.7	1	0.647
Neurological Examination					
Disease Duration (years)	6.7 ± 5.3	4.9 ± 1.1	8.1 ± 6.8	2	0.288
Unified Parkinson's Disease Rating Scale (Part III)	14.4 ± 11.5	9.1 ± 2.3	18.8 ± 14.1	2	**0.004**
Hoehn & Yahr Stage Score	1.7 ± 0.7	1.0 ± 0.0	2.2 ± 0.4	2	**<0.001**
Schwab & England Activities of Daily Living Scale	86.6 ± 7.5	90.0 ± 4.1	83.8 ± 8.5	2	0.056
Freezing of Gait Score	4.9 ± 5.2	2.7 ± 2.9	6.7 ± 6.0	2	**0.040**
Postural Instability and Gait Disorder Score	1.9 ± 1.6	0.8 ± 1.0	2.7 ± 1.6	2	**0.002**
Retropulsion Test	0.5 ± 0.7	0.2 ± 0.4	0.8 ± 0.9	2	0.083
Levodopa (mg/day)	618.3 ± 432.1	545.2 ± 350.7	677.8 ± 491.7	1	0.421
Dopamine Agonists	6 (20.7%)	2 (15.4%)	4 (25.0%)	3	0.468
Catechol-O-Methyl Transferase Inhibitors	9 (31.0%)	4 (30.8%)	5 (31.3%)	3	0.885
Monoamine Oxidase Inhibitors	10 (34.5%)	3 (23.1%)	7 (43.8%)	3	0.194
Benzodiazepine	1 (3.4%)	1 (7.7%)	0 (0.0%)	3	0.274

Note: Test 1 = One-way analysis of variance; Test 2 = Mann-Whitney U test; Test 3 = Chi-square test

Table 2: Spearman's Rho correlations between the clinical balance and mobility tests and the objective measures of walking rhythmicity for the entire PD cohort and the Mild and Moderate PD sub-groups.

			All PD		Mild PD		Moderate PD	
			Spearman's Rho	**p-value**	**Spearman's Rho**	**p-value**	**Spearman's Rho**	**p-value**
Retrospective Falls	6-Meter Walk Time		**-0.466**	**0.011***	-0.344	0.250	**-0.531**	**0.034***
	Timed Up and Go Total Time		-0.169	0.381	-0.194	0.526	-0.193	0.474
	Retropulsion Test		0.008	0.965	0.077	0.802	0.055	0.839
	Gait & Falls Questionnaire		**0.508**	**0.005***	0.274	0.365	**0.600**	**0.014***
	Activities-Specific Balance Confidence Scale		0.039	0.839	**0.555**	**0.049***	0.038	0.889
	Harmonic Ratio (Head)	AP	**-0.465**	**0.011***	-0.521	0.068	**-0.537**	**0.032***
		ML	**-0.448**	**0.015***	-0.320	0.286	**-0.579**	**0.019***
		VT	**-0.513**	**0.004***	-0.436	0.137	**-0.693**	**0.003***
	Harmonic Ratio (Trunk)	AP	**-0.524**	**0.004***	**-0.611**	**0.027***	-0.430	0.097
		ML	**-0.437**	**0.018***	-0.272	0.369	**-0.595**	**0.015***
		VT	**-0.623**	**<0.001***	-0.436	0.137	**-0.766**	**0.001***
6-Meter Walk Time	Gait Speed		**-1.000**	**<0.001***	**-1.000**	**<0.001***	**-1.000**	**<0.001***
	Timed up and Go Total Time		**0.519**	**0.004***	0.287	0.343	**0.624**	**0.010***
	Retropulsion Test		0.082	0.672	-0.286	0.344	0.268	0.315
	Gait & Falls Questionnaire		-0.134	0.487	-0.034	0.913	-0.158	0.560
	Activities-Specific Balance Confidence Scale		-0.197	0.307	-0.228	0.453	-0.474	0.064
	Harmonic Ratio (Head)	AP	0.163	0.397	0.571	0.571	0.174	0.520
		ML	**0.416**	**0.025***	**0.573**	**0.041***	0.365	0.165
		VT	0.035	0.857	0.174	0.571	-0.026	0.922
	Harmonic Ratio (Trunk)	AP	0.020	0.918	0.025	0.936	0.038	0.888
		ML	0.313	0.099	0.446	0.126	0.194	0.471
		VT	0.003	0.988	0.209	0.492	-0.091	0.737
Timed Up and Go Total	Gait Speed		**-0.519**	**0.004***	-0.287	0.343	**-0.624**	**0.010***
	Retropulsion Test		0.320	0.091	-0.171	0.577	0.413	0.112
	Gait & Falls Questionnaire		0.352	0.061	0.539	0.058	0.257	0.336
	Activities-Specific Balance Confidence Scale		**-0.565**	**0.001***	-0.472	0.104	**-0.708**	**0.002***
	Harmonic Ratio (Head)	AP	0.358	0.057	0.440	0.133	0.035	0.897
		ML	0.326	0.084	0.225	0.459	0.169	0.531
		VT	0.297	0.118	0.324	0.280	0.107	0.692

	Harmonic Ratio (Trunk)	AP	0.053	0.783	0.280	0.354	-0.187	0.488
		ML	0.278	0.145	0.473	0.103	-0.075	0.782
		VT	0.110	0.570	0.110	0.721	-0.097	0.720
Retropulsion Test	Gait Speed		-0.082	0.672	0.286	0.344	-0.268	0.315
	Gait & Falls Questionnaire		**0.434**	**0.019***	0.087	0.777	0.349	0.185
	Activities-Specific Balance Confidence Scale		**-0.595**	**0.001***	-0.143	0.641	**-0.652**	**0.006***
	Harmonic Ratio (Head)	AP	-0.297	0.118	-0.285	0.345	**-0.499**	**0.049***
		ML	-0.143	0.458	-0.513	0.073	-0.422	0.104
		VT	0.119	0.540	-0.057	0.853	-0.051	0.851
	Harmonic Ratio (Trunk)	AP	-0.102	0.597	0.342	0.253	-0.275	0.303
		ML	0.089	0.645	0.228	0.454	-0.173	0.523
		VT	0.116	0.550	0.114	0.711	-0.064	0.814
Gait & Falls Questionnaire	Gait Speed		0.134	0.487	0.034	0.913	0.158	0.560
	Activities-Specific Balance Confidence Scale		**-0.555**	**0.002***	0.007	0.982	**-0.521**	**0.038***
	Harmonic Ratio (Head)	AP	-0.176	0.360	0.067	0.827	**-0.526**	**0.036***
		ML	-0.107	0.579	0.079	0.799	**-0.538**	**0.032***
		VT	-0.042	0.828	0.163	0.595	-0.496	0.051
	Harmonic Ratio (Trunk)	AP	**-0.425**	**0.022***	-0.115	0.708	**-0.642**	**0.007***
		ML	-0.201	0.296	0.129	0.674	**-0.510**	**0.044***
		VT	-0.267	0.162	0.022	0.942	**-0.638**	**0.008***
Activities-Specific Balance Confidence Scale	Gait Speed		0.197	0.307	0.228	0.453	0.474	0.064
	Harmonic Ratio (Head)	AP	-0.119	0.540	0.025	0.936	-0.032	0.905
		ML	-0.256	0.181	0.014	0.964	0.159	0.557
		VT	-0.322	0.088	0.061	0.844	-0.291	0.274
	Harmonic Ratio (Trunk)	AP	-0.014	0.944	-0.505	0.078	0.126	0.641
		ML	-0.209	0.277	-0.356	0.233	-0.153	0.572
		VT	-0.158	0.414	0.168	0.583	-0.112	0.680

AP = Anteroposterior, ML = Mediolateral, VT = Vertical, * = Significant correlation

Table 3: Results of the linear regression analyses conducted between the clinical balance and mobility tests and the objective measures of walking rhythmicity for the entire PD cohort and the Mild and Moderate PD sub-groups.

			All PD			Mild PD			Moderate PD		
			Unstandardised beta (B)	Standardised Beta (β)	p-value	Unstandardised beta (B)	Standardised Beta (β)	p-value	Unstandardised beta (B)	Standardised Beta (β)	p-value
Retrospective Falls											
	Harmonic Ratio (Head)	AP	-0.499	-0.179	0.354	-0.668	-0.316	0.293	-0.491	-0.153	0.572
		ML	-0.478	-0.164	0.395	-0.301	-0.125	0.683	-0.787	-0.236	0.379
		VT	-0.671	-0.271	0.155	-0.469	-0.287	0.342	-1.074	-0.331	0.211
	Harmonic Ratio (Trunk)	AP	-0.755	-0.238	0.214	-0.868	-0.352	0.239	-0.671	-0.191	0.479
		ML	-0.437	-0.135	0.486	-0.218	-0.100	0.746	-0.729	-0.181	0.502
		VT	-0.683	-0.321	0.089	-0.506	-0.319	0.288	-0.934	-0.374	0.154
6-Meter Walk Time											
	Harmonic Ratio (Head)	AP	0.121	0.154	0.424	0.148	0.222	0.465	0.142	0.160	0.553
		ML	**0.348**	**0.382**	**0.041***	**0.500**	**0.585**	**0.036***	0.423	0.398	0.127
		VT	0.064	0.086	0.657	0.160	0.299	0.322	-0.003	-0.003	0.993
	Harmonic Ratio (Trunk)	AP	0.036	0.183	0.846	0.030	0.040	0.897	0.040	0.037	0.892
		ML	0.237	0.238	0.214	0.296	0.404	0.171	0.224	0.180	0.504
		VT	0.005	0.008	0.966	0.177	0.330	0.270	-0.076	-0.110	0.684
Timed Up and Go Total											
	Harmonic Ratio (Head)	AP	0.663	0.363	0.053	0.676	0.459	0.115	0.535	0.265	0.321
		ML	0.577	0.272	0.153	0.263	0.139	0.651	0.547	0.226	0.400
		VT	0.516	0.301	0.113	0.255	0.215	0.482	0.664	0.291	0.274
	Harmonic Ratio (Trunk)	AP	0.036	0.016	0.933	0.413	0.246	0.418	-0.256	-0.104	0.701
		ML	0.713	0.309	0.103	0.817	0.503	0.080	0.423	0.149	0.581
		VT	0.302	0.214	0.265	0.138	0.116	0.705	0.273	0.174	0.519
Retropulsion Test											
	Harmonic Ratio (Head)	AP	-0.243	-0.271	0.155	-0.128	-0.267	0.378	-0.491	-0.483	0.058
		ML	-0.124	-0.199	0.538	-0.259	-0.419	0.154	-0.402	-0.330	0.212
		VT	0.085	0.101	0.603	0.028	-0.072	0.815	-0.007	-0.006	0.982
	Harmonic Ratio (Trunk)	AP	-0.107	-0.098	0.612	0.153	0.280	0.354	-0.308	-0.249	0.352
		ML	0.059	0.052	0.790	0.044	0.084	0.785	-0.109	-0.077	0.778
		VT	0.051	0.074	0.703	0.020	0.053	0.864	-0.069	-0.087	0.748

Gait & Falls Questionnaire										
	AP	-3.309	-0.207	0.282	0.238	0.052	0.866	-8.161	-0.449	0.081
Harmonic Ratio (Head)	ML	-2.575	-0.154	0.425	0.765	0.147	0.631	-8.745	-0.465	0.070
	VT	-0.774	-0.055	0.779	0.557	0.158	0.607	-5.408	-0.295	0.268
	AP	-6.204	-0.341	0.071	-0.096	-0.018	0.954	-9.312	-0.469	0.067
Harmonic Ratio (Trunk)	ML	-3.315	-0.178	0.355	0.180	0.038	0.902	-8.699	-0.383	0.143
	VT	-2.140	-0.175	0.363	-0.402	-0.117	0.703	-5.602	-0.397	0.127
Activities-Specific Balance Confidence Scale										
	AP	-6.767	-0.199	0.300	-3.088	-0.329	0.272	-3.881	-0.108	0.691
Harmonic Ratio (Head)	ML	-9.947	-0.281	0.140	-4.230	-0.397	0.180	-4.687	-0.126	0.642
	VT	**-12.013**	**-0.399**	**0.032***	-0.922	-0.127	0.679	**-18.297**	**-0.504**	**0.047***
	AP	-6.616	-0.171	0.374	**-7.332**	**-0.669**	**0.012***	-7.555	-0.192	0.475
Harmonic Ratio (Trunk)	ML	-6.457	-0.164	0.395	-4.123	-0.424	0.149	-4.191	-0.093	0.731
	VT	-8.144	-0.315	0.096	-0.745	-0.106	0.731	-8.898	-0.319	0.229

AP = Anteroposterior, ML = Mediolateral, VT = Vertical, * = Significant correlation