ELSEVIER

Contents lists available at ScienceDirect

Human Movement Science



journal homepage: www.elsevier.com/locate/humov

Effect of disease, freezing of gait, and dopaminergic medication in the biomechanics of trunk and upper limbs in the gait of Parkinson's disease



Emanuele Los Angeles^a, Claudia Eunice Neves de Oliveira^a, Layla Cupertino^a, Solaiman Shokur^{b,c}, Mohamed Bouri^c, Daniel Boari Coelho^{a,d,*}

^a Center for Mathematics, Computation and Cognition, Federal University of ABC, São Bernardo do Campo, Brazil.

^b École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

^c The BioRobotics Institute and Department of Excellence in Robotics and AI, Scuola Superiore Sant'Anna, Pisa, Italy

^d Biomedical Engineering, Federal University of ABC, São Bernardo do Campo, SP, Brazil.

ARTICLE INFO

Keywords: Motor control Kinematics Levodopa Movement disorders

ABSTRACT

Introduction: Parkinson's disease (PD) causes gait abnormalities that may be associated with an arm swing reduction. Medication and freezing of gait (FoG) may influence gait characteristics. However, these comparisons do not consider differences in gait speed and clinical characteristics in individuals with PD. Objective: This study aims to analyze the effect of FoG and medication on the biomechanics of the trunk and upper limbs during gait in PD, controlling for gait speed and clinical differences between groups. Methods: Twenty-two people with a clinical diagnosis of idiopathic PD in ON and OFF medication (11 FoG), and 35 healthy participants (control) were selected from two open data sets. All participants walked on the floor on a 10-m-long walkway. The joint and linear kinematic variables of gait were compared: (1) Freezers and nonfreezers in the ON condition and control; (2) Freezers and nonfreezers in the OFF condition and control; (3) Group (freezers and nonfreezers) and medication. Results: The disease affects the upper limbs more strongly but not the trunk. The medication does not significantly influence the joint characteristics but rather the linear wrist displacement. The FoG does not affect trunk movement and partially influences the upper limbs. The interaction between medications and FoG suggests that the medication causes more substantial improvement in freezers than in nonfreezers. Conclusion: The study shows differences in the biomechanics of the upper limbs of people with PD, FoG, and the absence of medication. The future rehabilitation protocol should consider this

aspect.

https://doi.org/10.1016/j.humov.2024.103242

Received 24 November 2023; Received in revised form 17 March 2024; Accepted 2 June 2024

Available online 7 June 2024

^{*} Corresponding author at: Centre for Engineering, Modeling and Applied Social Sciences (CECS), Federal University of ABC (UFABC), Alameda da Universidade, s/no, Bairro Anchieta, São Bernardo do Campo, SP 09606-045, Brazil.

E-mail address: daniel.boari@ufabc.edu.br (D.B. Coelho).

^{0167-9457/© 2024} Elsevier B.V. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

1. Introduction

Among the activities compromised by Parkinson's disease (PD), difficulty in walking is one of the main complaints, causing a great decline in quality of life and frequent episodes of falls, the main cause of morbidity and mortality in this population (Hobert et al., 2019). Regarding the upper limbs during gait, PD is characterized by decreased arm swing and decreased peak arm velocity compared to healthy individuals (Navarro-Lopez et al., 2022). Reduced arm swing is present in the early stages of the disease (Schneider, Drude, Kasten, Klein, & Hagenah, 2012) and is a predictor of the occurrence of falls (Wood, Bilclough, Bowron, & Walker, 2002). According to Siragy and Nantel (2020), removing the arm swing during gait in PD caused compensatory responses in the lower and upper extremities, emphasizing the trunk. Given the importance of the trunk and upper limbs, this study aims to analyze the biomechanics of the trunk and upper limbs during gait in PD.

Few studies have sought to study the effects of medication on the trunk and upper limbs during gait in PD. Crenna et al. (2008) and Ferrarin, Rizzone, Lopiano, Recalcati, and Pedotti (2004) investigated the kinematics of the trunk during walking under the effect of levodopa; both demonstrated an increase in the amplitude of motion of the trunk in ON medication. Regarding the upper limbs, the results are controversial. Sterling et al. (2015) indicated that the sway amplitude of this limb substantially increased the ON medication. However, Crenna et al. (2008) and Warmerdam et al. (2021) show that the upper limbs are poorly responsive to medication. Additionally, a recent meta-analysis found no significant differences regarding the amplitude of arm movement between ON medication (Navarro-Lopez et al., 2022).

The meta-analysis performed by Fukuchi et al. (Fukuchi, Fukuchi, & Duarte, 2019) showed that, in older people, both cadence and step size decrease when individuals walk more slowly and, with increasing speed, cadence, step size, and stride size also increase. The authors suggested that to compare the gait parameters in groups with different self-selected speed, as occurs in the ON-OFF phenomenon, it is necessary to use methods or mathematical models that adjust the results according to the gait speed between the groups, thus reducing the impact of speed on the other variables analyzed. As dopaminergic medication alters the gait speed of individuals with PD, it is possible to assume that the change in the values of spatiotemporal gait parameters may be a consequence of the change in speed and not necessarily a direct effect of the medication on these parameters individually (Avila de Oliveira et al., 2021).

In addition to the classic features of parkinsonian gait, some individuals have freezing of gait (FoG), which is defined as "brief and episodic absence or marked reduction in the forward progression of the feet, despite the intention to walk" (Giladi & Nieuwboer, 2008). These episodes further affect the gait and distal joints, such as the ankle and knee, increasing the risk of falling (Shida et al., 2023). Gait speed, stride, and step length during walking are smaller in individuals with FoG (freezers) than without FoG (nonfreezers) (Ávila de Oliveira, Teixeira, & Coelho, 2023). Nonetheless, no studies have compared the effect of FoG and the effects of medication on freezers on the biomechanics of the trunk and upper limbs during gait in PD. In a turning task, McNeely and Earhart (2011) compared the effect of medication on subjects with and without FoG. Their results showed that in the OFF state, freezers performed worse on this task. However, with medication, both groups improved their performance on the task. Still, freezers showed a more pronounced improvement and reached a performance similar to that of nonfreezers in the ON medication. The authors concluded that this greater improvement occurred because freezers have a greater degree of disability in the OFF state and, therefore, a greater potential for improvement. Therefore, it is possible to assume that the improvement in gait induced by the medication may follow this pattern being more evident in freezers. However, the authors cite those freezers taking a higher drug dosage than nonfreezers as a limitation.

Given that studies do not analyze the biomechanics of the upper limbs during gait in individuals with PD, controlling for biomechanical and clinical aspects (Fukuchi et al., 2019; McNeely & Earhart, 2011), caution is needed when interpreting current results of trunk and upper limb biomechanics during gait in individuals with PD. This study aims to analyze the effect of FoG and antiparkinsonian medication on the biomechanics of the trunk and upper limbs during gait in PD, controlling for gait speed and clinical differences between groups. We hypothesize that there will be a smaller trunk and upper limb amplitude of motion during gait (a) in individuals with PD compared to age-controlled healthy individuals, (b) in the OFF state compared to ON in individuals with PD, and (c) in freezers compared to nonfreezers. We also expected medication to improve biomechanics of upper limb performance more in freezers relative to nonfreezers.

2. Methods

An open data set was used for the gait of individuals with PD (Shida et al., 2023) and another for healthy age-matched people (Kobayashi, Hida, Nakajima, Fujimoto, & Mochimaru, 2019). The two data sets were collected with the same experimental procedure. Below, we describe the methods and data available in these data sets.

2.1. Participants

Twenty-two individuals with PD participated in this study (11 with FoG, 17 men and 5 women; age: 64.1 ± 10.5 years), with a clinical diagnosis of idiopathic PD made by a neurologist. These individuals were between stages 1 and 4 of PD and classified by the criteria of the modified Hoehn and Yahr (H&Y) scale (Med = 2; minimum = 1; maximum = 4), obtained a minimum score of 15 (Med = 24; minimum = 15; maximum = 30) on the Montreal Cognitive Assessment (MoCA) scale, with self-declaration that they did not have any neurological impairment other than PD or musculoskeletal alterations that could interfere with task performance. All signed an informed consent form per procedures approved by the local research ethics committee. Inclusion criteria were as follows: (I) diagnosis of idiopathic PD confirmed by a neurologist specializing in movement disorders according to the UK Parkinson's Disease Society Brain Bank criteria; (II) absence of neurological dysfunctions (other than those associated with PD) and musculoskeletal

E. Los Angeles et al.

alterations that could interfere with the experimental task. The exclusion criteria adopted were: (I) being unable to attend scheduled visits; (II) impossibility of understanding or performing the task; (III) inability to walk without aid; (IV) change in medication dosage during the study.

Thirty-five participants were selected from the data set (Kobayashi et al., 2019) to match them by age with the individuals with PD collected (27 men and 8 women; age: 64.7 ± 7.4 years). All participants reported no orthopedic or neurological disease that could interfere with their gait patterns.

2.2. Task and equipment

Participants performed the tasks barefoot and in comfortable clothes. Participants walked on the ground on a 10-m-long walkway at a comfortable, self-selected speed. The participant's movement on a 10-m-long walkway was measured using a motion capture system with force platforms. The protocol consists of 19 anatomical reference points for the upper body, according to the model proposed by the Vicon Upper Limb Plug-In Gait model.

2.3. Experimental design and procedures

PD individuals were divided into two groups according to the presence (freezers, n = 11) or absence (nonfreezers, n = 11) of the FoG symptom. FoG was confirmed by score 1 of item 1 of the New Freezing of Gait Questionnaire, NFoQ-Q (Nieuwboer et al., 2009). PD patients participated in two experimental sessions: one of the sessions in the ON and the other in the OFF medication. To be considered ON medication, participants had taken medications one hour before starting the session to ensure dose stabilization (Araujo-Silva et al., 2022). In the OFF, participants spent at least 12 h without taking any medication for Parkinson's disease at the time of the experiment. The order of sessions was randomized among participants.

The initial evaluations consisted of an anamnesis form to collect clinical data, medication, and time of diagnosis of the disease. Two physical therapists applied the following rating scales: part III of the Unified Parkinson's Disease Rating Scale (UPDRS-III), H&Y, nFoGQ, MoCA, and the Balance Assessment System Mini-Test scale (Mini-BESTest).

After the initial clinical assessments, participants were given a 10-min rest period. Participants performed 20 trials of the experimental task in each condition. Participants were instructed to walk at a comfortable, self-selected speed for 10 m.

2.4. Data analysis

Only the side of the body most affected by individuals with PD was analyzed. Asymmetry was the difference between the UPDRS scores in the OFF condition and the body's right and left sides (items 3.3–3.9 and 3.15). The side of the body most affected was the highest UPDRS score. Asymmetric PD was defined as a side difference of UPDRS-motor score \geq 4 (Ham, Lee, Kim, Lee, & Sohn, 2015). For healthy people, half of the people were evaluated on the right side and the other half on the left side.

Data from C3D files were processed and analyzed in Visual 3D (C-motion) software. To define the gait cycle, it is necessary to detect the events of initial contact (foot strike) and the release of the foot (toe-off). These events are detected by the force platforms using a detection threshold of 20 N. The gait cycle was temporally normalized (0–100%) so that comparisons within the same subject (for example, between sides or between trials) or between subjects can be performed since small variations in the duration of this cycle may occur. Data were filtered using a fourth-order Butterworth filter and zero delay, a cutoff frequency of 6 Hz for the path. Subsequently, the following variables were calculated: (a) trunk flexion/extension amplitude [in degrees]; (b) shoulder flexion/extension amplitude [in degrees]; (c) elbow flexion/extension amplitude [in degrees]; (d) wrist amplitude for the mediolateral (ML) and vertical directions [in m]; (e) total wrist displacement [in m], length of wrist trajectory considering the three directions of movement; (f) amplitude of the 7th cervical vertebra (c7) [in m] for the mediolateral (ML) and vertical directions; (g) displacement of total oscillation of the 7th cervical vertebra (c7) [in m], length of trajectory of c7 considering the three directions of movement. Linear variables were related to each individual's hip movement.

2.5. Statistical analysis

The homogeneity of variances and normality in the data distribution and residuals was analyzed using the Levene and Shapiro-Wilk tests, respectively. In cases of non-normal data, the choice of data normalization method was selected from the Pearson P statistical function divided by the degrees of freedom (P/df); this ratio can be compared between the different forms of normalization and indicate which of the data follow the distribution closest to the normal (ratio close to 1). Clinical scales were analyzed using 2-way ANOVA (PD group x medication). For kinematics variables, linear mixed-effects models were fitted, using the Restricted Maximum Likelihood Estimation (REML), to investigate whether the results differ between groups (freezers and nonfreezers) and medication (ON and OFF), controlling for differences between groups found in demographic characteristics (disease duration), clinical scales (L-Dopa equivalent), and gait speed. In addition, the REML estimate was used to avoid bias due to the sample size. Participants were considered random intercepts to account for repeated measurements within each participant. To compare the effect of disease, the variance test (ANOVA) analysis was used for the groups (control, freezers, and nonfreezers) separately, under ON and OFF conditions. The significance level for all analyses was set at $\alpha = 0.05$, and for the analyzed interactions and differences found in the ANOVA test, Bonferroni's *post hoc* was used. The effect size was calculated by *Partial eta squared*, with "0.01" indicating a small effect, "0.06" indicating a medium effect, and "0.14" or more indicating a large effect. The analyses were performed using the R program (version 4.1.1). F

values and degrees of freedom of ANOVA are in the supplementary material.

3. Results

3.1. Participants

The clinical characteristics of the individuals with PD are described in Table 1. There was a significant group difference for L-Dopa equivalent units and UPDRS-III, with freezers showing higher values than nonfreezers. There was a significant difference between medication and miniBESTest, with ON showing lower values than OFF.

3.2. Gait parameters

Figs. 1 and 2 present the curves of each group's angular and linear variables. Individual values are in the supplementary material. Fig. 3 presents the boxplot of the kinematic variables.

Table 2 presents the *p*-values from the statistical analysis using the linear mixed effects model controlled for the disease duration, L-Dopa equivalent, and gait speed. Gait speed was higher on the ON medication than on the OFF medication. There was a significant difference in the interaction between the group and medication for wrist ML amplitude, with higher values in freezers than nonfreezers in the ON medication. Total wrist displacement showed a significant difference in medication, with higher ON values than OFF medication.

Table 3 presents the *p* values resulting from the statistical analysis performed using the ANOVA test comparing the PD group in the medication ON and the control group (PD ON x control) and the PD group in the medication OFF and the Control group (PD OFF x control). Gait speed was lower in PD than in the control group. In the ON medication: (1) the control group showed higher values in relation to freezers and nonfreezers, with no difference between them, for the variables: elbow flexion/extension amplitude, vertical wrist amplitude, and total wrist displacement, (2) the control group showed higher values in relation to freezers and nonfreezers, with no difference between them, for the variables: elbow flexion/extension amplitude. In the OFF medication, the control group showed higher values in relation to freezers, with no difference between them, for the variables: elbow flexion/extension amplitude.

4. Discussion

4.1. Disease Effect

Regarding the effect of the disease, the smaller amplitude of the trunk and upper limbs was hypothesized in individuals with PD

Table 1

Means (standard deviation) of anthropometric and clinical characteristics of participants with Parkinson's disease with and without freezing of gait separately by condition.

DP freezers		DP nonfreezers		p-value		
ON	OFF	ON	OFF	Group	Medication	Group*Medication
62.27		65.91		0.606		
(12.12)		(8.82)				
68.01		74.83		0.176		
(10.75)		(13.24)				
165.59		168.00		0.151		
(6.41)		(7.77)				
12.55	-	8.09	-	0.079	-	-
(5.94)		(5.32)				
1111.00	-	528.73	-	0.005 *	-	-
(545.14)		(283.36)				
2.45	2.64	2.09	2.09	0.135	0.161	0.161
(0.82)	(0.67)	(0.54)	(0.54)			
23.91	24.09	22.18	22.64	0.584	0.592	0.832
(2.51)	(3.02)	(5.53)	(5.10)			
30.36	30.09	17.64	22.82	0.043 *	0.287	0.239
(15.62)	(14.81)	(7.86)	(7.48)			
24.55	23.00	23.36	25.36	0.362	0.045 *	0.653
(6.30)	(6.87)	(3.96)	(3.98)			
	DP freezers ON 62.27 (12.12) 68.01 (10.75) 165.59 (6.41) 12.55 (5.94) 1111.00 (545.14) 2.45 (0.82) 23.91 (2.51) 30.36 (15.62) 24.55 (6.30)	DP freezers ON OFF 62.27 (12.12) 68.01 (10.75) 165.59 (6.41) 12.55 - (5.94) - 1111.00 - (545.14) 2.45 2.45 2.64 (0.82) (0.67) 23.91 24.09 (2.51) (3.02) 30.36 30.09 (15.62) (14.81) 24.55 23.00 (6.30) (6.87)	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

Freezers = with freezing of gait; nonfreezers = without freezing of gait; ON state = assessment made 1 h after administration of antiparkinsonian medications; OFF medication = evaluation performed 12 h after administration of antiparkinsonian medications; DDEL = equivalent daily dose of L-Dopa; MoCA = Montreal Cognitive Assement scale; UPDRS-III = Unified Parkinson's Disease Rating Scale, motor part; Mini-BESTest = Balance Assessment System Mini-Test. * indicates significant effect.



Fig. 1. Mean and error deviation of the angular displacement of the trunk, shoulder, and elbow joints in the three joint axes and linear kinematics of the marker in wrist and c7 during gait of the Parkinson's disease group without freezing of gait in ON (red) and OFF (gray) medication and the age-matched healthy control group (blue). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



Fig. 2. Mean and error deviation of the angular displacement of the trunk, shoulder, and elbow joints in the three joint axes and linear kinematics of the marker in wrist and c7 during gait of the Parkinson's disease group with freezing of gait in ON (red) and OFF (gray) medication and the age-matched healthy control group (blue). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)





Fig. 3. Boxplot of kinematic variables of participants with Parkinson's disease with and without freezing of gait and the control group of healthy control.

7

E. Los Angeles et al.

Table 2

P-values [effect size] resulting from the comparison between Parkinson's groups using the linear controlled mixed-effects model for the covariates (disease duration, L-Dopa equivalent and gait speed).

	Group	Medication	Group * Medication
Gait speed	0.054 [0.16]	<0.001*[0.12]	0.260 [<0.01]
Angular kinematics			
Trunk flexion/extension amplitude	0.568 [0.02]	0.398 [0.02]	0.496 [0.02]
Shoulder flexion/extension amplitude	0.255 [0.06]	0.110 [0.09]	0.435 [0.03]
Elbow flexion/extension amplitude	0.494 [0.02]	0.168 [0.06]	0.844 [<0.01]
Linear kinematics			
Wrist AP amplitude	0 382 [0 04]	0 116 [0 08]	0 395 [0 04]
Wrist vertical amplitude	0.629 [0.01]	0.082 [0.10]	0.315 [0.05]
Wrist ML amplitude	0.029 * [0.21]	0.186 [0.06]	0.016 * [0.26]
Total wrist displacement	0.159 [0.09]	0.044 * [0.13]	0.159 [0.09]
c7 vertical amplitude	0.090 [0.13]	0.974 [<0.01]	0.453 [0.03]
c7 ML amplitude	0.575 [0.02]	0.069 [0.11]	0.270 [0.06]
Total c7 displacement	0.643 [0.01]	0.933 [<0.01]	0.594 [0.01]

AP: anteroposterior. ML: mediolateral. c7: 7th cervical vertebra. * represents significant difference.

Table 3

P values [effect size] resulting from the ANOVA test comparing the group with Parkinson's disease in the ON and control (PD ON x control) and the group with Parkinson's disease in the OFF medication and control (PD OFF x control).

	DP ON x Control	DP OFF x Control
Gait speed	<0.001 * [0.43]	<0.001 * [0.57]
Angular kinematics		
Trunk flexion/extension amplitude	0.484 [0.03]	0.537 [0.02]
Shoulder flexion/extension amplitude	0.117 [0.08]	0.102 [0.08]
Elbow flexion/extension amplitude	< 0.001 * [0.26]	0.012 * [0.15]
Linear kinematics		
Wrist AP amplitude	0.129 [0.07]	0.036 * [0.12]
Wrist vertical amplitude	0.011 * [0.15]	0.029 * [0.12]
Wrist ML amplitude	0.163 [0.07]	0.343 [0.04]
Total wrist displacement	0.037 * [0.11]	0.067 [0.10]
c7 vertical amplitude	0.012 * [0.15]	0.166 [0.06]
c7 ML amplitude	0.974 [<0.01]	0.841 [0.01]
Total c7 displacement	0.462 [0.03]	0.481 [0.03]

AP: anteroposterior. ML: mediolateral. c7: 7th cervical vertebra. * represents significant difference.

than in healthy people. Our results are favorable to the hypothesis. Gait speed, elbow flexion/extension amplitude, and wrist vertical amplitude were smaller in individuals with PD. The constrained elbow flexion/extension amplitude in PD patients illustrates how rigidity surpasses mere muscle stiffness, affecting the fluidity and coordination of joint movements. This limitation reflects the severity of the motor symptoms and affects the natural arm swing during gait, further compromising gait dynamics and balance.

Regarding trunk variables, our results differ from previous works. For Ferrarin et al. (2004) and Crenna et al. (2008), individuals with PD had increased trunk stiffness. In the first, the amplitude of lateral flexion, torsion, and trunk rotation were lower in DP than controls. In the second, trunk rotation in the horizontal plane had reduced amplitude in PD. In our results, the biomechanics of the trunk joint showed no difference between groups. This difference was possibly due to the correction of gait speed. The only variable of the trunk affected by the disease was the vertical displacement of the c7. This decrease in the vertical amplitude of c7 possibly indicates that this lower variation in height may result from the shortening of the step length (Gordon, Ferris, & Kuo, 2009), a characteristic classic parkinsonian gait (Cheng et al., 2014; Mondal et al., 2019).

Regarding upper limb variables, our results correspond to previous studies (Crenna et al., 2008; Sterling et al., 2015). The primary purpose of the arm swing is to enhance lower limb movements during gait, promote dynamic balance, and decrease the energy expenditure associated with walking (Meyns, Bruijn, & Duysens, 2013). This characteristic holds particular significance for individuals with PD, as they commonly exhibit compromised dynamic balance and heightened energy expenditure during gait. Furthermore, the limitation of arm-swing movement decreased the average stride length and the time (Siragy, MacDonald, & Nantel, 2020). Furthermore, this reduction in sway in the lower limbs indicates a reduction in the degrees of freedom, generating a characteristic block movement in PD (Lewek, Poole, Johnson, Halawa, & Huang, 2010). Our study's diminished wrist vertical amplitude highlights the intricate nature of PD's impact on distal motor control. This reduction in movement can be attributed to a complex interplay between bradykinesia and rigidity, leading to a significant decrease in the dexterity and precision of hand movements.

The global bradykinesia in PD limited their arm mobility, thus reducing wrist magnitude and speed during gait. These motor impairments are likely a reflection of the neurological changes in PD, including the degeneration of dopaminergic neurons in the

substantia nigra, leading to the symptoms of bradykinesia and rigidity. Understanding these changes is crucial for developing targeted rehabilitation strategies to improve the quality of life for individuals with PD.

4.2. Medication Effect

As for the effect of the medication, smaller amplitudes of the trunk and upper limbs were hypothesized in the OFF compared to the ON medication. The results partially differed from the hypothesis. The medication did not affect any variable referring to the trunk and only one regarding the upper limb, with the total wrist displacement being smaller in OFF compared to ON medication.

In this case, the trunk's movement, or lack of alteration, suggests that the rigidity, postural instability, or other trunk-related symptoms in PD may not be significantly modulated by dopamine replacement therapy. This could be due to the complexity of postural control, which involves not just dopaminergic but also non-dopaminergic pathways, possibly explaining the limited efficacy of dopaminergic medication in this aspect.

The literature presented results in partial agreement with our results (Sterling et al., 2015; Warmerdam et al., 2021). Our results also showed no difference in the range of motion of the upper limbs. Our result suggests a nuanced effect of dopaminergic medication on upper limb function, particularly observed through the total wrist displacement during gait. When the medication is active (ON state), the wrist's range of motion seems to improve, indicated by greater total displacement. This could reflect the medication's efficacy in reducing rigidity and possibly improving fine motor control, at least in the wrist. The specific improvement in wrist displacement may indicate that certain aspects of motor function are more responsive to dopaminergic therapy than others, such as trunk movement. The wrist, being a more distal part of the limb, might exhibit more pronounced improvements due to its reliance on fine motor skills, which are heavily influenced by dopamine levels in the brain.

The linear displacement of the wrist is relevant, as the wrist represents the general mobility of the arm. The shoulder and elbow produce joint angles that culminate in wrist movement, the endpoint of displacement of all arm segments. The increase in this variable in ON medication may indicate that the upper limb stiffness was attenuated by medication. Our results are important for treatment. Augmenting the amplitude of arm swings has been observed to enhance pelvic movements during walking. This augmentation has several positive effects on gait parameters, including increased cadence, walking speed, stride length, and swing phase and decreased stride duration, double-support time, and stance phase (Meyns et al., 2013; Yoon et al., 2016).

The reduction in the range of motion of the upper limbs in PD during gait can be explained by the loss of dopaminergic neurons in the substantia nigra pars compacta (Sterling et al., 2015), which leads to striatal dopamine depletion. Isaias et al. (Isaias et al., 2012) show a linear correlation between arm amplitude reduction and corresponding putaminal dopaminergic depletion in PD. A dopaminergic striatal tone plays a modulatory role in upper-limb locomotor synergies while walking.

4.3. FoG Effect

The hypothesis consisted of smaller amplitudes of the trunk and upper limbs in freezers compared to nonfreezers. Our results were opposites of what was expected. Wrist mediolateral amplitude was greater in freezers. As the arm swing observed during gait decreases the body's angular momentum (Bruijn, Meijer, van Dieen, Kingma, & Lamoth, 2008), minimizing possible falls, and bradykinesia and hypometria of gait can be positively overcome by increasing the amplitude arm swing in individuals with PD (Zampier et al., 2018), we can hypothesize that the increase in wrist oscillation amplitude found in freezers indicates the use of a compensatory strategy for maintaining balance. Since FoG severely affects the lower limbs and disrupts forward progression, individuals might unconsciously increase upper body movements, including the wrists, to maintain balance and stability or to attempt to overcome the freezing episode. This exaggerated movement could also be an attempt to synchronize the upper and lower limbs, facilitating the initiation of steps when experiencing or anticipating FoG.

4.4. Group vs. Medication Interaction

We hypothesize that the medication induces a more pronounced improvement in gait in freezers. Corroborating our hypothesis, freezers had higher mediolateral wrist amplitude values than nonfreezers in ON medication. The persistence of higher mediolateral wrist amplitude in freezers despite medication underscores the multifaceted nature of motor control in PD. It suggests that FoG might involve distinct neural mechanisms separate from those that regulate general motor function, such as the coordination and amplitude of limb movements. This could indicate the involvement of non-dopaminergic pathways or a more complex interaction between dopaminergic deficits and other aspects of motor control and postural stability.

4.5. Limitations

The limitations of this study must be considered. The small sample size and diversity confer variability among participants, which may reduce the ability to detect small differences between groups. Another limitation is regarding the diagnosis of FoG. The study depended on the participants' reports of this symptom. Another limitation is the fact that it does not analyze the joint torques of the upper limb and trunk during gait.

5. Conclusion

Our study elucidates the nuanced impact of PD on motor functionality, emphasizing a pronounced disparity in the affliction of the upper limbs compared to the trunk. This disparity highlights considerable variances in motor capabilities between PD and healthy individuals, with the disease significantly impairing upper limb functions. Interestingly, the medication phase predominantly affects the linear displacement of the wrist, leaving the joint characteristics of both trunk and upper limbs relatively unchanged. This finding suggests a specific therapeutic effect of medication on fine motor control rather than on broader joint mobility. Furthermore, our analysis reveals that FoG spares trunk movements but partially impacts the upper limbs. Notably, the interaction between dopaminergic medication and FoG demonstrates a more pronounced beneficial effect on individuals experiencing FoG, indicating that medication may offer targeted relief for this challenging symptom. These insights advocate for personalized treatment strategies, focusing on the distinct aspects of motor impairment in PD.

Financial disclosures

This study was supported by Universidade Federal do ABC (UFABC/Brazil), by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES/Brazil), and by Leading House for the Latin American Region, the University of St. Gallen, Seed Money Grant, Switzerland.

Ethics approval

This investigation received study-specific approval by the local university ethics committee for research involving humans, and all participants provided informed consent before inclusion in the experiment.

CRediT authorship contribution statement

Emanuele Los Angeles: Writing – original draft, Visualization, Methodology, Data curation. **Claudia Eunice Neves de Oliveira:** Writing – original draft, Methodology, Formal analysis. **Layla Cupertino:** Methodology, Formal analysis, Data curation. **Solaiman Shokur:** Writing – review & editing. **Mohamed Bouri:** Writing – review & editing. **Daniel Boari Coelho:** Writing – review & editing, Supervision, Project administration, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

None.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humov.2024.103242.

References

Araujo-Silva, F., Santinelli, F. B., Felipe, I. I. L., Silveira, A. P. B., Vieira, L. H. P., Alcock, L., & Barbieri, F. A. (2022). Temporal dynamics of cortical activity and postural control in response to the first levodopa dose of the day in people with Parkinson's disease. *Brain Research*, 1775, Article 147727.

Avila de Oliveira, J., Bazan, P. R., de Oliveira, C. E. N., Treza, R. C., Hondo, S. M., Los Angeles, E., ... Coelho, D. B. (2021). The Effects of Levodopa in the Spatiotemporal Gait Parameters Are Mediated by Self-Selected Gait Speed in Parkinson's Disease. 54 pp. 8020–8028).

Ávila de Oliveira, J., Teixeira, L. A., & Coelho, D. B. (2023). Effect of antiparkinsonian medication on spatiotemporal gait parameters of individuals with Parkinson's disease: Comparison between individuals with and without freezing of gait. *BJMB*, *17*, 93–102.

Bruijn, S. M., Meijer, O. G., van Dieen, J. H., Kingma, I., & Lamoth, C. J. (2008). Coordination of Leg Swing, Thorax Rotations, and Pelvis Rotations During Gait: The Organisation of Total Body Angular Momentum. 27 pp. 455–462).

Cheng, K. Y., Lin, W. C., Chang, W. N., Lin, T. K., Tsai, N. W., Huang, C. C., ... Lu, C. H. (2014). Factors associated with fall-related fractures in Parkinson's disease. Parkinsonism & Related Disorders, 20, 88–92.

Crenna, P., Carpinella, I., Lopiano, L., Marzegan, A., Rabuffetti, M., Rizzone, M., Lanotte, M., & Ferrarin, M. (2008). Influence of basal ganglia on upper limb locomotor synergies. Evidence from deep brain stimulation and L-DOPA treatment in Parkinson's disease. *Brain: A Journal of Neurology*, 131, 3410–3420.

Perrarin, M., Rizzone, M., Lopiano, L., Recclarti, M., & Pedotti, A. (2004). Effects of subthalamic nucleus stimulation and L-dopa in trunk kinematics of patients with Parkinson's disease. Gait & Posture, 19, 164–171.

Fukuchi, C. A., Fukuchi, R. K., & Duarte, M. (2019). Effects of walking speed on gait biomechanics in healthy participants: A systematic review and meta-analysis. Systematic Reviews, 8, 153.

Giladi, N., & Nieuwbeer, A. (2008). Understanding and treating freezing of gait in parkinsonism, proposed working definition, and setting the stage. *Movement Disorders*, 23(Suppl. 2), S423–S425.

Gordon, K. E., Ferris, D. P., & Kuo, A. D. (2009). Metabolic and mechanical energy costs of reducing vertical center of mass movement during gait. Archives of Physical Medicine and Rehabilitation, 90, 136–144.

Ham, J. H., Lee, J. J., Kim, J. S., Lee, P. H., & Sohn, Y. H. (2015). Is dominant-side onset associated with a better motor Compensation in Parkinson's Disease?. 30 pp. 1921–1925).

Hobert, M. A., Nussbaum, S., Heger, T., Berg, D., Maetzler, W., & Heinzel, S. (2019). Progressive gait deficits in Parkinson's disease: A wearable-based biannual 5-year prospective study. Frontiers in Aging Neuroscience, 11, 22.

Isaias, I. U., Volkmann, J., Marzegan, A., Marotta, G., Cavallari, P., & Pezzoli, G. (2012). The influence of dopaminergic striatal innervation on upper limb locomotor synergies. PLoS One, 7, Article e51464.

Kobayashi, Y., Hida, N., Nakajima, K., Fujimoto, M., & Mochimaru, M. (2019). AIST Gait Database 2019. https://unit.aist.go.jp/harc/ExPART/GDB2019_e.html. Lewek, M. D., Poole, R., Johnson, J., Halawa, O., & Huang, X. (2010). Arm swing magnitude and asymmetry during gait in the early stages of Parkinson's disease. *Gait*

& Posture, 31, 256–260. McNeely, M. E., & Earhart, G. M. (2011). The effects of medication on turning in people with Parkinson disease with and without freezing of gait. Journal of

Parkinson's Disease, 1, 259–270. Meyns, P., Bruijn, S. M., & Duysens, J. (2013). The How and Why of Arm Swing During Human Walking. 38 pp. 555–562).

Mondal, B., Choudhury, S., Banerjee, R., Chatterjee, K., Ghosal, S., Anand, S. S., & Kumar, H. (2019). Analysis of gait in Parkinson's disease reflecting the effect of I-DOPA. Annals of Movement Disorders, 2, 21–27.

Navarro-Lopez, V., Fernandez-Vazquez, D., Molina-Rueda, F., Cuesta-Gomez, A., Garcia-Prados, P., Del-Valle-Gratacos, M., & Carratala-Tejada, M. (2022). Arm-swing kinematics in Parkinson's disease: A systematic review and meta-analysis. *Gait & Posture*, *98*, 85–95.

Nieuwboer, A., Rochester, L., Herman, T., Vandenberghe, W., Emil, G. E., Thomaes, T., & Giladi, N. (2009). Reliability of the new freezing of gait questionnaire: Agreement between patients with Parkinson's disease and their carers. *Gait & Posture*, *30*, 459–463.

Schneider, S. A., Drude, L., Kasten, M., Klein, C., & Hagenah, J. (2012). A study of subtle motor signs in early Parkinson's disease. *Movement Disorders*, 27, 1563–1566. Shida, T. K. F., Costa, T. M., de Oliveira, C. E. N., Treza, R. C., Hondo, S. M., Los Angeles, E., ... Coelho, D. B. (2023). A public data set of walking full-body kinematics and kinetics in individuals with Parkinson's disease. *Frontiers in Neuroscience*, 17, Article 992585.

Shida, T. K. F., de Oliveira, C. E. N., da Silva Fragoso de Campos, D., Los Angeles, E., Bernardo, C., Dos Santos de Oliveira, L., ... Coelho, D. B. (2023). Effect of Freezing of Gait and Dopaminergic Medication in the Biomechanics of Lower Limbs in the Gait of Patients With Parkinson's Disease Compared to Neurologically Healthy. 806 p. 137250).

Siragy, T., MacDonald, M. E., & Nantel, J. (2020). Restricted Arm Swing in People With Parkinson's Disease Decreases Step Length and Time on Destabilizing Surfaces. 11 p. 873).

Siragy, T., & Nantel, J. (2020). Absent arm swing and dual tasking decreases trunk postural control and dynamic balance in people with Parkinson's disease. Frontiers in Neurology, 11, 213.

Sterling, N. W., Cusumano, J. P., Shaham, N., Piazza, S. J., Liu, G., Kong, L., ... Huang, X. (2015). Dopaminergic modulation of arm swing during gait among Parkinson's disease patients. *Journal of Parkinson's Disease*, 5, 141–150.

Warmerdam, E., Romijnders, R., Hansen, C., Elshehabi, M., Zimmermann, M., Metzger, F. G., ... Maetzler, W. (2021). Arm swing responsiveness to dopaminergic medication in Parkinson's disease depends on task complexity. npj Parkinson's Disease, 7, 89.

Wood, B. H., Bilclough, J. A., Bowron, A., & Walker, R. W. (2002). Incidence and prediction of falls in Parkinson's disease: A prospective multidisciplinary study. Journal of Neurology, Neurosurgery, and Psychiatry, 72, 721–725.

Yoon, J., Park, J., Park, K., Jo, G., Kim, H., Jang, W., ... Youm, C. H. (2016). The Effects of Additional Arm Weights On Arm-Swing Magnitude and Gait Patterns in Parkinson's Disease. 127 pp. 693–697).

Zampier, V. C., Vitorio, R., Beretta, V. S., Jaimes, D. A. R., Orcioli-Silva, D., Santos, P. C. R., & Gobbi, L. T. B. (2018). Gait bradykinesia and hypometria decrease as arm swing frequency and amplitude increase. *Neuroscience Letters*, 687, 248–252.