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LOW TO MODERATE RELATIONSHIPS BETWEEN GAIT AND POSTURAL RESPONSES IN PARKINSON'S DISEASE

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Objective: To evaluate the relationship between spatiotemporal parameters of forward and backward gait and quality of compensatory stepping responses in forward and backward directions in people with Parkinson's disease with and without freezing of gait.

Design: Cross-sectional analysis.

Subjects: A total of 111 individuals with mild to moderate Parkinson's disease.

Methods: Forward and backward gait velocity and step length were evaluated using a GAITRite walkway. Forward and backward postural responses were evaluated using items from the Mini Balance Evaluation Systems Test and the Movement Disorders Society Unified Parkinson Disease Rating Scale motor subsection. Relationships between gait and postural responses were examined for the full sample and for sub-groups with and without freezing of gait.

Results: There were significant ($p < 0.05$) low to moderate correlations between postural responses and gait overall. Correlations were similar in the freezer and non-freezer sub-groups. Freezers performed worse than non-freezers on all gait parameters and backward postural response items ($p < 0.05$).

Conclusion: Low to moderate relationships between gait and postural responses indicate the complexity of postural control and the potential involvement of different neural circuitry across these tasks. Better understanding of the relationships between gait and postural deficits in Parkinson's disease may inform the future development of targeted interventions to address these impairments.

Key words: Parkinson's disease; gait; postural balance; freezing of gait.

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Parkinson's disease (PD) often involves impairments in gait and balance in addition to other motor and non-motor symptoms (1). Gait dysfunction, including reduced speed and stride length (2), worsens throughout the course of the disease and is thought to be at the leading edge of disability for those with PD (3). PD is

also characterized by compromised postural control that worsens with disease progression and may contribute to falls and injuries (4). Postural control deficits are present in both anticipatory and reactive balance tasks (5, 6). People with PD exhibit deficits in compensatory stepping after postural perturbation, with smaller step lengths and more steps taken to recover balance (5, 7).

In addition to general gait and postural decline, individuals are increasingly likely to exhibit freezing of gait (FOG) as PD progresses (8). FOG is a brief, episodic inability to produce effective stepping (9), typically preceded by reduced stride length with increased cadence (8). Overall balance performance is worse in people with PD with FOG, especially in reactive postural responses and stability of gait (10, 11). There is debate about whether FOG and postural response impairment share pathophysiology (11–13). As FOG is a significant source of disability in PD (13), understanding the relationships between gait and postural responses in this sub-group could be particularly useful.

Recent research has illuminated the relative independence of static balance and gait in PD. An exploratory factor analysis from sensor-based gait and balance data grouped static balance and gait into independent mobility factors, suggesting at least partially distinct mechanisms (14). However, as reactive postural responses induce dynamic, rather than static, instability, it is possible that reactive postural responses would involve mechanisms more similar to those required by gait than static balance. This is theoretically possible because successful compensatory stepping in postural responses requires rapid gait initiation, and instability in postural response is related to hypometric response amplitudes and step length (12). It is possible that deficits in reactive postural responses are related to impaired step length and speed during voluntary gait.

Although dynamic postural changes, bradykinesia, and hypokinesia are present in both gait and compensatory stepping responses in PD, it remains unclear whether and how these phenomena relate to one another. If a strong relationship between these different types of movements exists, such an understanding could guide future treatment efforts. We examined the relationships between gait parameters (velocity and step length) and performance on postural response items, specifically on the Mini Balance Evaluation

Systems Test (Mini-BESTest) and the Movement Disorders Society Unified Parkinson Disease Rating Scale motor subsection (MDS-UPDRS III), in people with mild to moderate PD. In addition, we examined these relationships in sub-groups of people with PD with or without a history of FOG (freezers and non-freezers). We hypothesized that there would be a strong relationship between gait parameters and postural responses overall, and that the relationships would be equal or stronger in the sub-group of freezers.

MATERIALS AND METHODS

Participants

This secondary, cross-sectional analysis was performed using baseline data from a clinical trial comparing the effect of different exercise interventions on motor function in PD. The protocol for this trial has been reported (15). Inclusion criteria were diagnosis of “definite” idiopathic PD (16, 17) including demonstrated benefit from dopamine replacement therapy, classification on the Hoehn & Yahr scale (18) between I and IV, and ability to walk independently for 3 m with or without an assistive device. All participants provided written informed consent, and the study protocol was approved by the Human Research Protection Office at Washington University School of Medicine in St Louis.

Outcome measures

Parameters of forward and backward preferred-pace gait were collected using a 4.8 m GAITRite computerized walkway (CIR Systems, Franklin, NJ, USA). Results from 3 trials in each condition were averaged. Both velocity and step length measures were normalized to leg length, to control for height differences among participants. Normalized step length was averaged between left and right sides.

Postural responses were assessed using items 4 and 5 on the Mini Balance Evaluation Systems Test (Mini-BESTest) (19), and item 3.12 on the motor subsection of the Movement Disorders Society Unified Parkinson Disease Rating Scale (MDS-UPDRS III) (20). Item 4 on the Mini-BESTest is a test of reactive postural response in the forward direction that involves the participant leaning forward into the examiner’s hands, which are placed on the participant’s shoulders. The examiner’s hands

are then moved away suddenly and the participant takes steps as needed to recover their balance. Item 5 on the Mini-BESTest involves a similar procedure, but with the participant leaning and stepping in the backward direction. Participants must lean far enough to require at least one recovery step when the examiner’s hands are moved away suddenly. Possible scores on these items are: 2, indicating a single step is needed to recover balance; 1, indicating more than 1 step is needed; or 0, indicating an absence of stepping response that would result in a fall. A summated score of postural response items on the Mini-BESTest was used in some analyses. This score (referred to as postural response summated score) includes Mini-BESTest items 4, 5, and 6, which test postural response in forward, backward, and lateral directions.

Item 3.12 on the MDS-UPDRS III is a test of postural stability in response to a backward perturbation that consists of the examiner pulling the participant’s shoulders suddenly with enough force that a stepping strategy is required. Possible scores on this item are: 0, indicating a normal stepping response of 1–2 steps; 1, indicating 3–5 steps taken; 2, indicating more than 5 steps needed with independent recovery; 3, indicating independent static standing but absence of postural response; or 4, indicating spontaneous loss of balance.

The summated score from gait items 10, 11, 12, 13, and 14 on the Mini-BESTest (gait summated score) was also used in some analyses. All gait items on the Mini-BESTest were performed on a 20-m walkway marked with tape. These items assess imbalance when changing walking speed (item 10), when turning one’s head during gait (item 11), when completing a walking pivot turn (item 12), when stepping over an obstacle (item 13), and when performing the Timed “Get Up and Go” test with a counting dual task (item 14). All 5 Mini-BESTest gait items are scored at 0, 1 or 2 points, with 0 indicating normal performance, 1 indicating moderately impaired performance, and 2 indicating severely impaired performance.

Procedures

All participants were assessed in the morning in the “off” anti-Parkinson medication state, after overnight withdrawal of at least 12 h. Participants wore shoes during evaluations and were allowed to rest as often as needed. The order of testing was the same for each participant, per the protocol of the larger clinical trial, and occurred as follows: (i) MDS-UPDRS III; (ii) Mini-BESTest; and (iii) GAITRite (15). Mini-BESTest and MDS-UPDRS III items were scored from video recordings of the tests by an MDS-certified blinded rater who did not perform the participant evaluations.

Table I. Participants’ characteristics at baseline

	All participants (n = 111)	Freezers (n = 46)	Non-freezers (n = 65)	p-values
Age, years, mean (95% CI)	66.5 (64.8, 68.2)	67.9 (65.2, 70.5)	65.6 (63.2, 67.9)	0.191
Sex, females, n	46	18	28	0.678
Hoehn & Yahr, participants per stage, n				
I	4	1	3	0.033*
II	88	33	55	
III	16	10	6	
IV	3	2	1	
Years since diagnosis, median (IQR)	4.0 (2.0–8.0)	5.0 (3.0–9.5)	4.0 (1.3–7.5)	0.015*
MDS-UPDRS III, median (IQR)	37.0 (30.0–43.0)	41.5 (32.8–46.3)	34.0 (29.0–39.0)	< 0.001*
Mini-BESTest, median (IQR)	19 (17–21)	17 (14.7–19.3)	21 (18–22)	< 0.0001*

p < 0.05. IQR: interquartile range; MDS-UPDRS III: Movement Disorders Society Unified Parkinson Disease Rating Scale motor subsection; Mini-BESTest: Mini Balance Evaluation Systems Test. Possible score range on MDS-UPDRS III is 0–132, where higher numbers indicate worse performance; possible score range on Mini-BESTest is 0–28, where higher numbers indicate better performance.

Table II. Relationships between tests and individual items for all participants, freezers, and non-freezers

	Mini-BESTest	MDS-UPDRS Item 3.12	Mini-BESTest Item 4	Mini-BESTest Item 5
<i>All</i>				
MDS-UPDRS III	-0.576*	0.513*	-0.314*	-0.478*
Mini-BESTest	-	-0.647*	0.635*	0.651*
<i>Freezers</i>				
MDS-UPDRS III	-0.578*	0.422*	-0.316*	-0.416*
Mini-BESTest	-	-0.600*	0.714*	0.638*
<i>Non-freezers</i>				
MDS-UPDRS III	-0.442*	0.453*	-0.251*	-0.423*
Mini-BESTest	-	-0.544*	0.540*	0.573*

*Relationships are significant at FDR-corrected $p < 0.05$. MDS-UPDRS III: Movement Disorders Society Unified Parkinson Disease Rating Scale motor subsection; Mini-BESTest: Mini Balance Evaluation Systems Test; FDR: false discovery rate.

Data analysis

Relationships between gait parameters and performance on postural response items were examined in the full cohort, as well as between categories of freezers and non-freezers. Freezers were participants who reported they had experienced at least one bout of freezing of gait in the month prior to assessment using the new Freezing of Gait Questionnaire (NFOG-Q) (21).

t-tests were used to compare age (normally distributed) between sub-groups, χ^2 tests were used to compare sex between sub-groups, and all other non-normally distributed or ordinal variables were compared between sub-groups with Mann-Whitney *U* tests. Relationships between non-normally distributed gait

parameters and ordinal postural response items in both forward and backward directions were examined using Spearman partial correlations, accounting for disease duration and MDS-UPDRS III score. Relationships between full tests and individual items, as well as between Mini-BESTest gait and postural response summated scores, were also examined with Spearman's correlations. False discovery rate (FDR) correction was applied to all correlational analyses to correct for multiple comparisons. The *a priori* level of significance was set at 0.05. Correlation coefficients were defined as little to none (0 to 0.300), low (0.300 to 0.500), moderate (0.500 to 0.700), and high (> 0.700) (22). All statistical analyses were conducted in IBM SPSS version 24.

RESULTS

The final cohort analysed included 111 participants with complete data for all variables of interest (Table I). Correlations between individual test items and the whole tests (MDS-UPDRS III, Mini-BESTest) were moderate for most items in freezers and non-freezers (Table II). Examining the cohort as a whole, all relationships between the 3 postural response items, gait velocity, and step length in the forward and backward directions were statistically significant ($p_{\text{corrected}} < 0.05$). Spearman partial correlation coefficients ranged between 0.267 and 0.463 (Table III), with better postural responses corresponding with better gait. In addition,

Table III. Relationships between gait parameters and performance on postural response items across all participants

	Mini-BESTest Item 4	Mini-BESTest Item 5	MDS-UPDRS Item 3.12	Forward velocity	Forward step length	Backward velocity	Backward step length
Mini-BESTest Item 4	-	-	-	-	-	-	-
Mini-BESTest Item 5	0.448*	-	-	-	-	-	-
MDS-UPDRS Item 3.12	-0.446*	-0.386*	-	-	-	-	-
Forward velocity	0.314*	0.267*	-0.331*	-	-	-	-
Forward step length	0.347*	0.348*	-0.394*	0.844*	-	-	-
Backward velocity	0.461*	0.344*	-0.335*	0.625*	0.602*	-	-
Backward step length	0.463*	0.380*	-0.364*	0.494*	0.677*	0.830*	-

*Relationships are significant at FDR-corrected $p < 0.05$. IQR: interquartile range; MDS-UPDRS III: Movement Disorders Society Unified Parkinson Disease Rating Scale motor subsection; Mini-BESTest: Mini Balance Evaluation Systems Test; FDR: false discovery rate.

Table IV. Comparisons between freezers and non-freezers on gait and postural response items

	All participants ($n = 111$)	Freezers ($n = 46$)	Non-freezers ($n = 65$)	p -values
Mini-BESTest Item 4, %				0.078
0	4	7	2	
1	62	67	58	
2	34	26	40	
Mini-BESTest Item 5, %				0.015*
0	10	17	5	
1	72	72	72	
2	18	11	23	
MDS-UPDRS Item 3.12, %				0.002*
0	35	26	42	
1	34	24	42	
2	13	20	8	
3	15	26	8	
4	3	4	2	
Forward velocity, median (IQR) ^a	1.35 (1.13–1.53)	1.23 (1.03–1.46)	1.37 (1.23–1.60)	0.002*
Forward step length, median (IQR) ^b	0.73 (0.66–0.83)	0.69 (0.63–0.80)	0.77 (0.71–0.84)	0.001*
Backward velocity, median (IQR) ^a	0.80 (0.59–0.97)	0.64 (0.46–0.83)	0.87 (0.67–1.02)	$< 0.001^*$
Backward step length, median (IQR) ^b	0.43 (0.32–0.52)	0.33 (0.24–0.44)	0.46 (0.39–0.55)	$< 0.001^*$

* $p < 0.05$. IQR: interquartile range; MDS-UPDRS III: Movement Disorders Society Unified Parkinson Disease Rating Scale motor subsection; Mini-BESTest: Mini Balance Evaluation Systems Test. ^acm/s/leg length (cm), ^bcm/leg length (cm).

Table V. Relationships between gait parameters and performance on postural response items among freezers and non-freezers

	Mini-BESTest Item 4		Mini-BESTest Item 5		MDS-UPDRS Item 3.12	
	Freezers	Non-freezers	Freezers	Non-freezers	Freezers	Non-freezers
Forward velocity	0.373*	0.253	0.277	0.235	-0.215	-0.408*
Forward step length	0.495*	0.273	0.338*	0.297*	-0.402*	-0.377*
Backward velocity	0.577*	0.398*	0.404*	0.264	-0.410*	-0.238
Backward step length	0.623*	0.335*	0.362*	0.306*	-0.382*	-0.257

*Relationships are significant at FDR-corrected $p < 0.05$.
MDS-UPDRS III: Movement Disorders Society Unified Parkinson Disease Rating Scale motor subsection; Mini-BESTest: Mini Balance Evaluation Systems Test; FDR: false discovery rate.

all 4 gait variables were significantly related to one another ($p_{\text{corrected}} < 0.05$), and all 3 postural response items were significantly related to one another ($p_{\text{corrected}} < 0.05$), with Spearman partial correlation coefficients between 0.386 and 0.844 (Table III). In all cases, better performance on 1 measure corresponded with better performance on the other correlated measure.

Freezers had a median NFOG-Q score of 10 (interquartile range = 5). Freezers performed significantly worse than non-freezers on all gait and postural response measures except Mini-BESTest item 4 ($p < 0.05$, Table IV). For both freezers and non-freezers, most relationships between postural response items and gait parameters in forward and backward directions were significant ($p_{\text{corrected}} < 0.05$, Table V). Spearman partial correlation coefficient magnitudes were similar between freezers and non-freezers, ranging between 0.215 and 0.623 for freezers, and 0.235 and 0.408 for non-freezers. Better postural responses corresponded with better gait for both groups.

Relationships between the gait summated score (Mini-BESTest items 10–14) and the postural response summated score (Mini-BESTest items 4–6) were low to moderate for all participants, as well as for freezers and non-freezers. Relationships between the gait summated score and the 4 spatiotemporal gait parameters were moderate (Table VI).

Table VI. Gait summated score (items 10–14 on Mini-BESTest) correlated with postural response summated score (items 4–6 on Mini-BESTest) and spatiotemporal parameters of gait for all participants, freezers, and non-freezers

	Mini-BESTest gait summated score		
	All participants	Freezers	Non-freezers
Postural response summated score	0.480*	0.550*	0.360*
Forward velocity	0.584*	0.505*	0.544*
Forward step length	0.625*	0.706*	0.514*
Backward velocity	0.591*	0.553*	0.527*
Backward step length	0.596*	0.604*	0.480*

*Relationships are significant at FDR-corrected $p < 0.05$.
Mini-BESTest: Mini Balance Evaluation Systems Test; FDR: false discovery rate.

DISCUSSION

The present study evaluated the relationships between postural responses and characteristics of gait in different directions in people with PD and in sub-groups of people with PD with or without a history of freezing of gait. The correlations between postural responses and gait observed in our results, though statistically significant, were only low to moderate. Furthermore, correlations between gait and postural responses were similar even for parameters of non-corresponding directions, suggesting that gait parameters in a particular direction are not uniquely predictive of postural responses in that direction. Likewise, tests of postural response in a particular direction are not uniquely predictive of gait speed and step length in that direction. This suggests that postural responses are complex phenomena. Although ability to take large steps and step quickly are significant contributors, deficits in proprioceptive integration and response scaling (23), impaired sense of vertical (5, 24), asymmetry in balance control (6), or impairments in executive function (5, 25) probably also contribute to postural impairments. The correlational results were comparable for the full sample and for the sub-groups of freezers and non-freezers.

In general, freezers performed worse on tests of backward postural response and had slower gait speeds and smaller step lengths. The Mini-BESTest forward postural response item did not differ between freezers and non-freezers. This could be due to compensatory postural mechanisms commonly seen among freezers to prevent forward falls, such as shifting the centre of gravity posteriorly (26). It is notable that correlations between gait and postural response items among freezers were similar to those of individuals with PD without FOG. Gait parameters are not more strongly predictive of postural response or vice versa, even in a PD sub-group with greater disease severity and impairment. Recent work by Nonnekes et al. suggests that postural instability and FOG have at least partly different pathophysiology; the hypokinesia that characterizes PD and is especially pronounced in FOG may not be the only contributing factor to postural instability (12).

Because the spatiotemporal parameters of gait and the postural response items varied in measurement type (continuous vs. ordinal), we correlated summated scores from the gait items (10–14) and postural response items (4–6) of the Mini-BESTest. In addition, we correlated the gait summated score with the spatiotemporal parameters of gait. By including ordinally scored gait items, we hoped to determine whether the scoring of the items influenced the correlation. The correlations between the gait and postural response summated scores for the whole group and for the sub-groups of freezers and non-freezers were similar to, or stronger

than, the correlations between the individual spatiotemporal parameters of gait and postural response items. The stronger correlations could reflect the fact that the gait summated score from the Mini-BESTest evaluates many aspects of gait and balance besides step quality, including anticipatory postural control, sensory orientation, reactive postural control, and dual tasking (27). These varied competencies may present a linkage between gait and postural response.

The weak relationship between compensatory stepping and voluntary stepping during gait suggests that these tasks might use different neural mechanisms. While voluntary stepping requires anticipatory postural adjustments to preserve balance before an internally generated perturbation (5), reactive postural adjustments and compensatory stepping happen more quickly than even the fastest voluntary stepping (28) in response to unplanned, abrupt movement (29). Our data support the hypothesis that different mechanisms control voluntary and compensatory stepping given that gait parameters in either direction are more strongly related to one another than are gait and postural response in the same direction. This suggests that neural circuits may be more distinct in different types of stepping (compensatory vs. voluntary) than for different directions.

There have been conflicting reports of whether postural responses can be directly altered with training (5, 7, 23, 30–32); conversely there is strong evidence to support improvements in gait parameters with a variety of interventions (for review, see (33)). One study found that 2 weeks of training with repeated perturbations not only increased compensatory step length and reduced delay in compensatory step initiation, but also increased stride length and velocity in voluntary gait (31), demonstrating the potential for generalized improvements across both gait and postural responses with targeted training for only 1 of these components. The significant low to moderate correlations we observed between individual gait and postural response items may suggest the presence of some similar elements or impairments across tasks in PD that could potentially be addressed simultaneously with 1 type of targeted training. Similarly, there is some evidence that training gait in 1 direction may have beneficial effects on gait in the opposite direction (34, 35), and the high correlations between forward and backward gait parameters observed in our data suggest that forward and backward gait impairments are related.

Because individuals with PD who exhibit postural instability and gait difficulty are at greater risk of rapid functional decline (36), it is essential that clinicians obtain an accurate picture of postural control to determine an optimal rehabilitation plan. Our results,

in combination with other studies, emphasize the importance of assessing reactive balance separately in the clinical setting, as reactive balance is not strongly nor consistently predicted by gait parameters or by anticipatory balance tasks (5, 37). For example, gait velocity measurements in isolation are not as effective at identifying fallers as is the Mini-BESTest (38). One limitation to this study was the relative insensitivity of the individual Mini-BESTest and the MDS-UPDRS III postural response items for assessing postural control. Each item is rated on either a 3- or 5-point scale that corresponds to a numerical range of compensatory steps taken or a fall. Most of the participants scored in the middle of the rating scales on each item; freezers and non-freezers were distinguished only by the extremes on the backward postural response items. In addition, these rating scales do not reflect stability during compensatory stepping, the participant's sense of control in responding to the perturbation, or the kinematic strategies adopted in the postural response. While these items are easy to administer and are clinically feasible, there may be a need for more sensitive quantitative measures, particularly in the research setting, to distinguish more subtle deteriorations and elucidate mechanisms of impairment in postural response. Sensor-based or full-body kinematic analyses should be conducted in the future to gain insight into the successful and unsuccessful strategies adopted by people with PD in response to postural perturbations (39, 40).

Similarly, the GAITRite system used here to analyse gait velocity and stride length is limited by its inability to assess walking kinematics or balance control. With the GAITRite, we captured measures of steady-state walking in the forward and backward directions. However, it is possible that the relationship between spatiotemporal measures of gait initiation and stepping during perturbation responses may be different from the relationships we observed between steady-state gait and postural responses. Future studies could assess relationships between postural responses and kinematic profiles during gait, particularly during gait initiation. These may also be more sensitive in differentiating those with PD with and without FOG.

Another limitation is that analyses were reported only in the off-medication state. We performed the analyses with off-medication data because this state most accurately reveals movement impairment due to PD. Off-medication analysis was also chosen to provide insight into the interplay of the deficits in walking and compensatory stepping due to the pathology of the disease, rather than the potentially asymmetrical or unequal benefit to walking vs postural responses that may be provided by levodopa (4, 14).

In addition, FOG was not elicited in the laboratory, but was ascertained only by self-report using the first question on the NFOG-Q. FOG is difficult to elicit in research and clinical settings, and the self-report method chosen is well-accepted in the field (21). However, we acknowledge as a limitation that we did not explore severity or characteristics of FOG as potential factors influencing gait and/or postural responses, and we did not measure FOG episodes in the laboratory to distinguish freezers from non-freezers.

In conclusion, spatiotemporal gait parameters and postural control are related in people with mild to moderate PD, but the correlations are low to moderate. Other factors, such as impaired stability and sense of vertical, executive function, or the use of different neural pathways may help to explain the weak relationships between these variables. Since spatiotemporal parameters of gait and the gait summated score on the Mini-BESTest have not been shown to be surrogate measurements for understanding postural response, clinicians should ensure that reactive postural responses are tested as part of routine assessment for PD. Future studies should examine detailed kinematic profiles of postural responses and gait to better evaluate whether certain patterns are more common in those with PD with FOG and whether overlapping components of these motor deficits could be addressed simultaneously by targeted rehabilitation interventions.

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The authors declare no conflicts of interest.

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