ANADOLU UNIVERSITY
FACULTY OF PHARMACY

European Journal of Life Sciences 2025; 4(2): 84-93

Research Article

Evaluation of functional movement parameters of Parkinson`s patients during ON and OFF states of dopaminergic medication

Ismail Bayram[1,2,3]

[1]Dresden Technical University, Faculty of Psychology, Psychology of Learning and Instruction, Dresden, Germany
[2]Dresden Technical University, Centre for Tactile Internet with Human in the Loop (CeTI), Dresden, Germany
[3]Istanbul Rumeli University, Faculty of Sport Sciences, Department of Coaching Training, Istanbul, Türkiye

Ismail Bayram
ismail.bayram@tu-dresden.de

https://doi.org/10.55971/EJLS.1727347

Received: 25.06.2025
Accepted: 17.08.2025
Available online: 31.08.2025

ABSTRACT

Parkinson`s Disease is a progressive neurodegenerative disease affecting sensory-motor systems and decreasing patients` quality of life. This study aims to find a sophisticated method for detecting characteristics of patients and comparing gait, balance and tremors between the ON and OFF periods. The data provided by the Xsens (Movella) company belongs to 3 anonymous patients, and the content is unique for all 3 patients since they were unable to perform the same movement patterns due to different disease severity. Their descriptive information was not provided due to patient privacy. Tremor, gait and balance assessments were asked to be performed via preferred approaches and methods by using MVN Analyze Software. Kinematic improvements were detected in gait parameters such as cadence (step/min), the number of steps, speed (m/s), total distance (m), stride and length. The provided data shows that patients have some difficulties during turns and initiation of gait (freezing gait). It accompanies a delay in the first step at the beginning of the gait and after turns as well. For the tremor assessment, a heat map was generated based on the magnitude and frequency of the tremors. Both the magnitude and frequency of the tremors were smaller under the dopaminergic medication (ON: amplitude:4.99 cm frequency:4.04 Hz; OFF: amplitude:7.78 cm frequency:5.17 Hz). We were unable to assess the balance due to time limitations. Most of the parameters show an improvement in gait and tremors during the ON period. Results are important in terms of individualization of drug intake time and dosage.

Keywords: Drug therapy, inertial measurement units, motion analyses, Parkinson´s disease

1. INTRODUCTION

Parkinson`s Disease (PD) is a progressive neurodegenerative disease affecting sensory-motor systems and significantly reducing patients' quality of life. The global burden of PD has grown substantially in recent decades, and the ambiguity in the data makes it difficult to assess PD´s global impact accurately. According to the World Health Organization, current estimates indicate that PD accounted for 5.8 million disability-adjusted life years and 329,000 deaths in 2019, representing increases of 81% and over 100%, respectively, since 2000 [1].

Levodopa is currently the dominant treatment for PD. Johansen et al. [2] reported more than 30% movement improvement in the ON state of dopaminergic medication. As PD advances, this therapy´s effectiveness diminishes, which causes

motor dysfunction and eventually requires the dose adjustment of levodopa to ensure appropriate motor functioning. Clinicians have found it difficult to pinpoint the best dosage of Levodopa since symptom responsiveness to Levodopa is variable due to disease severity and unique neurological differences among those with PD [3, 4].

Levodopa, while effective, is also associated with long-term complications, including motor fluctuations and dyskinesias [5, 6]. With the advancement of the disease and prolonged disease duration, some functional movement patterns of daily life connected to PD do not appear to react well to levodopa (or other dopaminergic medications) or seem to develop a resistance [4]. One possible explanation for this is the potential for pseudo-resistance, a phenomenon that describes dopamine-sensitive symptoms or signs appearing resistant to levodopa, despite other mechanisms causing inadequate dopaminergic efficacy [7]. These mechanisms may involve impaired gastrointestinal absorption, delayed stomach emptying, interactions with other medications, or inconsistent medication intake. Each of these can lower the amount of levodopa that reaches the brain, creating the appearance of resistance even though the drug itself remains effective. This confusing stage of the disease could be derived from the existence of particular motor and nonmotor PD symptoms that necessitate a substantially higher/lower levodopa dosage to be effective [8]. It is advised that patients should be prescribed a personalised medication dosage and time to manage these symptoms, which a neurological specialist can further standardise within the clinic [9].

However, PD drug development faces significant challenges due to the absence of definitive markers for tracking disease progression, which complicates the design and evaluation of effective treatments [10]. Moreover, even when individuals and their conditions are carefully assessed, the symptoms may manifest differently in the clinic than in their everyday life [11]. This is particularly important, as the neural control of many daily activities is governed by unconscious mechanisms, such as those controlled by the cerebellum [12], while more complex motor skills are developed through extensive practice [13]. Traditional clinical assessments, such as the Movement Disorders Society-Unified Parkinson`s Disease Rating Scale (MDS-UPDRS), are inherently subjective and conducted in clinical settings, potentially misrepresenting a patient`s actual functionality in real-world scenarios [10]. These conventional methods often fail to capture the subtle, subclinical changes in a patient`s condition and heavily rely on the patient`s recall, which can be particularly problematic as cognitive functions decline with disease progression [14]. Moreover, not all sufferers can accurately describe to the specialist how severe their symptoms are, and some patients are experiencing a special condition called “Levadopa phobia”, resulting in suboptimal control of the disease [15].

Therefore, it would be very beneficial if the symptoms could be objectively measured in a home environment, preferably for a longer period during daily activities. With this purpose in mind, the Department of Psychology, Health and Technology started a research project in the E-Health house at the University of Twente, measuring PD patients during a full day. The Xsens company launched a challenge in an attempt to find a way to guide PD patients about when and how much medication is needed based on Inertial Measurement Units (IMU) data. The goals of this challenge were to find a method to detect characteristic features of patients with Parkinson`s and compare those between the ON and OFF periods. The study focuses on the use of wearable IMU sensor technology to objectively quantify functional movement parameters in individuals with Parkinson`s disease, comparing their performance during the “ON” and “OFF” medication states. Wearable and digital health technologies have gained considerable international attention in recent years for their potential to provide objective, continuous, and ecologically valid assessments of motor symptoms in PD [9, 14]. Building on this growing body of research, our study applies a targeted IMU-based approach to assess medication-related motor performance differences in PD.

2. MATERIALS AND METHODS

The Xsens Biomechanics Challenge was announced at the beginning of March 2022. People were free to participate as individuals or as research/lab groups. After closing the registration on 20th April, people registered as individuals were informed that they could be matched with other individuals and create teams both for the current challenge and for future collaborations. The next day the case files were released and they included a prize delivery agreement, MDS-UPDRS, a case study document explaining project outputs, practicalities etc., and a data file with recordings belonging to 3 anonymous patients (P08, P21, P46). Teams worked on the files based on the explanations, and a Technical Training and Q&A Session was organised on 28th April. The 6th of May was the project delivery date, and after careful and detailed evaluation, selected teams presented their approach and findings on the 19th of May (**Figure 1**).

2.1. Project Flow and Parameters

The project outputs were based on three pillars as 1) Tremor, 2) Balance and 3) Gait assessments. The outputs demanded for tremor analysis were detecting tremors, defining characteristics of tremors in the kinematic data, and finding the differences in tremors between ON and OFF periods. During the first half of the day, the patients are without medication (OFF period) and are asked to perform a collection of daily tasks (e.g., ~10 m walk, sit-to-stand, sitting, lie down in bed, turning) in the house. At lunchtime, the patients take their medication (ON period) and continue in the house doing some more tasks in the afternoon. The outputs demanded for balance analysis were analysing balance, detecting when the patients were out of balance, and detecting differences in balance between the ON and OFF periods. Lastly, the outputs demanded for gait analysis were analysing gait and finding differences in gait parameters between the ON and OFF periods.

Data recorded using a triaxial Xsens IMU system (MTw Awinda, Movella/Xsens Technologies B.V., Enschede, Netherlands) comprising an accelerometer, gyroscope, and magnetometer with factory calibration and onboard sensor fusion. Sensors were affixed to the whole body with an Awinda full-body strap set to minimize motion artefacts. Data were sampled at 100 Hz and streamed wirelessly to the Xsens Awinda Station using the Xsens software suite.

A description of the methodology used to compute each parameter, background material to support the assumptions and calculations, and finally, the clinical relevance of the various conclusions derived from the findings was required for each of the parameters indicated above. When choosing the final projects, all of these considerations were taken into account by the evaluation committee.

2.2. Data Analysis

The data analysed in this challenge was provided by the Xsens (Movella) company. It belongs to 3 unanimous patients, and the content is not the same for all 3 patients since they were unable to perform the same movement patterns due to disease severity. Their descriptive information, such as age, height, weight, and laterality, has not been provided to keep them anonymous. For the tremor assessment, a custom-made signal analysis tool was developed in MATLAB (R2023a, MathWorks, USA) to process the acceleration data. The tool applied a 4th-order zero-lag Butterworth band-pass filter (3–15 Hz)

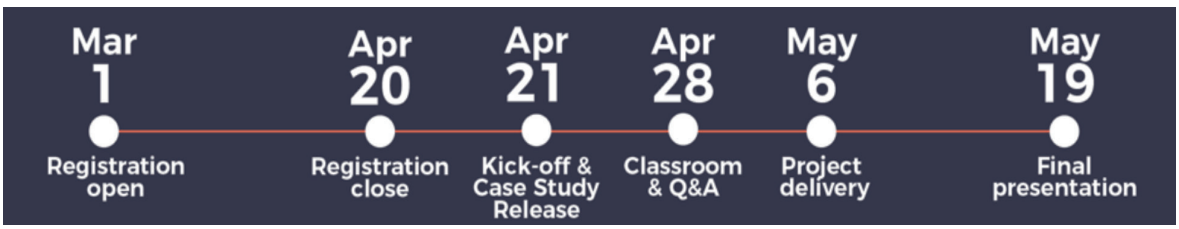

Figure 1. Timeline of the challenge from registration to final.

to isolate the tremor frequency range, followed by Fast Fourier Transform (FFT) to compute the power spectral density. Tremor amplitude was quantified as the peak power within the dominant frequency band. The tool was not formally validated, as the data collection system was not available to us for independent measurements, preventing comparison with data from healthy participants. For the gait assessment, the gait reports for patient P21 provided by the company have been used to assess any difference between ON and OFF states. Even though balance is such an important motoric feature, its assessment was not able to be performed since the data and MVN Analysis Software were provided for just 2 weeks.

3. RESULTS

Spatiotemporal gait parameters between the OFF and ON stages of dopaminergic medication revealed several notable improvements in gait performance and symmetry during the ON stage for the participant. Visual inspection of the provided data revealed that all three PD patients were having some difficulties during turns and initiation of gait. Most of the gait parameters of patient P21 differed between ON and OFF situations, as indicated in Table 1. Initiation of gait is a difficult task for PD patients. It accompanies a delay in the first step at the beginning of the gait and after turns as well.

General gait performance of the participant was enhanced during the ON stage, as indicated by a higher cadence (94.88 vs. 92.63 steps/min), increased speed (0.92 vs. 0.86 m/s), and a longer total distance covered (27.11 vs. 25.76 m). These improvements were accompanied by a reduction in the number of steps (18 vs. 22) and total walking duration (11.38 vs. 14.25 s), indicating a more efficient gait pattern under dopaminergic influence.

Stride lengths for both the left and right limbs increased significantly during the ON stage (Left: 116.87 ± 11.47 cm vs. 109.69 ± 12.47 cm; Right: 115.50 ± 12.10 cm vs. 108.65 ± 13.04 cm). Similarly, step length on the right improved significantly (56.33 ± 5.67 cm vs. 47.79 ± 7.59 cm), while the left step length remained comparable across conditions.

The gait cycle durations slightly decreased for both limbs in the ON stage (Left: 1.27 ± 0.15 s; Right: 1.27 ± 0.16 s), with a statistically significant reduction in left-side duration. The participant showed a shift in step time distribution: while the right step duration decreased significantly (0.63 ± 0.08 s vs. 0.69 ± 0.11 s), the left increased, leading to a more symmetrical step timing (difference reduced from -0.09 s to 0.02 s).

The ON stage induced a significant reorganization of gait phase durations. Notably, the swing phase duration decreased bilaterally (Left: 0.48 ± 0.04 s vs. 0.55 ± 0.07 s; Right: 0.48 ± 0.05 s vs. 0.50 ± 0.05 s), while the stance phase increased (Left: 0.79 ± 0.11 s vs. 0.74 ± 0.09 s; Right: 0.80 ± 0.12 s vs. 0.78 ± 0.14 s), suggesting a more stable gait pattern. Similarly, the single support phase durations decreased, whereas double support phase durations increased significantly (Total: 0.32 ± 0.08 s vs. 0.23 ± 0.05 s; %: 25.11 ± 4.01 vs. 18.01 ± 2.57), further reinforcing the observation of increased stability.

The loading response phase duration increased bilaterally during the ON stage (Left: 0.17 ± 0.03 s vs. 0.09 ± 0.03 s; Right: 0.15 ± 0.04 s vs. 0.13 ± 0.04 s), reflecting a more controlled initial contact and weight acceptance. There were minor changes in midstance, terminal stance, and pre-swing durations, with slight reductions in terminal stance times during the ON stage.

Overall, the gait pattern in the ON stage showed improved spatial symmetry (e.g., stride length and step width differences reduced) and temporal symmetry (e.g., equalized gait cycle times). These changes suggest that dopaminergic medication positively influenced the coordination and efficiency of gait in this participant.

For the tremor assessment, a heat map was generated based on the magnitude and frequency of the tremors. Both the magnitude and frequency of the tremors were smaller under the dopaminergic medication (ON: amplitude:4.99 cm, frequency: 4.04 Hz; OFF: amplitude:7.78 cm, frequency: 5.17 Hz).

Table 1. Gait parameters of patient P21 between the ON and OFF stages of dopaminergic medication

PARAMETERS*	OFF	ON
Cadence (step/min)	92.63	94.88
Duration (s)	14.25	11.38
Number of Steps	22	18
Speed (m/s)	0.86	0.92
Total distance (m)	25.76	27.11
Stride Length Left (cm)	109.69 ± 12.47	116.87 ± 11.47
Stride Length Right	108.65 ± 13.04	115.50 ± 12.10
Difference	1.04 (0.95%)	1.37 (1.17%)
Step Length Left (cm)	61.01 ± 6.48	60.81 ± 7.06
Step Length Right	47.79 ± 7.59	56.33 ± 5.67
Difference	13.22 (21,66%)	4.48 (7,36%)
Gait Cycle Left (s)	1.29 ± 0.16	1.27 ± 0.15
Gait Cycle Right	1.30 ± 0.20	1.27 ± 0.16
Difference	-0.01	0
Step Left (s, %)	0.60 ± 0.06 (46.68 ± 2.48)	0.65 ± 0.08 (51.62 ± 2.46)
Step Right	0.69 ± 0.11 (53.15 ± 3.02)	0.63 ± 0.08 (49.76 ± 2.88)
Difference	-0.09 s %-6.47	0.02 1.86
Swing Phase Left (s, %)	0.55 ± 0.07 (42.68 ±3.09)	0.48 ± 0.04 (38.23 ± 4.19)
Swing Phase Right	0.50 ± 0.05 (39.26±4.76)	0.48 ± 0.05 (38.35±5.03)
Difference	0.05 s %3.42	0 -0.12
Stance Phase Left (s, %)	0.74 ± 0.09 (57.51 ± 1.72)	0.79 ± 0.11 (62.52 ± 2.30)
Stance Phase Right	0.78 ± 0.14 (60.06 ± 2.90)	0.80 ± 0.12 (62.58 ± 3.30)
Difference	-0.04 s %-2.56	0 -0.07
Single Support Phase Left (s, %)	0.50 ± 0.05 (39.16 ± 3.11)	0.48 ± 0.05 (38.25 ± 2.75)
Single Support Phase Right	0.55 ± 0.07 (42.67 ± 3.42)	0.48 ± 0.04 (38.02 ± 2.61)
Difference	-0.05 s %-3.51	0 0.23
Double Support Phase Left (s, %)	0.09 ± 0.03 (7.52 ± 1.97)	0.17 ± 0.03 (13.36 ± 1.90)
Double Support Phase Right	0.13 ± 0.04 (10.48 ± 1.59)	0.15 ± 0.04 (11.74 ± 2.36)
Difference	-0,04 s %-2.96	0.02 1.63
Double Support Phase Total	0.23 ± 0.05 (18.01 ± 2.57)	0.32 ± 0.08 (25.11±4.01)
Loading Response Left (s, %)	0.09 ± 0.03 (7.52 ± 1.97)	0.17 ± 0.03 (13.36 ± 1.90)
Loading Response Right	0.13 ± 0.04 (10.48 ± 1.59)	0.15 ± 0.04 (11.74 ± 2.36)
Difference	-0.04 s %-2.96	0.02 1.63
Midstance Left (s. %)	0.21 ± 0.01 (17.04 ± 2.14)	0.22 ± 0.00 (17.75 ± 1.88)
Midstance Right	0.22 ± 0.00 (17.40 ± 2.71)	0.19 ± 0.04 (15.75 ± 4.07)
Difference	0 s %-0.36	0.03 s % 2
Terminal Stance Left (s. %)	0.28 ± 0.04 (22.12 ± 2.39)	0.26 ± 0.04 (20.50 ± 1.83)
Terminal Stance Right	0.33 ± 0.07 (25.26 ± 2.92)	0.28 ± 0.06 (22.27 ± 3.09)
Difference	-0.04 s % -15.36	-0.02 -9.11
Pre-swing Left (s. %)	0.14 ± 0.04 (10.82 ± 2.16)	0.14 ± 0.03 (10.89 ± 1.67)
Pre-swing Right	0.14 ± 0.04 (10.82 ± 2.16)	0.14 ± 0.03 (10.89 ± 1.67)
Difference	0.05 s % 3.92	-0.03 s %-1.93

*Since the data presented in this table pertain to a single participant (P21), no statistical analysis was conducted. The values are provided to illustrate individual changes in gait parameters between the OFF and ON stages of dopaminergic medication and should be interpreted descriptively.

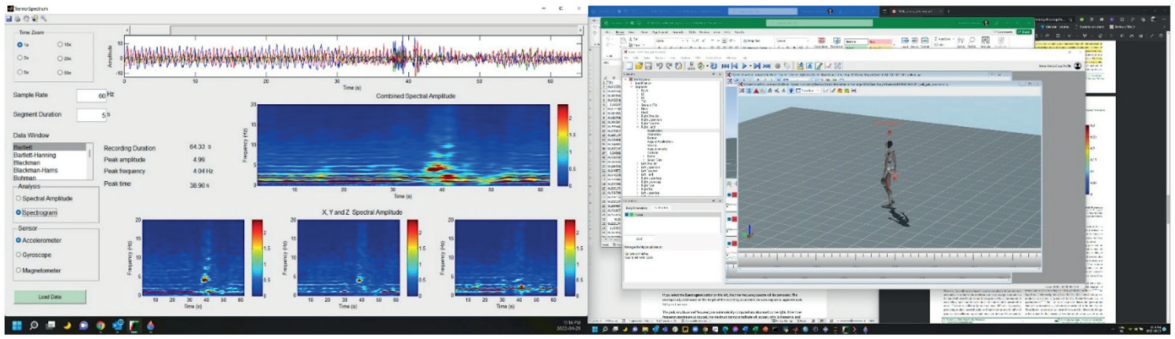

Figure 2. Magnitude and frequency of the tremors during ON stage of dopaminergic medication for patient P21.

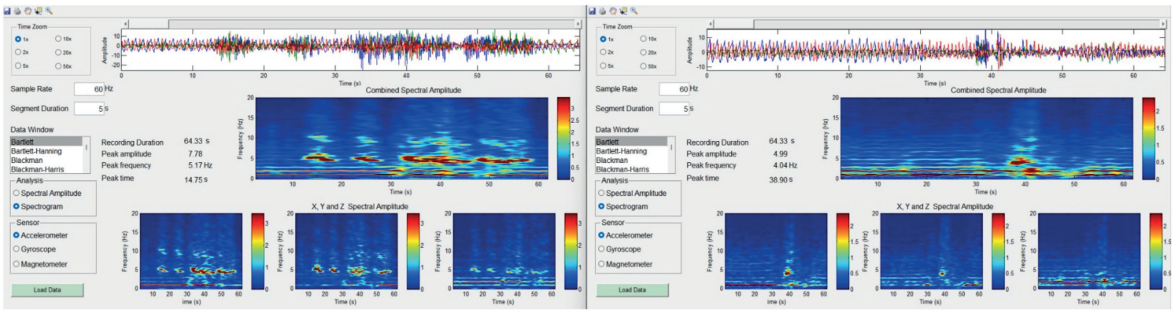

Figure 3. Magnitude and frequency of the tremors during OFF stage of dopaminergic medication for patient P21.

4. DISCUSSION

The goals of this study were to find a method to detect characteristic features of patients with PD and compare those between the ON and OFF periods. From a wider perspective, it is aimed to create an individual dose arrangement approach based on big movement data provided by IMU sensors. Even though Xsens company provided MVN Analysis Software for a limited time, participants were free to perform analyses via various tools (i.e., MATLAB, C++, Python). The approaches also varied, including machine learning, big data and artificial intelligence applications.

Most of the gait parameters were better when the patient was under the effect of dopaminergic medication, proving the effectiveness of the drug. Cadence, speed, and total distance were all greater during the ON stage, and the number of steps and total walking time were reduced as well, which suggests a more effective gait [16]. Patients with PD frequently exhibit gait abnormalities, which can be quantitatively evaluated using wearable accelerometers that track gait and postural sway [17]. These devices offer a practical method for objectively tracking how PD develops and how well treatments work [18]. Gait parameters improved markedly during the ON stage of dopaminergic medication, as evidenced by increased stride and step lengths, more symmetrical and efficient step timing, shortened gait cycle durations, enhanced stability through longer stance and double support phases, and a more controlled loading response, collectively indicating a more stable, coordinated, and efficient gait pattern.

Moreover, medication-induced improvements were observed in various gait parameters, including cadence, step count, speed, total distance, stride length, and step width, which aligns with the understanding that dopaminergic medication can enhance motor function in PD patients [19]. A prior study showed that Levodopa can increase gait pace, though postural stability may not improve during walking [20]. The observed improvements in stride length and step width during the ON period suggest that dopaminergic medication can positively influence the spatial aspects of gait, potentially leading to more stable and coordinated movements [21]. These results

are consistent with the established understanding that levodopa can enhance motor function in individuals with PD, particularly in alleviating bradykinesia and rigidity, which directly impact gait kinematics [22]. Initiation of gait is a complex motor task that is frequently impaired in individuals with Parkinson's disease, often manifesting as a delay in the first step and difficulties in initiating movement after turns [23]. The participant`s gait became more efficient and stable during the ON stage, highlighting the therapeutic value of medication in improving motor function in Parkinsonian gait.

Additionally, the magnitude and frequency of the tremors were both smaller under the dopaminergic medication (ON: a:4.99 cm f:4.04 Hz; OFF: a:7.78 cm f:5.17 Hz) in our study, which proved the effectiveness of the medication on tremor reduction. PD is characterized by a heterogeneous presentation, where some individuals exhibit prominent resting tremors while others do not, suggesting variability in the functional organization of the voluntary motor system [24].

The observed heterogeneity in PD underscores the importance of identifying markers that can track disease progression, facilitating personalized therapeutic strategies tailored to the advanced stages of the condition [25]. By using artificial intelligence tools and techniques, the researchers can potentially offer more personalised and effective treatments for PD, which is essential for improving the quality of life for individuals affected by this condition [26]. Advancements in understanding the neuropathology of PD and its molecular mechanisms have facilitated the development of new models and highly effective therapies [27]. However, the effectiveness of those therapies should also be tested on functional movement parameters of PD patients by using sophisticated data collection methods such as IMU [28-31].

The progressive nature of PD means that the benefits of treatments aimed at enhancing dopaminergic transmission, like levodopa, may reduce over time as symptoms worsen [32]. After 5–10 years of chronic L-DOPA therapy, several side effects are detected in most patients, reaching a point where the side effects are greater than the therapeutic benefits [29]. The prolonged use of levodopa is frequently associated with the emergence of motor complications, including fluctuations in motor response and the development of dyskinesias, which can significantly compromise gait patterns and postural control, thereby increasing the risk of falls and diminishing overall mobility [33]. These findings emphasize the importance of long-term data collection and evaluation.

The strength of the current study was the use of a comprehensive assessment of functional daily movement parameters in both ON and OFF medication states, allowing for a detailed comparison of the impact of dopaminergic medication on various aspects of motor function. Such observations highlight the critical role of optimized dopaminergic therapy in maintaining the functional independence and quality of life for individuals living with PD [34]. The combination of exercise therapy and movement strategy training has also demonstrated the potential to improve mobility, reduce falls risk, and enhance the quality of life for individuals with PD [35].

This study has several limitations that should be acknowledged. First, the data were obtained from only three anonymous individuals with PD, and no demographic or clinical information, such as age, sex, disease severity, or medication dosage, was available due to data protection constraints. This lack of contextual detail limits the interpretation of individual variability and prevents subgroup analyses that could have provided deeper insights into gait differences across disease stages. Additionally, no information was provided about the actual physical environment in which gait data were collected, which could have influenced some of the spatiotemporal parameters. The small sample size and absence of grouping possibilities restrict the generalizability of the findings, making it difficult to draw broad conclusions applicable to the wider PD population. Future studies with larger, well-characterized cohorts and controlled testing environments are needed to validate and expand upon these preliminary observations.

5. CONCLUSION

In conclusion, this challenge contributed to the creation of an open collaboration opportunity for many young researchers all around the world. It encourages the researchers to deal with a real-world problem by using sophisticated data analysis tools. Many data-driven parameters exhibited by different teams showed that dopaminergic medication positively affects the daily life of PD patients. However, the dosage and time of intake should be individualised precisely for each patient. Further research should be done to expand our results with more sophisticated methods such as big data, machine learning and artificial intelligence by including a larger sample size.

Acknowledgements

This study has been orally presented at the 1st Movement & Training Sciences Congress held by Fenerbahçe University in İstanbul, TÜRKİYE. The author would like to express his sincere appreciation to the participants who volunteered for the study and Xsens Company for organizing this challenge. The author also extends his gratitude to Jonathan Lyon Jacob Lommen for his valuable support in the data analysis phase of the study, despite his decision not to be listed as a co-author due to his non-academic career interests.

Ethical approval

Not applicable, because the data used in this article provided by the Xsens Company.

Author contribution

Conceptualization, I.B.; Methodology, I.B.; Software, I.B.; Validation, I.B.; Formal analysis, I.B.; Investigation, I.B.; Resources, I.B.; Data curation, I.B.; Writing—original draft preparation, I.B.; Writing—review and editing, I.B.; Visualization, I.B.; Supervision, I.B.; Project administration, I.B.; Funding acquisition, I.B. The author have read and agreed to the published version of the manuscript.

Source of funding

This study is partly funded by the German Research Foundation (DFG, Deutsche Forschungsgemeinschaft) as part of Germany`s Excellence Strategy – EXC 2050/1 – Project ID 390696704 – Cluster of Excellence “Centre for Tactile Internet with Human-in-the-Loop” (CeTI) of Technische Universität Dresden.

Conflict of interest

The author declares no conflict of interest. Although the data used in this study were provided by Xsens Company, the author has no financial or commercial relationship with the company, and no compensation or funding was received for conducting this research.

REFERENCES

1. World Health Organization (2022). Parkinson Disease: a Public Health Approach. Technical Brief. Retreived June 9, 2025 from https://www.who.int/publications/i/item/9789240050983
2. Silva S, Almeida AJ, Vale N. Importance of nanoparticles for the delivery of antiparkinsonian drugs. Pharmaceutics (2021);13:508. https://doi.org/10.3390/pharmaceutics13040508
3. Connolly BS, Lang AE. Pharmacological treatment of Parkinson disease. Jama (2014);311(16):1670-1683. https://doi.org/10.1001/jama.2014.3654
4. Malek N, Kanavou S, Lawton M, Pitz V, Grosset KA, Bajaj N, Barker RA, Ben-Shlomo Y, Burn DJ, Foltynie T, Hardy J, Williams N, Wood N, Morris HR, Grosset DG. L-dopa responsiveness in early Parkinson’s disease is associated with the rate of motor progression. Park Relat Disord. (2019);65:55-61. https://doi.org/10.1016/j.parkreldis.2019.05.022
5. Prasad EM, Hung S. Current therapies in clinical trials of Parkinson’s disease: a 2021 update. Pharmaceuticals. (2021);14(8):717. https://doi.org/10.3390/ph14080717
6. Chen JJ, Lew M, Siderowf A. Treatment strategies and quality-of-care indicators for patients with Parkinson’s disease. J Manag Care Spec Pharm. (2009);15(3 Supp A):1-22. https://doi.org/10.18553/jmcp.2009.15.s3.1
7. Vorovenci RJ, Biundo R, Antonini A. Therapy-resistant symptoms in Parkinson’s disease. J Neural Transm. (2016);123,19-30. https://doi.org/10.1007/s00702-015-1463-8

8. Nonnekes J, Timmer MHM, Vries NM de, Rascol O, Helmich RC, Bloem BR. Unmasking levodopa resistance in Parkinson's disease. J Mov Disord. (2016);31(11):1602-1609. https://doi.org/10.1002/mds.26712

9. Thomas I, Alam M, Bergquist F, Buvarp D, Memedi M, Nyholm D, Westin J. Sensor-based algorithmic dosing suggestions for oral administration of levodopa/carbidopa microtablets for Parkinson's disease: a first experience. J Neurol. (2019);266(3):651-658. https://doi.org/10.1007/s00415-019-09183-6

10. Khanna AJ, Adams J, Antoniades CA, Bloem BR, Carroll C, Cedarbaum JM, Cosman JD, Dexter DT, Dockendorf MF, Edgerton J, Gaetano L, Goikoetxea E, Hill D, Horak FB, Izmailova ES, Kangarloo T, Katabi D, Kopil C, Lindemann M, Mammen JR, Marek K, McFarthing K, Mirelman A, Müller MLTM, Pagano G, Peterschmitt M, Ren J, Rochester L, Sardar S, Siderowf A, Simuni T, Stephenson D, Swanson-Fischer C, Wagner JA, Jones GB. Accelerating Parkinson's disease drug development with federated learning approaches. npj Parkinsons Dis Nature Portfolio. (2024);10(1):225. https://doi.org/10.1038/s41531-024-00837-5

11. Jankovic J. Parkinson's disease: clinical features and diagnosis. J Neurol Neurosurg Psychiatry. (2008);79(4):368-376. https://doi.org/10.1136/jnnp.2007.131045

12. Ertan H, Bayram İ. Fundamentals of human movement, its control and energetics. In Comparative Kinesiology of the Human Body. London: Elsevier; (2020). p. 29-45. ISBN: 978-0-12-812162-7

13. Altan E, Seide SE, Bayram İ, Gizzi L, Ertan H, Röhrle O. A systematic review and meta-analysis on the longitudinal effects of unilateral knee extension exercise on muscle strength. Front Sports Act Living. (2020);2:518148. https://doi.org/10.3389/fspor.2020.518148

14. Stephenson D, Alexander R, Aggarwal V, Badawy R, Bain LJ, Bhatnagar R, Bloem BR, Boroojerdi B, Burton J, Cedarbaum JM, Cosman JD, Dexter DT, Dockendorf MF, Dorsey ER, Dowling AV, Evers LJW, Fisher K, Frasier M, Garcia-Gancedo L, Goldsack JC, Hill D, Hitchcock JM, Shulman J, Lawton MP, Lee SH, Lindemann M, Marek K, Mehrotra N, Meinders MJ, Minchik M, Oliva L, Romero K, Roussos G, Rubens R, Sadar S, Scheeren J, Sengoku E, Simuni T, Stebbins GT, Taylor KI, Yang B, Zach N. Precompetitive consensus building to facilitate the use of digital health technologies to support parkinson disease drug development through regulatory science. Digit Biomark. (2020);4(Suppl. 1):28–49. https://doi.org/10.1159/000512500

15. Titova N, Levin O, Katunina E, Chaudhuri KR. 'Levodopa Phobia': a review of a not uncommon and consequential phenomenon. npj Parkinsons Dis Nature Portfolio. (2018);4:31. https://doi.org/10.1038/s41531-018-0067-z

16. Rhyu HS, Rhi SY. The effects of training on different surfaces, on balance and gait performance in stroke hemiplegia. Rev Bras Med Esporte. (2021);27:592-596. https://doi.org/10.1590/1517-8692202127062020_0089

17. Fine AS, Kaufman ML, Goodman J, Turk BR, Bastian AJ, Lin D, Fatemi A, Keller J. Wearable sensors detect impaired gait and coordination in LBSL during remote assessments. Ann Clin Transl Neurol. (2022);9(4):468. https://doi.org/10.1002/acn3.51509

18. Pandis MFD, Tomino C, Proietti S, Rotondo R, Gaglione M, Casali M, Corbo M, Biase L di, Galli M, Goffredo M, Stocchi F. Mechanical peripheral stimulation for the treatment of gait disorders in patients with Parkinson's disease: a multi-centre, double-blind, crossover randomized controlled trial. J NeuroEng Rehabil. (2025);22:77. https://doi.org/10.1186/s12984-025-01574-3

19. Slevin JT, Gerhardt GA, Smith CD, Gash DM, Kryscio RJ, Young B. Improvement of bilateral motor functions in patients with Parkinson disease through the unilateral intraputaminal infusion of glial cell line—derived neurotrophic factor. J Neurosurg. (2005);102(2):216-222. https://doi.org/10.3171/jns.2005.102.2.0216

20. Mancini M, Afshari M, Almeida QJ, Huffmaster SLA, Balfany K, Camicioli R, Christiansen CL, Dale ML, Dibble LE, Earhart GM, Ellis TD, Griffith G, Hackney ME, Hopkins JO, Horak FB, Jones KE, Li L, O'Keefe JA, Kwei K, Olivier GN, Rao AK, Sivaramakrishnan A, Corcos DM. Digital gait biomarkers in Parkinson's disease: susceptibility/risk, progression, response to exercise, and prognosis. npj Parkinsons Dis Nature Portfolio. (2025);11:51. https://doi.org/10.1038/s41531-025-00897-1

21. Muñoz B, Valderrama J, Paredes JDA, Pino YJC, Navarro A, Orozco JL. Objective arm swing analysis in early-stage parkinson's disease using an rgb-d camera (Kinect®)1. J Parkinsons Dis. (2018);8(4):563-570. https://doi.org/10.3233/jpd-181401

22. Pieterman M, Adams S, Jog M. Method of levodopa response calculation determines strength of association with clinical factors in Parkinson disease. Front Neurol. (2018);9:260. https://doi.org/10.3389/fneur.2018.00260

23. Radder DLM, Lima ALS de, Domingos J, Keus SHJ, Nimwegen M van, Bloem BR, Vries NM de. Physiotherapy in Parkinson's disease: a meta-analysis of present treatment modalities. Neurorehabil Neural Repair. (2020);34(10):871-880. https://doi.org/10.1177/1545968320952799

24. Helmich RC, Bloem BR, Toni I. Motor imagery evokes increased somatosensory activity in parkinson's disease patients with tremor. Hum Brain Mapp. (2012);33:1763-1779. https://doi.org/10.1002/hbm.21318

25. Palermo G, Giannoni S, Bellini G, Siciliano G, Ceravolo R. Dopamine transporter imaging, current status of a potential biomarker: A comprehensive review. Int J Mol Sci. (2021);22(20):11234. https://doi.org/10.3390/ijms222011234

26. Islam MdS, Rahman W, Abdelkader A, Lee S, Yang PT, Purks JL, Adams J, Schneider RB, Dorsey ER, Hoque E. Using AI to measure Parkinson's disease severity at home. npj Digit Med. (2023);6:156. https://doi.org/10.1038/s41746-023-00905-9

27. Padilla-Godínez FJ, Ruiz-Ortega LI, Guerra-Crespo M. Nanomedicine in the face of Parkinson's disease: from drug delivery systems to nanozymes. Cells. (2022);11(21):3445. https://doi.org/10.3390/cells11213445

28. Lawton M, Ben-Shlomo Y, May M, Baig F, Barber TR, Klein J, Swallow DMA, Malek N, Grosset KA, Bajaj N, Barker RA, Williams N, Burn DJ, Foltynie T, Morris HR, Wood N, Grosset DG, Shulman J. Developing and validating Parkinson's disease subtypes and their motor and cognitive progression. J Neurol Neurosurg Psychiatry. (2018);89:1279-1287. https://doi.org/10.1136/jnnp-2018-318337

29. Monge-Fuentes V, Mayer AB, Lima MR, Geraldes LR, Zanotto LN, Moreira KG, Martins OP, Piva HL, Felipe MSS, Amaral AC, Bocca AL, Tedesco AC, Mortari MR. Dopamine-loaded nanoparticle systems circumvent the blood–brain barrier restoring motor function in mouse model for Parkinson's Disease. Sci Rep. (2021);11:15185. https://doi.org/10.1038/s41598-021-94175-8

30. Grétarsdóttir HM, Widman E, Johansson A, Nyholm D. Personalized medicine approach in treating parkinson's disease, using oral administration of levodopa/carbidopa microtablets in clinical practice. J Pers Med. (2021);11(8):720. https://doi.org/10.3390/jpm11080720

31. He X, Mo C, Zhang Y, Cai Y, Yang X, Qian Y, Xiao Q. Effect of acute levodopa up-titration on blood pressure in patients with early stage Parkinson's disease: results of a levodopa challenge test. Front Aging Neurosci. (2022);13:778856. https://doi.org/10.3389/fnagi.2021.778856

32. Catalán MJ, Antonini A, Calopa M, Băjenaru O, Fábregues O de, Mínguez-Castellanos A, Odin P, García-Moreno JM, Pedersen SW, Pirtošek Z, Kulisevsky J. Can suitable candidates for levodopa/carbidopa intestinal gel therapy be identified using current evidence? eNeurologicalSci. (2017);8:44-53. https://doi.org/10.1016/j.ensci.2017.06.004

33. Laar T van, Chaudhuri KR, Antonini A, Henriksen T, Trošt M. Infusion therapies in the treatment of Parkinson's disease. J Parkinsons Dis. (2023);13(5):641-657. https://doi.org/10.3233/jpd-225112

34. Kalia LV, Lang AE. Parkinson's disease. The Lancet. (2015);386(9996):896-912. https://doi.org/10.1016/s0140-6736(14)61393-3

35. Georgy EE, Barsnley S, Chellappa R. Effect of physical exercise-movement strategies programme on mobility, falls, and quality of life in Parkinson's disease. Int J Ther Rehabil. (2012);19(2):88-96. https://doi.org/10.12968/ijtr.2012.19.2.88