

#### Article

# Comprehensive assessment of lower limb coordination during the heel strike phase in Parkinson's disease

# Roberta Minino<sup>1</sup>, Pierpaolo Limone<sup>1</sup>, Francesco Peluso Cassese<sup>1</sup>, Mariam Maisuradze<sup>2</sup>, Francesco Tafuri<sup>3,\*</sup>, Francesca Latino<sup>1</sup>, Emahnuel Troisi Lopez<sup>1</sup>

<sup>1</sup>Pegaso University, 80143 Napoli NA, Italy

<sup>2</sup> University of Naples "Parthenope", 80133 Napoli NA, Italy

<sup>3</sup>Niccolò Cusano University, 00166 Roma RM, Italy

\* Corresponding author: Francesco Tafuri, francesco.tafuri@unicusano.it

#### CITATION

Minino R, Limone P, Peluso Cassese F, et al. Comprehensive assessment of lower limb coordination during the heel strike phase in Parkinson's disease. Molecular & Cellular Biomechanics. 2025; 22(3): 1389. https://doi.org/10.62617/mcb1389

#### ARTICLE INFO

Received: 16 January 2025 Accepted: 26 January 2025 Available online: 18 February 2025

#### COPYRIGHT



Copyright © 2025 by author(s). *Molecular & Cellular Biomechanics* is published by Sin-Chn Scientific Press Pte. Ltd. This work is licensed under the Creative Commons Attribution (CC BY) license. https://creativecommons.org/licenses/ by/4.0/ Abstract: Parkinson's disease (PD) is character rised by numerous motor symptoms, including impaired coordination of the lower limbs, which reduces stability. The heel strike phase is crucial in gait, as it follows the single step phase and precedes the transfer of weight between limbs, requiring precise control to maintain balance. Impaired coordination during this phase can therefore compromise gait and stability. Therefore, this study aimed to investigate physiological coordination patterns of the lower limbs during the heel strike phase and identify potential alterations in patients with PD. Twenty-three patients with PD and 23 healthy controls participated in this study. Gait of each participant was recorded with a stereophotogrammetric system with 55 reflective markers and data were trimmed to  $\pm 15$  milliseconds and analysed to assess joint coordination of ankles, knees and hips. Lower limb joint coordination was assessed through pairwise correlations of their acceleration time series. The results showed that PD patients exhibited reduced coordination during the left heel strike, involving all three joints of the left lower limb and ankle and hip of the right lower limb. However, increased coordination between knees was observed, possibly indicating compensatory mechanisms. Furthermore, the difference in coordination between each PD patient and the average coordination of the healthy control group significantly correlated with both disease duration and UPDRS-III scores, highlighting the association between coordination impairments, PD severity, and disease progression. In conclusion, individuals with PD show significant alterations in lower limb coordination during the heel strike phase. These alterations are associated with disease severity and progression, emphasising the need for targeted interventions to address gait dysfunction in PD.

Keywords: biomechanics; physiology; anatomy; exercise; neurodegenerative disorder

## **1. Introduction**

Parkinson's disease (PD) is a neurodegenerative disorder that affects approximately 10 million people worldwide [1]. In Italy, it is estimated that around 250,000 individuals are affected by this disease, with a prevalence of about 300 cases per 100,000 inhabitants [2]. The prevalence of the disease increases with age: it affects about 1% of the population over 60 years old and reaches 4% among individuals over 85 years old [3]. Furthermore, in 2023, adults aged 60 or older accounted for over 90% of the prevalent Parkinson's cases diagnosed in the seven major markets, with an age distribution highlighting a higher prevalence among older individuals [4].

It is characterized by a progressive loss of dopaminergic neurons in the substantia nigra, leading to a reduction dopamine levels in the brain [5]. This intricate

neurodegenerative process arises from complex molecular and cellular mechanisms that remain an active area of research. Over time, the loss of dopaminergic neurons in the substantia nigra disrupts the normal neural circuitry that depends on dopamine for proper functioning. Not only does the number of neurons decrease, but the integrity of their connections and the efficiency of neurotransmission are also severely compromised [6]. The reduction of dopamine level leades to a range of motor and non-motor symptoms, including resting tremor, muscle rigidity, bradykinesia, freezing and postural instability [7,8]. These symptoms can significantly diminish the quality of life for individuals with PD, making daily activities increasingly challenging and reducing their overall independence.

One of the most affected aspects in patients with PD is gait, which is often characterized by short steps, reduced arm swing, and difficulties in initiating and maintaining movement. The gait alterations are not only hallmark features of PD but also serve as a critical indicators for diagnosing the disease. PD patients frequently exhibit excessive flexion of the trunk, arms, hips, and knees during the stance phase of gait, along with a reduced range of motion in the lower limb joints [9]. The postural changes reflect the muscle rigidity and bradykinesia commonly associated with PD, further hindering their ability to walk normally. Overall, these alterations result in a diminished ability to maintain balance and a disruption of smooth gait execution [10]. There duction in balance and impaired gait significantly increase the risk of falls, which can lead to serious injuries such as fractures. Impaired gait also limits mobility and independence, making everyday activities, such as shopping or visiting friends, particularly challenging [11]. As the disease progresses, these gait-related issues often worsen, further reducing the patient's quality of life.

In healthy individuals, the complex interaction between lower limb joints ensures proper force distribution and balance maintenance, which are essential for both static and dynamic postural control [12]. It should be noted that coordination involves not only the alignment and movement of the hip, knee, and ankle joints within each leg, but also the synchronized functioning of the left and right limbs [13]. According to Günther et al., all leg joints contribute to the maintenance of quiet posture in humans, highlighting the phase synchronization of the three leg joints during standing and emphasizing the importance of inter-articular coordination [14,15]. This evidence supports the idea that joint coordination is a key element for maintaining stability and ensuring efficiency of movement in both static and dynamic conditions. The assessment of joint coordination during walking provides valuable insights into the motor impairments experienced by patients with PD. Evaluating how different joints work together can help identify specific deficits in motor control, offering a deeper understanding of the characteristic gait disturbances in PD [16].

The majority of studies investigating inter-limb coordination during walking, both under physiological and pathological conditions, have primarily analyzed gait as a whole, without delving into the complexity of individual phases [17–20]. However, a specific phase of the gait cycle, the initial heel-strike, which marks the beginning of the stance phase [21], requires precise coordination between the lower limb joints to absorb impact and ensure body stability. During the heel strike phase, the ankle, knee and hip joints work together harmoniously to ensure stability, absorb the impact of ground contact and prepare the body for the next movement. It is a crucial moment in

the gait cycle, and each joint plays a specific role. When the heel touches the ground, the ankle is in slight dorsiflexion, i.e. with the foot slightly raised upwards. This positioning allows for controlled contact with the ground. Immediately afterwards, thanks to the dorsal flexor muscles, such as the tibialis anterior, the ankle slowly moves towards plantar flexion [22]. This controlled movement is essential to absorb the impact of the foot on the ground and progressively distribute the weight from the heel to the front of the foot, preparing it for the next phase. The knee, on the other hand, comes into play to further absorb the impact. At the time of contact, it is slightly flexed, about 5 degrees, a position that helps reduce the stress that is generated on the joints. The quadriceps muscles, which are located at the front of the thigh, work eccentrically to control the movement of the knee and ensure that it does not collapse under body weight [23]. This mechanism works like a shock absorber, allowing a smooth transition to the full support phase. Finally, there is the hip, which is slightly flexed at this stage, at an angle of about 20 to 30 degrees. This position helps to position the leg correctly for contact with the ground. Extensor muscles, such as the gluteus maximus and hamstrings, are activated to stabilize the hip and begin to prepare it for the extension needed to propel the body forward [24]. At the same time, the abductor muscles, such as the gluteus medius, work to keep the pelvis stable, preventing it from sagging on the opposite side, which could compromise balance during the gait. In summary, the ankle, knee and hip work together in perfect synergy during heel strike. The ankle controls the initial impact and distributes weight, the knee absorbs shock and ensures a smooth transition, while the hip stabilizes the pelvis and prepares the body for the push. It is this coordination that makes smooth, safe and efficient movement possible [25].

In patients with PD, this particular moment is often characterized by prolonged stance time and reduced push-off force, contributing to a less efficient and more unstable gait [9]. During heel-strike, the motor impairments of PD patients become particularly evident, significantly affecting their ability to maintain balance and execute smooth, coordinated movements. Indeed, the complexity of heel strike phase in PD seems to be associated with several altered gait parameters, which are crucial for understanding the broader impact of PD on movement and stability [26,27].

Given the critical role of limb coordination in maintaining balance and movement efficiency, we hypothesize that PD patients exhibit significant alterations in lower limb coordination patterns during the heel strike phase. In particular, these alterations are likely not confined to dysfunction in individual joint, but are instead manifestations of broader, systemic impairments in the motor network that governs lower limb coordination.

To investigate this hypothesis, we adopted an innovative approach that integrates traditional kinematic analysis with advanced motion network analysis, called Kinectome. The Kinectome approach enables mapping and analysis of the dynamic interactions between different joints, treating the musculoskeletal system as an interconnected network rather than a series of isolated segments. By analyzing the synchronization and coupling between joints during the heel strike phase, this method provides a more comprehensive understanding of how coordination deficits manifest in PD.

On this basis, the aim of this study was to understand the physiological coordination pattern of the lower limbs during the heel strike phase, and to explore potential alterations in PD patients, with a specific focus on lower limb coordination during this critical phase of walking.

## 2. Materials and methods

#### 2.1. Participants

Twenty-three subjects with PD and twenty-three matched healthy controls (HC) were recruited for this cross-sectional study. The inclusion criteria for the PD patients were: a minimum age of 45 years; disease duration <15 years; Hoehn & Yahr (H&Y) score <3 during off-medicament. The inclusion criteria for the HC patients were: a minimum age of 45 years; no history of Parkinson's disease; no comorbidities that could affect motor function or gait. Participants from both groups were excluded if they met any of the following exclusion criteria: a Mini-Mental State Examination (MMSE) score <24, a Frontal Assessment Battery (FAB) score <12, a Beck Depression Inventory II (BDI-II) score >13, neurological or psychiatric disorders, the use of psychoactive drugs, or the existence of physical or medical conditions that can affect gait (**Table 1**). Informed consent was obtained from all participants, in accordance with the Declaration of Helsinki. The study was approved by the AORN "A. Cardarelli" Ethic Committee (protocol number: 00019628).

Characteristic	<b>PD</b> Group ( <i>n</i> = 23)	HC Group $(n = 23)$
Age (years)	$58 \pm 5$	$60 \pm 5$
Sex (M/F)	60%/40%	50%/50%
Disease duration (years)	$8\pm2$	Not applicable
UPDRS III (score)	$20\pm5$	Not applicable
Hoehn & Yahr scale (H&Y)	$2.0\pm0.4$	Not applicable
Symptom lateralization	55% Right/45% Left	Not applicable
MMSE (score)	$28 \pm 1.5$	$29\pm1$
FAB (score)	15 ± 1	$16 \pm 1$
BDI-II (score)	$8\pm2$	$6 \pm 1$
Comorbidities	Hypertension (35%), diabetes (10%)	Hypertension (25%), diabetes (5%)
Medication use	Levodopa (85%), dopamine agonists (50%)	None
Blood pressure (mmHg)	$128/78 \pm 8$	$120/75 \pm 5$

Table 1.	Characteristic	of the sample.
----------	----------------	----------------

#### 2.2. Protocol

Participants in both groups underwent gait analysis in the movement analysis laboratory of the University of Naples "Parthenope", located in the Hermitage Diagnosis and Treatment Clinic in Capodimonte (Naples). Prior to acquisition, PD patients, who had not taken their levodopa dose in the last 14–16 h, underwent the UPDRS III clinical motor assessment.

Gait data was collected using a motion analysis system composed of eight infrared cameras (ProReflex Unit—Qualisys Inc., Gothenburg, Sweden). Fifty-five passive markers were placed on anatomical landmarks of the participants' bodies, following the modified Davis protocol [28]. Both groups were asked to walk in the middle of a 10-metre-long carpet, back and forth at their preferred walking speed. The best trials, characterised by high visibility of all markers, were selected, resulting in the collection of 8 gait cycles per participant, and recordings during changes of direction were excluded from the study.

#### 2.3. Data analysis

To analyse the data, heel strike events were identified and then clipped within a window of +/-15 milliseconds in order to capture both the preparation and execution phases of the heel strike. To analyse joint coordination, we adopted a network approach, called Kinectome in which the joints were considered the nodes of the network, while the connections between the nodes were represented by the kinetic relationships between the time series of each pair of joints. The kinetic relationships were calculated using Pearson's correlation coefficient, which measures coordination as standardised covariance.

Furthermore, in order to assess the overall differences between each patient and the average control group, error scores were calculated, referred to as 'coordination error'. This value represents the difference between the coordination value of each patient and the average of the values obtained from the control group. Subsequently, the coordination error was correlated with the duration of the disease and the UPDRSIII clinical scale score with the aim of analysing how the duration of the diagnosis and the severity of the motor symptoms could affect the patients' performance in the task.

A chi-square test  $(\chi^2)$  was conducted to compare the lateralization of motor symptoms between the two groups. Finally, a multivariate analysis was performed to examine the relationship between motor symptom lateralization (left vs. right) and variables such as disease duration, medications taken, comorbidities, and walking surface. A multivariate logistic regression can be used.

Statistical analysis was performed in MATLAB 2020a. The significant differences between the PD group and the HC control group in the standard deviation of kinectomes was assessed by permutation test, randomly shuffling the group labels 10,000 times. The correlation analysis between the Coordination Error value with both UPDRS III clinical scale score and disease duration was performed by Spearman's correlation test. The p-values were corrected for multiple comparisons using the false discovery rate (FDR) [29] and the statistical significance was set at p < 0.05.

#### **3. Results**

Before presenting the statistical results, it is essential to describe the procedures adopted to ensure the quality and reliability of the analyses. In this study, a methodical approach was used to select participants and collect data, ensuring they were representative and free from significant biases. A total of 23 patients with PD and 23 HC were recruited, matched by age and sex to minimize differences unrelated to the disease. Inclusion and exclusion criteria were rigorously applied to rule out medical conditions or environmental factors that could influence the results, such as neurological or psychiatric comorbidities, the use of psychotropic drugs, or the use of non-standard surfaces during walking trials. After participant selection, a control phase was carried out to identify and reduce the impact of potential confounding variables, including disease duration, medications taken, and comorbidities. Finally, specific analyses, such as tests of statistical significance and multivariate regressions, were conducted to investigate the associations between key variables and the phenomena under study. These steps were essential to ensure that the statistical analyses were robust and accurate, allowing for reliable conclusions to be drawn regarding the impact of PD and related variables on the outcomes of interest.

Comparison between the group with PD and the HC revealed a significant impairment in coordination during the left heel strike phase (**Figure 1**).



**Figure 1.** Correlation matrices and significant differences between the HC and the group with PD during the left heel strike (HS) and right heel strike (HS) phase.

**Figure 1a**: Joint-to-joint correlation values for the HC group (left - HC L; right - HC R) and the PD group (left - PD L; right - PD R). The horizontal and vertical axes indicate the joints analysed. The colour in the cells represents the correlation coefficients: colours closer to yellow indicate higher positive correlation, while blue colours indicate negative correlations. **Figure 1b**: Significant correlation differences by False Discovery Rate (FDR) method between the HC group and the PD group for the left and right heel strike phase. The yellow cells represent statistically significant differences between the two groups, highlighting impaired joint coordination in Parkinson's patients compared with healthy controls.

This impairment involved both lower limbs and specifically affected the right ankle and right hip (p < 0.05), the left knee and left hip (p < 0.001), as well as the left ankle and left hip (p < 0.01), showed reduced coordination in the PD group than in the

HC group. In contrast, coordination between the left knee and right knee was greater in PD group than in HC group (p < 0.05). In addition, the difference in coordination between each patient and the average HC group coordination significantly correlated with both disease duration and UPDRS-III scores, underlining the association with PD severity and progression (**Figure 2**).



**Figure 2.** Correlation analysis. (a) Correlation analysis between left heel strike coordination error and disease duration in PD patients. (b) correlation analysis between left heel strike coordination error and UPDRS III (unified pd rating scale – motor examination) score.

The chi-square test yielded a  $\chi^2 = 0.52$  with a *p*-value = 0.47, indicating that there is no significant difference in the lateralization of motor symptoms between the PD group and the control group.

The multivariate analysis yielded the following results (Table 2):

Disease duration ( $\beta_1 = 0.12$ , p = 0.02): The positive coefficient indicates that, with the increase in disease duration, there is a higher likelihood of motor symptoms being lateralized to the left, controlling for other factors. The significance of the *p*-value (p = 0.02) suggests that this factor is statistically significant.

Medications taken ( $\beta_2 = 0.15$ , p = 0.71): The positive coefficient suggests that patients who take Levodopa may have a higher likelihood of left lateralization compared to those who do not take it. However, the *p*-value (p = 0.71) is not significant, indicating that Levodopa use does not have a significant effect on motor symptom lateralization.

Comorbidities ( $\beta_3 = -0.23$ , p = 0.45): The negative coefficient suggests that patients with hypertension may have a lower likelihood of left-lateralized motor symptoms, but this effect is not significant (p = 0.45). Therefore, comorbidities do not appear to be a significant predictor for motor symptom lateralization.

Walking surface ( $\beta_4 = -0.10$ , p = 0.79): The negative coefficient suggests that walking on an inclined surface may reduce the likelihood of left-lateralized symptoms, but again, the *p*-value (p = 0.79) indicates that this effect is not significant.

		5	
Variable	Coefficient ( <i>β</i> )	Standard Error (SE)	<i>p</i> -value
Intercept (β <sub>0</sub> )	-0.34	0.45	0.46
Disease duration	0.12	0.05	0.02*
Medication taken (Levodopa)	0.15	0.40	0.71
Comorbidities (Hypertension)	-0.23	0.30	0.45
Walking surface	-0.10	0.39	0.79

Table 2. Multivariate analysis.

#### 4. Discussion

This study aims to investigate the possible impairment of lower limbs coordination during heel strike phase in PD patients.

Initially, we compared the joint coordination matrices of patients with those of the control group. This comparison was carried out with meticulous attention to detail, using advanced statistical and computational methods. The matrices were carefully constructed to accurately represent the complex relationships between different joints during the gait cycle. Each element within the matrix corresponded to a specific aspect of joint movement, such as joint rotation timing, angular displacement magnitude, and relative forces exerted between joints. Through this comprehensive comparison, we were able to discern even the subtlest differences in joint coordination patterns. This analysis revealed a reduction in lower limb joint coordination during the heel strike phase in PD patients, compared to controls. Specifically, these alterations affected the left heel strike, involving all three joints of the left lower limb (ankle, knee and hip), and the ankle and hip of the right lower limb. In contrast, no changes were shown during right heel strike for both the right and left joints. The scientific literature indicates that PD leads to a reduction in the range of motion (ROM) of the lower limbs joints [30,31] and a decrease in coordination. Previous research has delved deep into understanding these phenomena. Researchers have used various techniques, including high - resolution motion capture systems and in - depth electromyography studies, to explore the underlying mechanisms. They have found that the reduction in ROM is not only due to muscle stiffness but also to changes in the neural signals that control joint movement [32]. The decrease in coordination is thought to be a result of disruptions in the complex neural networks that govern the synchronous movement of multiple joints. These disruptions can lead to a breakdown in the precise timing and force application required for smooth gait. Recent studies have observed how these motor alterations are closely linked to the clinical features of the disease. Sofuwa et al. [33], documented a significant reduction in the ROM of hip and ankle joints in PD patients compared to healthy controls, attributing this limitation primarily to muscle stiffness and alterations in neuromuscular control. This impairment negatively affects general motor function, increasing the risk of instability and falls.

Our results demonstrate a clear asymmetry, with a greater prevalence of coordination impairment in the left limb. This asymmetry was a particularly intriguing finding. We conducted additional analyses to rule out potential confounding factors, examining medical histories, disease duration, medications, and comorbidities, as well as environmental factors such as the walking surface on which they walked during the experiments. After careful consideration, we were confident that the observed

asymmetry was a characteristic feature of the motor deficits in PD patients. Specifically, the multivariate analysis indicated that disease duration is a significant predictor of motor symptom lateralization, with a positive effect suggesting a higher likelihood of left lateralization as the disease duration increases. Medications taken, comorbidities, and walking surface did not show a significant effect on motor symptom lateralization in patients with PD. In summary, disease duration is the only variable that had a significant impact on motor symptom lateralization, while other factors such as medications, comorbidities, and walking surface did not prove to be influential. It is worth emphasising that the PD group, as well as the group of healthy controls, consisted exclusively of right-handed individuals, and the patient group consisted of patients with left and right lateral impairment without showing a significant difference in the group. Our findings suggest that, although motor symptoms are present on both sides (left and right) in the PD group, there is no significant difference in the lateralization of symptoms when compared to the control group, with a p-value exceeding the threshold of 0.05. A possible explanation for this asymmetry could lie in the dominance of motor control associated with manual lateralisation [34]. Manual lateralization is a well - studied phenomenon in neuroscience [35–37]. In right - handed individuals, the neural pathways that control the dominant hand are also thought to have an impact on the control of the lower limbs. The left hemisphere of the brain, which is often more dominant in right - handed people for language and fine motor control of the right hand, may also play a role in coordinating the left leg's movements during gait. This may explain why the left leg, which serves a stabilizing role in walking for right - handed, is more affected in PD patients. Indeed, from a biomechanical point of view, in right-handed individuals, the left leg often plays a stabilising role during activities such as walking, acting as a pivot in order to maintain balance, whereas the right leg is mainly involved in propulsion and dynamic movements [38]. Consequently, the role of the left leg during the left heel strike is crucial to ensure stability during walking, requiring precise inter-articular coordination not only within the left limb, but also in synchrony with the contralateral limb. Furthermore, it is also notable that the absence of coordination deficits during right heel strike may reflect the relatively lower demands for stability placed on the left leg when acting as a swing limb in right-handed individuals. This may mean that, in PD patients, dysfunctions in motor control systems may compromise this stabilising function, leading to the deficits observed during the left heel strike [39].

According to Sadeghi et al., the dominance of one limb over another is the result of neurological specialization that reflects hemispheric asymmetry and contralateral motor control. Neurological specialization is a complex and fascinating area of study. Scientists have long been intrigued by how the brain's hemispheres develop distinct functions. Through a combination of genetic programming and environmental influences during development, the left and right hemispheres of the brain take on different roles [40]. In the context of motor control, the left hemisphere typically controls the right side of the body and vice versa. This contralateral arrangement is a fundamental aspect of human movement regulation. Hemispheric asymmetry, which is observable in various cognitive and motor functions, plays a significant part in determining limb dominance. For example, in most right - handed individuals, the left hemisphere is more dominant in fine motor control tasks [41]. This asymmetry is not only limited to the upper limbs but also extends to the lower limbs, as Sadeghi et al. pointed out. The left leg, despite being less mobile in some respects compared to the right leg in right - handers, has a unique role in postural stabilization due to these neurological underpinnings. This asymmetry might be relevant for understanding why the left leg, despite being less dominant in terms of mobility, plays a crucial role in postural stabilization in right-handers [42].

Although our results show a general reduction in lower-limb coordination, the study also shows an increase in coordination between the right and left knee in the PD group compared to the HC group. When we first analyzed the data, this increase in knee coordination was a rather unexpected finding. We carefully re - examined the data collection process to ensure its accuracy. We double - checked the calibration of the motion - tracking devices and the reliability of the data analysis algorithms. After confirming the validity of the result, we delved into possible explanations. The increase in knee coordination seemed to be a distinct compensatory mechanism emerging in PD patients. To further understand this, we compared our findings with other related studies on movement adaptation in neurological disorders. The increase in knee coordination during the heel strike in the PD compared to the HC group could be explained as a compensatory mechanism. The reduction of the range of motion (ROM), particularly of the ankle, a fact now widely confirmed in the literature, seems to lead both knees to a slight simultaneous flexion, probably to absorb the impact and maintain postural stability [43]. The ankle, being a key joint in gait, is highly sensitive to the effects of Parkinson's disease. The reduced ROM in the ankle is a consequence of multiple factors, including muscle stiffness, altered neural signaling, and joint degeneration. As the ankle's ability to move freely is compromised, the body needs to find alternative ways to manage the forces generated during walking. The simultaneous flexion of both knees serves as a crucial adaptation. When the heel strikes the ground, the knees flex in tandem to cushion the impact. This is similar to how a shock - absorber system in a vehicle works. By flexing, the knees can distribute the force more evenly across the lower limb, reducing the stress on other joints and soft tissues. This coordinated movement also helps in maintaining the body's center of mass, which is essential for postural stability. This coordinated flexion could reduce the joint excursion required of other structures, ensuring a more efficient movement. It is also widely demonstrated that PD patients exhibit a general flexion of the joints, which could induce this coordinated flexion during a delicate phase such as the heel strike [44]. However, this interpretation remains speculative, as there are currently no data in the literature directly confirming or refuting this hypothesis. The scientific community has been actively exploring the mechanisms underlying Parkinson's disease, yet this particular aspect of knee compensation in the context of reduced joint range of motion remains a grey area. However, the specific compensatory role of the knees in such a nuanced scenario has somehow slipped through the cracks of existing research efforts. Without direct evidence from previous studies, our proposed interpretation is based on a combination of biomechanical reasoning, observed patterns in our data, and an understanding of how the body typically adapts to motor impairments. We are essentially treading on uncharted territory, and while our hypothesis seems plausible, it urgently requires validation through dedicated research. It remains necessary to investigate the compensatory role of the knees in conditions of reduced joint ROM with specific studies. These findings suggest that the observed deficits are not limited to individual joints but reflect a more systemic impairment in motor control. Moreover, the severity of these coordination errors was significantly correlated with both disease duration and UPDRS-III scores, underscoring the association between motor impairments, PD progression, and symptom severity. The UPDRS-III is a well-established tool for assessing the motor symptoms of PD. By correlating the coordination error values with the UPDRS-III scores and disease duration, we were able to draw a clear line between the worsening of motor control and the progression of the disease. As the disease progresses over time, the loss of dopaminergic neurons accumulates, leading to more severe motor impairments. The coordination errors, which are a manifestation of these impairments, become more pronounced. This correlation not only validates our findings but also provides valuable insights for clinicians. It can help them better predict the progression of the disease in individual patients and adjust treatment plans accordingly. Furthermore, in order to assess the level of impairment of coordination in the PD group compared to the HC group, we calculated a Coordination Error value, defined as the difference between each patient's coordination value with the mean of the control group's coordination value), and correlated these Coordination Error values with the UPDRS III motor scores and disease duration. The calculation of the Coordination Error value was a meticulous process. First, we had to ensure the accuracy of the coordination values obtained from both the PD and HC groups. This involved carefully calibrating the motion - tracking equipment and validating the data analysis algorithms. Once we had reliable coordination values, we subtracted the mean coordination value of the control group from each patient's coordination value in the PD group. This gave us a numerical representation of how much each PD patient's coordination deviated from the norm. We then entered these Coordination Error values into a statistical analysis software, along with the corresponding UPDRS III motor scores and disease duration data. The goal was to determine if there was a relationship between these variables, and if so, how strong it was. Correlation analysis showed that these values correlated positively with both (as shown in **Figure 2**). This result strengthens the data of this study, confirming that as each patient's Coordination Error increases, the UPDRS III score increases and the disease time increases.

This study has some limitations that need to be mentioned. Firstly, the examined sample is relatively reduced, which may limit the generalizability of the results. Future studies with a larger number of participants will be necessary to confirm the reported observations. Furthermore, the results regarding coordination during the heel strike phase should be compared with other phases of the gait cycle, in order to better understand motor coordination mechanisms within a more holistic overview of the movement. This analysis could reveal specific coordination patterns or significant differences between the various phases of the stride cycle.

#### **5.** Conclusion

This study reveals significant alterations in joint coordination of the lower limb joints during the gait cycle in patients with PD during the heel strike phase. In particular, the observed increase in coordination error, which correlates positively with both UPDRS III motor scores and disease duration, underlines the progressive impairment of motor coordination associated with PD. Exploring and understanding the alterations in joint coordination of the lower limbs during gait provides valuable insights into the biomechanical adaptations that occur in PD. These findings could serve as a basis for the development of targeted rehabilitation interventions aimed at improving gait quality, reducing the risk of falls, and improving the autonomy and quality of life of PD patients. By focusing on restoring joint coordination, rehabilitation strategies could more effectively support functional movement and overall mobility in people with PD.

Furthermore, this holistic approach provides a more comprehensive framework for the assessment of coordination during walking. It shifts the focus from viewing these disorders as isolated deficits within specific joints or segments to understanding them as the result of complex and dynamic interactions between various parts of the body. This perspective recognizes the integrated nature of movement and emphasises the importance of addressing the entire biomechanical system to develop more effective rehabilitation strategies.

Author contributions: Conceptualization, RM.; methodology, RM.; software, ETL. and FL; validation, PL and FPC.; formal analysis, ETL. and FL; investigation, FT; resources, FT; data curation, RM; writing—original draft preparation, RM; writing—review and editing, FL; visualization, MM; supervision, FT; project administration, RM; funding acquisition, FT. All authors have read and agreed to the published version of the manuscript.

**Ethical approval:** The study was conducted in accordance with the Declaration of Helsinki and approved by the AORN "A. Cardarelli" Ethic Committee (protocol number: 00019628).

Conflict of interest: The authors declare no conflict of interest.

# References

- 1. Stocchi F, Barone P, Ceravolo R, et al. Advanced Parkinson's disease treatment patterns in Italy: an observational study interim analysis. Annals of Medicine. 2024; 56(1). doi: 10.1080/07853890.2024.2315226
- Zenesini C, Belotti LMB, Baccari F, et al. Validation of Administrative Health Data Algorithms for Identifying Persons with Parkinson's Disease and the 10-Year Prevalence Trend in Bologna, Italy. Neuroepidemiology. 2023; 57(5): 336-344. doi: 10.1159/000533362
- 3. Marini K, Seppi K, Kiechl S, et al. Comparison of different risk scores for Parkinson disease in a population-based 10-year study. European Journal of Neurology. 2023; 30(10): 3347-3352. doi: 10.1111/ene.15971
- 4. Bonato G, Antonini A, Pistonesi F, et al. Genetic mutations in Parkinson's disease: screening of a selected population from North-Eastern Italy. Neurological Sciences. 2024; 46(1): 165-174. doi: 10.1007/s10072-024-07690-7
- 5. Morris HR, Spillantini MG, Sue CM, Williams-Gray CH. The pathogenesis of Parkinson's disease. The Lancet. 2024; 403(10423): 293-304. doi: 10.1016/S0140-6736(23)01478-2
- Coukos R, Krainc D. Key genes and convergent pathogenic mechanisms in Parkinson disease. Nature Reviews Neuroscience. 2024; 25(6): 393-413. doi: 10.1038/s41583-024-00812-2
- 7. di Biase L, Di Santo A, Caminiti ML, et al. Gait Analysis in Parkinson's Disease: An Overview of the Most Accurate Markers for Diagnosis and Symptoms Monitoring. Sensors. 2020; 20(12): 3529. doi: 10.3390/s20123529
- 8. Romano A, Liparoti M, Minino R, et al. The effect of dopaminergic treatment on whole body kinematics explored through network theory. Scientific Reports. 2024; 14(1). doi: 10.1038/s41598-023-50546-x

- 9. Švehlík M, Zwick EB, Steinwender G, et al. Gait Analysis in Patients with Parkinson's Disease Off Dopaminergic Therapy. Archives of Physical Medicine and Rehabilitation. 2009; 90(11): 1880-1886. doi: 10.1016/j.apmr.2009.06.017
- Cioni M, Richards CL, Malouin F, et al. Characteristics of the electromyographic patterns of lower limb muscles during gait in patients with Parkinson's disease when OFF and ON L-Dopa treatment. The Italian Journal of Neurological Sciences. 1997; 18(4): 195-208. doi: 10.1007/bf02080464
- 11. Negida A, Altamimi FQ, Elsayed M, et al. Epidemiology and risk factors of Parkinson's disease. Essential Guide to Neurodegenerative Disorders; 2025.
- 12. Winter DA. Human balance and posture control during standing and walking. Gait & posture. 1995; 3(4): 193-214. doi: 10.1016/0966-6362(96)82849-9
- Saegner K, Romijnders R, Hansen C, et al. Inter-joint coordination with and without dopaminergic medication in Parkinson's disease: a case-control study. Journal of NeuroEngineering and Rehabilitation. 2024; 21(1). doi: 10.1186/s12984-024-01416-8
- 14. Günther M, Grimmer S, Siebert T, et al. All leg joints contribute to quiet human stance: A mechanical analysis. Journal of Biomechanics. 2009; 42(16): 2739-2746. doi: 10.1016/j.jbiomech.2009.08.014
- 15. Günther M, Putsche P, Leistritz L, et al. Phase synchronisation of the three leg joints in quiet human stance. Gait & Posture. 2011; 33(3): 412-417. doi: 10.1016/j.gaitpost.2010.12.014
- Chen L, Bedard P, Hallett M, et al. Dynamics of Top-Down Control and Motor Networks in Parkinson's Disease. Movement Disorders. 2021; 36(4): 916-926. doi: 10.1002/mds.28461
- Goetschalckx M, Moumdjian L, Feys P, et al. Interlimb coordination and spatiotemporal variability during walking and running in children with developmental coordination disorder and typically developing children. Human Movement Science. 2024; 96: 103252. doi: 10.1016/j.humov.2024.103252
- 18. Ravi D. A recommendation of 'Interlimb coordination in Parkinson's Disease is minimally affected by a visuospatial dual task.' Peer Community In Health and Movement Sciences; 2024.
- 19. Li C, Chen X, Zhang X, et al. Research on the electromyography-based pattern recognition for inter-limb coordination in human crawling motion. Frontiers in Neuroscience. 2024; 18. doi: 10.3389/fnins.2024.1349347
- 20. Chung JW, Bower AE, Malik I, et al. fMRI changes during multi-limb movements in Parkinson's disease. Frontiers in Human Neuroscience. 2023; 17. doi: 10.3389/fnhum.2023.1248636
- 21. Perry J. Gait Analysis: Normal and Pathological Function, Second Edition, 2nd ed. SLACK, Incorporated; 2010.
- 22. Louie KH, Lu C, Abdallah T, et al. Gait phase triggered deep brain stimulation in Parkinson's disease. Brain Stimulation. 2021; 14(2): 420-422. doi: 10.1016/j.brs.2021.02.009
- 23. Zhang X, Fan W, Yu H, et al. Single- and dual-task gait performance and their diagnostic value in early-stage Parkinson's disease. Frontiers in Neurology. 2022; 13. doi: 10.3389/fneur.2022.974985
- 24. Wu Z, Jiang X, Zhong M, et al. Mild Gait Impairment and Its Potential Diagnostic Value in Patients with Early-Stage Parkinson's Disease. Soto H, ed. Behavioural Neurology. 2021; 2021: 1-8. doi: 10.1155/2021/6696454
- 25. Zhu S, Wu Z, Wang Y, et al. Gait Analysis with Wearables Is a Potential Progression Marker in Parkinson's Disease. Brain Sciences. 2022; 12(9): 1213. doi: 10.3390/brainsci12091213
- 26. Alcock L, Galna B, Perkins R, et al. Step length determines minimum toe clearance in older adults and people with Parkinson's disease. Journal of Biomechanics. 2018; 71: 30-36. doi: 10.1016/j.jbiomech.2017.12.002
- 27. Ghislieri M, Agostini V, Rizzi L, et al. Atypical Gait Cycles in Parkinson's Disease. Sensors. 2021; 21(15): 5079. doi: 10.3390/s21155079
- 28. Davis RB, Õunpuu S, Tyburski D, Gage JR. A gait analysis data collection and reduction technique. Human Movement Science. 1991; 10(5): 575-587. doi: 10.1016/0167-9457(91)90046-Z
- Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. Journal of the Royal Statistical Society Series B: Statistical Methodology. 1995; 57(1): 289-300. doi: 10.1111/j.2517-6161.1995.tb02031.x
- Sande de Souza, L. A. P., Nascimento, M. B., Souza dos Santos, A., & Dionisio, V. C. (2024). Motor Control in Parkinson's Disease During the Performance of Multi-Joint Reversal Movements. Journal of Motor Behavior, 56(5), 533-544. doi: 10.1080/00222895.2024.2350723
- 31. Raiola G, Lipoma M, Tafuri D. Postural control in young soccer players: differences between the cognitive approach and ecological-dynamic one. Journal of Human Sport and Exercise. 2015; 10(Proc1). doi: 10.14198/jhse.2015.10.proc1.29

- 32. Zanardi APJ, da Silva ES, Costa RR, et al. Gait parameters of Parkinson's disease compared with healthy controls: a systematic review and meta-analysis. Scientific Reports. 2021; 11(1). doi: 10.1038/s41598-020-80768-2
- Sofuwa O, Nieuwboer A, Desloovere K, et al. Quantitative Gait Analysis in Parkinson's Disease: Comparison With a Healthy Control Group. Archives of Physical Medicine and Rehabilitation. 2005; 86(5): 1007-1013. doi: 10.1016/j.apmr.2004.08.012
- 34. Lin Z, Zhang C, Li D, et al. Lateralized effects of deep brain stimulation in Parkinson's disease: evidence and controversies. npj Parkinson's Disease. 2021; 7(1). doi: 10.1038/s41531-021-00209-3
- 35. Gan C, Wang L, Ji M, et al. Abnormal interhemispheric resting state functional connectivity in Parkinson's disease patients with impulse control disorders. npj Parkinson's Disease. 2021; 7(1). doi: 10.1038/s41531-021-00205-7
- 36. Roussakis AA, Zeng Z, Lao-Kaim NP, et al. Parkinson's disease laterality: a 11C-PE2I PET imaging study. Journal of Neurology. 2020; 268(2): 582-589. doi: 10.1007/s00415-020-10204-y
- 37. Mundorf A, Ocklenburg S. The Clinical Neuroscience of Lateralization. Routledge; 2021.
- 38. Sadeghi H, Allard P, Prince F, Labelle H. Symmetry and limb dominance in able-bodied gait: A review. Gait & Posture. 2000; 12(1): 34-45. doi: 10.1016/S0966-6362(00)00070-9
- 39. Camargo CHF, Ferreira-Peruzzo SA, Ribas DIR, et al. Imbalance and gait impairment in Parkinson's disease: discussing postural instability and ataxia. Neurological Sciences. 2023; 45(4): 1377-1388. doi: 10.1007/s10072-023-07205-w
- 40. Takakusaki K, Takahashi M, Noguchi T, et al. Neurophysiological mechanisms of gait disturbance in advanced Parkinson's disease patients. Neurology and Clinical Neuroscience. 2022; 11(4): 201-217. doi: 10.1111/ncn3.12683
- Bohnen NI, Costa RM, Dauer WT, et al. Discussion of Research Priorities for Gait Disorders in Parkinson's Disease. Movement Disorders. 2021; 37(2): 253-263. doi: 10.1002/mds.28883
- 42. Qadir RMAB, Hassan A, Buttar TUR, et al. Microinstability of Major Joints in Movement Disorders: The Hidden Challenge. Cureus. 2024; 16(10): e71449. doi: 10.7759/cureus.71449
- 43. Pinto C, Salazar AP, Hennig EM, et al. Dual-task walking reduces lower limb range of motion in individuals with Parkinson's disease and freezing of gait: But does it happen during what events through the gait cycle? McKay JL, ed. PLOS ONE. 2020; 15(12): e0243133. doi: 10.1371/journal.pone.0243133
- 44. Mangalam M, Kelty-Stephen DG, Seleznov I, et al. Older adults and individuals with Parkinson's disease control posture along suborthogonal directions that deviate from the traditional anteroposterior and mediolateral directions. Scientific Reports. 2024; 14(1). doi: 10.1038/s41598-024-54583-y