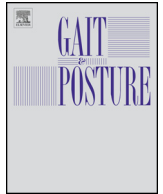




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The effect of levodopa on postural stability evaluated by wearable inertial measurement units for idiopathic and vascular Parkinson's disease

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ABSTRACT

Background: Postural stability analysis has shown that postural control is impaired in untreated idiopathic Parkinson's disease (IPD), even in the early stages of the disease. Vascular Parkinson's disease (VPD) lacks consensus clinical criteria or diagnostic tests. Moreover, the levodopa effect on postural balance remains undefined for IPD and even less so for VPD.

Objective: To characterize postural stability, using kinematic analysis with wearable inertial measurement units, in IPD and VPD patients without clinical PI, and to subsequently analyze the response to levodopa.

Methods: Ten patients with akinetic-rigid IPD and five patients with VPD were included. Clinical and postural stability kinematic analysis was performed before and after levodopa challenge, on different standing tasks: normal stance (NS), Romberg eyes open (REO) and Romberg eyes closed.

Results: In the "off state", VPD patients had higher mean distances and higher maximal distance of postural sway on NS and REO tasks, respectively. VPD patients maintained a higher range of anterior–posterior (AP) postural sway after levodopa. In the absence of PI and non-significant differences in UPDRS-III, a higher mPIGD score in the VPD patients was mainly due to gait disturbance. Gait disturbance, and not UPDRS-III, influenced the degree of postural sway response to levodopa for VPD patients.

Conclusion: Quantitative postural sway evaluation is useful in the investigation of Parkinsonian syndromes. VPD patients have higher AP postural sway that is correlated with their gait disturbance burden and also not responsive to levodopa. These observations corroborate the interconnection of postural control and locomotor networks.

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1. Introduction

Postural control encompasses the acts of aligning the body with respect to gravity and maintaining, achieving or restoring the body center of mass (COM) relative to the base of support or, more

generally, within the limits of stability during daily activities. Postural control is achieved by the complex integration and coordination of multiple body systems, including the vestibular, visual, auditory, motor, and higher level premotor systems [1], often unconsciously [2]. Postural instability (PI) is one of the most disabling features of idiopathic Parkinson's disease (IPD) and, generally, it is a manifestation of the late stages of the disease [3]. Yet, there is some evidence that postural control is already impaired in early stage of IPD without overt clinical PI [4]. Postural control can be characterized by the following four main postural control systems: (1) balance during quiet stance, (2) reactive

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postural adjustments to external perturbations, (3) anticipatory postural adjustments in preparation for voluntary movements, and (4) dynamic balance during movements, such as gait [5]. In this sense, postural control has a fundamental role in gait of establishing and maintaining appropriate postural orientation of body segments relative to each another and to the environment as well as to ensure dynamic stability of the moving body [6].

Vascular Parkinsonism (VPD) is a Parkinsonian syndrome that is typically characterized by lower body parkinsonism, marked gait difficulty, less tremor, less rigidity, better hand dexterity, relatively symmetrical symptomatic distribution, association with pyramidal tract signs, more frequent dementia, and poor response to levodopa treatment compared to IPD [7]. However, there are no consensus clinical criteria for VPD or its specific clinical features; additionally, there is a lack of diagnostic tests to differentiate VPD from IPD [8]. In terms of treatment, although it is recognized that the dopaminergic benefit tends to fade away with the progression of IPD, the objective effect of dopaminergic therapy on postural balance remains controversial for IPD and is even more questionable for VPD. There is increasing research to understand what and how networks of postural control and gait, both dopaminergic and non-dopaminergic, interact [9]. VPD, which is pathologically different from Parkinsonian syndrome but with clinical similarities to IPD [8], may serve as a good comparison model for investigating the postural stability on different and increasingly demanding postural and cognitive tasks and its response to levodopa.

Objective measures of balance using wearable inertial sensors are sensitive, specific and responsive to postural balance testing on clinical practice [10] and act as a diagnostic tool that is complementary to the traditional force plate measurements [4]. To characterize postural stability in IPD and VPD patients and to subsequently analyze the response to levodopa, we evaluated postural stability using kinematic analysis derived from wearable inertial measurement units on early disease akinetic-rigid IPD and VPD patients without clinical PI.

2. Materials and methods

2.1. Subjects and clinical assessment

Patients were consecutively recruited from our Movement Disorders outpatient consult, fulfilling criteria for IPD (UKPDS Brain Bank criteria) or VPD [8]. IPD and VPD patients had normal clinical postural stability measured by the retropulsion test (item 12 on MDS-UPDRS-III), and they had no dyskinesia. IPD patients had an Hoehn&Yahr of ≤ 2 (“off state”) and an akinetic-rigid profile. VPD patients predominantly presented with lower body Parkinsonism with independent but impaired gait; they were short stepped and stooped, which was related to an acute or chronic cerebrovascular disease, fulfilling the proposed criteria for VPD [8]. VPD patients had subcortical or basal ganglia focal lesions without large vessels stroke that were qualitatively classified from the neuroradiologist’s reports. Patients were considered as being on their best “on” dopaminergic regimen in the three previous months. The exclusion criteria were dementia, orthopedic, musculoskeletal, vestibular disorder, significant visual or auditory deficit, and alcohol abuse. VPD patients with motor deficits, whether related to stroke or not, were also excluded.

Age has been associated with kinetic performance for postural stability [11]. Therefore, VPD and IPD age-matched patients were included. The collected variables consisted of demographic (gender, age, and education) and biometric data reported as influencing kinetic performance, such as weight, height, body mass index. The center of mass (COM) was determined at 55% of a patient’s height above the ground [12]. Clinical data were also collected, including years of disease duration; Movement Disorder

Society-Unified Parkinson’s Disease Rating Scale III (MDS-UPDRS III) (scored as either an “off” or on “on” state); Levodopa Equivalent Levodopa Daily Dose [13]; Levodopa suprathereshold challenge dose; and motor benefit (percentage of the difference between “off” and “on” states). The modified Postural Instability Gait Disorder (PIGD) score part III was derived from the sum of MDS-UPDRS items (3.9 (arising from chair), 3.10 (gait), 3.11 (freezing of gait), 3.12 (postural stability), 3.13 (posture), and 3.14 (global spontaneity of movement)) [14]. A brief neuropsychological examination was performed using the Portuguese version of the Montreal Cognitive Assessment test (MoCA) with scores normalized to the Portuguese population [15] no more than 1 month prior to the kinetic assessment. The levels of education were categorized by years of schooling as follows: 0 (analphabetic), 1 (1–4 years), 2 (5–9 years), 3 (10–12 years), and 4 (>12 years). The study protocol derived from the ICVS-3Bs and the Algoritmi Center and was approved by hospital local ethics committee. Written informed consent was received from all participants in the study.

2.2. Kinematic postural tasks

Five kinetic sensing modules, harboring an 8051 microprocessor embedded in CC2530 *Texas Instrument* SoC (System on Chip), and a wearable inertial measurement unit MPU6000 (tri-axial accelerometer and gyroscope) [16] operating with a sample rate frequency of 113 Hz on a SD card were attached to the following five body segments: trunk (on the COM); both legs (middle of ankle-knee) and both thighs (middle of knee-iliac crest) by Velcro bands. Video capture (sample rate of 60 fps) and data logging were synchronized by a bidirectional radio signal transmission through a USB coordinator node connected to a PC with custom designed Matlab[®] software.

Our methodology and mathematical formulas for kinematic acquisition have been previously published [17]. We focused on some kinematic measurements that were derived from the wearable sensor unit placed at the COM, including the total length of sway (cm); maximal and mean distance of sway (cm) with respect to the origin; maximal linear velocity (cm/s); and range of medial-lateral (ML) and anterior-posterior (AP) sway (cm) (on the X and Y axis transverse planes, respectively). As one of the human’s mechanisms of maintaining balance is to vary the height and COM by bending the knees and trunk, kinematic data was constantly adjusted to real height adjusted from the wearable sensor units placed on the shanks and thighs.

Subjects were instructed to perform the following three different tasks, first in the “off” and then in the “on state”: normal comfortable standing, Romberg test with eyes open, and Romberg with eyes closed. Patients were clinically and kinematically evaluated in the “off state”, in the morning, after a 12-h period without any dopaminergic medication. Afterwards, they were given a suprathereshold dopaminergic medication of 150% of their usual morning dose and were re-examined 90 min later regardless of the intensity of their subjective response.

Subjects performed the Romberg test barefoot with the medial aspects of the feet touching each other. During the tasks, subjects stood quietly with their arms hanging at their sides and their head in a normal forward-looking eye position directed to an object placed at 2 m away. All tasks were explained, and subjects had the chance to train before the definitive trial. Each task was performed for 30 s; during that time, the kinematic data were recorded. The trial was invalidated and started again if subjects moved any part of their body, spoke, opened their eyes for visual aid or performed a corrective step.

2.3. Statistical analysis

Gender comparisons were analyzed by the χ^2 Fisher exact test. Given the small number of subjects, statistical analysis was carried

out with a non-parametric exact test, the Mann–Whitney test (comparison between groups), and by a Wilcoxon matched pair test for the magnitude of change (intragroup) after levodopa challenge and for the effect of the visual suppression effect. Intragroup correlation of the basal (“off state”) mPIGD score and the total MDS-UPDRS III score with a change in postural sway variables after levodopa challenge was evaluated with the Spearman test. Statistical analyses were conducted with software (SPSS 20.0) using a 95% level of significance.

3. Results

Five patients with VPD and ten patients with IPD were included. Thirteen patients fulfilling the criteria for VPD were excluded due to dementia (seven patients) and/or motor deficit and/or orthopedic problems (six patients). The demographic and anthropometric characteristics of the two groups are summarized in Table 1.

All VPD patients were males, but gender has not been described to influence postural sway [18]. Groups did not differ in age or anthropometric characteristics. Additionally, baseline clinical characteristics (years of disease duration, “off state” MDS-UPDRS III score, Equivalent Levodopa Daily Dose; Levodopa challenge dose; and Motor Benefit) were not significantly different between groups. VPD patients had a higher mPIGD score 8 [5,10], ($U = 4.0$; $z = -2.602$; $p = 0.006$) due essentially to a higher score on posture and gait. After levodopa challenge, both groups differed significantly on the MDS-UPDRS III ($U = 0.0$; $z = -3.062$; $p = 0.001$) and mPIGD score ($U = 1.5$; $z = -2.907$; $p = 0.002$), reflecting, as expected, a lower motor benefit of levodopa for patients with VPD ($U = 0.0$; $z = -3.067$; $p = 0.001$).

Concerning postural sway analysis (Table 2, Fig. 1), we observed that in both groups, the requirement for postural control

increased for the different tasks. This was evident in the higher values of total sway length and distance of sway in the ML and AP planes.

On “off state”, in the normal stance, VPD patients had a higher mean distance of sway ($U = 7.0$; $z = -2.205$; $p = 0.028$), and on the REO task, they had a higher maximal distance ($U = 8.0$; $z = -2.08$; $p = 0.04$) and higher range of anterior–posterior sway ($U = 8.0$; $z = -2.082$; $p = 0.04$). In the “on state,” VPD patients on the REO task also had a higher range of anterior–posterior sway ($U = 5.0$; $z = -2.449$; $p = 0.013$). Of note, in the “on state,” there were no significant differences in the distance of sway between the two groups.

In intragroup analysis of the levodopa effect, only IPD patients had significant changes in the normal stance task. The total length (IPD: 6.07 [−5.98, 10.81]; VPD: 1.05 [−7.39, 7.39]) ($z = -2.191$, $p = 0.027$), maximal distance (IPD: 0.65 [−0.18, 2.57]; VPD: 0.14 [−2.63, 1.18]) ($z = -2.497$, $p = 0.01$), range of ML (IPD: 0.63 [−0.01, 2.03]; VPD: 1.19[−1.18, 1.88]) ($z = -2.701$, $p = 0.04$) and AP sway (IPD: 0.64 [−0.73, 2.15]; VPD: −0.17 [−5.11,1.15])($z = -1.988$; $p = 0.049$) were significantly increased in only the IPD group. When analyzing the effect of visual suppression, only IPD patients, and only in the “off state”, registered a significant effect, and there was an increase in the total length ($z = -2.191$, $p = 0.027$) and maximal distance of sway ($z = -1.988$, $p = 0.049$). For the IPD group, there were no significant correlations in the basal mPIGD score (“off state”) with the change in postural sway variables after levodopa challenge. In contrast, VPD patients had a significant correlation between the basal mPIGD score (OFF state) and the total length of sway in normal stance ($\rho = -0.949$, $p = 0.014$) and range of AP sway on the REC task ($\rho = 0.9$, $p = 0.037$). The basal MDS-UPDRS-III total score (“off state”) had no significant correlation with any of the postural sway variables in either group.

Table 1
Demographics, anthropometric and clinical variables in idiopathic Parkinson's disease and vascular Parkinson's disease patients.

	IPD (n = 10)	VPD (n = 5)	Inter-group comparison
Gender (female/male)	6/4	0/5	* $p = 0.044$
Age	73 [61,79]	77 [63, 84]	$U = 18.0$; $z = -0.086$; $p = 0.418$
Height (m)	1.61 [1.52, 1.71]	1.61 [1.55, 1.68]	$U = 24.5$; $z = -0.062$; $p = 0.981$
Weight (kg)	73.2 [55, 85]	76.5 [68, 89]	$U = 15$; $z = -1.225$; $p = 0.254$
Body Mass Index (kg/m ²)	29 [24, 32]	31 [27, 34]	$U = 11.5$; $z = -1.673$; $p = 0.098$
Center of mass (cm)	88.3 [84, 94]	88 [85, 92]	$U = 24.5$; $z = -0.062$; $p = 0.981$
Level of Education	1 [1, 4]	1 [1, 1]	$\chi^2 = 2.359$; $p = 0.267$
MOCA	23 [16, 30]	12 [10, 15]	$U = 0.0$; $z = -3.067$; $p = 0.001$
Disease duration in years	6 [5, 10]	5 [3, 9]	$U = 25.0$; $z = -0.0$; $p = 1.0$
MDS-UPDRS III Off stage	30 [16, 53]	44 [33, 57]	$U = 10.0$; $z = -1.839$; $p = 0.075$
mPIGD off stage	3 [1, 7]	8 [5, 10]	* $U = 4.0$; $z = -2.602$; $p = 0.006$
Arising from chair	0 [0, 1]	1 [0, 2]	$p = 0.059$
Gait	0 [0, 2]	2 [1, 2]	$p = 0.005$
Freezing of gait	0 [0, 0]	0 [0, 0]	$p = 1.0$
Postural stability	0 [0, 0]	0 [0, 0]	$p = 1.0$
Posture	1 [0, 3]	3 [1, 3]	$p = 0.067$
Global spontaneity of movement	2 [0, 3]	2 [2, 3]	$p = 0.114$
MDS-UPDRS III On stage	13.5 [1, 24]	39 [26, 46]	$U = 0.0$; $z = -3.062$; $p = 0.001$
mPIGD on stage	2 [0, 6]	7 [5, 8]	* $U = 1.5$; $z = -2.907$; $p = 0.002$
Arising from chair	0 [0, 1]	1 [0, 2]	$p = 0.032$
Gait	0 [0, 0]	1 [1, 2]	$p = 0.001$
Freezing of gait	0 [0, 0]	0 [0, 0]	$p = 1.0$
Postural stability	0 [0, 0]	0 [0, 0]	$p = 1.0$
Posture	1 [0, 3]	2 [1, 3]	$p = 0.121$
Global spontaneity of movement	1 [0, 2]	2 [1, 3]	$p = 0.017$
Levodopa equivalent daily dose	685 [300, 1532]	750 [500, 1124]	$U = 24$; $z = -0.123$; $p = 0.931$
Levodopa challenge dose	300 [150, 400]	350 [200, 400]	$U = 18.5$; $z = -0.82$; $p = 0.458$
Motor benefit (%)	57.5 [47, 94]	19 [11, 26]	* $U = 0.0$; $z = -3.067$; $p = 0.001$

Data is presented as median [minimum, maximum].

IPD—idiopathic Parkinson's disease; VPD—vascular Parkinson's disease; COM—55% of individual's height; mPIGD—modified postural instability and gait disorder score (mPIGD) derived from the sum of the MDS-UPDRS items (arising from chair, gait, freezing of gait, postural stability, posture, global spontaneity of movement).

* Significant at exact Fisher test.

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Table 2
Postural kinematic variables on different postural tasks in idiopathic Parkinson's disease and vascular Parkinson's disease.

Kinematic variables	Normal stance			Romberg test with eyes open (REO)			Romberg test with eyes closed (REC)			REO vs.	REO vs.
	Off stage	On stage	p-Value ^a	Off stage	On stage	p-Value ^a	Off stage	On stage ^a	p-Value ^a	REC off stage	REC on stage
Total length of sway (cm)											
IPD	13.4 [8.3, 21.1]	19.4 [12.8, 25.4]	p=0.027 [*]	21.0 [10.5, 36.8]	22.1 [8.9, 32.8]	p=0.922	24 [13.8, 39.6]	23.2 [12.5, 47.2]	p=0.846	p=0.027 [*]	p=0.064
VPD	13.7 [12.8, 41.2]	20.2 [10.3, 33.9]	p=1.0	20.9 [18.7, 35.7]	21.3 [16.0, 50.0]	p=0.31	21.8 [14.4, 38.4]	23.3 [16.2, 57.3]	p=0.313	p=0.625	p=0.625
p-Value ^b	p=0.254	p=0.953		p=0.679	p=0.513		p=0.953	p=0.768			
Maximal distance of sway (cm)											
IPD	1.56 [0.92, 2.93]	2.46 [1.60, 3.55]	p=0.01 [*]	2.04 [1.36, 3.66]	2.5 [1.4, 4.3]	p=0.23	2.43 [1.46, 4.70]	2.43 [1.13, 8.4]	p=0.625	p=0.049 [*]	p=0.695
VPD	1.82 [1.46, 6.50]	3.0 [1.8, 4.0]	p=0.81	3.7 [1.9, 9.2]	3.2 [2.0, 5.9]	p=0.81	2.4 [1.64, 6.25]	3.26 [1.8, 5.4]	p=0.625	p=0.188	p=0.438
p-Value ^b	p=0.206	p=0.440		p=0.04 [*]	p=0.129		p=0.953	p=0.594			
Mean distance of sway (cm)											
IPD	0.57 [0.45, 1.32]	1.03 [0.42, 1.98]	p=0.084	1.15 [0.71, 2.04]	1.2 [0.65, 2.24]	p=0.492	1.17 [0.48, 2.79]	1.22 [0.53, 4.18]	p=0.432	p=0.57	p=0.77
VPD	1.15 [0.61, 2.50]	0.98 [0.5, 2.6]	p=0.623	1.8 [0.78, 4.3]	1.6 [0.82, 2.5]	p=0.081	1.1 [0.7, 2.3]	1.64 [0.8, 3.2]	p=0.438	p=0.313	p=0.625
p-Value ^b	p=0.028 [*]	p=.953		p=0.129	p=0.165		p=0.679	p=0.513			
Maximal linear velocity (cm/s)											
IPD	0.85 [0.22, 2.78]	1.3 [0.24, 1.77]	p=0.43	0.6 [0.28, 2.6]	1.27 [0.37, 1.82]	p=0.275	0.65 [0.43, 2.9]	1.64 [0.46, 3.72]	p=0.064	p=0.275	p=0.084
VPD	0.79 [0.5, 7.20]	1.5 [0.5, 8.2]	p=0.43	1.46 [0.58, 2.8]	2.2 [0.41, 5.5]	p=0.188	1.48 [0.17, 3.8]	1.1 [0.06, 5.7]	p=0.813	p=1.0	p=0.31
p-Value ^b	p=0.371	p=0.59		p=0.679	p=0.055		p=0.254	p=0.859			
Range of ML sway (cm)											
IPD	0.8 [0.33, 3.4]	1.82 [0.86, 3.96]	p=0.004 [*]	2.68 [1.64, 5.29]	2.03 [1.04, 5.39]	p=0.275	2.49 [1.33, 5.47]	2.28 [1.23, 7.3]	p=0.695	p=0.625	p=0.105
VPD	1.75 [0.67, 2.0]	2.38 [0.36, 3.63]	p=0.188	2.4 [1.76, 3.20]	3.24 [2.38, 3.72]	p=0.063	2.4 [1.9, 2.5]	2.4 [1.8, 5.9]	p=0.625	p=1.0	p=1.0
p-Value ^b	p=0.165	p=0.44		p=0.679	p=0.129		p=.768	p=0.768			
Range of AP sway (cm)											
IPD	1.96 [0.99, 2.70]	2.86 [1.89, 3.78]	p=0.049 [*]	2.32 [1.3, 3.87]	2.45 [0.9, 4.2]	p=0.77	2.24 [1.77, 3.85]	2.04 [1.30, 4.40]	p=0.492	p=0.557	p=1.0
VPD	2.5 [1.6, 12.0]	2.74 [2.16, 6.9]	p=0.625	4.14 [1.75, 9.96]	5.3 [2.7, 10.9]	p=0.125	3.0 [1.7, 6.2]	3.3 [2.2, 7.3]	p=1.0	p=0.18	p=0.063
p-Value ^b	p=0.371	p=0.44		p=0.04 [*]	p=0.013 [*]		p=0.371	p=0.055			

Data is presented as median [minimum, maximum]. IPD—idiopathic Parkinson's disease; VPD—vascular Parkinson's disease; ML—medial-lateral; AP—anterior–posterior.

^a Wilcoxon statistical analysis (intragroup analysis).

^b Mann–Whitney statistical analysis (intergroup analysis).

^{*} Significant at exact Fisher test.

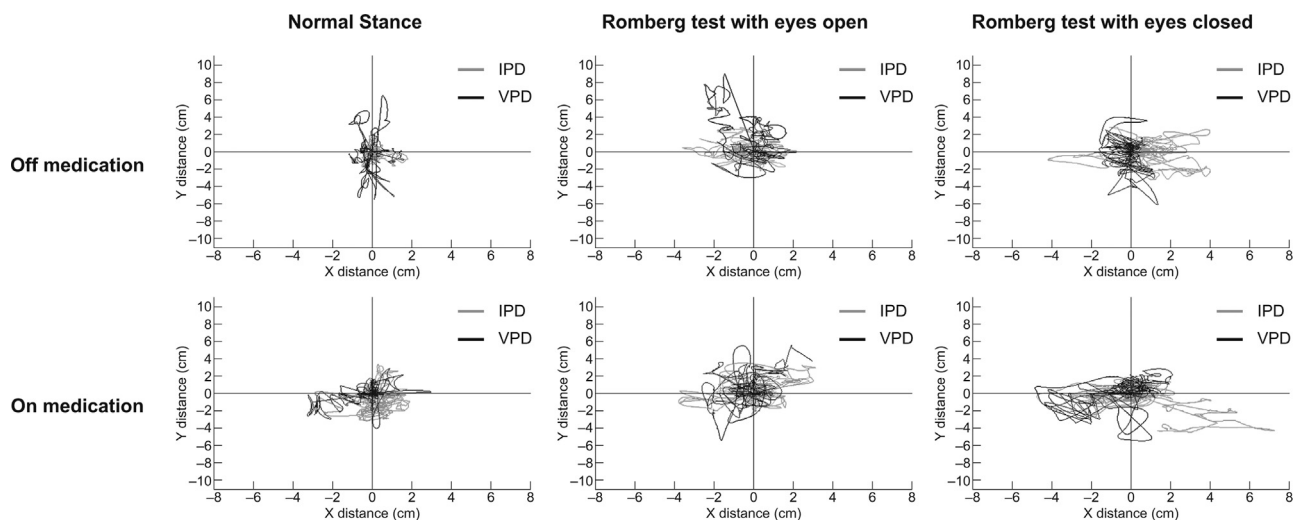


Fig. 1. Displacement on x-axis (medial-lateral) and y-axis (anterior–posterior) of inertial measurement unit on center of mass (55% of Height), plotted on different conditions (before (off) and after levodopa challenge (on)), for all subjects (idiopathic Parkinson's disease (IPD); vascular Parkinson's disease (VPD) patients).

4. Discussion

The present results indicated subclinical differences in postural sway between VPD and AR-IPD patients. This finding is in agreement with clinical evidence, diagnostic criteria and the different etiopathology of these two entities [8]. In agreement with the data from previous force platforms and IMU studies, we also found a significant increase in the displacement of sway from the origin after levodopa [19]. This is relevant because the role attributed to levodopa on postural control in IPD remains unclear due to conflicting results. Herein, we also demonstrate that levodopa only had a significant effect on IPD but not on VPD. Sway in patients with IPD who are in the “on state” are larger and faster than when in the “off state”, which is perhaps because levodopa reduces the rigidity without improving control of posture or because subclinical dyskinesia increases body motion [20]. Additionally, the decrease in sway after dopaminergic medication has been correlated with a smaller risk of falling, whereas no change or increased postural sway correlated with higher risk [21]. In our study, levodopa did not have a positive effect on the range of the AP postural sway in VPD patients. Interestingly, the main difference between IPD and VPD was in the AP sway measures both in the “off” and “on” states. AP sway involves the inverted pendulum and ankle muscle sway strategy of postural control, which may be less affected in IPD than in VPD.

The etiology of the postural misalignment and flexed posture in IPD is not clear, but background muscle tone is larger, especially in flexor muscles. In spite of their forward inclination in the upright posture, IPD patients tend to fall backwards very easily, with both axial rigidity and poor trunk coordination contributing to the poor stability of IPD patients in response to backward body sway [22]. The more flexed posture of VPD patients, demonstrated in their mPIGD scores, may have contributed, but the larger AP range of sway can also represent a distinctive variable of VPD and higher risk of falling even without overt clinical PI.

More demanding postural control tasks, such as the Romberg under visual suppression, may have put our patients on higher cognitive alert and effort to control COM under stable limits. This may have attenuated the subclinical dyskinesia and increased postural sway that was only observed in the normal relaxed stance. Visual suppression increases the postural instability, making the patient more dependent on other systems, including the vestibular, proprioceptive inputs and postural controls nucleus such as the

pedunculopontine nucleus [5]. We observed a significant effect of visual suppression on the postural sway of our IPD patients, which is concordant with other studies on early stage IPD [19]. This vulnerability was only present for IPD patients, which was evident in the “off state” and showed a positive response to levodopa, as previously reported [19]; importantly, we failed to find a positive response in VPD patients.

Increasing evidence suggests an important role of cognitive factors, such as executive function and attention, in the control of balance during standing and walking [23,24]. Many studies have shown that gait in IPD is more dependent on focused attention and external cues and that the frontal cortex may play a crucial role in controlling gait patterns [14]. The disruption of the microstructural organization of the frontal lobe white matter has been associated with the severity of VPD, reinforcing the hypothesis of the frontal lobe disconnection for gait problems and that the involvement of fibers related to the prefrontal cortex is crucial for the core features of VPD. In this respect, we cannot exclude that some findings in VPD patients can also be explained by their lower cognitive performance (lower values on MoCa), albeit without the criteria of dementia.

In the absence of clinical postural instability, the higher mPIGD score in both groups was mainly due to gait disturbance, especially prevalent in the VPD patients. After levodopa challenge, VPD patients had a higher basal mPIGD basal score, which is correlated with the lower total length postural sway change in normal stance; interestingly, this lower sway apparently persisted in the AP plane. In most cases of VPD, gait and postural stability are simultaneously impaired [25]. In this particular cohort of VPD patients, in the absence of clinically assessed postural instability, gait impairment influenced the degree of the postural sway response to levodopa. Locomotor generators and postural control are interconnected [26], and if postural control is still modulated by dopamine at least in the early stages of IPD without PI, this was not evident in VPD. Unlike for mPIGD, the UPDRS-III total score did not influence the postural sway response after levodopa challenge. A pure mechanical process, with less rigidity after levodopa influencing postural sway, is not the sole explanation for this; central postural control circuits, both dopaminergic and non-dopaminergic, could be involved [27].

4.1. Study limitations

It is important to note that we opted to include only the akynetic-rigid IPD subtype and age-matched VPD patients.

Therefore, our methodological concerns about the purity and homogenization of the VPD and IPD groups, excluding variables with potential bias on postural control, such as neuromuscular, osteoarticular and motor deficits, although theoretically a strength, led to the exclusion of a significant number of patients encountered in clinical practice. The small clinical sample of VPD patients limits the statistical inferences of comparison between groups. This difficulty in including a large number of VPD patients affects clinical cross-sectional studies [28]. Our evaluation of cerebrovascular disorder on brain MRI was merely qualitative. However, there is still no specific abnormal structural imaging pattern for VPD [25], and the terminology and definitions of the imaging features of cerebral small vessel disease vary widely, although recent advances have attempted to address this problem [29]. Nevertheless, quantitative analysis of the impact of the cerebrovascular system on brain MRI has been correlated with the severity of VPD [14]. Additionally, the volume of parietal white matter lesions has been associated with the MoCA score in VPD patients [30].

5. Conclusion

The results of our pilot study suggest that a quantitative postural sway evaluation is a useful tool for investigating the levodopa effect on Parkinsonian syndromes. VPD patients have higher AP postural sway, which is correlated with the gait clinical burden, and not responsive to levodopa. These observations corroborate the interconnection of postural control and locomotor networks, especially the non-dopaminergic ones.

Further studies with larger sample sizes that use less restrictive inclusion criteria and perform multivariate analyses are needed to determine the effect of the dopaminergic system and cognition on postural stability. Investigation should also be extended to patients with postural instability, monitoring the progression to more advanced stages of IPD, different profiles of VPD patients and even other Parkinsonian disorders, and a future study should include a correlation with a quantitative gait analysis.

Conflict of interest statement

There are no conflicts of interest to report.

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