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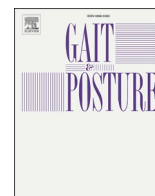
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Full length article



Functional limits of stability and standing balance in people with Parkinson's disease with and without freezing of gait using wearable sensors

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ABSTRACT

Background: People with from Parkinson's disease (PD) and freezing of gait (FoG) have more frequent falls compared to those who do not freeze but there is no consensus on which, specific objective measures of postural instability are worse in freezers (PD + FoG) than non-freezers (PD-FoG).

Research question: Are functional limits of stability (fLoS) or postural sway during stance measured with wearable inertial sensors different between PD + FoG versus PD-FoG, as well as between PD versus healthy control subjects (HC)?

Methods: Sixty-four PD subjects with FoG (MDS-UPDRS Part III: 45.9 ± 12.5) and 80 PD subjects without FoG (MDS-UPDRS Part III: 36.2 ± 10.9) were tested Off medication and compared with 79 HC. Balance was quantified with inertial sensors worn on the lumbar spine while performing the following balance tasks: 1) fLoS as defined by the maximum displacement in the forward and backward directions and 2) postural sway area while standing with eyes open on a firm and foam surface. An ANOVA, controlling for disease duration, compared postural control between groups.

Results: PD + FoG had significantly smaller fLoS compared to PD-FoG ($p = 0.004$) and to healthy controls ($p < 0.001$). However, PD-FoG showed similar fLoS compared to healthy controls ($p = 0.48$). Both PD+FoG and PD-FoG showed larger postural sway on a foam surface compared to healthy controls ($p = 0.001$) but there was no significant difference in postural sway between PD+FoG and PD-FoG.

Significance: People with PD and FoG showed task-specific, postural impairments with smaller fLoS compared to non-freezers, even when controlling for disease duration. However, individuals with PD with or without FoG had similar difficulties standing quietly on an unreliable surface compared to healthy controls. Wearable inertial sensors can reveal worse fLoS in freezers than non-freezers that may contribute to FoG and help explain their more frequent falls.

1. Introduction

Postural stability is defined as the ability to maintain equilibrium under both dynamic and static conditions [1]. Traditionally, the excursion of the center of pressure (COP) during dynamic and static balance tasks has been used to characterize postural stability. For example, functional limits of stability (fLoS), measured as the maximum displacement of the COP while voluntary leaning forward and

backward, has been used as measure of dynamic postural stability [2–4]. fLoS are important to successfully carry out fall-prone motor tasks such as reaching, initiating gait and transitioning from sitting to standing [5]. It has been previously shown that fLoS are impaired in people with PD compared to healthy elderly but improve with levodopa [2,6]. Postural stability during quiet standing has traditionally been measured by from COP displacements under the base of support although recent studies show comparable measures using an inertial sensor on the lumbar spine

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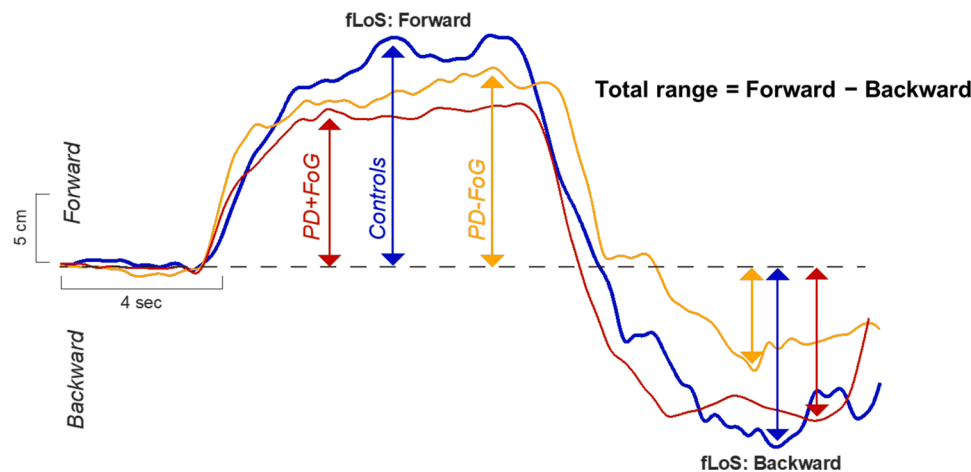


Fig. 1. Representative signal of center of pressure during the limits of stability task.

Blue line represents a control subject, red line a subject with Parkinson's disease (PD) and freezing of gait (FoG), and orange line a PD subject without FoG. fLoS, functional limits of stability (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

[3]. Several studies have shown that people with PD have larger sway area, velocity, and jerkiness when standing with eyes open, but not with eyes closed, compared to healthy controls [2–6]. Although both postural sway and fLoS have been shown to worsen with PD duration, it is not known whether freezing of gait (FoG) is associated with worse sway or fLoS, regardless of disease duration [6,7].

FoG affects up to 80 % of people with PD and is characterized by a brief absence or marked reduction of forward progression of the feet despite the intention to walk [8,9]. This phenomenon happens mainly during gait initiation, turning, approaching narrow spaces, or performing a dual-task, and it is usually worse Off medications. Although it has been suggested that people with FoG show worse postural stability than people without FoG [9], only one study showed the effects of FoG on fLoS [6]. Specifically, reduced fLoS in the anterior, but not posterior, direction (quantified as maximum forward and backward leaning) has been found in subjects with PD and FoG (PD + FoG) compared to subjects without FoG (PD-FoG) or healthy controls. However, this study evaluated participants only while On levodopa medication using a force plate to quantify fLoS.

In addition, although previous studies have shown that PD + FoG and PD-FoG have similar postural sway deficits while standing in the Sensory Organization Test in simple and complex conditions (conditions with unreliable visual and/or proprioceptive input [10], and while standing on a firm surface with eyes open or closed [11,12]), others found different results. In fact, two studies have reported larger anteroposterior sway in PD + FoG compared to PD-FoG during quiet stance on a firm surface [7]. Furthermore, PD + FoG showed greater postural impairments compared to PD-FoG, particularly when standing on a surface with unreliable proprioceptive inputs [13]. Such discrepancy could be explained by the fact that often PD + FoG have longer disease duration compared to PD-FoG, but rarely studies account for disease duration, making it difficult to determine whether FoG or disease severity or both are related to worse postural stability.

Recent advances in inertial measurement units (IMUs) have demonstrated the ability to collect objective measures of postural stability outside of the laboratory. IMUs are small, low-cost and quicker to use by clinicians compared to a force plate [3]. Previous studies have shown the validity of IMUs to quantify postural sway while standing, compared to traditional force plate COP measures in people with PD [3, 14,15]. In fact, while the COP reflects the acceleration of the center of mass, the IMUs are capturing sway that is controlled by the COP or related kinetic adjustments to segment movement. Due to this relationship, COP and segmental accelerations are highly correlated [16], although they reflect different aspects of postural stability. No previous

study has compared the fLoS and postural sway in PD + FoG versus PD-FoG using IMUs.

The aim of this study was to use IMUs to investigate the effect of FoG in people with PD on postural stability while Off anti-Parkinson's medication, measured by fLoS and postural sway while standing under 2 sensory conditions. We hypothesized that PD + FoG would have smaller fLoS compared to PD-FoG, independent of disease severity, but similar sway measures during quiet standing.

2. Methods

2.1. Participants

A total of 144 subjects with idiopathic PD and 79 age-matched healthy elderly subjects (free of any neurological or musculoskeletal disorders) were recruited through the Parkinson's Center of Oregon at the Oregon Health & Science University (OHSU), the Portland VA Medical Center or in the community. Individuals were excluded if they were not able to stand or walk for 2 min without an assistive device. Furthermore, people were excluded if they had any musculoskeletal or vestibular disorder that could affect balance or gait. People with idiopathic PD were diagnosed based on the United Kingdom Brain Bank criteria, and of the 144 subjects with PD, 64 were classified as freezers (PD + FoG) and 80 subjects were classified as non-freezer (PD-FoG). Freezers were classified based on question 1 of the New Freezing of Gait Questionnaire (NFOGQ) [17] or if freezing of gait was clinically detected during the assessment (by an experienced neurologist J. G. N.). All subjects were tested in the practical Off state, after withholding PD medication for at least 12 h. All subjects signed informed consent forms approved by the OHSU Institutional Review Board (approval #4131) and the joint OHSU and Veterans Affairs Portland Health Care System (VAPORHCS) Institutional Review Board (approval #8979). All work was conducted in accordance with the declaration of Helsinki (1964).

2.2. Procedure

The following clinical tests characterized the cohort: 1) the MDS-UPDRS [18], 2) the Activities-specific Balance Confidence scale (ABC-scale) [19], 3) the Montreal Cognitive Assessment (MoCA) [20], 4) the NFOGQ, 5) and the Parkinson's Disease Questionnaire 39 (PDQ-39) [21]. In addition, subjects were asked about how many falls they experienced in the past six months. A fall was defined as a loss of balance where the person inadvertently came to rest on the ground or other lower level [22]. Subjects then took off their shoes and wore 8 wireless

Table 1
Demographic and clinical characteristics.

	HC (N = 79)		FoG+ (N = 64)		FoG- (N = 80)		p-value			
	Mean	SD	Mean	SD	Mean	SD	All Groups	HC vs. FoG+	HC vs. FoG-	FoG + vs. FoG-
Male/Female	48/31		44/20		49/31		0.554 ^a	–	–	–
Age	68.2	8.1	68.1	8.0	68.8	8.0	0.857	1.000	1.000	1.000
Height	171.5	10.0	173.0	10.5	173.6	9.5	0.412 ^b	0.888	0.660	1.000
Weight	73.7	13.1	80.0	15.4	79.3	18.1	0.027	0.053	0.075	1.000
MoCA	26.8	2.3	25.5	3.8	26.0	3.1	0.205 ^b	0.324	0.462	1.000
ABC scale	95.9	5.3	73.8	17.6	85.8	13.0	< 0.001b	< 0.001	< 0.001	0.001
Falls (N)	0.17	0.05	1.85	0.36	0.51	0.13	<0.001b	< 0.001	0.486	< 0.001
Disease duration (years)	–		7.8	5.4	5.0	4.2	–	–	–	< 0.001
MDS-UPDRS Part III	–		45.9	12.5	36.2	10.9	–	–	–	< 0.001
PDQ-39	–		21.6	11.8	14.6	11.0	–	–	–	< 0.001c
NFOGQ	–	–	12.1	7.1	0.0	0.0	–	–	–	< 0.001c
HY stage (I/ II/ III/ IV)	–		0/44/10/10		1/71/5/3		–	–	–	0.011a

Groups compared using ANOVA, Kruskal-Wallis test, Mann-Whitney U test or Chi-squared test and significance level of 0.05 (a: Chi-squared test, b: Kruskal-Wallis test, c: Mann-Whitney U test). Bold values indicate significant differences between groups.

HC, healthy controls; FoG, freezing of gait; MoCA, montreal cognitive assessment; ABC scale, the activities-specific balance confidence scale; Falls, the number of falls in the past 6 months; MDS-UPDRS, movement disorder society-sponsored revision of the unified Parkinson’s disease rating scale; PDQ-39, Parkinson’s disease questionnaire-39.

inertial sensors (Opals by APDM, Inc. Portland, OR, USA) on the lumbar back, sternum, both feet, shins, and wrists, applied with an elastic velcro belt. The sensor included triaxial accelerometers, triaxial gyroscopes, and magnetometer recording at 128 Hz. Subjects performed one trial each of the fLoS and Sway task. This study came from baseline data of a larger, interventional trial [23].

The fLoS task required subjects to stand still with their arms at their sides and with a consistent foot position using a template between the feet with 10 cm between heels [24]. After standing still for 5 s, subjects were asked to lean forward as far as possible that they could hold for 5 s, then to lean backward as far as possible, hold for 5 s and then to come back to an upright position. Participants were instructed to lean forward and backward without lifting their toes or heels and not to bend their knees or hips [2]. If participants flexed their hips or knees, or lifted their heel/toes, the trial was repeated.

The sway task required subjects to stand quietly for 30 s in two different conditions, standing on a firm or foam (Balance-pad, Airex AG, Sins, Switzerland) surface with eyes open (EOFirm or EOFoam). Subjects were asked to look at an art poster 6 m ahead while standing. Their hands were kept on their hips and their entire medial borders of the feet immediately adjacent in both sway tasks.

2.3. Outcome measures

Analysis focused on 3 measures of fLoS and 7 measures of postural sway. Measures characterizing fLoS were calculated offline using a custom-made algorithm in MATLAB R2018b (The Mathworks Inc., Natick, MA, USA). Specifically, data from the accelerometers at the lumbar level were low-pass filtered (2 Hz, fourth-order, zero-lag, Butterworth filter) and the COP antero-posterior displacement was estimated from the acceleration at the center of mass level (from the lumbar sensor) via an inverted-pendulum model [24]. In addition to the maximum forward and backward fLoS, the total fLoS range was calculated as the difference between forward and backward fLoS (Fig. 1). Furthermore, the mean fLoS was calculated during 3 s, including the maximum peak leaning in the forward and backward directions. The objective measures of sway were computed online with APDM’s Mobility Lab™ (APDM Inc., Portland, OR, USA). The following sway measures were extracted from the Opal accelerometer placed on the lumbar region: sway area, jerk in mediolateral (ML) or anteroposterior

(AP) direction, mean velocity in ML or AP direction, and the root mean square (RMS) in ML or AP direction.

2.4. Statistical analysis

The distribution for demographic and clinical characteristics of the three groups (healthy controls, PD-FoG, and PD + FoG) was examined by the Shapiro-Wilk test or one-way ANOVA. In addition, an independent t-test was used to examine possible differences in disease duration and the MDS-UPDRS score. A chi-square test was used for gender distribution and the Hoehn and Yahr stage rating.

To determine possible differences in fLoS and sway measures among the three groups, a one-way ANOVA was used. Differences between groups were further evaluated with post-hoc analysis using Bonferroni pairwise comparison. Since disease duration significantly differed between PD-FoG and PD + FoG (see Results), disease duration was used as a covariate in a general linear model. Prior to analyzing group differences in objective measures, they were transformed to their natural logarithms to ensure a normal distribution. All statistical analyses were processed using SPSS Statistics version 25.0 (IBM, Armonk, NY, USA). The statistical significance was set to $p < 0.05$.

3. Results

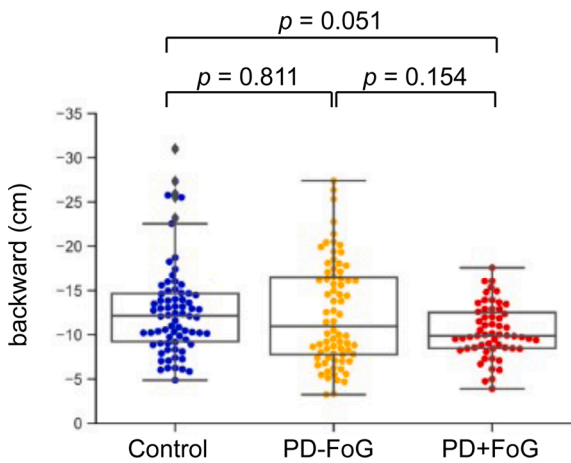
3.1. Demographics and clinical measures among PD subgroups and healthy controls

All 3 groups had similar age, height, weight, sex, and MoCA scores (Table 1). However, both PD subgroups showed significantly worse balance confidence (ABC scale) compared to the control group. In addition, the PD + FoG group showed significantly worse MDS-UPDRS III, PDQ-39, ABC scale, NFOGQ, and significantly longer disease duration and significantly more falls compared to the PD-FoG group.

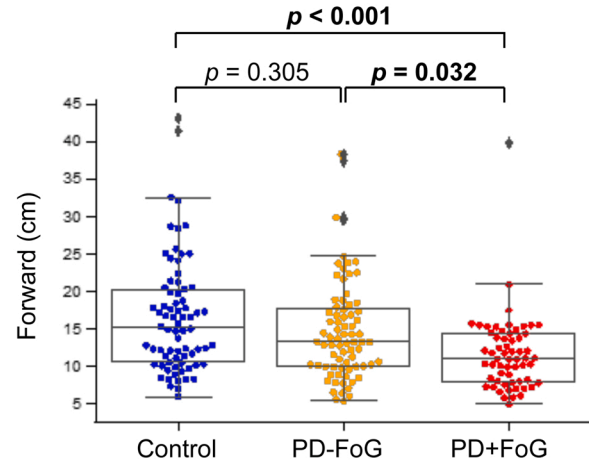
3.2. fLoS and Sway measures among PD subgroups and healthy controls

9 % of people with FoG, 7 % of people without FoG, and 6 % of control could not complete or had to be caught during the fLoS task. Similarly, 6 % of people with FoG and 1 % of people without FoG could not complete the 30 s sway EOFirm or had to be caught. Also, 17 % of

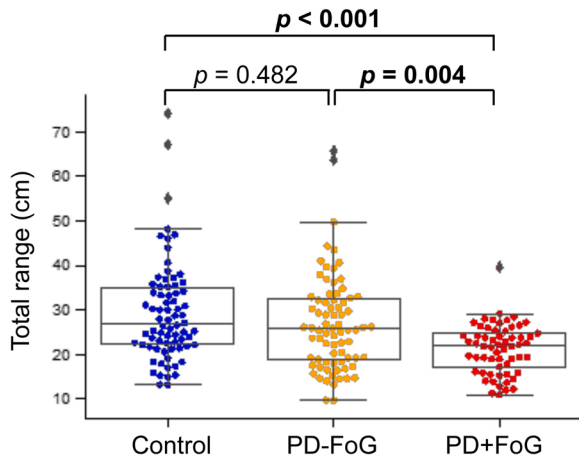
(A) Peak Functional limits of stability



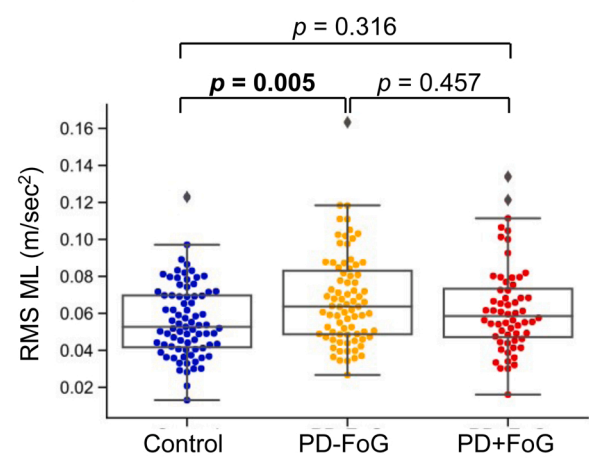
(B) Peak Functional limits of stability



(C) Peak Functional limits of stability



(D) Eyes open on firm surface



(E) Eyes open on foam surface

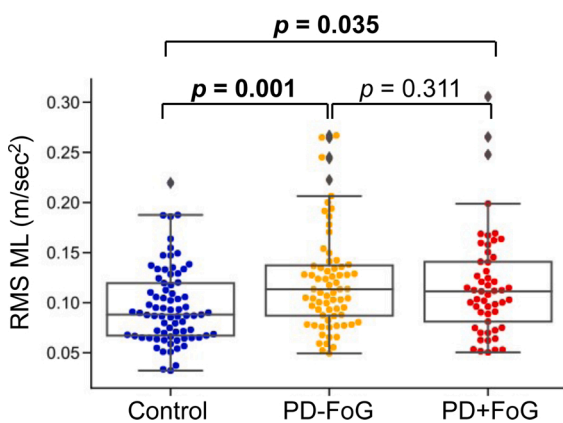


Fig. 2. Functional limits of stability (A, B and C), and objective sway measures (D and E) in healthy controls, non-freezers (PD-FoG), and freezers (PD + FoG). Dots indicate a value of each subject, boxes the interquartile range, middle lines the median, whiskers the min–max value. The p-value after correcting for disease duration is shown. Bold values indicate significant effects at $p < 0.05$. RMS, root mean square; ML, mediolateral.

people with FoG, 11 % of people without FoG, and 2 % of controls could not complete the 30 s sway EOfoam or had to be caught. No people with FoG history experienced freezing during the tasks of fLoS or Sway.

The PD + FoG group had significantly smaller fLoS (fLoS forward

direction and fLoS range) than the PD-FoG ($p = 0.007$ and $p = 0.003$) or the healthy control groups ($p < 0.001$) (Fig. 2B and C). The smaller forward fLoS in PD + FoG compared to PD-FoG remained statistically significant even after controlling the analysis for disease duration.

Table 2
Differences between groups for objective measures.

	HC		FoG+		FoG-		p-value All Groups	GLM			
	Mean	SD	Mean	SD	Mean	SD		HC vs. FoG+	HC vs. FoG-	FoG + vs. FoG-	FoG + vs. FoG-
Peak fLoS											
Backward (cm)	-12.8	5.3	-10.4	3.0	-12.4	5.9	0.057	0.051	0.811	0.513	0.154
Forward (cm)	16.5	7.6	11.6	5.1	14.8	6.7	< 0.001	< 0.001	0.305	0.007	0.032
Total range (cm)	29.3	11.3	21.2	5.5	26.9	10.7	< 0.001	< 0.001	0.482	0.003	0.004
Mean fLoS											
Backward (cm)	-10.2	4.9	-7.2	5.9	-8.4	2.8	0.207	0.250	0.753	1.000	0.377
Forward (cm)	14.3	7.2	10.0	4.7	13.0	6.1	< 0.001	< 0.001	0.817	0.007	0.026
Total range (cm)	24.5	10.4	18.4	6.3	22.5	9.4	0.001	< 0.001	0.471	0.029	0.045
Sway, EOFirm											
Sway area (m ² /sec ⁴)	0.08	0.05	0.09	0.06	0.11	0.08	0.017	0.273	0.014	1.000	0.174
Jerk ML (m ² /sec ⁵)	1.46	1.09	1.89	2.75	1.75	1.68	0.712	1.000	1.000	1.000	0.396
Jerk AP (m ² /sec ⁵)	1.72	1.27	2.42	2.80	2.03	1.86	0.515	0.913	1.000	1.000	0.754
Velocity ML (m/sec)	0.09	0.05	0.12	0.07	0.12	0.07	0.002	0.011	0.006	1.000	0.631
Velocity AP (m/sec)	0.15	0.09	0.17	0.12	0.17	0.12	0.886	1.000	1.000	1.000	0.907
RMS ML (m/sec ²)	0.06	0.02	0.06	0.02	0.07	0.02	0.007	0.316	0.005	0.537	0.457
RMS AP (m/sec ²)	0.07	0.03	0.08	0.03	0.08	0.04	0.245	0.429	0.484	1.000	0.698
Sway, EOFoam											
Sway area (m ² /sec ⁴)	0.19	0.14	0.32	0.28	0.31	0.27	< 0.001	0.001	< 0.001	1.000	0.865
Jerk ML (m ² /sec ⁵)	6.63	6.19	6.33	7.31	6.15	5.71	0.789	1.000	1.000	1.000	0.203
Jerk AP (m ² /sec ⁵)	5.81	5.54	8.29	10.20	6.62	8.22	0.257	0.310	1.000	1.000	0.806
Velocity ML (m/sec)	0.12	0.08	0.17	0.09	0.17	0.11	< 0.001	< 0.001	0.001	1.000	0.460
Velocity AP (m/sec)	0.17	0.10	0.24	0.15	0.22	0.14	0.002	0.002	0.038	0.809	0.436
RMS ML (m/sec ²)	0.10	0.04	0.12	0.05	0.12	0.05	0.001	0.035	0.001	1.000	0.311
RMS AP (m/sec ²)	0.10	0.04	0.13	0.05	0.13	0.05	< 0.001	< 0.001	0.001	0.717	0.389

Groups compared using ANOVA and general linear model using disease duration as a covariate. General linear model (GLM) used disease duration as a covariate. Bold values indicate significant effects at $p < 0.05$.

FoG, freezing of gait; fLoS, functional limits of stability; EOFirm, standing on a firm surface with eyes open; EOFoam, standing on a foam surface with eyes open; ML, mediolateral; AP, anteroposterior; RMS, root mean square.

Specifically, the difference between freezers' and nonfreezers' fLoS in the forward direction ($p = 0.032$) and fLoS total range ($p = 0.004$) was confirmed. No significant difference was found between PD-FoG and HC for fLoS in the forward direction nor fLoS range ($p = 0.305$ and $p = 0.482$). On the other hand, all 3 groups showed similar fLoS in the backward direction (Table 2). The mean fLoS showed very similar results as the peak fLoS (Table 2 and Appendix 1). In addition, the PD + FoG group showed significantly smaller fLoS compared to the PD-FoG group after controlling the analysis for age (fLoS forward: $p = 0.001$, fLoS Total range: $p = 0.004$) and sex (fLoS forward: $p = 0.001$, fLoS Total range: $p = 0.003$).

In contrast to fLoS, no differences were found between PD + FoG and PD-FoG in the sway measures, either on the foam or firm surfaces (Table 2 and Fig. 2D, E). However, both PD + FoG and PD-FoG showed larger sway area ($p = 0.001$, $p < 0.001$), RMS (AP: $p < 0.001$, $p = 0.001$; ML: $p = 0.035$, $p = 0.001$), and sway velocity (AP: $p = 0.002$, $p = 0.038$; ML: $p < 0.001$, $p = 0.001$), compared to healthy controls in the EOFoam condition, for both the AP and ML directions (Table 2 and Fig. 2E). Fewer differences, mainly in the ML direction, were present between PD and healthy controls in the EOFirm condition (Table 2). Specifically, PD-FoG showed larger sway area ($p = 0.014$), velocity ML ($p = 0.006$) and RMS ML ($p = 0.005$; Fig. 2D), compared to healthy controls; whereas PD + FoG only showed larger sway velocity in the ML direction compared to healthy controls ($p = 0.011$).

4. Discussion

Our findings showed that people with PD and FoG have smaller fLoS compared to people with PD and without FoG or healthy controls, even after controlling for disease duration, when tested Off medication. In contrast, postural sway did not differ between PD subjects with FoG versus without FoG, although people with PD showed greater postural instability compared to healthy controls when standing on a foam surface with eyes open.

Consistent with previous results using a force plate, people with PD and FoG showed smaller fLoS in the forward (but not backward)

direction compared to healthy controls and people with PD without FoG [6]. Our study is the first to demonstrate that fLoS measures differentiated between PD + FoG and PD-FoG, even when controlling the analysis for disease duration. This finding suggests that fLoS may be specifically related to freezing rather than deterioration of postural control with disease progression, and therefore may be a sensitive, objective measure differentiating freezers from non-freezers. In contrast to PD + FoG, PD-FoG showed no significant difference in fLoS compared to age-matched, healthy controls. This result was partly inconsistent with previous studies reporting reduced limits of stability in people with PD [2] with or without FoG [6]. These differences may be explained by medication status since the previous study measured fLoS while On levodopa, whereas our study tested participants Off levodopa. However, this would suggest that levodopa may worsen, rather than improve, fLoS in non-freezers, and this wouldn't be consistent with the previous study reporting improvement in fLoS with levodopa [2]. Therefore, future investigations should compare fLoS Off and On levodopa in a larger sample of people with PD with varied disease severity and with versus without FoG.

Interestingly, our results showed that people with PD and FoG had smaller fLoS in the forward direction and smaller total range of fLoS compared to people without FoG or healthy controls. An explanation for the smaller fLoS in PD + FoG may be their lower balance confidence. Fear of falling has been associated with fLoS in healthy older adults [25] and could reduce fLoS in people with PD who have FoG. Another explanation could be that the reduced ability to lean forward is compensatory to try to avoid falls when a rescue step may be impaired [6]. In fact, most falls in people with PD, and especially freezers, are in the forward direction [6,26].

In contrast to fLoS, people with PD with and without FoG showed similar postural sway impairments compared to healthy controls, consistent with previous studies using COP [10–12]. However, postural sway was impaired in people with PD compared to elderly controls while standing on a foam surface, but not on a firm surface. The ability to maintain a stable, upright stance depends on a complex integration of somatosensory, vestibular, and visual stimuli with the motor, premotor,

and brainstem systems. A previous study showed that people with PD show difficulties in switching from unreliable sensory information to more reliable sensory information for posture control [27]. Inability to quickly switch sensory weighting from proprioceptive information to visual and vestibular could explain why standing on foam was more difficult for people with PD [28].

Our study is consistent with a previous study showing that people with PD exhibit larger sway velocity in the ML direction compared to healthy controls while standing on a firm surface [5]. Surprisingly, we found that larger postural sway, mainly in the ML direction as measured by RMS ML, was found only in PD-FoG compared to healthy controls. Our findings also confirm that postural sway in the ML direction maybe a more sensitive measure to distinguish people with PD from healthy controls and it could be related to the risk of falls [5]. Hip abduction/adduction is used to control postural sway in the ML direction, whereas postural sway in AP direction involves an ankle strategy, that may be less affected by PD [29]. ML sway velocity when standing is controlled by spinal and hip muscles that may be stiffer, due to rigidity, in the PD + FoG group than controls [30]. Stiffer, co-contracting muscles could lead to increased sway velocity, without increased sway amplitude.

The fact, that fLoS, but not postural sway, differs between people with and without FoG may suggest that selective domains of balance are further impaired in people with FoG [9]. In addition, this could be the result of further impairments in the control of balance in a dynamic task (fLoS) versus static task (sway) in people with FoG compared to people without FoG.

There are several limitations to this study. One limitation is our PD group was relatively milder compared to previous studies (HY stage) [2, 6], which may underestimate the balance dysfunction caused by PD, especially in the fLoS of the PD-FoG group. The strength of our study is that we asked participants to lean their bodies as far as possible without flexing at their hips and without focusing on speed of movement. With this protocol, subjects were given ample time to reach their actual stability limits. However, it meant that the velocity of lean could not be included as an outcome in this study.

In conclusion, PD individuals with FoG had reduced fLoS compared to non-freezers and healthy controls, even when controlling for disease duration. On the contrary, similar postural sway impairments were found in people with PD compared to healthy controls regardless of the existence of FoG while standing on an unreliable surface. Clinicians should consider using objective measures of balance in addition to clinical assessments to detect important postural disorders not apparent from rating scales, distance reached or time maintaining a stance position. Future studies should investigate whether abnormal fLoS or lateral postural sway are related to future fall risk in people with PD.

Declaration of Competing Interest

Dr. Horak has an equity interest in APDM Wearable Technologies, an ERT company that may have a commercial interest in the results of this study. This potential conflict of interest has been reviewed and managed by the Research and Development Committee at the VA Portland Medical Health Care System and Oregon Health and Science University. They have put in place a plan to help ensure that this research study is not affected by the financial interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.gaitpost.2021.04.023>.

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