



Del Din S, Galna B, Godfrey A, Bekkers EMJ, Pelosin E, Nieuwhof F, Mirelman A, Hausdorff JM, Rochester L.

Analysis of free-living gait in older adults with and without Parkinson's disease and with and without a history of falls: identifying generic and disease specific characteristics.

Journals of Gerontology Series A: Medical Sciences 2017
DOI: https://doi.org/10.1093/gerona/glx254

## Copyright:

This is a pre-copyedited, author-produced version of an article accepted for publication in Journals of Gerontology Series A: Medical Sciences following peer review. The version of record is available online at: https://doi.org/10.1093/gerona/glx254

## Date deposited:

05/01/2018

## **Embargo release date:**

30 December 2018



This work is licensed under a <u>Creative Commons Attribution-NonCommercial 3.0 Unported License</u>

# Journal of Gerontology, Series A: Medical Sciences.

DOI: https://doi.org/10.1093/gerona/glx254

Analysis of free-living gait in older adults with and without Parkinson's disease and with and without a history of falls: identifying generic and disease specific characteristics.

Silvia Del Din<sup>1</sup>, PhD, Brook Galna<sup>1,2</sup>, PhD, Alan Godfrey<sup>1,3</sup>, PhD, Esther MJ Bekkers<sup>4</sup>, MSc, Elisa Pelosin<sup>5</sup>, PhD, Freek Nieuwhof <sup>6</sup>, PhD, Anat Mirelman<sup>7</sup>, PhD, Jeffrey M Hausdorff<sup>7,8,9</sup>, PhD, Lynn Rochester<sup>1,10</sup>, PhD.

<sup>1</sup> Institute of Neuroscience/Newcastle University Institute for Ageing, Clinical Ageing Research Unit, Campus for Ageing and Vitality, Newcastle University, Newcastle upon Tyne, UK

<sup>&</sup>lt;sup>2</sup> School of Biomedical Sciences, Newcastle University, Newcastle upon Tyne, UK

<sup>&</sup>lt;sup>3</sup> Department of Computer and Information Science, Northumbria University, Newcastle upon Tyne, NE2 1XE

<sup>&</sup>lt;sup>4</sup> KU Leuven, Department of Rehabilitation Sciences, Neuromotor Rehabilitation Research Group, Leuven, Belgium

<sup>&</sup>lt;sup>5</sup> Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics and Maternal Child Health, University of Genova, Genova, Italy

<sup>&</sup>lt;sup>6</sup> Departments of Geriatric Medicine and Neurology, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, The Netherlands

<sup>&</sup>lt;sup>7</sup> Center for the study of Movement, Cognition and Mobility, Department of Neurology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

<sup>&</sup>lt;sup>8</sup> Department of Physical Therapy, Sackler School of Medicine and Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel

<sup>9</sup> Rush Alzheimer's Disease Center and Department of Orthopaedic Surgery, Rush University

Medical Center

<sup>10</sup> Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK

# **Corresponding Author**

Prof. Lynn Rochester

Institute of Neuroscience/Newcastle University Institute for Ageing, Newcastle University;

Newcastle upon Tyne Hospitals NHS Foundation Trust

Clinical Ageing Research Unit,

Campus for Ageing and Vitality,

Newcastle upon Tyne

NE4 5PL, UK

Email: <a href="mailto:lynn.rochester@ncl.ac.uk">lynn.rochester@ncl.ac.uk</a>

Phone: +44 (0) 191 208 1291

Fax: +44 (0) 191 208 1251

**Abstract** 

BACKGROUND: Falls are associated with gait impairments in older adults (OA) and

Parkinson's disease (PD). Current approaches for evaluating falls risk are based on self-report

or one-time assessment and may be suboptimal. Wearable technology allows gait to be

measured continuously in free-living conditions. The aim of this study was to explore generic

and specific associations in free-living gait in fallers and non-fallers with and without PD.

METHODS: 277 fallers (155 PD, 122 older adults (OA)) who fell twice or more in the

previous 6 months and 65 non-fallers (15 PD, 50 OA) were tested. Free-living gait was

characterised as the volume, pattern, and variability of ambulatory bouts (Macro), and 14

discrete gait characteristics (Micro). Macro and Micro variables were quantified from free-

living data collected using an accelerometer positioned on the low back for one week.

**RESULTS:** Macro variables showed that fallers walked with shorter and less variable

ambulatory bouts than non-fallers, independent of pathology. Micro variables within

ambulatory bouts showed fallers walked with slower, shorter and less variable steps than non-

fallers. Significant interactions showed disease specific differences in variability with PD

fallers demonstrating greater variability (step length) and OA fallers less variability (step

velocity) than their non-faller counterparts (p < 0.004).

**CONCLUSIONS:** Common and disease specific changes in free-living Macro and Micro gait

highlight generic and selective targets for intervention depending on type of faller (OA-PD).

Our findings support free-living monitoring to enhance assessment. Future work is needed to

confirm the optimal battery of measures, sensitivity to change and value for fall prediction.

**Keywords:** falls, gait, Parkinson's, wearable technology

3

#### Introduction

Falls are frequent among older adults (OA) and people with Parkinson's disease (PD); approximately 30% of people over 65 years of age fall each year with the fall rate increasing with age and for people with PD to 60% (1, 2). As the majority of falls occur while walking, gait impairments are commonly associated with and predict falls even in falls-naïve PD (1, 3). Fall related injuries cause loss of functional independence, poor quality of life and have associated costs to health of £1.7 billion per year in the United Kingdom alone (4), a figure estimated to rise due to increased longevity. Understanding falls risk and identifying key fall-related characteristics is critical to determine effective treatment and prevention strategies (3, 5).

Clinical falls risk assessment is often based on questionnaires or one-time assessments of balance, gait and other falls risk factors. Due to their brief, subjective and sporadic nature, these approaches may not fully capture everyday falls risk and therefore may be suboptimal (1, 6). Assessments based on recall such as falls diaries may be further compromised by cognitive impairment, thus limiting their utility. Falls also occur and may be precipitated by everyday activities and the environmental context, which is difficult to capture in a one-off assessment (7). It appears evident then that monitoring performance continuously during normal everyday activity may offer significant added benefits to understand falls risk and to enhance assessment of risk.

In this context, wearable technology (e.g. accelerometers) is a valid and inexpensive tool to assess falls risk (8-12), walking activity, and gait impairment (13, 14). Continuously monitoring activity during unsupervised and everyday activities (free-living) may provide an objective and more sensitive measure of falls risk than instrumented clinical-based assessments, being able to discriminate between fallers and non-fallers better than the clinical

gait assessments (12). Free-living monitoring allows activity to be described by a broad framework that captures macro-structural characteristics (e.g. volume, pattern and variability of walking bouts) (referred to as Macro) and micro-structural characteristics that make up each walking bout (e.g. spatial-temporal characteristics, gait stability outcomes, gait (a) symmetry outcomes, gait adaptability) (referred to as Micro or quality outcomes). Other models based on 'quantity' (e.g. volume) and 'quality' (e.g. endurance, variability, adaptability) measures of gait have also been shown to be promising in discriminating fall status in either PD or OA (10-12, 15, 16). To date, however, it is not clear if Macro and Micro characteristics of falls risk are similar in older adults and PD or different. Comparing Macro and Micro gait characteristics with respect to falls risk and pathology may therefore be useful to highlight generic (i.e. fallers/non-fallers) or disease specific (PD fallers/OA fallers) differences. This nuanced understanding of falls risk could stress whether to target specific intervention across groups rather than a "one-size-fits-all" approach. Further work is therefore required to understand the nature of the relationship between free-living walking activity and falls risk to ultimately better inform strategies to reduce falls risk.

The aim of this study was to describe free-living walking activity taking a broad framework which encapsulated both Macro and Micro features of walking and to compare differences in fallers and non-fallers. Secondly, we wanted to establish generic (across all participants) and PD-specific associations between features of walking and a history of falls. Our primary hypothesis was that fallers would be less active and have more impaired gait with respect to non-fallers; and that this these differences would be more evident in people with PD compared to OA.

#### Methods

### 2.1 Participants

Fallers (F) were enrolled in the V-TIME study at five clinical centres across five countries (17). Participants were included in the study if they had fallen twice or more in the 6 months prior to assessment (17). Non-fallers (NF) were recruited from the Incidence of Cognitive Impairment in Cohorts with Longitudinal Evaluation-GAIT (ICICLE-GAIT) study, participants were included if they had not fallen for at least 18 months. ICICLE-GAIT is a collaborative study with ICICLE-PD, an incident cohort study (Incidence of Cognitive Impairment in Cohorts with Longitudinal Evaluation—Parkinson's disease) conducted between June 2009 and December 2011 (18). PD participants were diagnosed with idiopathic PD according to the UK Parkinson's Disease Brain Bank criteria and were excluded if they presented with significant cognitive impairment (Mini Mental State Exam (MMSE) < 21 for V-TIME study and 24 for ICICLE-GAIT study (19)), psychiatric comorbidities, any neurological (other than PD), orthopaedic or cardiothoracic conditions that may have markedly affected their walking or safety during the testing sessions.

Age and sex were recorded for each participant. The severity of PD motor symptoms was measured using the Hoehn and Yahr scale (20) and section III of the modified Movement Disorder Society version of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS (21)). For both studies, people with PD were assessed approximately one hour after their medication intake. V-TIME study testing took place at the five clinical sites (17). ICICLE-GAIT study testing took place at the Clinical Ageing Research Unit, Newcastle University. Both studies were conducted according to the declaration of Helsinki and were approved by local Ethics Committees (17, 18). All participants signed an informed consent form prior to testing.

## 2.2 Free-living data collection: protocol

At the end of a laboratory testing session participants were asked to wear a tri-axial accelerometer (Axivity AX3, York, UK) on the lower back for one week as detailed in previous work (22). The water-proof device was programmed to capture data for seven days at 100Hz (range  $\pm 8g$ ), for more details see Supplementary methods.

## 2.3 Data processing and analysis

## 2.3.1 Data processing and variable extraction

Once the device was received, data were downloaded and segmented (per day) and individual ambulatory bouts (ABs) were extracted via MATLAB® (23). Detailed data processing can be found in the Supplementary methods.

Outcome measures were described according to a broad framework of Macro and Micro characteristics (24). Macro (behavioural outcomes) representing the volume of walking (total walking time per day, percentage (%) of walking time per day, number of bouts and steps per day), mean AB length were generated based on the AB detected over the seven days. In addition, a set of non-linear descriptors were also derived: (i) pattern of ABs derived using a power-law distribution (alpha,  $\alpha$ ) based on a logarithmic scale from their density and length and (ii) the within AB variability ( $S_2$ ) estimated using a maximum likelihood technique (22, 25, 26).

Micro gait characteristics (n=14 describing pace, rhythm, variability, asymmetry and postural control) were also determined for each walking bout. Characteristics were selected based upon a model of gait validated both in OA and in people with PD (27, 28). For further details on quantification of Micro outcomes see Supplementary Methods.

#### 2.3.2 Data considerations

All ABs with more than three steps (minimum bout length) were taken into account for the analysis (10, 14, 29, 30); a threshold of 2.5 seconds was set for the maximum resting period between consecutive ABs (23). Each AB was considered individually to ensure robustness for the evaluation of the gait characteristics, to avoid sources of error in step detection, and facilitate the calculation of variability and asymmetry characteristics (13). Micro outcomes were evaluated for each AB and then averaged over the seven days; pooled seven-day data were used for quantifying Macro outcomes. No further threshold was applied to ABs length when evaluating Macro outcomes (all ABs greater than three steps were included) (11, 12, 23), whilst in agreement with previous work ABs >10s were included into the analysis for the Micro outcomes (13, 31).

## 2.3.3 Statistical analysis

Statistical analysis was carried out using SPSS v19 (IBM). Normality of data and homoscedasticity were tested with Shapiro-Wilk test and Levene's Test of Equality of Variances respectively. Descriptive statistics were reported as means and standard deviations (SD). Clinical characteristics were described but not used in further analysis. Effect of pathology and falls history were examined using general linear modelling. Fall history (F vs. NF) and pathology (OA vs. PD) were entered as within-person factors. Age, sex and BMI were included as covariates. When a pathology x fall history interaction was found, post-hoc secondary analysis was carried out using Tukey's test. We used a threshold of p < 0.05 to guide statistical interpretation for the main effects, while a Bonferroni corrected threshold (p < 0.0083) was used accounting for the multiple comparisons (fall status x pathology) of the post-hoc analysis. Further analysis of Macro outcomes was then repeated on walking bouts grouped by bout length: medium (ABs >60s) and long (ABs>120s) ABs to explore the impact of AB length on results.

## **Results**

277 fallers (F: 122 Older Adult Fallers (OA<sub>F</sub>), 155 PD Fallers (PD<sub>F</sub>), age: 73.33±6.78 years), together with 65 non-fallers (NF: 50 Older Adult Non-Fallers (OA<sub>NF</sub>), 15 PD Non-Fallers (PD<sub>NF</sub>), age: 69.05±7.67 years) were assessed. F were older (p<0.001) and included proportionally less women (F: 42%, NF: 56%). Clinical and demographic characteristics are shown in Table 1.

## Macro gait characteristics

Mean bout length and variability were related to fall history where F walked with shorter and less variable walking bouts (lower  $S_2$ ) (Figure 1a). Volume of walking bouts (e.g. total walking time per day, % of walking time per day, total number of steps and bouts per day) was not related to fall history.

When exploring differences based on walking bout length, a different picture emerged. ABs >60s represented less than 10% of the total amount of ABs, and volume of walking (based on total walking time per day and % of walking time per day) was significantly less in F. Longer ABs (>120s) represented less than 2% of the total amount of ABs, and once again volume of walking (based on total walking time per day, % of walking time per day and in addition number of bouts per day) was significantly less in F (Figure 1b and 1c).

There were no interactions between fall history and pathology for any of the outcomes (Supplementary Table 2), indicating that Macro based outcomes respond in a similar manner irrespective of PD.

## Micro gait characteristics

Characteristics relating to pace (step velocity, step length) and variability (step length variability) were significantly different between F and NF. F walked with reduced velocity and shorter, less variable steps (Supplementary Table 3, Figure 2). A significant interaction was found for fall history and PD in rhythm (step time, swing time, stance time) and variability (step length variability and step velocity variability) characteristics (Supplementary Table 3, Figure 2). PD<sub>NF</sub> had a slower step time, swing time and stance time compared to  $OA_{NF}$  (p < 0.004, Figure 3). Although non-significant,  $OA_F$  tended to walk at a slower cadence (higher step time, swing time and stance time) compared to  $OA_{NF}$ . In contrast PD<sub>F</sub> had a quicker time on all of these characteristics compared to PD<sub>NF</sub>, indicated a faster cadence overall (Figure 3). Variability characteristics (step length and step velocity) also showed significant interactions effects. Post-hoc analysis showed increased step length variability for PD<sub>F</sub> compared to PD<sub>NF</sub> (p = 0.004) in contrast to  $OA_F$  who had reduced step velocity variability compared to  $OA_{NF}$  (p = 0.004) in contrast to  $OA_F$  who had reduced step velocity variability compared to  $OA_{NF}$  (p = 0.004). Figure 3.

#### **Discussion**

We quantified gait using a framework that captured Macro and Micro gait characteristics measured during free-living with a wearable accelerometer worn for one week and compared findings with respect to falls risk and pathology. We found an association between falls history, activity pattern and variability of walking bouts (Macro outcomes) regardless of pathology. In contrast, discrete Micro gait characteristics were not only different with respect to falls status but also revealed generic and PD specific associations between gait impairment and a history of falls. Together these findings highlight generic differences and disease specific differences in macro and micro characteristics that inform a nuanced understanding of falls risk and intervention across groups.

#### Macro characteristics

Our findings partly support our primary hypothesis that fallers would be less active than non-fallers, irrespective of pathology. We found that fallers were as active as non-fallers, irrespective of pathology, when considering the total amount of activity and our findings concur with others (12, 15). However, when taking bout length into account a different picture emerged. Fallers spent less time walking during bouts over one minute, and even less during bouts of two minutes. These findings are in agreement with previous studies (32, 33).

Differences were also observed in the pattern and variability of all walking bouts. We found that fallers had a greater number of shorter walking bouts, in agreement with previous work reporting a higher short-walk exposure for fallers (12). Fallers also had less variability in walking bout duration. This may reflect restricted engagement in sustained walking bouts. Contrasting results have been reported for measures representing walking bout variability with reports of increased (16) or decreased variability (34) in fallers when compared to non-fallers. Comparison across studies however is difficult due to different methodological approaches and metrics used for describing across bout variability. Our findings that changes in Macro characteristics were similar for OA and PD fallers not only extend previous work, they also suggest that these may be fundamental features of falls risk.

Agreement with previous work validates the veracity of our findings while at the same time raising interesting questions about the relationship between activity levels and fall risk/exposure (33). Falls often occur when individuals are engaged in dynamic activities such as walking (5, 7, 33), and therefore it is often assumed that individuals reduce overall exposure to falls risk by becoming less active. The data, however, suggest that the relationship of fall risk and activity is more complex and influenced by duration of walking bouts, particularly

longer duration bouts (33). Differences observed in patterns of walking through a reduction in longer walking bouts may be due to compensatory change to reduce risk, possibly by reducing duration of walking bouts either by limiting access to the community or exercise. Alternatively, these changes may be related to fundamental features of falls risk. Reduction in variability of walking bout length in fallers may also be due to changes in patterns of walking behaviours indicating reduced confidence and a less varying walking "routine". We performed further analysis to support this hypothesis and found that falls efficacy scale (FES-I) scores were negatively correlated with Macro variability (r < -0.149), showing that fallers who were less confident (higher FES-I score) also had a less variable walking pattern (lower variability). Compensatory strategies or higher attentional load (e.g. dual task) required for walking during free-living conditions may also play a role in modifying Macro level outcomes. At present, this is unclear and further work is required to understand the relationship with activity and falls more fully.

Either way, the relationship of reduced activity, health comorbidity (such as cardiovascular disease and diabetes) and function is an important consideration. A reduction in sustained bouts of walking is problematic given the putative positive benefits of activity and the subtle, insidious nature of inactivity on health and disease burden. Interventions should aim to find a balance of maintaining activity whilst minimising falls risk, as well as the need to understand the relationship between these characteristics (35).

### Micro gait characteristics

As hypothesised, gait impairment was more evident in fallers who walked with a slower gait and shorter step length compared to non-fallers. Our findings agree with previously published work in free-living gait (12, 16). However, of more interest were the interactions in select Micro

characteristics (related to rhythm and variability) indicating a different response in PD<sub>F</sub> and OA<sub>F</sub> compared to their non-falling counterparts. For example, variability of step velocity and step length showed an interesting pattern with respect to pathology and falls status with older adult fallers typically showing reduced variability in these characteristics and PD fallers increased variability compared to their non-falling counterparts. Although to date no studies have compared older adult and PD fallers, independent analysis of these groups in free-living studies lends support to our findings. For example, previous reports have shown that PD fallers have increased variability (represented by width of dominant frequency) to PD non-fallers (16). Studies of older adult fallers have reported both higher and lower variability compared to nonfallers depending on the outcome measure. For example, when considering the amplitude and slope of the dominant frequency (measures of variability of the 'quality' of walking), OA fallers were significantly more variable in the vertical axis but had less variability in the mediolateral axis (15). Others reported lower (although non-significant) between-walk variability ('adaptability') (12) but higher within-walk variability or mode variability (10). The intrinsic meaning of these differences is still unclear. Variability measured in the laboratory or clinic is typically greater in fallers compared to non-fallers (34) and has been reported to be predictive of future falls (36, 37). For Micro level variability in free-living, the picture is not as clear but it seems that it is influenced by the environment or context (38). Possible explanations for this dichotomy could be related to the different type metrics (and therefore methods) used to describe variability (e.g. frequency based, within-walk variability, between-walk adaptability, etc.) which may indicate different constructs. Moreover while some studies focused on steady-state walking for evaluating variability, in the current approach we included also short bouts of walking. The influence of "embedded" dual-task nature of real-life on walking poses additional challenges and ability to adapt, and our findings raise the possibility of a different adaption and control strategy in OA compared to PD. Whether they

reflect compensatory adaptations or primary pathological disturbances in gait underpinning falls is as yet unclear. These selective differences however, suggest the need for strategies dependant on type of faller (OA or PD) targeting specific Micro gait characteristics (e.g. increase variability for PD and decrease for OA) in order to reduce falls risk.

Consistent with previous results (15, 16, 39), our findings corroborate the suggestion that 'variability' measures may represent different constructs. Higher variability in Macro outcomes ('behaviour') may be "good" - representing ability to engage and adapt in a wider variety of walking activities. Whilst higher variability in Micro outcomes may be "good" or "bad" representing either compensatory adaptions to minimise risk (e.g. in OA) or impaired control and inability to minimise risk (e.g. in people with PD).

## Clinical Implications

Similar to what has been reported when investigating differences between fallers and non-fallers both in PD and OA (10, 11, 16), we found that Micro outcomes seem to be more sensitive than Macro to identify selective faller x pathology "type" dependant differences (e.g. OA<sub>F</sub> and PD<sub>F</sub>). However, both contribute to a bigger picture that suggests group specific and generic features as targets for intervention development.

#### Limitations

This study informs understanding of the association between walking activity quantified via a range of Macro and Micro outcomes and falls history, however further work is required to identify the merits of this exploratory analysis especially in a larger sample of non-fallers. We acknowledge that use of different studies (V-TIME an ICICLE-GAIT) for populations of fallers and non-fallers and the limited number of PD fallers may affect generalisability of the

results. Only one model of gait including specific Macro and Micro gait characteristics was included in this work, in the future other reported models and outcomes should be considered to identify best measure (or combination of measures) for falls risk detection. In addition, examination of other pathologies with fall history will allow us to determine whether free-living Macro and Micro outcomes can be a selective tool for identification of "pathology-dependant" falls risk. Future work is also needed to examine the effect of merging short ABs, turning and freezing of gait on results, and to confirm if Macro and Micro outcomes can predict falls in order to provide an insight into falls risk for guiding clinical decision-making.

#### **Conclusions**

We found common and disease specific changes in Macro and Micro gait characteristics that highlight generic and selective targets for intervention in older adults and PD fallers allowing a more nuanced approach to falls intervention development. Macro outcomes seem to be associated with fall history regardless of pathology, while Micro outcomes seem to be a more sensitive outcome for detecting disease specific falls risk. Our findings support a role for free-living monitoring and the use of wearable technology to enhance assessment and understanding of falls risk. Future work is needed to confirm the optimal battery of measures and to fully understand the relationship of walking in the real-world and falls risk, especially its prognostic utility to enhance clinical decision-making and intervention development.

#### **Conflict of Interest**

The authors declare that they have no conflict of interest.

#### **Funding**

The work was supported by the V-TIME project, which is a European Union 7th Framework Programme (FP7) under the Health theme (FP7 - 278169). The ICICLE-GAIT study was

supported by Parkinson's UK (J-0802, G-1301) and by the NIHR Newcastle Biomedical Research Centre. SDD is supported by the Newcastle Biomedical Research Unit (BRU) based at Newcastle upon Tyne and Newcastle University. The work was also supported by the NIHR/Wellcome Trust Clinical Research Facility (CRF) infrastructure at Newcastle upon Tyne Hospitals NHS Foundation Trust. All opinions are those of the authors and not the funders.

## Acknowledgments

The authors would like to thank all the V-TIME participants and all the members of the V-TIME project who have provided assistance with data collection. The authors would also like to thank Mrs Dadirayi Mhiripiri, Dr Rosie Morris and Philip Brown for their assistance with data collection for the ICICLE-GAIT study.

### References

- 1. Allen NE, Schwarzel AK, Canning CG. Recurrent falls in Parkinson's disease: a systematic review. Parkinson's disease. 2013;**2013**:906274.
- 2. Peel NM. Epidemiology of falls in older age. Canadian Journal on Aging/La Revue canadienne du vieillissement. 2011;**30**:7-19.
- 3. Lord S, Galna B, Yarnall AJ, Coleman S, Burn D, Rochester L. Predicting first fall in newly diagnosed Parkinson's disease: Insights from a fall-naive cohort. Mov Disord. 2016;**31**:1829-1836.
- 4. Age UK. Falls in the over 65s cost NHS £4.6 million a day. Press Release. 2010; http://www.ageuk.org.uk/latest-press/archive/falls-over-65s-cost-nhs/.
- 5. Ross A, Yarnall AJ, Rochester L, Lord S. A novel approach to falls classification in Parkinson's disease: development of the Fall-Related Activity Classification (FRAC). Physiotherapy. 2016.
- 6. Cho CY, Kamen G. Detecting balance deficits in frequent fallers using clinical and quantitative evaluation tools. J Am Geriatr Soc. 1998;**46**:426-430.
- 7. Lamont RM, Morris ME, Menz HB, McGinley JL, Brauer SG. Falls in people with Parkinson's disease: A prospective comparison of community and home-based falls. Gait Posture. 2017;55:62-67.
- 8. Del Din S, Godfrey A, Mazzà C, Lord S, Rochester L. Free-living monitoring of Parkinson's disease: Lessons from the field. Mov Disord. 2016;**31**:1293-1313.
- 9. Maetzler W, Domingos J, Srulijes K, Ferreira JJ, Bloem BR. Quantitative wearable sensors for objective assessment of Parkinson's disease. Mov Disord. 2013;**28**:1628-1637.
- 10. Brodie M, Lord S, Coppens M, Annegarn J, Delbaere K. Eight weeks remote monitoring using a freely worn device reveals unstable gait patterns in older fallers. IEEE transactions on bio-medical engineering. 2015;62:2588-2594.
- 11. Brodie MA, Okubo Y, Annegarn J, Wieching R, Lord SR, Delbaere K. Disentangling the health benefits of walking from increased exposure to falls in older people using remote gait monitoring and multi-dimensional analysis. Physiological measurement. 2017;38:45-62.

- 12. Brodie MA, Coppens MJ, Ejupi A, Gschwind YJ, Annegarn J, Schoene D, *et al.* Comparison between clinical gait and daily-life gait assessments of fall risk in older people. Geriatrics & gerontology international. 2017.
- 13. Del Din S, Godfrey A, Galna B, Lord S, Rochester L. Free-living gait characteristics in ageing and Parkinson's disease: impact of environment and ambulatory bout length. J Neuroeng Rehabil. 2016;**13**:46.
- 14. Brodie MA, Coppens MJ, Lord SR, Lovell NH, Gschwind YJ, Redmond SJ, *et al.* Wearable pendant device monitoring using new wavelet-based methods shows daily life and laboratory gaits are different. Medical & biological engineering & computing. 2015;**54**:663-674.
- 15. Weiss A, Brozgol M, Dorfman M, Herman T, Shema S, Giladi N, *et al.* Does the evaluation of gait quality during daily life provide insight into fall risk? A novel approach using 3-day accelerometer recordings. Neurorehabil Neural Repair. 2013;**27**:742-752.
- 16. Weiss A, Herman T, Giladi N, Hausdorff JM. Objective assessment of fall risk in Parkinson's disease using a body-fixed sensor worn for 3 days. PloS one. 2014;9:e96675.
- 17. Mirelman A, Rochester L, Maidan I, Del Din S, Alcock L, Nieuwhof F, *et al.* Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial. Lancet (London, England). 2016;**388**:1170-1182.
- 18. Yarnall AJ, Breen DP, Duncan GW, Khoo TK, Coleman SY, Firbank MJ, *et al.* Characterizing mild cognitive impairment in incident Parkinson disease: the ICICLE-PD study. Neurology. 2014;**82**:308-316.
- 19. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. Journal of psychiatric research. 1975;12:189-198.
- 20. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology. 1967;17:427-442.
- 21. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, *et al.* Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. Mov Disord. 2008;**23**:2129-2170.
- 22. Godfrey A, Lord S, Galna B, Mathers JC, Burn DJ, Rochester L. The association between retirement and age on physical activity in older adults. Age Ageing. 2014;**43**:386-393.
- 23. Hickey A, Del Din S, Rochester L, Godfrey A. Detecting free-living steps and walking bouts: validating an algorithm for macro gait analysis. Physiological measurement. 2017;38:N1-n15.
- 24. Lord S, Galna B, Rochester L. Moving forward on gait measurement: toward a more refined approach. Mov Disord. 2013;**28**:1534-1543.
- 25. Lord S, Godfrey A, Galna B, Mhiripiri D, Burn D, Rochester L. Ambulatory activity in incident Parkinson's: more than meets the eye? J Neurol. 2013;**260**:2964-2972.
- 26. Lara J, O'Brien N, Godfrey A, Heaven B, Evans EH, Lloyd S, *et al.* Pilot Randomised Controlled Trial of a Web-Based Intervention to Promote Healthy Eating, Physical Activity and Meaningful Social Connections Compared with Usual Care Control in People of Retirement Age Recruited from Workplaces. PloS one. 2016;11:e0159703.
- 27. Godfrey A, Del Din S, Barry G, Mathers JC, Rochester L. Instrumenting gait with an accelerometer: A system and algorithm examination. Med Eng Phys. 2015;**37**:400-407.
- 28. Del Din S, Godfrey A, Rochester L. Validation of an accelerometer to quantify a comprehensive battery of gait characteristics in healthy older adults and Parkinson's disease: toward clinical and at home use. IEEE J Biomed Health Inform. 2016;**20**:838-847.

- 29. de Bruin ED, Najafi B, Murer K, Uebelhart D, Aminian K. Quantification of everyday motor function in a geriatric population. Journal of rehabilitation research and development. 2007;44:417-428.
- 30. Schwenk M, Hauer K, Zieschang T, Englert S, Mohler J, Najafi B. Sensor-derived physical activity parameters can predict future falls in people with dementia. Gerontology. 2014;60:483-492.
- 31. van Schooten KS, Pijnappels M, Rispens SM, Elders PJ, Lips P, van Dieen JH. Ambulatory fall-risk assessment: amount and quality of daily-life gait predict falls in older adults. J Gerontol A Biol Sci Med Sci. 2015;**70**:608-615.
- 32. Hiorth YH, Larsen JP, Lode K, Tysnes OB, Godfrey A, Lord S, *et al.* Impact of falls on physical activity in people with Parkinson's disease. Journal of Parkinson's disease. 2015;**6**:175-182.
- 33. Mactier K, Lord S, Godfrey A, Burn D, Rochester L. The relationship between real world ambulatory activity and falls in incident Parkinson's disease: influence of classification scheme. Parkinsonism Relat Disord. 2015;21:236-242.
- 34. Howcroft J, Kofman J, Lemaire ED, McIlroy WE. Analysis of dual-task elderly gait in fallers and non-fallers using wearable sensors. J Biomech. 2016;**49**:992-1001.
- 35. Ahlskog JE. Does vigorous exercise have a neuroprotective effect in Parkinson disease? Neurology. 2011;77:288-294.
- 36. Mirelman A, Herman T, Brozgol M, Dorfman M, Sprecher E, Schweiger A, *et al.* Executive function and falls in older adults: new findings from a five-year prospective study link fall risk to cognition. PloS one. 2012;7:e40297.
- 37. Hausdorff JM, Rios DA, Edelberg HK. Gait variability and fall risk in community-living older adults: a 1-year prospective study. Archives of physical medicine and rehabilitation. 2001;82:1050-1056.
- 38. Rispens SM, Van Dieen JH, Van Schooten KS, Cofre Lizama LE, Daffertshofer A, Beek PJ, *et al.* Fall-related gait characteristics on the treadmill and in daily life. J Neuroeng Rehabil. 2016;**13**:12.
- 39. Moe-Nilssen R, Aaslund MK, Hodt-Billington C, Helbostad JL. Gait variability measures may represent different constructs. Gait & posture. 2010;**32**:98-101.

Table 1 Clinical and demographic characteristics for Older Adult Non-Fallers ( $OA_{NF}$ ), Older Adult Fallers ( $OA_{F}$ ), participants with Parkinson's disease non-fallers ( $PD_{NF}$ ) and participants with Parkinson's disease fallers ( $PD_{F}$ ).

Characteristic	OA <sub>NF</sub> (n=50)	OA <sub>F</sub> (n=122)	PD <sub>NF</sub> (n=15)	<b>PD</b> <sub>F</sub> ( <b>n=155</b> )	p	<i>p</i> *	<i>p</i> **	p***	$p^{\dagger}$	p§
Characteristic	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	OA <sub>NF</sub> vs OA <sub>F</sub>	OA <sub>NF</sub> vs PD <sub>NF</sub>	OA <sub>NF</sub> vs PD <sub>F</sub>	OA <sub>F</sub> vs PD <sub>NF</sub>	OA <sub>F</sub> vs PD <sub>F</sub>	PD <sub>NF</sub> vs PD <sub>F</sub>
Female (n, %)	23, 46%	95, 77.9%	4, 26.7%	59, 38.1%	<.001	.183	.319	<.001	<.001	.383
Age (years)	70.40 (6.88)	75.58 (6.32)	64.54 (8.64)	71.55 (6.44)	<.001	.014	.700	<.001	<.001	.001
BMI (kg/m <sup>2</sup> )	28.30 (4.23)	26.28 (4.29)	28.45 (4.91)	25.75 (3.69)	.017	.999	.001	.204	.709	.067
MMSE	28.40 (1.74)	28.52 (1.36)	28.87 (1.60)	28.04 (1.72)	.974	.760	.554	.859	.105	.235
				HY 2 - 48.05%						
Hoehn & Yahr	-	-	HY 2 - 100%	HY 2.5 - 11.69%	-	-	-	-	-	.310
(HY) stage (%)				HY 3 - 40.26%						
MDS-UPDRS III	-	-	28.60 (5.65)	31.42 (13.17)	-	-	-	-	-	<.001
Freezing of gait			13.3%,	43.2%,						224
(%, Score)	-	-	7.71 (9.03)	2.13(5.64)	-	-	-	-	-	.002

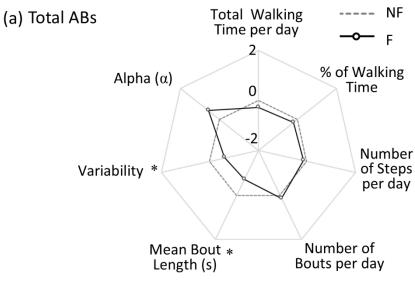
FES-I (16-64)	-	28.68 (7.68)	-	35.46 (12.00)	-	-	-	-	<.001	-
ABCs (0-100%) 9	1.02 (11.66)	-	85.64 (15.73)	-	-	.185	-	-	-	-

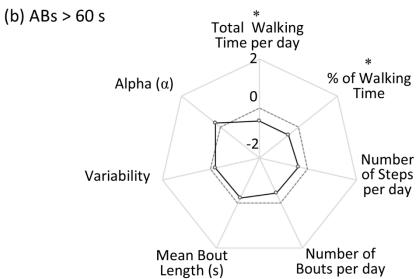
BMI: Body Mass Index; MMSE: Mini Mental State Examination; MDS-UPDRS III: Movement Disorder Society Unified Parkinson's Disease Rating Scale part III; FES-I: Falls Efficacy Scale; ABCs: Activities specific balance confidence scale. In bold significant p-values (p < 0.05).

## **Figure Captions**

## Figure 1.

Radar plot illustrating the free-living Macro gait characteristics for Fallers (F), compared to Non Fallers (NF), evaluated in free-living conditions for total ambulatory bouts (ABs > three steps, panel a), ABs > 60s (panel b), and ABs > 120s (panel c). The central dotted line represents NF data, deviation from zero along the axis radiating from the centre of the plot represents how many standard deviations the F differ from NF (range:  $\pm$  2 SD, z score based on NF means and standard deviations). \* represents significant differences between F and NF (effect of Fall History) (p values < 0.05).





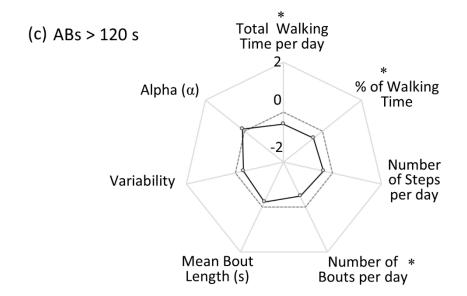
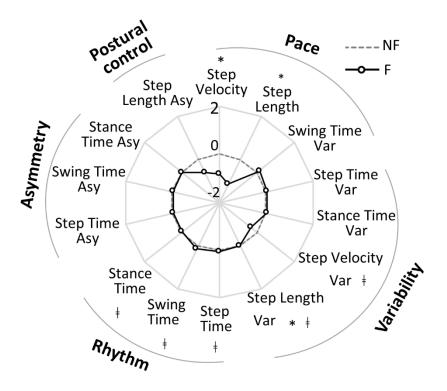


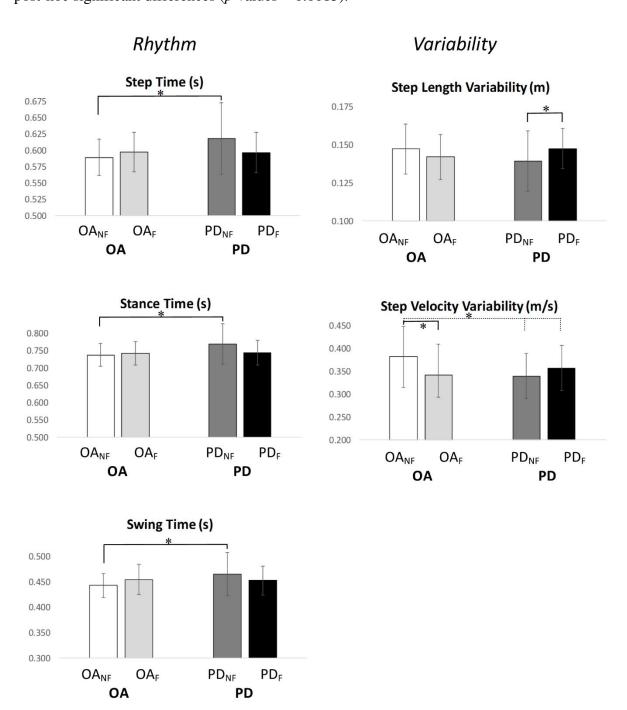
Figure 2.

Radar plot illustrating the free-living Micro gait characteristics for Non Fallers (NF) and Fallers (F) evaluated in free-living conditions for ambulatory bouts > 10 seconds. The central dotted line represents NF data, deviation from zero along the axis radiating from the centre of the plot represents how many standard deviations (range:  $\pm$  2 SD, z score based on NF means and standard deviations) the F differ from NF. \* represents significant differences between F and NF (effect of Fall History), ‡ represents Fall History x Pathology interactions (p values < 0.05). (Var: Variability, Asy: Asymmetry).



## Figure 3.

Post-hoc analysis results for interactions found in free-living Micro gait characteristics for Older Adult Fallers ( $OA_F$ , in light grey), Non Fallers ( $OA_{NF}$ , in white), people with Parkinson's disease Fallers ( $PD_F$ , in black) and Non Faller ( $PD_{NF}$ , in dark grey) evaluated in free-living conditions for ambulatory bouts > 10s. Error bars represent standard deviations. \* represents post-hoc significant differences (p values < 0.0083).



## **Supplementary Methods**

## 2.2 Free-living data collection: protocol

At the end of a laboratory testing session participants were asked to wear a tri-axial accelerometer (Axivity AX3, York, UK; dimensions: 23.0 × 32.5 × 7.6 mm; weight: 11 grams) for one week (1). The device has been validated for its suitability in capturing high-resolution data akin to human movement (2). It was located on the fifth lumbar vertebrae with a hydrogel adhesive (PAL Technologies, Glasgow, UK) and covered with additional tape (Hypafix bandage) for extra support. Participants were asked to continue their daily activities as usual and not to change their routine. Upon completion of recording, participants removed the device and posted it back to the researcher as detailed in previous work (3).

## 2.3 Data processing and analysis

## 2.3.1 Data processing and variable extraction

Once the device was received, data were downloaded, segmented (per calendar day) and analysed using bespoke MATLAB® programs. For each day, a logical heuristics paradigm was embedded into walking bout identification and quantification algorithm which has shown to be accurate in detecting ambulatory bouts (ABs) and step count in free-living conditions (4). Individual ABs were extracted via MATLAB®, where a 'bout' was defined as the continuous length of time spent walking with at least three consecutive steps (3, 4). Ambulatory bouts were detected by applying selective thresholds on the triaxial acceleration data as detailed elsewhere (4).

#### Micro outcomes

Micro gait characteristics (n=14) were also determined for each walking bout. Characteristics were selected based upon a model of gait validated both in OA and in people with PD (5, 6). Briefly, the initial contact and final contact events within the gait cycle were identified and allowed the estimation of step, stance and swing time. Initial contact events were also used to estimate step length using the inverted pendulum model. Step velocity was calculated as the ratio between step length and time (6). To calculate step variability, the standard deviation (SD) from all steps (left and right combined) was calculated. Asymmetry was determined as the absolute difference between left and right steps for each AB, averaged across all ABs (6, 7).

## **Supplementary References**

- 1. van Schooten KS, Rispens SM, Elders PJ, Lips P, van Dieen JH, Pijnappels M. Assessing physical activity in older adults: required days of trunk accelerometer measurements for reliable estimation. Journal of aging and physical activity. 2015;23:9-17.
- 2. Ladha C, Jackson, Dan, Ladha, Karim, Olivier, Patrick. Shaker table validation of OpenMovement AX3 accelerometer. 3rd International Conference on Ambulatory Monitoring of Physical Activity and Movement. Ahmerst; 2013:69-70.
- 3. Godfrey A, Lord S, Galna B, Mathers JC, Burn DJ, Rochester L. The association between retirement and age on physical activity in older adults. Age Ageing. 2014;43:386-393.
- 4. Hickey A, Del Din S, Rochester L, Godfrey A. Detecting free-living steps and walking bouts: validating an algorithm for macro gait analysis. Physiological measurement. 2017;38:N1-n15.
- 5. Godfrey A, Del Din S, Barry G, Mathers JC, Rochester L. Instrumenting gait with an accelerometer: A system and algorithm examination. Med Eng Phys. 2015.

- 6. Del Din S, Godfrey A, Rochester L. Validation of an accelerometer to quantify a comprehensive battery of gait characteristics in healthy older adults and Parkinson's disease: toward clinical and at home use. IEEE J Biomed Health Inform. 2016;20:838-847.
- 7. Galna B, Lord S, Burn DJ, Rochester L. Progression of gait dysfunction in incident Parkinson's disease: Impact of medication and phenotype. Mov Disord. 2014.

# **Supplementary Table 2**

Free-living Macro gait characteristics for participants grouped as Non Fallers (NF), Fallers (F), Older Adult Non-Fallers (OA<sub>NF</sub>), Older Adult Fallers (OA<sub>F</sub>), participants with Parkinson's disease Non-Fallers (PD<sub>NF</sub>) and participants with Parkinson's disease fallers (PD<sub>F</sub>). Data are presented for total ambulatory bouts (ABs > three steps), ABs > 60s and ABs > 120s.

Total ABs	NF (n=65)	F (N=277)	$OA_{NF}$ (n=50)	$OA_{F}$ (n=122)	$PD_{NF}$ (n=15)	PD <sub>F</sub> (n=155)
Total Walking						
Time per Day	188.557 (78.459)	167.812 (68.695)	192.063 (77.529)	176.327 (66.084)	176.867 (83.144)	161.111 (70.168)
(Min)						
Percentage of						
Walking	12.730 (5.689)	11.654 (4.771)	13.172 (5.561)	12.245 (4.589)	11.257 (6.056)	11.188 (4.873)
Time						
Number of steps	10(01 (5405)	11052 (5045)	12005 (5(20)	12400 (4002)	11(77 (5000)	11416 (5060)
per Day	12691 (5497)	11853 (5045)	12995 (5629)	12408 (4992)	11677 (5082)	11416 (5060)
Bouts per	602 (221)	639 (219)	609 (222)	667 (206)	578 (221)	617 (226)
Day						
Mean Bout Length	10 (57 (4 100)	15 705 (4 022)	10.051 (2.055)	15 750 (2 401)	10.012 (5.052)	15 ((0 (4 470)
(sec) a	18.657 (4.188)	15.705 (4.033)	18.851 (3.855)	15.759 (3.401)	18.013 (5.253)	15.662 (4.478)

1.642 (0.061)			0.86 (0.096)	0.82 (0.09)
	1.604 (0.052)	1.636 (0.06)	1.629 (0.074)	1.646 (0.062)
45.185 (31.17)	64.781 (36.617)	46.683 (30.419)	65.9 (47.676)	44.001 (31.801)
2.120 (2.165)	4.400 (0.540)	2.242 (2.112)	4.55( (0.011)	2.056 (2.200)
3.138 (2.165)	4.499 (2.543)	3.242 (2.112)	4.576 (3.311)	3.056 (2.208)
4014 (2910)	5393 (3310)	4278 (2978)	4896 (2962)	3806 (2848)
18 (12)	24 (13)	18 (10)	24 (15)	18 (13)
150.015 (44.124)	164.091 (59.503)	153.19 (44.526)	159.889 (37.038)	147.503 (43.786)
0.575 (0.135)	0.599 (0.137)	0.586 (0.14)	0.594 (0.086)	0.565 (0.131)
2.687 (0.502)	2.615 (0.376)	2.678 (0.545)	2.524 (0.344)	2.695 (0.467)

Total Walking							
Time per Day	44.784 (30.972)	29.867 (23.667)	44.153 (29.133)	32.043 (24.326)	46.886 (37.529)	28.174 (23.079)	
(Min) a							
Percentage of	3.110 (2.151)	2.074 (1.644)	3.066 (2.023)	2.225 (1.689)	3.256 (2.606)	1.957 (1.603)	
Walking Time <sup>a</sup>	3.110 (2.131)	2.074 (1.044)	3.000 (2.023)	2.223 (1.009)	3.230 (2.000)	1.937 (1.003)	
Number of steps	2712 (2(22)	2700 (2272)	2707 (27(7)	2000 (2522)	2424 (2101)	2550 (2220)	
per Day	3713 (2633)	2790 (2373)	3797 (2767)	3099 (2522)	3434 (2191)	2550 (2229)	
Bouts per Day <sup>a</sup>	9 (6)	7 (4)	9 (5)	7 (4)	10 (6)	6 (5)	
Mean Bout Length	202 540 (125 222)	265 275 (96 672)	207 504 (147 521)	272.06 (91.240)	275 729 (92 926)	250 221 (00 207)	
(sec)	292.540 (135.232)	265.275 (86.672)	297.584 (147.531)	273.06 (81.349)	275.728 (83.836)	259.221 (90.397)	
Variability (S <sub>2</sub> )	0.522 (0.164)	0.463 (0.15)	0.53 (0.179)	0.49 (0.155)	0.495 (0.096)	0.442 (0.142)	
Alpha	2.918 (0.772)	2.997 (1.405)	2.946 (0.855)	2.978 (1.877)	2.824 (0.398)	3.011 (0.887)	

Significant (p < 0.05) effect of Fall History (a, difference between NF and F) are shown for each variable. No effect of Fall History x Pathology was found

# **Supplementary Table 3**

Free-living Micro gait characteristics for participants grouped as Non Fallers (NF), Fallers (F), Older Adult Non-Fallers (OA<sub>NF</sub>), Older Adult Fallers (OA<sub>F</sub>), participants with Parkinson's disease Non-Fallers (PD<sub>NF</sub>) and participants with Parkinson's disease fallers (PD<sub>F</sub>). Data are presented for ABs > 10s.

ABs > 10s	NF (n=65)	F (N=277)	OA <sub>NF</sub> (n=50)	OA <sub>F</sub> (n=122)	PD <sub>NF</sub> (n=15)	PD <sub>F</sub> (n=155)
Pace						
Step Velocity (m/s) <sup>a</sup>	1.11 (0.112)	1.019 (0.110)	1.127 (0.105)	1.050 (0.113)	1.055 (0.120)	0.994 (0.100)
Step Length (m) <sup>a</sup>	0.612 (0.04)	0.567 (0.049)	0.615 (0.038)	0.587 (0.048)	0.603 (0.046)	0.551 (0.045)
Swing Time Var (s)	0.143 (0.023)	0.146 (0.018)	0.142 (0.019)	0.139 (0.015)	0.147 (0.032)	0.152 (0.017)
Variability						
Step Velocity Var (m/s) b	0.372 (0.066)	0.351 (0.049)	0.382 (0.067)	0.342 (0.048)	0.340 (0.049)	0.358 (0.049)
Step Length Var (m) a,b	0.146 (0.017)	0.145 (0.014)	0.147 (0.016)	0.142 (0.015)	0.139 (0.020)	0.148 (0.013)
Step Time Var (s)	0.172 (0.028)	0.174 (0.023)	0.171 (0.023)	0.164 (0.020)	0.177 (0.043)	0.181 (0.023)
Stance Time Var (s)	0.185 (0.031)	0.186 (0.026)	0.184 (0.025)	0.175 (0.022)	0.190 (0.046)	0.194 (0.026)
Rhythm						
Step Time (s) b	0.596 (0.037)	0.597 (0.031)	0.589 (0.028)	0.597 (0.03)	0.618 (0.055)	0.597 (0.031)
Swing Time (s) b	0.448 (0.030)	0.454 (0.029)	0.443 (0.024)	0.455 (0.03)	0.466 (0.043)	0.453 (0.029)
Stance Time (s) b	0.745 (0.042)	0.743 (0.034)	0.738 (0.033)	0.742 (0.033)	0.769 (0.060)	0.744 (0.035)

A ~-		4
AS	ymn	ietry

Step Time Asy (s)	0.071 (0.019)	0.071 (0.016)	0.069 (0.014)	0.067 (0.016)	0.079 (0.029)	0.073 (0.016)
Swing Time Asy (s)	0.064 (0.019)	0.064 (0.014)	0.061 (0.012)	0.061 (0.013)	0.074 (0.033)	0.066 (0.013)
Stance Time Asy (s)	0.072 (0.021)	0.071 (0.016)	0.069 (0.014)	0.067 (0.015)	0.082 (0.033)	0.073 (0.017)
Postural Control						
Step Length Asy (m)	0.075 (0.010)	0.069 (0.014)	0.075 (0.010)	0.073 (0.015)	0.075 (0.012)	0.066 (0.012)

Var: Variability; Asy: Asymmetry. Significant (p < 0.05) effect of Fall History ( $^a$ , difference between NF and F) are shown for each variable and effect of Fall History x Pathology ( $^b$ ).