BMC Geriatrics

RESEARCH

Open Access

Do the gait domains change in PD patients with freezing of gait during their 'interictal' period?

Jiahao Zhao[1], Chen Liu[1], Ying Wan[1], Xiaobo Zhu[1], Lu Song[1], Zhenguo Liu[1*] and Jing Gan[1*]

Abstract

Objectives Freezing of Gait (FOG) is one of the disabling symptoms in patients with Parkinson's Disease (PD). While it is difficult to early detect because of the sporadic occurrence of initial freezing events. Whether the characteristic of gait impairments in PD patients with FOG during the 'interictal' period is different from that in non-FOG patients is still unclear.

Methods The gait parameters were measured by wearable inertial sensors. Exploratory factor analysis was used to investigate the inherent structure of diverse univariate gait parameters, with the aim of identifying shared characteristics among the gait variables.

Results This cross-sectional study involved 68 controls and 245 PD patients (167 without FOG and 78 with FOG). The analysis yielded six distinct gait domains which were utilized to describe the impaired gait observed during the "interictal" period of FOG. Both PD-nFOG and PD-FOG groups exhibited significant impairments in the pace domain, kinematic domain, gait phase domain, and turning process domain compared to the healthy control. The gait phase domain was different in the PD-FOG group compared to the PD-nFOG group (p corrected = 0.004, Cohen's d = -0.46). And it was identified as independent risk factor for FOG (OR = 1.64, 95% CI = 1.05–2.55, $p = 0.030$), as well as other risk factors: gender (OR = 2.67, 95% CI = 1.19–5.99, $p = 0.017$), MDS-UPDRS IV score (OR = 1.23, 95% CI = 1.10–1.37, $p < 0.001$), and PIGD subscore (OR = 1.50, 95% CI = 1.30–1.73, $p < 0.001$). The model demonstrated a correct discrimination rate of 0.78 between PD-FOG and PD-nFOG, with an area under the receiver operating characteristic curve (AUC) of 0.87.

Conclusions FOG was found to be associated with abnormal alterations in the gait phase domain during the interictal period. Models constructed using gait phase domain, PIGD subscore, gender, and severity of motor complications can better differentiate freezers from no-freezers during 'interictal' period.

Keywords Parkinson's disease, Freezing of gait, Wearable inertial sensor, Exploratory factor analysis, Gait domain

Introduction

Walking safely and comfortably is critical to patients with Parkinson's disease (PD). As we know, freezing of gait (FOG) is one of the main risk factors for falls in PD [1]. The tendency of the trunk to move forward while the feet are relatively "frozen" in place during walking can easily lead to balance dysfunction and falls, which reduce the ability to move independently and impair the quality of life of PD patients. PD-FOG patients present a brief,

*Correspondence:
Zhenguo Liu
liuzhenguo@xinhuamed.com.cn
Jing Gan
ganjing@xinhuamed.com.cn
[1] Department of Neurology, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China

involuntary, and unexpected disruption of gait that persists for several seconds or longer. It is not evident to observe the onset of FOG in outpatient visits due to its "episodic" nature [2]. During the outpatient visit, the gait performance of Parkinsonians with FOG may be improved by increased attention and alertness, especially in patients with mild or less frequent FOG episodes, which are difficult to elicit in the clinic [2–4]. Consequently, it is crucial to detect even subtle changes in gait characteristics in PD patients who experience FOG, even when an episode is not directly observed by clinicians.

With the development of technology-based gait analysis in PD, subtle changes in gait characteristics can be captured using wearable sensors [5–7], and these quantified gait parameters can provide more information on how PD gait converts to FOG gait. Several studies showed the gait characteristics during FOG episodes. There is a decrease in gait frequency, variability of gait speed, stride length, and mean lateral displacement amplitude during FOG [8]. A typical FOG event occurs with a progressive decrease in step length and eventually a freeze, also known as the sequence effect [9]. The sequence effect prior to a FOG episode is a direct description of how gait impairment develops prior to a FOG episode [10, 11].

Our hypothesis is that gait impairments in PD-FOG patients may be preserved in some form and to some extent during the "interictal" period. The term "interictal" period in the context of FOG refers to the intervals between episodic FOG events, during which patients do not experience an acute FOG event but may still exhibit gait impairments that contribute to the susceptibility to FOG. These "interictal" gait changes in gait characteristics may predict that these patients are prone to develop FOG events and even further exacerbation of these gait impairments may lead to the onset of FOG events. One study has shown that some gait abnormalities, including reduced gait rhythmicity, decreased asymmetry and bilateral dyscoordination were found during the "interictal" period in PD [12]. We propose that these hidden gait abnormalities during the "interictal" period may serve as risk factors for developing FOG. This view is supported by a review, which underscores the idea of gait abnormalities occurring between freezing episodes, potentially signifying early signs of freezing [12].

To test our hypothesis, we analyzed the gait parameters of PD patients with FOG during their "interictal" period using wearable inertial measurement sensors. We extracted several gait domains to better describe gait impairment by grouping numerous univariate gait parameters with the exploratory factor analysis (EFA). Our objective is: (1) to find the distinct abnormal gait domains in FOG patients from non-FOG patients during interictal period; (2) to analyze the relevant influencing factors of FOG by integrating clinical information and abnormal gait domain characteristics.

Material and methods

Participants

Two hundred forty-five patients with idiopathic PD who visited the Department of Neurology, Xinhua Hospital Affiliated to Shanghai Jiao Tong University, School of Medicine were enrolled in this study from November 2019 to December 2021. The inclusion criteria for the PD group were: (1) the diagnosis of PD was based on International Movement Disorders Society (MDS) PD diagnostic criteria 2015 [13]; (2) Hoehn and Yahr (H-Y) stages ≤ 3; (3) walking independently for at least 10 m without any assistive device; (4) Mini-Mental State Examination (MMSE) > 24 points. The exclusion criteria were: (1) were diagnosed with parkinsonism-plus syndromes or other diseases that may affect gait performance (e.g., stroke, trauma, orthopedic disease, abnormal vision and serious cardio-pulmonary diseases); (2) Severe psychiatric symptoms, dementia, and inability to cooperate with the completion of the examination.

The age-matched healthy controls (HC group) were partners of patients with PD or volunteers of the nearby community during the same period. They were excluded if they reported previous neurological, orthopedic, abnormal vision or musculoskeletal disorders that could impact gait.

Clinical assessments

A detailed medical history (including age, sex, height, weight, education, time of disease onset, first symptoms, antiparkinsonian drugs, etc.) was collected. The time of disease onset was defined as the onset of subjective perceived motor symptoms of PD. The motor assessment scales included the MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and the H-Y stage. The motor subscores were calculated as the bradykinesia subscore (sum of items 3.4–3.8 and 3.14), rigidity subscore (sum of item 3.3), tremor subscore (sum of items 3.15–3.18), and postural instability and gait difficulty (PIGD) subscore (sum of items 3.9–3.13) based on the MDS-UPDRS part III. Information on pharmacological treatment was collected and calculated in total daily levodopa equivalent dose (LED) [14]. The New Freezing of Gait Questionnaire (NFOG-Q) was used to determine the presence and severity of the freezing of gait. The Mini Balance Evaluation Systems Test (mini-BESTest) was used to evaluate the balance function. The cognitive and emotional assessment scales included the MMSE, the Montreal Cognitive Assessment (MoCA), the Hamilton Anxiety Scale (HAMA), the Hamilton Depression Scale (HAMD), and the Frontal Assessment Battery (FAB). The

8-item Parkinson's Disease Questionnaire (PDQ-8) was used to assess the quality of life. According to the scores from the Part I of the NFOG-Q, PD patients were divided into two groups: a PD-FOG group with a score = 1, and a PD-nFOG group with a score = 0. All assessments were performed during the "ON" period.

The study was a cross-sectional study, approved by the Research Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (XHEC-C-2015–019-2), and all subjects were fully informed of the purpose and content of the study and provided written informed consent.

Kinematic analysis of gait

Gait testing was performed by the MATRIX (a Wearable Movement and Gait Quantitative Assessment System). The MATRIX (GYENNO Science, Shenzhen, China) were applied to collect kinematic parameters [7, 15]. The sampling frequency of the MATRIX is set at 100 Hz, and the accelerometer has a range of ± 8 g with a resolution of 0.00024 g, while the gyroscope has a range of ± 2000°/s and a resolution of 0.0305°/s. Participants wore ten inertial sensors fixed to the lower back (L5), anterior chest (sternum), bilateral thighs, ankles, feet, and wrists by elastic bands (Supplementary Fig. 1). After the sensors were placed correctly, the participants were asked to perform the Timed Up and Go Test (TUG): (1) stand up from the chair; (2) walk straight for a 5-m distance at their regular pace; (3) turn and walk back to the starting point; and (4) sit down. Prior to commencing the test, the subjects were initially instructed on the process by the researcher and subsequently allowed to practice it once. Subjects in the PD group completed the test during their "ON" period.

Wearable sensor signals are transmitted via Bluetooth to the computer for 3D motion posture reconstruction to assess gait, arm swing, whole-body coordination, and other indicators. If the investigator observed or the device automatically identified a FOG episode during walking, the patient was excluded from the final analysis. All parameters which we can obtain were calculated automatically during the motor test using built-in algorithms (Appendix 1).

Statistical analysis

The Shapiro–Wilk test combined with Q-Q plots was used to determine the distribution of continuous variables. Normally distributed measures were expressed using the mean ± standard deviation (SD), and non-normally distributed measures were expressed using the median (quartiles). The independent t-test/Mann–Whitney U test was used for comparison of measures between independent groups, and X^2 test/Fisher exact probability method was used for comparison of numerical data. Differences in baseline clinical characteristics and gait parameters among controls, PD-nFOG patients, and PD-FOG patients were assessed using analysis of covariance (ANCOVA) and Bonferroni post hoc tests, and homogeneity of variance was determined by plotting scatter plots and performing Levene's tests. Forward stepwise binomial logistic regression was used to analyze factors associated with FOG, and the degree of influence was evaluated using the odds ratio (OR) and 95% confidence interval (CI). The Box-Tidwell method is used to test whether there is a linear relationship between the logit transformed values of the continuous independent and dependent variables. Tolerance and variance inflation factor (VIF) was calculated to diagnose the presence of multicollinearity between the independent variables.

Exploratory factor analysis (EFA) was used to explore the intrinsic structure of the 22 gait variables and to identify the common features behind the gait variables to categorize and extract several major gait domains that represent different gait characteristics [16, 17]. Each gait variable was first transformed separately by normalization. Each value was subtracted from the mean value of the parameter in the whole sample (including the PD and HC groups), respectively, and the difference was divided by the standard deviation of the whole sample. The Kaiser–Meyer–Olkin (KMO) sampling fitness test and Bartlett's sphericity test were used to clarify whether the 22 variables were suitable for factor analysis among themselves. Horn's parallel analysis [18] was then used to determine the appropriate number of factors, namely, the number of gait domains. The maximum likelihood method was used for factor extraction. Further, the oblimin oblique rotation method was used to improve the interpretability of their loadings to avoid possible correlations between potential factors. Variables with loadings up to 0.5 were considered significant. After EFA analysis, the Thurstone method [19] was used to summarize each parameter's standard score coefficients based on EFA's results and calculate the factor scores for each gait domain separately. The obtained factor scores were converted to a Z-score with HC as the reference value [e.g., factor 1 Z-score = (factor 1—mean of factor 1 in HC group)/standard deviation of factor 1 in HC group] to draw radar plots for comparing the different levels of impairment in the gait domain between the PD-nFOG group and PD-FOG group relative to the subjects in the HC group.

Statistical analyses were performed with R (version number: 4.1.2) (R Foundation for Statistical Computing, Vienna, Austria). The threshold for statistically significant differences was set at a two-tailed $p < 0.05$.

Results

The differences in clinical characteristics among the HC group, PD-nFOG group and PD-FOG group

A total of 245 patients with PD were enrolled (124 males and 121 females) in our study. The mean age was 67.07 ± 7.80 years, height was 164.92 ± 7.80 cm, the mean disease duration was 5.45 ± 4.52 years, the H-Y stage was 2.13 ± 0.75, and the MDS-UPDRS III score was 25.55 ± 14.26. Sixty-eight healthy controls (27 males and 41 females) were enrolled in the HC group with a mean age of 66.44 ± 8.76 years and a mean height of 163.22 ± 8.19 cm.

According to the scale of the NFOG, the patients with PD were classified into the PD-FOG group and PD-nFOG group (Table 1). Seventy-eight (31.84%) of the 245 PD patients had FOG, of which 55 were levodopa responsive, and 19 were levodopa unresponsive. No difference in gender, age, height, and education was found among the HC group, PD-nFOG group, and PD-FOG group ($p > 0.05$). Compared with PD-nFOG patients, PD-FOG patients had a longer disease duration (7.65 ± 4.95 vs. 4.43 ± 3.91, t = −5.07, $p < 0.001$), a higher H-Y stage (2.51 ± 0.64 vs. 1.95 ± 0.73, t = −5.84, $p < 0.001$), and higher doses of LED (632.29 ± 352.10 vs. 398.82 ± 333.90,

Table 1 Clinical characteristics of control, PD-nFOG group and PD-FOG group

	HC	PD-nFOG	PD-FOG	t/U/χ^2/F	p-value
No	68	167	78		
Gender (male/female)	27/41	78/89	46/32	5.74	0.057
Age (years)	66.44 ± 8.76	66.90 ± 8.27	67.42 ± 6.72	0.30	0.738
Height (cm)	163.22 ± 8.19	165.70 ± 7.84	163.15 ± 7.54	1.39	0.240
Education					
Illiteracy or primary school graduates	11	32	6	7.60	0.668
Middle school graduates	46	110	55		
High school graduates or above	11	23	14		
Disease duration (years)	/	4.43 ± 3.91	7.65 ± 4.95	−5.07	**< 0.001**
H-Y stage	/	1.95 ± 0.73	2.51 ± 0.64	−5.84	**< 0.001**
LED (mg/d)	/	398.82 ± 333.90	632.29 ± 352.10	−4.96	**< 0.001**
MDS-UPDRS I	/	9.13 ± 5.23	10.97 ± 5.55	−2.30	**0.022**
MDS-UPDRS II	/	9.98 ± 6.23	16.89 ± 7.75	−6.87	**< 0.001**
MDS-UPDRS III	/	22.86 ± 13.43	31.31 ± 29.50	−4.48	**< 0.001**
MDS-UPDRS IV	/	0 (0, 2)	4 (0, 7.5)	2838.50	**< 0.001**
Moto symptom	/				
Bradykinesia subscore	/	11.42 ± 7.02	16.17 ± 7.37	−4.83	**< 0.001**
Rigidity subscore	/	2.64 ± 3.10	3.52 ± 3.91	−1.73	0.087
Tremor subscore	/	3.77 ± 3.85	3.34 ± 4.08	0.79	0.430
PIGD subscore	/	3.41 ± 2.42	6.23 ± 3.25	−6.79	**< 0.001**
NFOG-Q	/	/	18.31 ± 6.81		
Mini-BESTest	/	22.95 ± 4.88	17.96 ± 5.10	4.39	**< 0.001**
Levodopa response of FOG	/				
Levodopa responsive	/	/	55		
Levodopa unresponsive	/	/	19		
Other	/	/	4		
Non-motor symptom					
MMSE	/	28 (27, 30)	28 (26, 29)	5209.50	0.097
MoCA	/	25 (21, 27)	24 (19, 26)	4218.50	0.193
HAMA	/	7.62 ± 5.43	9.18 ± 6.17	−1.97	0.050
HAMD	/	8.10 ± 6.85	10.45 ± 6.88	−2.30	**0.023**
FAB	/	16 (15, 18)	15 (13, 17)	1383.50	**< 0.001**
PDQ-8	/	0.56 ± 0.91	1.70 ± 1.45	−5.11	**< 0.001**

MDS-UPDRS MDS-Unified Parkinson's Disease Rating Scale, *H-Y stage* Hoehn & Yahr stage, *LED* levodopa equivalent dose, *PIGD* postural instability and gait difficulty, *NFOG-Q* New Freezing of Gait Questionnaire, *mini-BESTest* Mini Balance Evaluation Systems Test, *MMSE* Mini-Mental State Examination, *MoCA* Montreal Cognitive Assessment, *HAMA* Hamilton Anxiety Scale, *HAMD* Hamilton Depression Scale, *FAB* Frontal Assessment Battery, *PDQ-8* 8-item Parkinson's Disease Questionnaire

t = −4.96, $p < 0.001$). The scores of MDS-UPDRS were significantly higher in the PD-FOG group than those in the PD-nFOG group with part I (10.97 ± 5.55 vs. 9.13 ± 5.23, t = −2.30, $p = 0.022$), part II (16.89 ± 7.75 vs. 9.98 ± 6.23, t = −6.87, $p < 0.001$), part III (31.31 ± 29.50 vs. 22.86 ± 13.43, t = −4.48, $p < 0.001$) and part IV (Mann–Whitney U = 2838.50, $p < 0.001$). Moreover, compared to the PD-nFOG group, the PD-FOG group obtained higher bradykinesia subscore (16.17 ± 7.37 vs. 11.42 ± 7.02, t = −4.83, $p < 0.001$) and PIGD subscore (6.23 ± 3.25 vs. 3.41 ± 2.42, t = −6.79, $p < 0.001$). At the same time, there was no difference in rigidity subscore and tremor subscore between these two groups ($p > 0.05$). The PD-FOG group performed worse balance based on the mini-BESTest (t = 4.39, $p < 0.001$), and in terms of non-motor symptoms of PD, the PD-FOG group presented a more elevated HAMD score (10.45 ± 6.88 vs. 8.10 ± 6.85, t = −2.30, $p = 0.023$) and lower FAB score (Mann–Whitney U = 1383.50, $p < 0.001$) than those in PD-nFOG group. No difference in MMSE and HAMA scores was found between the two groups ($p > 0.05$). PD patients with FOG had significantly lower quality of life (1.70 ± 1.45 vs. 0.56 ± 0.91, t = −5.11, $p < 0.001$).

Differences in gait parameters among the HC group, PD-nFOG group and PD-FOG group

Table 2 showed the gait parameters during walking, turning, and sit-stand shift tasks among the HC group, PD-nFOG group, and PD-FOG group.

During the sit-to-stand task, there were statistical differences in mean duration, trunk sagittal peak velocity, and trunk sagittal ROM among these three groups ($F = 8.15$, $p < 0.001$; $F = 26.49$, $p < 0.001$; $F = 7.73$, $p < 0.001$, respectively), after adjusting for age, gender, and height. The HC group had a shorter mean duration, faster trunk sagittal peak velocity, and larger trunk sagittal RoM than PD-FOG or PD-nFOG patients. At the same time, there was no difference between PD-FOG and PD-nFOG group after post hoc tests with Bonferroni correction. There were similar differences in these three parameters above during the stand-to-sit task among the three groups.

During the walking process, there were significant differences in step length ($F = 17.42$, $p < 0.001$), stride velocity ($F = 10.38$, $p < 0.001$), and stride length ($F = 17.41$, $p < 0.001$) among these three groups. However, no difference was found in step frequency ($F = 1.42$, $p = 0.243$) and gait cycle ($F = 1.20$, $p = 0.302$).

The differences between the PD-FOG and PD-nFOG groups were mainly reflected in the decrease in the proportion of the double support phase (p corrected = 0.007, Cohen's d = 0.43) and the increase in the proportion of the swing phase (p corrected = 0.010, Cohen's d = −0.42) during walking. Regarding gait variability parameters: step length CV was significantly greater in the PD-FOG group compared to the HC group (p corrected = 0.005, Cohen's d = −0.53), and there were no statistical differences in swing phase CV, double support phase CV, cadence CV, and stride velocity CV among the three groups ($p > 0.05$). Regarding kinematic gait parameters: shank RoM ($F = 23.97$, $p < 0.001$) and peak shank angular velocity ($F = 14.21$, $p < 0.001$) were significantly reduced in both PD-nFOG and PD-FOG groups compared to the HC group. Trunk coronal peak velocity ($F = 5.36$, $p = 0.005$), trunk coronal RoM ($F = 23.08$, $p < 0.001$), trunk sagittal peak velocity ($F = 4.76$, $p = 0.009$), trunk sagittal RoM ($F = 6.79$, $p = 0.001$), trunk transverse peak velocity ($F = 9.25$, $p < 0.001$), trunk transverse RoM ($F = 8.84$, $p < 0.001$) and arm RoM ($F = 14.93$, $p < 0.001$) were reduced both in the PD-nFOG and PD-FOG groups when compared to the HC group. The arm peak velocity ($F = 5.31$, $p = 0.005$) was decreased in the PD-nFOG group compared to the HC group, while there was no difference between the PD-FOG group and the HC group. Regarding the parameters of gait asymmetry: the swing asymmetry ($F = 5.08$, $p = 0.007$) and shank RoM asymmetry ($F = 4.37$, $p = 0.013$) increased in the PD-nFOG group compared to the HC group, while the PD-FOG group did not differ from the HC group. The arm symmetry index increased both in the PD-nFOG and PD-FOG groups compared to the HC group ($F = 5.73$, $p = 0.004$). There were no statistical differences in the stride length asymmetry ($F = 2.98$, $p = 0.052$), shank symmetry index ($F = 0.84$, $p = 0.433$), and phase coordination index ($F = 1.52$, $p = 0.220$) among the three groups.

During turning, the mean duration of turning was longer both in the PD-FOG and PD-nFOG groups compared to the HC group ($F = 7.85$, $p < 0.001$). The mean number of steps in the turning process increased in the PD-FOG group compared to the PD-nFOG and HC groups ($F = 8.79$, $p < 0.001$). The peak angular velocity of the turning process decreased both in the PD-FOG and PD-nFOG groups compared to the HC group ($F = 41.93$, $p < 0.001$).

Obtain the gait domains and factor scores

The EFA approach was used to extract the gait domains and to reduce the dimensionality of gait parameters. We first performed KMO sampling fitness tests on 22 representative gait variables, and the results are shown in Appendix 2. The total KMO was 0.78, and each variable individually had KMO > 0.5. Bartlett's test of sphericity $X_2 = 8552.20$, $p < 0.001$, indicating that the correlation between the variables was appropriate and suitable for further factor analysis.

Table 2 Differences in gait parameters among the PD-nFOG group, PD-FOG group, and HC group

Gait parameters	HC	PD-nFOG	PD-FOG	Corrected *p*-value (age、gender、height)	Post hoc tests	
					HC vs PD-nFOG&PD-FOG	PD-nFOG vs PD-FOG
Sit-to-stand						
SiSt—Average Duration (s)	1.43 ± 0.49	1.80 ± 0.78	1.95 ± 0.97	< 0.001	HC < < PD; HC < < < FOG	—
SiSt—Trunk Sagittal Peak Velocity (degree/s)	85.73 ± 23.94	65.55 ± 18.76	63.78 ± 18.95	< 0.001	HC > > > PD, FOG	—
SiSt—Trunk Sagittal RoM (degree)	37.44 ± 10.56	32.8 ± 7.78	32.49 ± 7.97	< 0.001	HC > > PD, FOG	—
Walking						
Step Length (cm)	55.11 ± 9.82	49.24 ± 10.18	46.55 ± 10.36	< 0.001	HC > > > PD, FOG	—
Stride Velocity (m/s)	1.01 ± 0.22	0.90 ± 0.22	0.86 ± 0.20	< 0.001	HC > > > PD, FOG	—
Stride Length (cm)	109.19 ± 19.70	97.57 ± 20.10	92.22 ± 20.27	< 0.001	HC > > > PD, FOG	—
Cadence (step/min)	111.87 ± 13.97	110.18 ± 11.99	113.61 ± 12.88	0.243	—	—
Gait Cycle (s)	1.11 ± 0.14	1.11 ± 0.13	1.08 ± 0.12	0.302	—	—
Double Support (%)	21.85 ± 5.34	23.19 ± 7.18	20.56 ± 5.13	0.009	—	PD > > FOG
Swing Phase (%)	39.62 ± 2.90	38.82 ± 3.81	40.19 ± 2.78	0.010	—	PD < FOG
Swing Phase CV (%)	5.93 ± 3.13	6.74 ± 2.74	6.61 ± 2.70	0.165	—	—
Double Support CV (%)	14.76 ± 5.82	16.22 ± 7.41	16.96 ± 7.15	0.182	—	—
Cadence CV (%)	7.50 ± 8.10	8.32 ± 10.86	8.16 ± 4.45	0.773	—	—
Gait Cycle CV (%)	4.15 ± 1.86	4.66 ± 2.45	5.13 ± 3.73	0.121	—	—

Table 2 (continued)

Gait parameters	HC	PD-nFOG	PD-FOG	Corrected *p*-value (age、gender、height)	Post hoc tests	
					HC vs PD-nFOG&PD-FOG	PD-nFOG vs PD-FOG
Stride Velocity CV (%)	8.81 ± 4.95	9.94 ± 5.23	10.89 ± 5.90	0.071	—	—
Step Length CV (%)	6.01 ± 3.05	7.66 ± 5.69	8.87 ± 7.16	0.007	HC < < FOG	—
Shank RoM (degree)	70.43 ± 10.72	59.87 ± 11.78	60.77 ± 11.08	< 0.001	HC > > > PD, FOG	—
Peak Shank Angular Velocity (degree/s)	357.38 ± 60.09	314.97 ± 57.76	311.52 ± 57.74	< 0.001	HC > > > PD, FOG	—
Trunk Coronal Peak Velocity (degree/s)	24.70 ± 6.55	21.62 ± 6.82	21.83 ± 7.46	0.005	HC > > PD; HC > FOG	—
Trunk Coronal RoM (degree)	5.02 ± 2.20	3.31 ± 1.70	3.49 ± 1.59	< 0.001	HC > > > PD, FOG	—
Trunk Sagittal Peak Velocity (degree/s)	36.42 ± 12.28	31.16 ± 11.31	31.58 ± 9.03	0.009	HC > PD, FOG	—
Trunk Sagittal RoM (degree)	4.85 ± 1.47	3.99 ± 1.67	4.29 ± 1.28	0.001	HC > > > PD	—
Trunk Transverse Peak Velocity (degree/s)	45.29 ± 12.5	38.01 ± 11.77	37.71 ± 11.16	< 0.001	HC > > > PD, FOG	—
Trunk Transverse RoM (degree)	10.32 ± 3.36	8.05 ± 3.72	8.70 ± 3.45	< 0.001	HC > > > PD; HC > FOG	—
Arm Peak Velocity (degree/s)	182.11 ± 59.48	151.07 ± 66.08	159.91 ± 79.91	0.005	HC > > PD	—
Arm RoM (degree)	34.41 ± 14.07	24.52 ± 12.28	25.97 ± 14.05	< 0.001	HC > > > PD, FOG	—
Stride Length Asymmetry (%)	3.62 ± 2.62	3.63 ± 3.00	4.49 ± 2.68	0.052	—	—

Table 2 (continued)

Gait parameters	HC	PD-nFOG	PD-FOG	Corrected *p*-value (age、gender、height)	Post hoc tests	
					HC vs PD-nFOG&PD-FOG	PD-nFOG vs PD-FOG
Swing Asymmetry (%)	6.37 ± 4.42	8.28 ± 3.93	8.10 ± 4.25	0.007	HC < < PD	—
Shank RoM Asymmetry (%)	6.96 ± 5.30	9.67 ± 8.38	7.95 ± 5.31	0.013	HC < PD	—
Shank Symbolic Symmetry Index (%)	11.72 ± 3.30	11.73 ± 2.83	11.20 ± 2.48	0.433	—	—
Phase Coordination Index (%)	7.63 ± 4.54	9.00 ± 5.38	8.82 ± 5.67	0.220	—	—
Arm Symbolic Symmetry Index (%)	34.95 ± 5.54	37.31 ± 5.29	37.10 ± 5.25	0.004	HC < < PD; HC < FOG	—
Turning						
Turning—Average Duration (s)	1.51 ± 0.25	2.09 ± 1.26	2.09 ± 1.07	< 0.001	HC < < < PD; HC < < FOG	—
Turning—Average Steps	2.10 ± 0.74	2.53 ± 1.74	3.27 ± 2.30	< 0.001	HC < < < FOG	PD < < FOG
Turning—Peak Velocity (degree/s)	166.83 ± 31.99	129.15 ± 31.51	126.56 ± 30.08	< 0.001	HC > > > PD, FOG	—
Turning—Average Angular Velocity (degree/s)	122.29 ± 13.21	99.77 ± 26.46	100.71 ± 27.14	< 0.001	HC > > > PD, FOG	—
Stand-to-sit						
StSi—Average Duration (s)	1.99 ± 0.53	2.30 ± 0.89	2.17 ± 0.71	0.024	HC < PD	—
StSi—Trunk Sagittal Peak Velocity (degree/s)	86.47 ± 27.00	64.28 ± 22.18	62.41 ± 19.11	< 0.001	HC > > > PD, FOG	—

Table 2 (continued)

Gait parameters	HC	PD-nFOG	PD-FOG	Corrected *p*-value (age、gender、height)	Post hoc tests	
					HC vs PD-nFOG&PD-FOG	PD-nFOG vs PD-FOG
StSi—Trunk Sagittal RoM (degree)	40.76 ± 11.80	33.95 ± 9.38	33.67 ± 10.17	< 0.001	HC > > > PD, FOG	—

Statistically significant differences between groups after Bonferroni correction were expressed as follows: (> or <), $p < 0.05$; (> > or < <), $p < 0.01$; (> > > > or < < <), $p < 0.001$. All results were adjusted for age, gender, and height by analysis of covariance

The results of the parallel analysis method suggest that six factors/domains are the optimal number of factors to explain the data distribution. These six factors explained a total of 74.23% of the variance in the data set, with 16.83% of the variance explained by factor 1, 14.77% by factor 2, 11.52% by factor 3, 12.76% by factor 4, 9.37% by factor 5, and 8.98% by factor 6. Based on the loadings of the gait variables in each factor, we grouped them into six gait domains: the pace factor (including stride length, step length, stride velocity, shank RoM, and stride velocity CV), the kinematic factor (including trunk transverse RoM, trunk coronal RoM, trunk sagittal RoM, trunk transverse peak velocity, trunk sagittal peak velocity, and trunk coronal peak velocity), gait phase factor (including double support phase, swing phase and double support phase CV), turning process factor (including turning process average duration, turning process average steps, turning process average angular velocity and turning process peak velocity), rhythm factor (including gait cycle and cadence) and asymmetry factor (including swing phase CV and swing asymmetry) (Table 3). We further summarize the standard score coefficients of each parameter based on the results of EFA and use the Thurstone method to calculate the factor scores of each gait domain separately.

Differences in gait domains impairment in the PD-nFOG group and PD-FOG group in comparison to HC group

Each group's gait domain factor scores were separately transformed to a Z-score with HC as the reference value. The mean value of each variable in the HC group was 0, and the standard deviation was 1 after the transformation. Radar plots were used to indicate the degree of impairment and the direction of change in the gait domain in the PD-nFOG and PD-FOG groups relative to the HC group (Fig. 1). The results showed that the factor scores of pace and kinematic domain were reduced in both two groups compared to the HC group. The gait phase domain factor score was significantly higher in the PD-FOG group compared to the PD-nFOG group (p corrected = 0.004, Cohen's d = −0.46). The turning process domain factor score was greater in both the PD-nFOG and PD-FOG groups compared to the HC group by approximately two standard deviations ($F = 16.72$, $p < 0.001$). The differences in asymmetry and rhythm factors were not statistically significant among the three groups ($p > 0.05$).

The related factors of FOG through the combination of clinical and gait domain characteristics

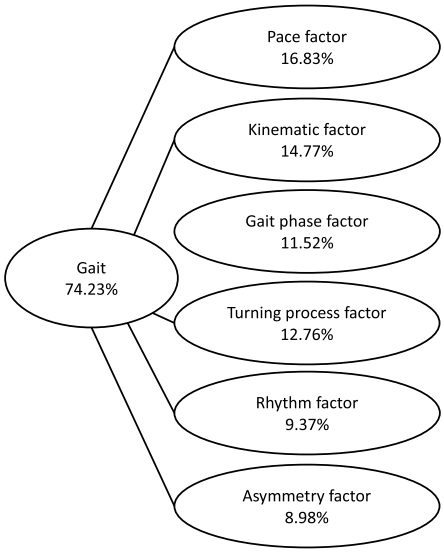
We constructed a binomial logistic regression model with the presence or absence of FOG as the dependent variable, and independent variables with p-values < 0.1 were included in the model based on the results of the univariate analysis. After eliminating the independent variables with excessive covariance, the final independent variables included in the multinomial model were: gender, height, disease duration, H-Y stage, MDS-UPDRS II score, MDS-UPDRS IV score, bradykinesia subscore, rigidity subscore, PIGD subscore, HAMD score, MMSE score, gait phase domain factor score, and LEDD. The results showed that gender (OR = 2.67, 95% CI = 1.19–5.99, $p = 0.017$), MDS-UPDRS IV score (OR = 1.23, 95% CI = 1.10–1.37, $p < 0.001$), gait phase domain (OR = 1.64, 95% CI = 1.05–2.55, $p = 0.030$) and PIGD subscore (OR = 1.50, 95% CI = 1.30–1.73, $p < 0.001$) were independent risk factors for FOG after forward stepwise (likelihood ratio) selection (Table 4). The Hosmer–Lemeshow test showed a good model fit ($X_2 = 1.09$, degrees of freedom = 8, $p = 0.998$). The model had a sensitivity of 0.78 and a specificity of 0.77 for differentiating FOG and PD patients at a cut-off value of 0.28, with an accuracy of 0.78 and an area under the receiver operating characteristic curve (AUC) was 0.87 (Fig. 2).

Discussion

In this study, we found that some characteristics of gait impairments in PD patients with FOG were different from those of non-FOG patients when FOG episode was not present. Common gait characteristics contained in twenty-two gait variables were identified, and six gait domains were categorized and extracted to represent a synthetic description of gait. Among these gait domains, the impairment of the gait phase domain was the critical abnormality in identifying potential PD-FOG from PD-nFOG patients during an interictal period of freezing. Combined with the clinical information, males, with higher MDS-UPDRS IV score, higher PIGD subscore, and higher gait phase domain factor score were independent risk factors for FOG.

We used wearable sensors for gait detection, which has the advantages of being portable and less restricted by the testing environment compared to a 3D optical motion analysis system [7, 20, 21]. Some studies previously focused on the changes in gait parameters during FOG episodes [8]. The decrease in gait frequency during FOG episodes can be explained by the tendency of the trunk to walk continuously forward. Still, the inability of the feet to produce an effective stride length makes the walking movement collapse and reduces the number of steps. FOG may result from dysfunctional stride control. In addition, FOG events are often preceded by postural instability when FOG patients compensate by increasing the duration of the double support phase [22]. It has also been found that an anterior tilt of the pelvis occurs prior to the onset of a FOG event, suggesting an impaired

Table 3 Factor loading of gait parameters on three factors rotated and extracted by exploratory factor analysis



	Factor						
	1	2	3	4	5	6	Uniqueness
Stride Length (cm)	**0.99**	0.01	0.01	-0.02	-0.10	-0.01	0.00
Step Length (cm)	**0.99**	0.01	0.03	-0.02	-0.11	-0.00	0.01
Stride Velocity (m/s)	**0.86**	0.01	0.02	-0.02	0.33	-0.02	0.00
Shank RoM (degree)	**0.48**	0.33	0.19	-0.18	-0.03	-0.08	0.24
Stride Velocity CV (%)	**-0.38**	0.15	0.08	0.21	-0.19	0.19	0.61
Trunk Transverse RoM (degree)	-0.10	**0.78**	0.12	-0.07	-0.10	-0.06	0.31
Trunk Coronal RoM (degree)	0.02	**0.77**	-0.07	0.05	-0.03	-0.02	0.45
Trunk Sagittal RoM (degree)	0.07	**0.71**	0.19	-0.03	-0.09	0.13	0.36
Trunk Transverse Peak Velocity (degree/s)	0.07	**0.63**	-0.13	-0.17	0.11	-0.11	0.45
Trunk Sagittal Peak Velocity (degree/s)	0.22	**0.54**	-0.06	-0.04	0.19	-0.00	0.53
Trunk Coronal Peak Velocity (degree/s)	0.14	**0.50**	-0.22	0.03	0.09	-0.07	0.72
Double Support (%)	-0.04	-0.00	**-0.94**	0.06	-0.00	0.11	0.01
Swing Phase (%)	0.03	0.03	**0.93**	-0.05	0.02	-0.12	0.00
Double Support CV (%)	0.01	-0.04	**0.63**	0.10	0.14	0.44	0.49
Turning - Average Duration (s)	0.05	-0.04	-0.16	**0.88**	-0.01	0.02	0.17
Turning - Average Steps	-0.18	0.25	0.18	**0.77**	0.16	0.00	0.26
Turning - Average Angular Velocity (degree/s)	0.03	0.25	0.12	**-0.76**	0.10	0.05	0.13
Turning - Peak Velocity (degree/s)	0.17	0.24	-0.02	**-0.56**	0.19	-0.03	0.31
Gait Cycle (s)	0.00	0.03	-0.04	0.01	**-0.94**	0.09	0.07
Cadence (step/min)	-0.03	-0.02	0.02	0.00	**0.87**	0.06	0.26
Swing Phase CV (%)	-0.02	0.06	-0.05	0.03	-0.04	**0.97**	0.00
Swing Asymmetry (%)	-0.01	-0.14	-0.13	-0.11	-0.00	**0.78**	0.29

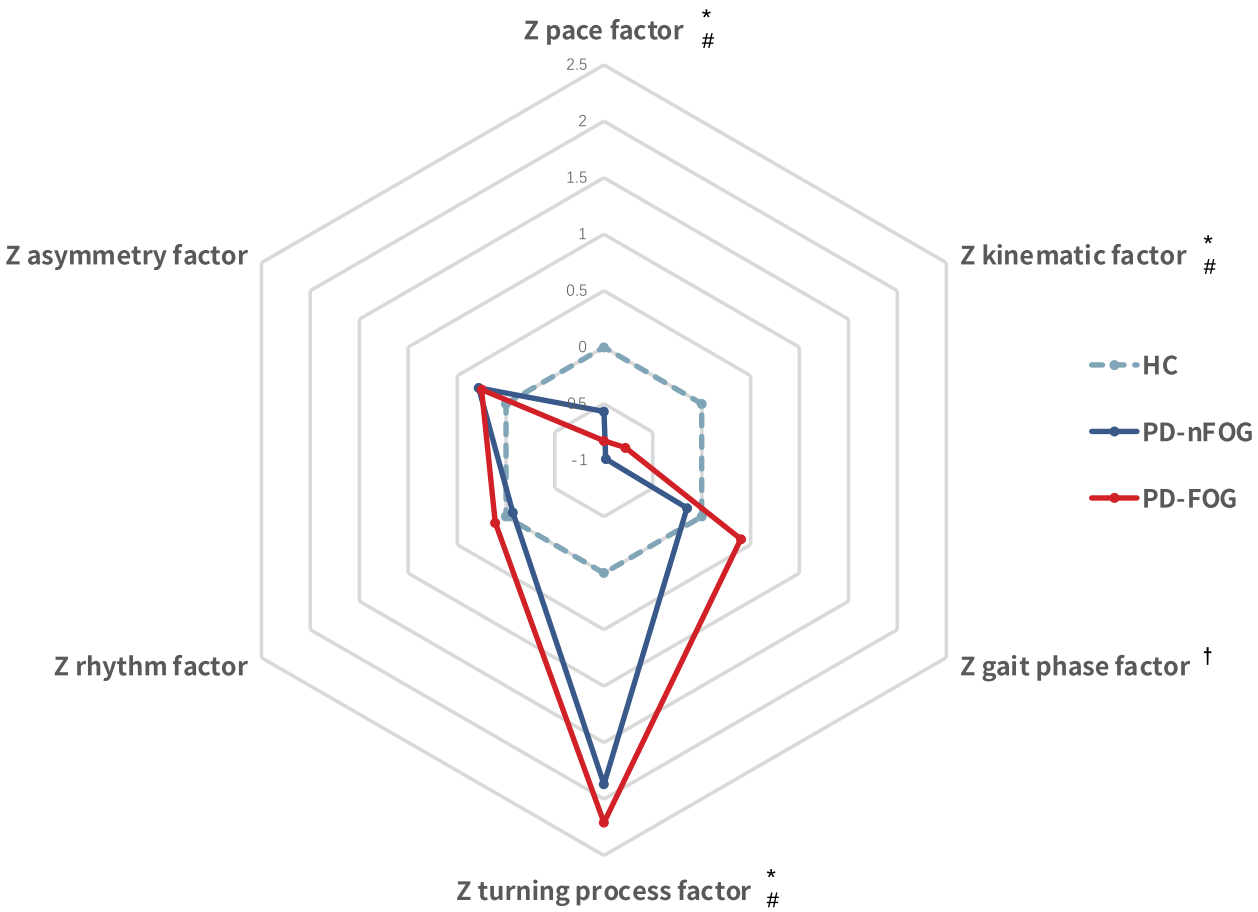


Fig. 1 Radar plot illustrating the z-scores of PD-nFOG, PD-FOG, and HC for the six factors of the gait domains

Table 4 The related factors of FOG through Logistic regression

Predictor	Estimate	SE	Z	p-value	OR	95% Confidence Interval	
						Lower	Upper
Intercept	−4.20	0.59	−7.08	< 0.001	0.02	0.00	0.05
MDS-UPDRS IV	0.21	0.06	3.65	< 0.001	1.23	1.10	1.37
PIGD subscore	0.41	0.07	5.67	< 0.001	1.50	1.30	1.73
Gait phase factor	0.49	0.23	2.18	0.030	1.64	1.05	2.55
Gender:							
Male–Female	0.98	0.41	2.39	0.017	2.67	1.19	5.99

MDS-UPDRS MDS-Unified Parkinson's Disease Rating Scale, *PIGD* postural instability and gait difficulty, *OR* odds ratio. Estimate represents the log odds of PD-FOG vs. PD-nFOG

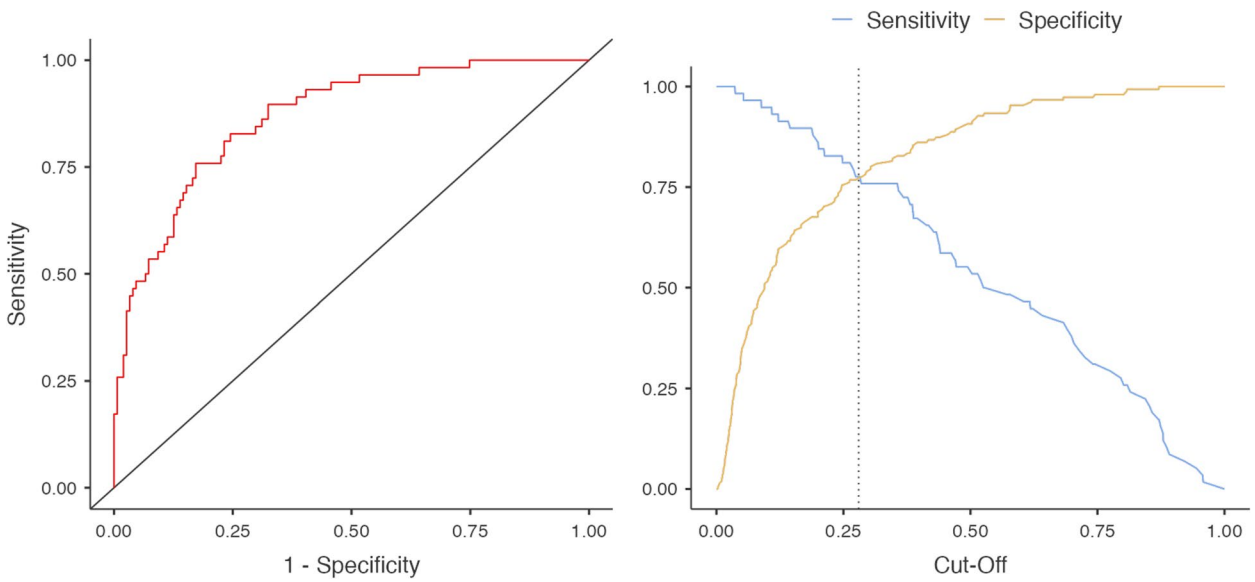


Fig. 2 ROC analysis and cut-off plot for prediction of FOG

anticipatory postural adjustment, leading to an increased risk of falling forward [23, 24]. However, few studies have examined the gait characteristics of FOG patients during the "interictal" period.

Our results found that patients with FOG had a reduced double-support phase time, a relatively increased swing phase during the interictal period compared to PD patients without FOG, and a significant increase in the number of steps during turning. Some hypotheses on the pathophysiological mechanisms of FOG point to an impairment in the coordination of the gait cycle in FOG patients, as evidenced by increased step frequency variability, gait asymmetry, and double support phase [25, 26]. The double-support phase represents the period of the gait cycle when both feet are in contact with the ground at the same time, during which the body has better control over the movement of the center of gravity. An increase in the percentage of the double support phase suggests impaired dynamic balance and postural control [27]. It has been suggested that the percentage of the double support phase significantly increased during FOG events, reflecting that patients are in the double support phase to correct the interference of FOG on balance postural control [22]. The percentage of the double support phase is also related to the walking speed, which may increase as the walking speed decreases [27]. However, in the present study, the double support phase percentage was reduced, and the swing phase was relatively increased during the interictal period in PD-FOG patients, and there was no significant difference between the two groups regarding gait speed. Another possibility is that during the "interictal period," by shortening the double support phase and increasing the swing time, patients may attempt to speed up the transition between steps, thereby reducing the risk of freezing episodes. This

suggests that patients are attempting to avoid freezing events through compensatory gait adaptations. This suggests that the typical gait cycle control impairment pattern of FOG is not present in the interictal period and is even slightly better than in the average PD-nFOG patient. Consistent with the results of other studies, gait characteristics such as gait speed, stride length, stride variability, and left–right asymmetry were impaired to varying degrees in PD patients relative to healthy controls [28].

With the aid of gait analysis systems, we can obtain multi-variables. However, these parameters are too many to highlight PD's gait impairment characteristic and to be unsatisfactory in descript or distinguishing FOG. Previous studies have attempted to describe gait in PD with different approaches and analyzed numerous spatiotemporal and kinematic parameters. However, the extracted variables are not readily interpretable from a clinical standpoint and are frequently analyzed in isolation from clinical correlations, thus disregarding the comprehensive features of gait. Moreover, many gait parameters are often widely correlated with each other, and the problem of collinearity among variables limits the multinominal analysis of gait [29, 30]. Exploratory factor analysis (EFA) has been widely used in social science and medical research and is less commonly used in the field of chronic non-communicable diseases. Some recent studies have attempted to use EFA methods to reveal complex correlations among variables, identify potential common factors among variables, and further explain the practical significance of each factor [16]. For example, one study obtained four gait domains (variability, asymmetry, postural control, and pace/cadence factors) after factor analysis of gait parameters for assessing the gait characteristics of elderly patients with hip fractures [17]. Few studies are using EFA to characterize the gait of PD patients, especially the gait characteristics of FOG patients in the 'interictal' period relative to PD patients without FOG symptoms are uncertain. Therefore, in this study, we used EFA to analyze the differences in the changes in gait characteristics between PD-FOG patients and PD-nFOG patients compared to healthy controls in six gait dimensions: pace, kinematics, gait phase, turning process, rhythm and asymmetry, and to describe the degree of impairment in different gait domains. Our results showed that the pace, kinematic, gait phase, and turning process domains were impaired in both PD-nFOG and PD-FOG groups compared to healthy controls. Among them, the difference between the PD and FOG groups in the interictal period was mainly in the domain of the gait phase. This suggested that gait phase parameters were important indicators to distinguish PD-FOG patients from PD-nFOG patients in the interictal period.

The present study also showed that patients with FOG had a longer disease duration, more progressive disease, poorer balance, and more severe motor and non-motor symptoms, with more prominent aspects of bradykinesia and PIGD. These results are also consistent with the findings of other previous studies [31]. Notably, motor complications were more severe in patients with FOG, which may also be related to the longer disease duration and higher doses of antiparkinsonian medication in patients with FOG. The results of the multinominal analysis showed that gender, motor complications, PIGD, and impaired gait phase domain are associated with FOG and that these indicators could effectively distinguish PD patients with FOG in the interictal period from those without FOG.

There were some limitations of this study. Firstly, the gait test was completed during the "ON" period, and this might inaccurately reflect the degree of gait impairment of PD patients because of the differences in drug effect on motor symptoms and gait control among individuals. Secondly, visual judgment is currently the gold standard for FOG identification. Still, the standard definitions of the beginning and end of FOG events are inconsistent or not even clearly defined in many studies [32, 33]. This also reduces the comparability between different studies. Our study focused on people with interictal periods of FOG episodes, and the presence or absence of FOG events was determined by visual observation. There may be a problem of low identification accuracy, which in turn may introduce some patients with FOG events but mild symptoms into the population. Finally, FOG is a highly heterogeneous symptom, and there may be differences in the gait characteristics of patients with different types of FOG (complete blocking, shuffling forward with small steps, and trembling on the spot). Therefore, future prospective studies with larger sample sizes and less heterogeneous candidates are needed to further clarify these changes in FOG patients.

Conclusions

This study focused on analyzing the characteristic differences of gait parameters in FOG patients during the 'interictal' period. We focused not only on a single gait variable but also on revealing the common features behind numerous gait parameters and extracting independent gait domains. Abnormal change in the gait phase domain was associated with FOG during the interictal period. Models constructed using gait phase domain factor score, PIGD subscore, gender, and severity of motor complications can better differentiate patients with interictal FOG. These features, while not directly causing

freezing of gait, may serve as risk markers due to their persistent impairments in gait patterns. FOG is not an isoated phenomen, but rather part of a broader spectrum of gait disturbances that evole over time in PD patients. We provided a more comprehensive understanding of the factors that cause FOG, both just prior to and further away from the events. Preventive interventions to reduce the risk of FOG can also be informed by understanding the interictal period and its role in the progression of gait disturbance.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12877-024-05673-z.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3: Supplementary Figure 1. Illustration of the placement of the ten inertial measurement units on the subjects' bodies.

Acknowledgements
We thank PAR (Psychological Assessment Resources) for granting us permission to use the Chinese version of the MMSE in this study. An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified with PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR (www.parinc.com).

Authors' contributions
ZJH contributed to data collection, methodology, writing the original draft. LC contributed to data curation and formal analysis. WY and ZXB contributed to data collection, data curation. SL contributed to study conceptualization, funding acquisition, investigation. LZG contributed to study conceptualization, funding acquisition, investigation, project administration, supervision. GJ contributed to study conceptualization, funding acquisition, project administration, and review and editing of the paper. All authors reviewed the manuscript.

Funding
This study was funded by grants from the Shanghai Committee of Science and Technology (22Y11904100), the National Natural Science Foundation of China (82271274, 82171242), Shanghai Pujiang Program (21PJD046).

Data availability
The datasets generated or analysed from the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This manuscript reports a study involving human participants. All procedures were carried out with written informed consent of the participants. This study was conducted in accordance with the Declaration of Helsinki. The ethical approval for the study was obtained from the Research Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine with the approval number XHEC-C-2015–019-2 to which none of the authors was affiliated.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

Received: 23 March 2024 Accepted: 30 December 2024
Published: 9 January 2025

References

1. Camicioli R, Morris ME, Pieruccini-Faria F, Montero-Odasso M, Son S, Buzaglo D, Hausdorff JM, Nieuwboer A. Prevention of Falls in Parkinson's Disease: Guidelines and Gaps. Mov Disord Clin Pract. 2023;10(10):1459–69.
2. Mancini M, Bloem BR, Horak FB, Lewis SJG, Nieuwboer A, Nonnekes J. Clinical and methodological challenges for assessing freezing of gait: Future perspectives. Mov Disord. 2019;34(6):783–90.
3. Barthel C, Mallia E, Debû B, Bloem BR, Ferraye MU. The Practicalities of Assessing Freezing of Gait. J Parkinsons Dis. 2016;6(4):667–74.
4. van Dijsseldonk K, Wang Y, van Wezel R, Bloem BR, Nonnekes J. Provoking Freezing of Gait in Clinical Practice: Turning in Place is More Effective than Stepping in Place. J Parkinsons Dis. 2018;8(2):363–5.
5. Bouça-Machado R, Jalles C, Guerreiro D, Pona-Ferreira F, Branco D, Guerreiro T, Matias R, Ferreira JJ. Gait Kinematic Parameters in Parkinson's Disease: A Systematic Review. J Parkinsons Dis. 2020;10(3):843–53.
6. Sotirakis C, Conway N, Su Z, Villarroel M, Tarassenko L, FitzGerald JJ, Antoniades CA. Longitudinal Monitoring of Progressive Supranuclear Palsy using Body-Worn Movement Sensors. Mov Disord. 2022;37(11):2263–71.
7. Gan J, Wu X, Wan Y, Zhao J, Song L, Wu N, Wang H, Yin Y, Liu Z. Evolution characteristics of dynamic balance disorder over the course of PD and relationship with dopamine depletion. Front Aging Neurosci. 2022;14:1075572.
8. Mitchell T, Conradsson D, Paquette C. Gait and trunk kinematics during prolonged turning in Parkinson's disease with freezing of gait. Parkinsonism Relat Disord. 2019;64:188–93.
9. Chee R, Murphy A, Danoudis M, Georgiou-Karistianis N, Iansek R. Gait freezing in Parkinson's disease and the stride length sequence effect interaction. Brain. 2009;132(Pt 8):2151–60.
10. Iansek R, Huxham F, McGinley J. The sequence effect and gait festination in Parkinson disease: contributors to freezing of gait? Mov Disord. 2006;21(9):1419–24.
11. Cao SS, Yuan XZ, Wang SH, Taximaimaiti R, Wang XP. Transverse Strips Instead of Wearable Laser Lights Alleviate the Sequence Effect Toward a Destination in Parkinson's Disease Patients With Freezing of Gait. Front Neurol. 2020;11:838.
12. Plotnik M, Hausdorff JM. The role of gait rhythmicity and bilateral coordination of stepping in the pathophysiology of freezing of gait in Parkinson's disease. Mov Disord. 2008;23(Suppl 2):S444–50.
13. Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, Obeso J, Marek K, Litvan I, Lang AE, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. 2015;30(12):1591–601.
14. Tomlinson CL, Stowe R, Patel S, Rick C, Gray R, Clarke CE. Systematic review of levodopa dose equivalency reporting in Parkinson's disease. Mov Disord. 2010;25(15):2649–53.
15. Lin S, Gao C, Li H, Huang P, Ling Y, Chen Z, Ren K, Chen S. Wearable sensor-based gait analysis to discriminate early Parkinson's disease from essential tremor. J Neurol. 2023;270(4):2283–301.
16. Horak FB, Mancini M, Carlson-Kuhta P, Nutt JG, Salarian A. Balance and Gait Represent Independent Domains of Mobility in Parkinson Disease. Phys Ther. 2016;96(9):1364–71.
17. Thingstad P, Egerton T, Ihlen EF, Taraldsen K, Moe-Nilssen R, Helbostad JL. Identification of gait domains and key gait variables following hip fracture. BMC Geriatr. 2015;15:150.
18. Horn JL. A RATIONALE AND TEST FOR THE NUMBER OF FACTORS IN FACTOR ANALYSIS. Psychometrika. 1965;30:179–85.
19. Thurstone LL. Multiple-factor analysis; a development and expansion of The Vectors of Mind. University of Chicago Press; 1947.
20. Prasanth H, Caban M, Keller U, Courtine G, Ijspeert A, Vallery H, von Zitzewitz J. Wearable sensor-based real-time gait detection: a systematic review. Sensors (Basel). 2021;21(8):2727.
21. Ossig C, Antonini A, Buhmann C, Classen J, Csoti I, Falkenburger B, Schwarz M, Winkler J, Storch A. Wearable sensor-based objective assessment of motor symptoms in Parkinson's disease. J Neural Transm (Vienna). 2016;123(1):57–64.

22. Nieuwboer A, Dom R, De Weerdt W, Desloovere K, Fieuws S, Broens-Kaucsik E. Abnormalities of the spatiotemporal characteristics of gait at the onset of freezing in Parkinson's disease. Mov Disord. 2001;16(6):1066–75.
23. Alice N, Fabienne C, Anne-Marie W, Kaat D. Does freezing in Parkinson's disease change limb coordination? A kinematic analysis J Neurol. 2007;254(9):1268–77.
24. Schlenstedt C, Mancini M, Nutt J, Hiller AP, Maetzler W, Deuschl G, Horak F. Are Hypometric Anticipatory Postural Adjustments Contributing to Freezing of Gait in Parkinson's Disease? Front Aging Neurosci. 2018;10:36.
25. Okuma Y. Practical approach to freezing of gait in Parkinson's disease. Pract Neurol. 2014;14(4):222–30.
26. Okuma Y. Freezing of gait in Parkinson's disease. J Neurol. 2006;253 Suppl 7:Vii27-32.
27. Williams DS, Martin AE. Gait modification when decreasing double support percentage. J Biomech. 2019;92:76–83.
28. Rehman RZU, Del Din S, Guan Y, Yarnall AJ, Shi JQ, Rochester L. Selecting Clinically Relevant Gait Characteristics for Classification of Early Parkinson's Disease: A Comprehensive Machine Learning Approach. Sci Rep. 2019;9(1):17269.
29. Godi M, Arcolin I, Giardini M, Corna S, Schieppati M. A pathophysiological model of gait captures the details of the impairment of pace/rhythm, variability and asymmetry in Parkinsonian patients at distinct stages of the disease. Sci Rep. 2021;11(1):21143.
30. Arcolin I, Corna S, Giardini M, Giordano A, Nardone A, Godi M. Proposal of a new conceptual gait model for patients with Parkinson's disease based on factor analysis. Biomed Eng Online. 2019;18(1):70.
31. Sawada M, Wada-Isoe K, Hanajima R, Nakashima K. Clinical features of freezing of gait in Parkinson's disease patients. Brain Behav. 2019;9(4):e01244.
32. Palmerini L, Rocchi L, Mazilu S, Gazit E, Hausdorff JM, Chiari L. Identification of Characteristic Motor Patterns Preceding Freezing of Gait in Parkinson's Disease Using Wearable Sensors. Front Neurol. 2017;8:394.
33. Mazilu S, Blanke U, Hardegger M, Troster G, Hausdorff JM. GaitAssist: a wearable assistant for gait training and rehabilitation in Parkinson's disease. In: 2014 IEEE International Conference on Pervasive Computing and Communication Workshops (PERCOM WORKSHOPS). 2014.

Publisher's Note