Gait and trunk kinematics during prolonged turning in Parkinson's disease with freezing of gait

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Running Head: Prolonged turning in PD with freezing of gait

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Abstract

INTRODUCTION: Although turning during walking is known to trigger freezing of gait (FOG) in Parkinson's disease (PD), little is known about kinematic strategies used by individuals with PD and FOG while performing prolonged turning.

OBJECTIVE: Our aim was to compare gait and trunk kinematics during straight walking and continuous turning over 20-minutes in PD with and without FOG.

METHODS: 18 individuals with idiopathic PD (n=9 with FOG, n=9 without FOG), performed two 20-minute walking tasks: straight ahead, and turning, in a laboratory setting in their OFF medication state. Accelerometer-based spatial and temporal gait parameters and trunk kinematics (range of motion, peak velocity, variability of range of motion and peak velocity) were analyzed.

RESULTS: During turning, PD with FOG reduced cadence more compared to PD without FOG ($P < 0.045$), despite similar decline in stride velocity (28-32%) and stride length (24-27%). Participants with FOG had decreased variability of gait speed ($P < 0.011$), stride length ($P < 0.035$), frontal trunk range of motion ($P < 0.040$) and peak trunk velocity ($P < 0.017$) compared to PD without FOG during turning, whereas there was no difference between groups during straight walking. Gait speed variability and cadence between these two tasks differentiated the PD groups (sensitivity 89% and specificity 78%).

CONCLUSIONS: We demonstrate that PD with FOG decreased cadence and reduced variability of walking speed, stride length, and lateral flexion of the trunk compared to PD without FOG during prolonged turning. These real-life gait markers are observable during lab-based gait that is similar to daily-life.

Keywords: Parkinson's disease, freezing of gait, gait variability, trunk

1. Introduction

Freezing of gait (FOG) occurs in a subset of people with Parkinson's disease (PD) and is characterized by a transient inability to produce effective steps and is significantly related to falls [1, 2]. One important trigger of FOG is walking while turning, which makes up more than 50% of our daily steps [3]. This could be in part due to the complex control required for the asymmetric nature of turning, where spatially and temporally asymmetric stepping is required for each leg to travel a different distance but maintain the same step time. Turning while walking naturally induces instability to the body as it requires center of mass to momentarily be shifted outside the lateral boundaries of the base of support [4]. These aspects of irregular gait are thought to pose a greater challenge in individuals with FOG, who have impaired executive functions and require increased voluntary control for tasks that are typically automatic such as gait [5, 6]. Thus, understanding changes to the gait pattern under these challenging and cognitively demanding conditions could provide insight to the pathophysiology underlying freezing as well as identify alternate markers of gait impairment in PD with FOG.

Spatial and temporal turning performance deficits in individuals with FOG exist for single walking turns as slight as 30 degrees and are characterized by reduced step length, increased cadence [7], and impaired inter-limb coordination [8]. These impairments are thought to contribute to an increased head-pelvis coupling and reduced trunk range of motion in PD with FOG where turns are performed "en bloc" [9, 10]. While these studies have all employed single walking turn paradigms, few studies have examined performance over several conscutive turns which more realistically resembles real-life situations [11]. It has also been proposed that assessing gait over multiple turns is more sensitive for the detection of mobility impairments compared to single turns

[12, 13]. However, it has not yet been determined how the spatial and temporal gait and trunk kinematics may be impaired during repeated walking turns as compared to steady-state walking.

The aim of this paper was therefore to compare the gait pattern and trunk kinematics during prolonged straight walking and turning in PD with and without FOG. We hypothesized that a lab-based turning paradigm that is more similar to gait in daily-life would provide more information about real-life gait markers for PD with FOG compared to the existing literature mostly assessing trunk and gait kinematics during non-ecological paradigms consisting of just one turn.

2. Methods

2.1. Subjects

Eighteen individuals with a clinical diagnosis of idiopathic PD according to the UK Brain Bank criteria, Hoehn and Yahr stage 2 or 3, and the ability to walk for 20 minutes without assistance were recruited from the Quebec Parkinson Network in Montreal, Canada. Nine participants with a score ≥ 1 on Part I of the New Freezing of Gait Questionnaire (NFOGQ) [14] were classified as experiencing FOG (FOG+) and nine participants with a score <1 were classified as not experiencing FOG (FOG-). Participants in both groups were assessed for the presence of cognitive impairment by the Montreal Cognitive Assessment (MoCA) or coexisting neurological disorders via health questionnaires [15]. Severity of motor symptoms, disease duration, medication dosage, age, gender, BMI, and cognitive functions were similar between the FOG+ and FOG- groups (see Table 1). This study was approved by the McGill Faculty of Medicine Institutional Review Board for Human Subjects and all participants provided written informed consent in accordance with the Declaration of Helsinki before entering the study.

2.2. Experimental procedure

Data collection comprised three separate visits to our laboratory. At the first visit, subjects were screened in the on medication state using clinical assessments and classified as FOG- or FOG+ using Part I of the NFOGQ (Table 1). Individuals in the FOG+ group were assessed for severity of freezing and its effect on daily life using Parts II and III of the NFOGQ which included eight additional questions (Maximum score: 29), with higher scores indicating greater severity of freezing. During this visit, all participants were given brief practice of each gait task.

On two subsequent visits to the laboratory, subjects performed two 20-minute continuous gait tasks (straight walking and turning) on separate days in randomized order. Assessment of motor symptoms and gait was performed in the OFF medication state, i.e. after overnight withdrawal of all anti-Parkinson medication (average off time = 12 hours 15 minutes). Motor severity was assessed immediately prior to the first gait task using Part III of the Movement Disorders Society Unified Parkinson's Disease Rating Scale (UPDRS-III) and Hoehn and Yahr scale [16]. The experimental paradigm included three long walking lanes (1.2 m width by 28 m length) delineated by 30 yellow and orange disc cones (height: 5 cm, diameter: 19 cm) (**Figure 1**). For the straight walking task, participants were required to walk straight at a self-selected comfortable speed in the middle of each lane. In the turning task, an identical setup was used and participants were instructed to consecutively turn around the yellow cones at their self-selected speed. The average distance between the yellow turning cones was 1.63 metres. Cones were placed in a semi-random unpredictable pattern that required participants to constantly adjust their walking trajectory and turn at varying degrees and the same setup was used across all participants.. This 20-minute turning task required continuous adjustment of the walking trajectory and ongoing motor planning for selection of relevant targets. All participants were given an additional practice

session for each task immediately prior to task performance. A safety harness with handles was worn so that a research assistant following closely behind could quickly grab the harness in case of a fall [17].

The gait pattern and trunk kinematics were measured using the APDM Mobility Lab System (Opal™, APDM Inc., Portland, OR) [18]. Participants wore six light-weight wireless inertial sensors that each contained a tri-axial accelerometer, tri-axial gyroscope, and a tri-axial magnetometer, placed on the sternum, sacrum, left and right wrist, and left and right lower shank. Data was sampled at 128 Hz throughout the entire walking trial and exported through Mobility Lab™ software for further analyses. Gait performance outcomes were variability depicted by stride velocity variability (standard deviation: SD); hereafter referred to as gait speed variability, and stride length variability (SD), spatial and temporal measures of pace (i.e., stride length normalized to leg length, stride velocity, step time variability), rhythm (i.e., step time, cadence, percentage of gait cycle spent in stance and swing), and asymmetry (i.e., step time asymmetry, stride length asymmetry) [18]. Asymmetry variables were calculated as the absolute percent difference between the right and left leg. To further assess the kinematics of straight walking and turning, average and variability (SD) of trunk range of motion and peak velocity in the horizontal and frontal plane were analyzed using the APDM system. The data were binned into epochs of 30 seconds duration and an mixed-effect ANOVA for task and time was conducted to determine if stride velocity, stride length, and step time asymmetry were constant across the trials. There were no significant differences in any gait measures between epochs ($P > 0.05$) and there was no interaction of task and time ($P > 0.05$). Thus, means were obtained over the entire 20-minutes for each gait task.

Freezing events were recorded using a stopwatch to quantify the total duration spent in FOG throughout the entire 20-minute gait task. The onset of a freezing episode was determined when there was (i) shuffling of steps with minimal forward movement, (ii) trembling of the legs with absence of forward movement, or (iii) complete motor arrest [19]. The same experienced observer measured freezing episodes across all participants. To validate these measurements, another researcher blinded to participant group independently measured the number and duration of freezing episodes via video-based analysis [19]. There was high level of agreement between raters ($r = 0.98$, $P < 0.001$).

2.3. Statistical Analysis

IBM SPSS (version 21.0, IBM, Armonk, NY, USA) was used for statistical analysis. Two-way repeated measures analyses of variance (ANOVA) were used to determine effects of group (FOG+ and FOG-) and task (straight walking and turning) on spatial and temporal gait parameters and outcomes of trunk kinematics. Because gait speed could affect biomechanical outcomes, all analyses were adjusted for difference in gait speed. Bonferroni post-hoc tests were performed whenever a significant interaction effect (i.e. group x task) occurred with the significance level set at $P < 0.05$. To determine if any of our outcomes could successfully differentiate between the PD groups, significant between-group gait outcomes were used as independent variables in a binary logistic regression using forward selection method. Receiver operating characteristic (ROC) analyses were conducted on the selected variables to determine the accuracy in classifying the two groups.

3. Results

3.1. Freezing during straight walking and turning

Eight of nine of the participants in the FOG+ group presented at least one freezing event during the turning task, whereas only two experienced a freezing event during the straight walking task. The mean ± SD number of freezing episodes during the 20-minute steering task was 11 ± 16 and the percentage of time spent freezing during the turning task ranged from 0 to 2.6% of the total trial. No subjects in the FOG- group exhibited freezing during either task.

3.2. Differences in gait pattern between turning and straight walking

For both PD groups, gait speed during turning was slower compared to straight walking (FOG+: -32 %, FOG-: -28 %, Task: $P < 0.001$) and FOG+ walked slower than FOG- across tasks, Group: $P < 0.009$ (see **Table 2**). FOG+ walked with shorter stride length during straight walking ($P < 0.009$), whereas there was no difference between groups during turning ($P = 0.112$) (Group x Task: $P < 0.004$). The FOG+ group showed different changes in cadence between straight walking and turning compared to FOG- (Group x Task: $P < 0.045$). FOG+ had a greater decrease in cadence for turning relative to straight walking ($P < 0.001$) compared to FOG- ($P < 0.005$). FOG+ adjusted both gait speed variability and stride length variability differently during turning compared to FOG- (Group x Task: $P \leq 0.035$). That is, FOG+ had reduced gait speed and stride length variability compared to FOG- during turning ($P \leq 0.028$), whereas there was no difference between groups during straight walking ($P \geq 0.476$).

3.3. Differences in trunk kinematics between straight walking and turning

Both groups demonstrated increased trunk range of motion (Frontal: FOG+: 37 %, FOG-: 41 %; Horizontal: FOG+: 22 %, FOG-: 33 %) and peak velocity in the frontal plane (FOG+: 18

%, FOG-: 31 %) during turning compared to straight walking (See **Table 2**, Task: $P \leq 0.043$). FOG+ showed different changes in trunk variability between turning and straight walking compared to FOG- in the frontal plane (Group x Task: $P \leq 0.040$). While FOG+ had reduced variability of frontal trunk range of motion ($P = 0.028$) and frontal peak velocity variability ($P = 0.013$) compared to FOG- during turning, no group differences were found for these outcomes during straight walking ($P \geq 0.365$).

3.4. Differentiating FOG+ and FOG-

Difference in stride velocity variability and cadence were selected in the logistic regression as significant predictors of PD group (FOG+ or FOG-). ROC represented good accuracy (area under the curve: .89) with 89% sensitivity and 78% specificity.

4. Discussion

This study was the first to explore changes to gait and trunk control during prolonged straight walking and turning in individuals with PD with and without FOG. We observed that PD with FOG have reduced cadence during prolonged turning compared to PD without FOG, despite a similar reduction in speed across groups. We also found that PD with FOG had decreased variability of gait speed and lateral flexion of the trunk during turning. Our results support the assertion that FOG is related to an overall task-specific performance deficit involving lower-limb and trunk control in PD with FOG and provide unique information about the performance of continuous turns. Gait speed variability and cadence between these two tasks were able to differentiate the two PD groups with relatively high specificity and sensitivity. Moreover, we

provide evidence for useful gait biomarkers to identify PD with FOG during lab-based gait that is similar to behavior in daily life.

Few studies have included continuous turning paradigms in the study of gait impairment in Parkinson's disease that is more similar to gait in daily-life [13, 20-22], as opposed to non-ecological single turn paradigms [7-9, 23-25]. Importantly, continuous turning paradigms such as the one used in the present study are more likely to induce freezing epsiodes due to increased number of repetitive turns. These paradigms have previously shown to differ from gait outcomes of single turn paradigms [20] and seem to be a more sensitive approach for the detection of mobility impairments [12, 13]. This could be because, variable turn angles [26] and unpredictability of turns [27] are associated with poorer turn performance in PD. Group differences in cadence and speed variability among the FOG+ group were evident during turning only, highlighting task-specific deficits in this sub-group of PD. Our findings are similar to previous research that examined turning in daily life using an inertial sensor over 72 hours, demonstrating that PD with FOG have reduced variability of medio-lateral jerkiness during moderate to large turn angles ($<120^{o}$ and $>260^{o}$) compared to PD without FOG [20]. In addition, this study also showed that disease progression was associated with reduced variability during turning in PD [20], a finding that was attributed to impaired postural adjustments for a variety of turning angles and a more "en-bloc" turning strategy. Importantly, our findings and previous findings differ from research on single 180^{o} turns that show increased stride length variability in freezers [28]. Indeed, impaired motor adaptation of stride variability between straight walking and turning could be related to freezing episodes, since too little or too much stride variability is associated with falls among elderly persons [29]. In addition, in contrast to previous findings of increased cadence during single walking turns (180^{o} and 360^{o}) in PD with FOG compared to PD without FOG [7],

we observed decreased cadence during continuous turning in the group with FOG. This finding could indicate that freezers may adopt a strategy for reduced cadence in order to compensate for other motor planning deficits involved in the execution of varying turn angles. Therefore, our prolonged turning tasks reflects general locomotor changes associated with PD with FOG behavior rather than changes specific to a freezing episode.

Both PD with and without FOG increased trunk range of motion and peak velocity between straight walking and steering. However, PD with FOG demonstrated reduced variability of trunk frontal movements (i.e. lateral flexion) compared to PD without FOG during turning. We also observe reduced peak velocity variability in the horizontal plane (i.e., axial rotation) for PD with FOG, with range of motion showing a similar trend. This finding in combination with our observations of impaired walking imply an overall or whole-body coordination deficit among individuals experiencing FOG. Our results are in line with research revealing reduced movement in the horizontal plane in PD with FOG, characterized by increased head-pelvis coupling during turning ("en bloc") compared to a top-down sequential rotation of the head, thorax, and pelvis for turning used by PD without FOG and healthy controls [9]. Previous research has similarly found reduced frontal and horizontal trunk rotation in PD compared to healthy controls during turning [30]. Moreover, our results may indicate that PD with FOG inadequately adjust trunk and stride measures for variable and potentially larger turn angles, similar to those used in daily life.

To the best of our knowledge, this is the first study of prolonged turning in individuals with PD in the OFF medication state. We assessed walking and turning in the OFF medication state since dopaminergic medication has variable effects on gait characteristics in PD [31] and its role in mediating freezing behaviour is unclear [19]. The current findings should be replicated in the ON medication state in order to determine medication effects on continuous gait under conditions

of daily life. Although we include a carefully selected sample of patients with FOG, one limitation of this study is the moderate sample size, and thus results should be validated in a larger cohort.

We found that freezers adopted a reserved strategy characterized by reduced variability during continuous turning that could be related to reduced movement amplitude or a fear of falling. Furthermore, the UPDRS-III sub-score for postural instability and gait disturbance demonstrated greater impairment in these domains for freezers (mean ± SD: 7.0 ± 1.7) compared to non-freezers (5.8 ± 3.6) (*P = 0.050*). We lack information about fear of falling in this study sample. Moreover, poor postural stability and possibly a fear of falling could be related to the reserved gait strategy and further investigations regarding the influence of these factors are warranted. Finally, since freezing episodes made up a very low percentage of the total gait task (0-2.3%), our results represent typical gait patterns during non-steady state gait. Indeed, investigations of non-steady state walking in FOG represents an important gap in the literature due to the well-known role of irregular gait in triggering freezing episodes.

4.1. Conclusion

This is the first study to show that PD with FOG demonstrates an impaired ability to adjust cadence, as well as variability of stride length, gait speed, and frontal trunk motion during prolonged turning compared to straight walking. These deficits in temporal and spatial gait characteristics and trunk kinematics are able to differentiate PD with FOG compared to PD without FOG. We encourage future research to investigate continuous turning paradigms that are more similar to daily-life to better understand mechanisms of gait impairment and vailidate these useful gait biomarkers in PD with FOG.

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Conflict of Interest declaration

The authors report no competing interests.

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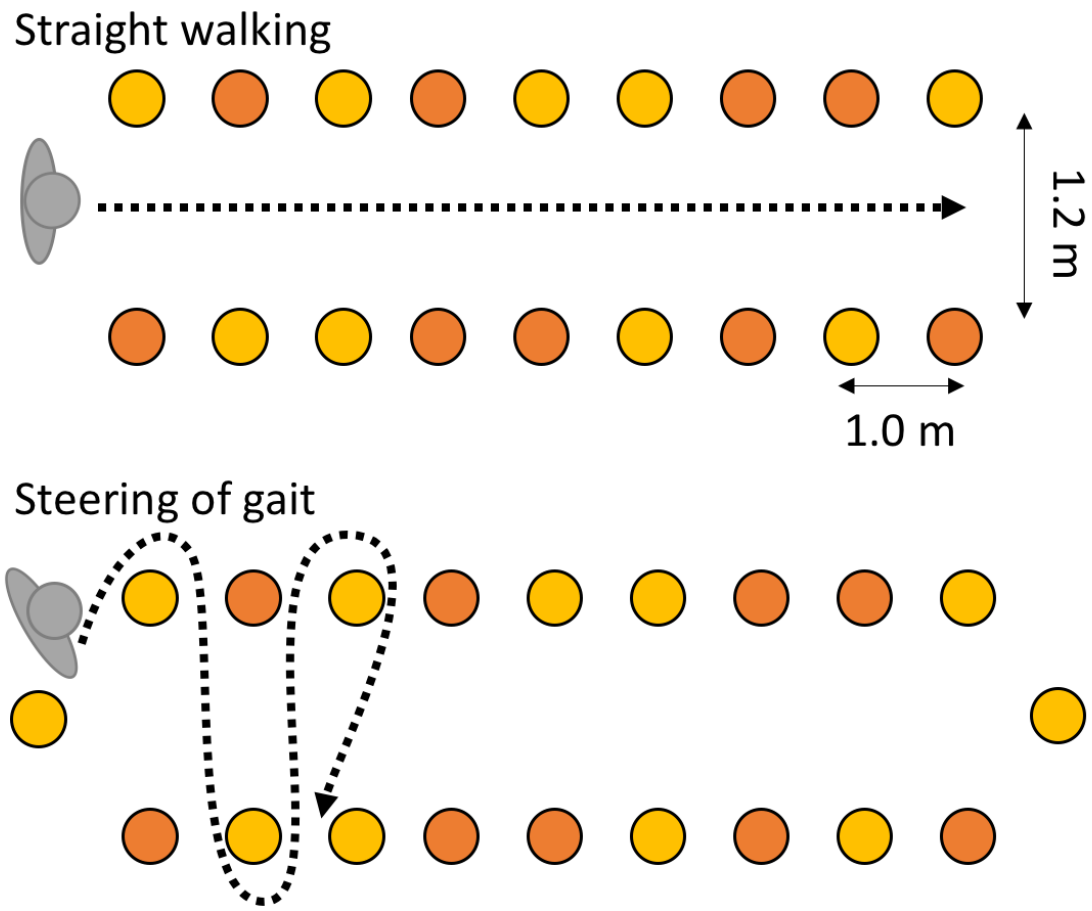
Figure legends

Figure 1. Top-view of the walkway. In the straight walking task, participants were instructed to walk straight in the middle of the markers, making 180 degree turns in the adjacent walking lane. In the turning task, participants were instructed to continuously turn around the yellow coloured markers.

Figure 2. Gait outcomes for pace, rhythm, and variability

(A) Pace (stride length and stride velocity), (B) Rhythm (cadence and step time), (C) Variability (variability of stride length and stride velocity), and (D) Trunk Variability (variability of frontal trunk range of motion and peak velocity). Bars represent means and error bars are SD. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.


Straight walking
1.2 m
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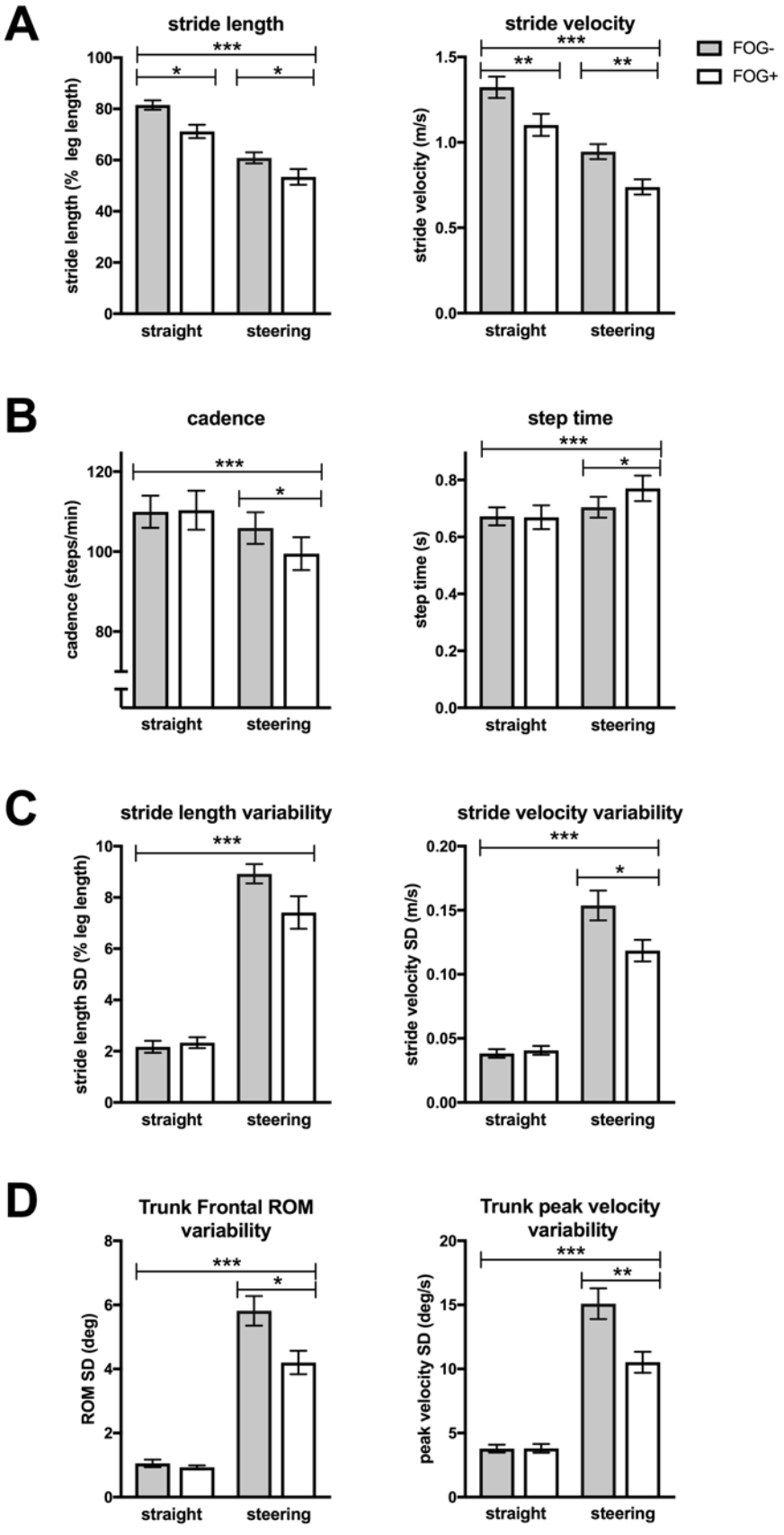
Steering of gait


A
stride length
stride length (% leg length)
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80
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straight
steering
stride velocity
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1.5
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stride length SD (% leg length)
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Trunk peak velocity variability
peak velocity SD (deg/s)
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15
10
5
0
***
**
straight
steering

Table 1. Participant characteristics

Variables	**FOG+ (n=9)**	**FOG- (n=9)**	**p-value**
Gender, male/female	5/4	7/2	0.310
Age (years)	69 (6)	65 (4)	0.190
BMI	23.7 (2.3)	24.0 (4.8)	0.775
Montreal Cognitive Assessment	28 (2)	29 (2)	0.546
Hoehn & Yahr Scale (II/III)	4/5	7/2	0.113
MDS-UPDRS-III score (off-state)	51 (11)	42 (3)	0.050
MDS-UPDRS-III PIGD sub-score (off-state)	7 (1)	5 (0)	0.050
Disease duration (years)	6 (4)	9 (4)	0.258
Dopa equivalent dose (mg)	950 (890)	786 (151)	0.606
Most affected side (right/left)	3/6	2/7	0.500
NFOG – Questionnaire score	10 (14)	0 (0)	0.000

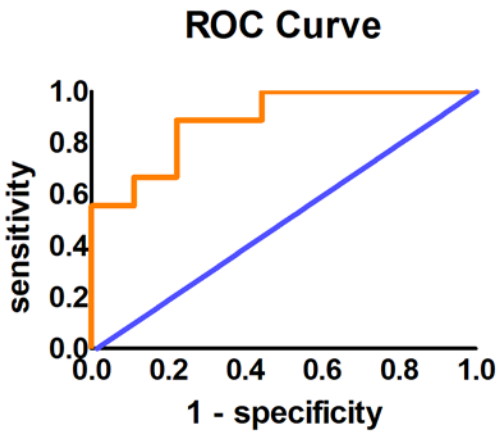
Values are median (interquartile range) for all variables except gender, Hoehn & Yahr, and most affected side, that were presented as proportions. Mann-Whitney U tests were used to compare subject characteristics between groups. Abbreviations: MDS-UPDRS-III; Movement Disorder Society Unified Parkinson's disease rating scale Part III, PIGD; postural instability and gait disorder subscore, NFOG - Questionnaire; New freezing of gait Questionnaire

1 Table 2. Summary of gait measures during straight walking and turning

	FOG+				**FOG-**				**Group**	**Task**	**Group x task**
Gait Outcomes	*Straight*		*Turning*		*Straight*		*Turning*		*p-value*	*p-value*	*p-value*
Pace											
Stride velocity (m/s)	1.10	(.06)	0.74	(.04)	1.32	(.06)	0.95	(.04)	**.009**	**.000**	.818
Stride length (% leg length)	71.33	(2.25)	54.47	(2.28)	81.40	(2.35)	59.82	(2.28)	**.031**	.097	**.004**
Step time variability (m/s)	.030	(.003)	.077	(.007)	.019	(.003)	.064	(.007)	.089	.806	.805
Rhythm											
Cadence (steps/min)	108.8	(4.1)	98.8	(4.1)	111.5	(4.1)	106.4	(4.1)	.391	.084	**.045**
Step time (s)	.68	(.03)	.77	(.04)	.66	(.03)	.70	(.04)	.386	.137	.063
Swing (% gait cycle)	39.49	(.87)	36.89	(.91)	39.36	(.87)	37.88	(.91)	.714	.088	.312
Stance (% gait cycle)	60.56	(.87)	63.22	(.93)	60.65	(.87)	62.23	(.93)	.707	.108	.330
Variability (SD)											
Stride velocity variability (m/s)	.041	(.004)	.116	(.010)	.038	(.004)	.156	(.010)	**.023**	.076	**.011**
Stride length variability (% leg length)	2.38	(.23)	7.28	(.51)	2.13	(.23)	9.06	(.51)	.052	.066	**.035**
Asymmetry											
Step time asymmetry	.037	(.004)	.092	(.008)	.023	(.004)	.085	(.008)	.166	.703	.566
Stride length asymmetry	.003	(.001)	.008	(.001)	.004	(.001)	.010	(.001)	.440	.359	.695
Trunk Kinematics											
Trunk Horizontal ROM (°)	4.28	(.50)	5.48	(.69)	4.46	(.50)	6.64	(.69)	.405	**.043**	.197
Trunk Horizontal ROM variability	.63	(.05)	1.47	(.23)	.64	(.05)	1.92	(.23)	.247	**.004**	.142
Trunk Horizontal peak velocity (°/s)	18.67	(1.37)	21.48	(2.38)	21.28	(1.37)	27.19	(2.38)	.092	.081	.336
Trunk Horizontal peak velocity variability	2.22	(.14)	4.73	(.59)	2.50	(.14)	6.35	(5.9)	**.036**	**.011**	.158
Trunk Frontal ROM (°)	6.21	(.80)	9.87	(.86)	7.45	(.80)	12.65	(.86)	**.029**	**.006**	.379
Trunk Frontal ROM variability	.93	(.10)	4.27	(.43)	1.06	(.10)	5.75	(.43)	**.025**	**.000**	**.040**

Trunk Frontal peak velocity (°/s)	29.10	(2.45)	35.28	(3.21)	33.02	(2.45)	47.42	(3.21)	**.023**	**.002**	.134
Trunk Frontal peak velocity variability	3.73	(.32)	10.76	(1.01)	3.86	(.32)	14.85	(1.01)	**.017**	**.000**	**.017**

Values are mean (standard deviation) for all variables, adjusted for the gait speed difference between tasks. Significance P < 0.05 (two-tailed) indicated in bold type.



ROC curve for classification of FOG+ and FOG- based on gait and trunk and kinematics