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Composite measures of motor performance and self-efficacy are better determinants of postural instability and gait difficulties than individual clinical measures in Parkinson's disease

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Abstract

Objective: Postural instability and gait difficulties (PIGD) are a significant cause of lower quality of life (QoL) in Parkinson's Disease. Most research on clinical predictors of PIGD measures have focused on individual clinical often motor performance variables, However, PIGD motor features often result in fear of falling (FoF) lowering a patient's self-efficacy. We assessed composite measures of motor and self-efficacy of PIGD motor features in PD and compare these to analysis of individual clinical metrics.

Methods: 75 PD participants underwent detailed motor and non-motor test batteries. Principal component analysis (PCA) was used to identify clusters of covarying correlates of slow walking, imbalance, falls, freezing of gait (FoG). Traditional univariate analyses were also performed.

Results: A single PCA-derived measure of motor performance and self-efficacy of mobility was the most robust determinant of all PIGD motor features except for falls. In contrast, analysis of the individual clinical variables showed more limited and diverging findings, including evidence of better cognitive performance but more severe motor parkinsonian ratings in the falls group.

Conclusion: Composite measures of motor performance and self-efficacy of mobility are robust determinants of all PIGD motor features except for falls. Univariate analysis of individual clinical

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measures showed limited correlation with PIGD motor features. Patient's own perception of motor performance, FoF, and QoL deserve more attention as PIGD therapeutic targets in PD.

Keywords

Parkinson's disease; Postural instability and gait difficulties; fear of falling; freezing of gait; falls

Introduction

Postural instability and gait difficulties (PIGD) are a major cause of falls and lower quality of life (QoL) in advanced Parkinson's disease (PD) [1–3]. PIGD motor features include imbalance, gait alterations (slow walking, and FoG). Falls are the result of a complex interaction of multiple systems. Factors contributing to falls are typically older age, more severe motor symptoms, impaired cognition, prior history of falls, vision impairments, postural instability, sleepiness, and fatigue [4]. However, psychological factors related to falls, including balance confidence and fear of falling (FoF) cannot be overlooked [5]. To date, several studies studied risk factors of PIGD motor features using predominant clinical motor measures [6–7]. However, mechanisms of PIGD motor features are heterogeneous and may not be fully captured or predicted by a single clinical characteristic. Therefore, the purpose of this study was to use a clustering technique (PCA) to investigate and capture multiple factors of PIGD motor features and compare these to traditional logistic regression approaches. To achieve this goal, we analyzed a multidimensional clinical test battery. Our main hypothesis was that self-efficacy mobility measures significantly associate with PIGD motor features beyond pure motor measures. We focused on the four major PIGD motor features: slow walking, imbalance, falls and FoG. We additionally hypothesized that self-efficacy measures play an increasing role with increasing disability from slow walking to imbalance to falls and most significant for FoG.

Materials and Methods

Idiopathic PD patients diagnosed by movement disorders neurologists were recruited from the University of Michigan and Ann Arbor VA medical centers. All data was collected during a dopaminergic medication ON state except for a Movement Disorder Society Unified Parkinson Disease Rating Scale part III (MDS-UPDRS), the Mini Balance Evaluation Systems Test (Mini-BESTest), the timed up and go (TUG), and Romberg eyed-closed on foam surface (Romberg EC foam) which were performed during OFF state. Participants completed a comprehensive multidimensional clinical test battery. The Montreal Cognitive Assessment (MoCA) was used for cognitive assessment. were used to assess for dynamic balance and postural instability functions. Lower limb sensory function was assessed for cold temperature (small sensory nerve fiver) and duration of vibration at the malleolus using a 128-Hz tuning fork (large sensory fiber). The presence of ankle jerks was also rated. The short version of Fall Efficacy Scale (sFES) and the short version of Activities-specific Balance Confidence Scale (sABC) were used to assess for Fear of falling (FoF). The Physical activity questionnaire, Instrumental Activities of Daily Living Scale (IADL), and Schwab and England Activities of Daily Living Scales were used for activities of daily living assessment. Fatigue Severity Scale (FSS) and Epworth scale were used to

assess fatigue and sleepiness, respectively. The Benton Judgment of Line Orientation (JoLO) and Rabin tests were used for visuospatial and visual contrast assessments. The Parkinson's disease questionnaire (PDQ-39) was used for quality-of-life assessment. Demographical data and clinical assessments such as Levodopa equivalent dose (LED), disease duration, history of falls, etc. were obtained during visit.

The study protocol was reviewed and approved by the institutional review boards from University of Michigan and Ann Arbor VA medical center. Written informed consent was obtained from all participants.

Statistical analysis

We performed a cross-sectional analysis to examine the potential risk predictors for the four main PIGD motor features: Impaired balance, slow walking, falls, and FoG (all as dichotomous variables).

Impaired balance was defined as Hoehn and Yahr (H&Y) ≥ 2.5 as previously reported [3]. Slow walking status was defined as a walking speed of less than 1 m/s. Fall status was determined by history of falls in the preceding one year. FoG status was defined as MDS-UPDRS item 3.11 > 0.

Group comparisons were performed by a Chi-square test for categorical data and Mann-Whitney U for continuous variables. PCA was used to cluster significant covarying variables. Varimax rotation factors with Eigenvalue ≥2 was retained. Factor loadings ≥ 0.5 were used to compute factor scores. Further analysis was performed by univariate logistic regression with adaptive Holm adjustment for correction of multiple testing in post-hoc analyses.

Univariate logistic regression models with imbalance, slow walking, falls, and FoG as the dependent variables and the sociodemographic and clinical features (gender, age, disease duration, LED, MoCA, JoLO, MDS-UPDRS II, III, Mini-BEST total, TUG, Romberg EC foam, ankle vibration, ankle jerks, cold temperature sensory leg gradient, PDQ-39, physical activities, sFES, sABC, Epworth, FSS, iADL, Schwab, and Rabin) as the independent variables were used to calculate unadjusted odds ratio (OR), Wald, OR, 95% confidence interval [CI]. Multivariate logistic forward stepwise regression models with sociodemographic and clinical features with $p<0.2$ at the univariate linear regression analyses were used to calculate an adjusted OR (Wald, OR, 95% confidence interval [CI]) for possible confounding effects. Multicollinearity analysis was used to find the correlation between variables before performing Multivariate regression analysis.

All tests were two-tailed with a P-value < 0.05. Statistical analyses were performed using SPSS (version 28) statistical software.

Results

75 patients (54 males and 21 females) with PD (mean age 67.2±6.3 years, mean disease duration at 6.4±4.1 years and median H&Y stage of 2.5) were included in the study. See table S1 for more details.

Principal component analysis

29 demographic and clinical test batteries were entered into the PCA, yielding five factors accounting for 48% of total variance. PCA1 consisted of measures of motor performance and self-efficacy of mobility (16.3%); PCA2 reflect deep tendon reflex functions(8.3%); PCA2, small sensory nerve fiber functions(8.1%); PCA4 large sensory nerve fiber functions (8.1%), and PCA5 measures of postural control (7.3%) (table 1).

Univariate logistic regression with adaptive Holm adjustment for multiple testing identified motor performance and self-efficacy of mobility as a determinant of imbalance (χ2=9.237, OR=1.71, 95% CI = 1.21–2.416, p=0.002), slow walking (χ2=12.275, OR=1.678, 95% CI = 1.256–2.241, p=0.0005), and FoG (χ2=10.44, OR=1.579, 95% CI = 1.197–2.082, p=0.001). In addition, postural and balance control components (χ2=3.286, OR=0.631, 95% CI = 0.383–1.038, p=0.007) also associated with FoG (Table 2).

No significant PCA predictor was found for the fall group.

Traditional Logistic Regression Analyses

Multivariate logistic forward stepwise regression showed that MDS-UPDRS part II score (χ2=5.761, OR=1.149, 95% CI = 1.026–1.287, p=0.016), Romberg EC foam (χ2=3.872, OR=0.861, 95% CI = 0.742–0.999, p=0.049) were significant determinants of imbalance (Table S2).

Similar results showed that LED (χ2=4.19, OR=1.005, 95% CI = 1.000–1.009, p=0.041), FSS (χ2=5.008, OR=1.178, 95% CI = 1.021–1.359, p=0.025) significantly associated with slow walking (Table S2).

MoCA (χ2=4.135, OR=1.247, 95% CI = 1.008–1.542, p=0.042), and MDS-UPDRS part III score (χ2=6.265, OR=1.057, 95% CI = 1.012–1.104, p=0.012) associated with fall status (Table S2).

Finally, disease duration (χ2=7.341, OR=1.594, 95% CI = 1.138–1.737, p=0.007), and TUG (χ2=9.76, OR=1.404, 95% CI = 1.135–1.737, p=0.002) were significant predictors of FoG (Table S2).

Discussion

This study is the first study to examine the risk factors from various motor and non-motor test batteries of four PIGD motor features by using PCA and compare the results with traditional regression analyses. Findings of the PCA in this study provides evidence that PIGD motor features in this cohort of PwPD resulted from a complex interaction of multiple

systems and self-efficacy and FoF measures rather than pure motor outcome measures. We found that motor performance and self-efficacy of mobility component which consisted of a high score of fear of falling (sABC and sFES), severe motor symptoms (MDS-UPDRS II and III), and disease duration were significant determinants of imbalance, slow walking, and FoG PIGD motor features. In addition, PCA5 or postural and balance control component, consisting of reduced ability of standing with eyed closed on foam surface, lower score on mini-BESTest, and vision impairment were also significant correlates of FoG. In contrast, our more traditional mainly univariate analyses of individual clinical measures confirmed prior studies in demonstrating that a longer disease duration, and presence of postural instability are risk factors of FoG [8–9]. Our findings that PCA factor 1 was a significant determinant of imbalance, slow walking, and FoG suggests that decreased motor performance and lower self-efficacy of mobility functions are intrinsically related. Furthermore, FoG seems to involve even more factors compared to the imbalance and slow walking PIGD motor features. This is likely because FoG occurs in a later and more severe stage of PD. When comparing the relative degree of PCA associations with the various PIGD motor features, the PCA also suggested increasing statistical model variances from slow walking to imbalance and highest for FoG.

Unexpected, we did not find any risk significant factors of the fall group in our PCA analysis. However, we found that MoCA and a severity of motor symptoms had significant association with fall status in the traditional clinical variable logistic regression analyses. Our findings contrast prior studies which were shown that FoF was a significant predictor of falls [6–7, 10]. A likely explanation may relate to the heterogeneity of multiple fall etiologies and circumstances in daily life and also the stochastic nature of falls in general. Our univariate analysis showed the lower cognitive performance and more severe parkinsonian motor performance associated with fall status. There results were not captured in our PCA analysis where severity of motor impairment covaried highly with self-efficacy measures of mobility rather than directly with cognition. This may suggest that more progressive motor impairment is not a necessary correlate of more severe cognitive changes in PD.

Prior studies have mainly used traditional logistic regression approaches to examine the risk factors of PIGD motor features and generally capturing only one or two variables. We found similar results using traditional logistic regression. For example, we found that having a higher score of MDS-UPDRS part II and decreased ability of standing with eyed close on foam surface were the only two significant predictors of imbalance. Higher LED and greater fatigue in FSS associated with slow walking. Longer duration of disease and lower score on Mini-BESTest were the only two significant predictors of FoG. Better MoCA and worse MDS-UPDRS part III scores associated with falls. The findings of a trending higher MoCa score in the fall compared to the non-fall group contrasts with previous studies [4]. However, falls are the result of a complex interaction of multiple systems and may not be driven by better cognition per se.

In our study, FoF and self-perceived efficacy (sABC and sFES) were high loading variables within PCA 1. FoF has been recognized as an important feature in PD with PIGD motor features. Prior studies, like Mak *et al.* demonstrated that perceived balance efficacy was

independently associated with a lower performance on the 6-minute walking test (after correcting for other factors like age and disease symptoms). There have also been attempts to address FoF in prior intervention studies. A study from Chow *et a*l [11] explored 3 different interventions based on 3 different mechanisms likely involved with FoG: cognition, anxiety (limbic system), and proprioception, using cognitive training, limbic training (using cognitive-behavioral therapy, CBT), and proprioceptive training. However, results were mixed, and the authors emphasized the need for individualized and combinatorial treatments as these three diverging interventions when performed in isolation lacked sufficient clinical efficacy.

Collectively, our study findings indicate that balance and gait confidence and efficacy do not exist in a vacuum because of a substantial covarying relationship between the motor performance and self-efficacy of mobility variables with more pure motor ratings. This should not come as a surprise as multiple studies have shown a reciprocal relationship between self-efficacy and exercise or physical activities performance [10]. Such intertwined relationship between self-efficacy and motor performances underscores the importance of a holistic integrated therapeutic approach that integrates both motor and behavioral to improve symptom management for PIGD motor features in PD.

Significant outcomes

There are multiple implications of our findings. We discovered that three of the four motor features of PIGD (imbalance, slow walking, and FoG) all associated with the conglomerate PCA factor 1 score consisting of measures of motor performance and self-efficacy of mobility. Higher levels of association between PCA 1 scores andFoG compared to the imbalance and slow walking groups implies the increasing relevance of not only motor severity but also compromised self-efficacy of mobility functions with more severe PD.

Recommendation for future research

In our PCA analysis, clinical assessment related to neuropathy was shown in PCA factors 2–4. However, we did not find any significant association. Interestingly, a prior study [12] showed that lower-limb peripheral neuropathy is significantly associated with more falls and gait difficulties in PD. Future studies can focus more on sensitive assessment of neuropathic features as these are predicter to contribute to PIGD motor features in PD. As fear of falling is an important covarying component of PIGD motor features, more studies are needed to assess interventions to reduce fear of falling. Future research should also explore the effect of interventions that integrate all the components of motor performance and self-efficacy of mobility rather than emphasizing motor performance alone.

Conclusion

Conglomerate measures of not only motor severity and postural control variables but also substantial covarying presence of patient’s own perception of motor performance, and fear of falling are more robust determinants of PIGD motor features than findings obtained in traditional analysis of individual clinical variable, especially freezing of gait.

Lack of significant determinants in the fall group may represent the small sample size, heterogeneous etiologies or the more stochastic nature of falls.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Authors' roles:

1. Research Project: A. Conception, B. Organization, C. Execution

2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique

3. Manuscript: A. Writing of the First Draft, B. Review and Critique

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Mr. Roytman has nothing to disclose.

Dr. van Emde Boas has nothing to disclose.

Ms. Dickinson has nothing to disclose.

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Table 1.

Principal component analysis of clinical measures

ALL			
PCA 1: Motor performance and self-efficacy of mobility	MDS-UPDRS II (0.868)	16.3%	48.0%
	sFES (0.834)		
	sABC (−0.822)		
	MDS-UPDRS III (0.774)		
	Disease duration (0.531)		
PCA 2: Deep tendon reflexes	Ankle Jerk L (0.903)	8.3%	
	Ankle Jerk R (0.814)		
PCA 3: Small sensory nerve fiber legs	Cold gradient R (0.902)	8.1%	
	Cold gradient L (0.851)		
PCA 4: Large sensory nerve fiber ankles	Vibration L (0.920)	8.1%	
	Vibration R (0.890)		
PCA 5: Postural and balance control	Romberg EC foam (0.837)	7.3%	
	Mini-BEST Total (0.702)		
	Rabin (0.595)		

LED: Levodopa Equivalent Dose; JoLO: Judgment of Line Orientation; MDS-UPDRS: International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; Mini-BESTest: Mini Balance Evaluation Systems Test; TUG: Timed Up and Go; PDQ: Parkinson's disease questionnaire; sFES: The short version of Fall Efficacy Scale; sABC: the short version of Activities-specific Balance Confidence Scale.

Table 2.

Multiple regression analysis of PCA correlates of each PIGD motor features with post-hoc adaptive Holm adjustment for multiple testing (shown in bold font).

		Wald (χ2)	P-value	OR	95% CI	
					Lower	Upper
Imbalance	PCA1	9.237	**0.002**	1.710	1.210	2.416
	PCA2	0.182	0.670	1.070	0.785	1.457
	PCA3	0.482	0.487	1.110	0.827	1.491
	PCA4	0.105	0.746	0.954	0.716	1.271
	PCA5	3.756	0.053	0.637	0.404	1.005
Slow walking	PCA1	12.275	**0.0005**	1.678	1.256	2.241
	PCA2	2.821	0.093	0.745	0.529	1.050
	PCA3	1.124	0.289	1.202	0.855	1.691
	PCA4	0.016	0.898	1.020	0.759	1.370
	PCA5	0.116	0.734	0.931	0.618	1.403
Falls	PCA1	3.315	0.069	1.226	0.985	1.527
	PCA2	1.700	0.192	1.218	0.906	1.638
	PCA3	0.240	0.624	1.074	0.808	1.426
	PCA4	0.633	0.426	1.124	0.843	1.499
	PCA5	0.194	0.660	0.921	0.639	1.328
FOG	PCA1	10.440	**0.001**	1.579	1.197	2.082
	PCA2	1.459	0.227	0.779	0.519	1.168
	PCA3	1.450	0.229	1.314	0.843	2.048
	PCA4	0.334	0.563	0.899	0.626	1.291
	PCA5	3.286	**0.070**	0.631	0.383	1.038

PCA: Principal Component Analysis; PCA1: motor performance and self-efficacy of mobility; PCA2: Small sensory nerve fiber; PCA3: Large sensory nerve fiber; PCA4: Deep tendon reflexes; PCA5: Postural and balance control.