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Associations between daily-living physical activity and laboratory-based assessments of motor severity in patients with falls and Parkinson's disease

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ABSTRACT

Introduction: Recent work suggests that wearables can augment conventional measures of Parkinson's disease (PD). We evaluated the relationship between conventional measures of disease and motor severity (e.g., MDS-UPDRS part III), laboratory-based measures of gait and balance, and daily-living physical activity measures in patients with PD.

Methods: Data from 125 patients (age: 71.7±6.5 years, Hoehn and Yahr: 1-3, 60.5% men) were analyzed. The MDS-UPDRS-part III was used as the gold standard of motor symptom severity. Gait and balance were quantified in the laboratory. Daily-living gait and physical activity metrics were extracted from an accelerometer worn on the lower back for 7 days.

Results: In multivariate analyses, daily-living physical activity and gait metrics, laboratory-based balance, demographics and subject characteristics together explained 46% of the variance in MDS-UPDRS-part III scores. Daily-living measures accounted for 62% of the explained variance, laboratory measures 30%, and demographics and subject characteristics 7% of the explained variance. Conversely, demographics and subject characteristics, laboratory-based measures of gait symmetry, and motor symptom severity together explained less than 30% of the variance in total daily-living physical activity. MDS-UPDRS-part III scores accounted for 13% of the explained variance, i.e., <4% of all the variance in total daily-living activity.

Conclusions: Our findings suggest that conventional measures of motor symptom severity do not strongly reflect daily-living activity and that daily-living measures apparently provide important information that is not captured in a conventional one-time, laboratory assessment of gait, balance or the MDS-UPDRS. To provide a more complete evaluation, wearable devices should be considered.

Key words: Parkinson's disease, wearable device, accelerometers, inertial measurement units, digital health**,** daily-living activity

INTRODUCTION

Difficulties in gait, balance, and mobility are major contributors to disability, diminished quality of life and fall risk in patients with Parkinson disease's (PD). In the past, these symptoms have generally been quantified in the laboratory and in clinical settings. Emerging evidence suggests that there are key differences between gait measured in the clinic or laboratory setting versus measures assessed during daily-living[1-4]. Furthermore, measures based on community ambulation apparently may help to predict important outcomes such as fall risk[5,6] and quality of life[7]. These findings support the idea that the assessment of mobility during daily-living provides information that is complementary to more conventional clinic and laboratory assessments of gait and motor function.

Several recent studies used wearable sensors to characterize and quantify daily-living physical activity among patients with PD[8-13]. Not surprisingly, the results of these studies suggest that everyday mobility differs in people with PD, as compared with age-matched controls, and that daily-living activity measures have utility in assessing and tracking PD by reflecting the subject's movement at home and in the community. Since activity and every-day function may be influenced by factors such as cognitive function, affect, environment, and social interactions, measures of daily-living may capture features that are not reflected in a single test in a laboratory or clinical setting. However, it has not been fully explored if and how the quality and quantity of daily-life physical activity characteristics relate to the conventional assessment of motor symptom severity in PD.

The assessment of disease severity is routinely conducted in the clinic using the Unified Parkinson’s Disease Rating Scale (MDS-UPDRS)[14]. The motor section subscale of the MDS-UPDRS (part III) evaluates motor symptom severity and is often used as the primary outcome for clinical studies in PD. It is widely accepted that gait performance, when measured in the clinic, correlates with disease severity[15]. It is also well-established that daily-living physical activity is related to morbidity and mortality and that it may positively modify disease severity, improving a wide range of global and specific motor and non-motor symptom in PD[16-18]. Nonetheless, the relationships between the severity of the motor symptoms in PD, gait, and balance, as measured during a one-time visit to the clinic, and measures based on daily-living mobility are not clearly understood.

One could speculate that people with more severe motor symptoms are less active. However, since activity may be affected by more than just motor symptoms and abilities, this relationship may be more complex. Several studies found associations between some items of the UPDRS-part III with sensor-derived gait acceleration in PD patients[19-21]. Yet, those studies did not explore the motor severity–daily-living physical activity relationship considering gait and balance assessed in the laboratory setting. Therefore, in the present analysis, we evaluated the relationship between PD motor symptom severity and metrics based on the laboratory-based assessment of mobility, on the one hand, and the daily-living assessment of mobility, on the other. In addition, since total daily-living physical activity is associated with many positive and negative health care outcomes (e.g., dementia, mortality) and since its benefits are well established[22,23], we investigated the relationship between total daily-living physical activity (based on objective ambulatory monitoring), clinic-based assessment of disease severity (MDS-UPDRS part I-III) and clinic-based metrics of mobility (gait and balance).

METHODS

Participants

The present analysis is based on the baseline assessment of subjects who participated in a randomized controlled trial designed to reduce fall rates in older adults, as detailed previously[24]. Briefly, the study was conducted at 5 clinical centers (Belgium, Israel, Italy, the Netherlands, and United Kingdom). The inclusion criteria for the present analyses were: (a) People diagnosed with PD according to the UK Brain Bank criteria by a movement disorders specialist (b) age 60-90 years, (c) Hoehn and Yahr stage I-III, (d) taking anti-parkinsonian medications and with stable prescriptions at least for the past month, (e) had at least two falls in the 6 months prior to assessment, and (f) able to walk at least 5 minutes without assistance and (f) physical activity recording times greater than 3 days. Subjects were excluded if they had other significant comorbidities, clinical diagnosis of dementia or severe cognitive impairment (Mini Mental State Exam score, MMSE<21). The study was approved by each clinical site's ethics committee. All participants provided informed written consent prior to testing.

Assessment of demographics and other subject characteristics

Age, gender, and other subject characteristics were collected. Motor symptom severity was assessed using the motor part of the MDS-UPDRS, i.e., part III[14] in a self-reported ON stage. Parts I and II of the MDS-UPDRS evaluated motor and non-motor experiences of daily-living based on-self-report.

Laboratory-based assessment of mobility

The participants walked back and forth in a well-lit corridor of 15 meters for one minute at a preferred, usual walking pace. Gait measures (e.g., speed, step length, and stride time variability) were collected using a Zeno instrumented walkway and PKMAS software, (Havertown, PA, USA)[25] and an inertial measurement unit placed on the lower back (Opal, APDM, Portland, OR, USA). Only straight-line walks, defined as sagittal progression walking, were analyzed. To compare laboratory to daily-living gait, only acceleration-based features were calculated from the inertial measurement unit. To further assess balance, the Mini-Balance Evaluation Systems Test (Mini-BESTest) and the Four Square Step Test were used. Endurance was evaluated using the Two Minute Walk Test by measuring the total distance covered[26].

Daily-living assessment of physical activity

At the end of the laboratory testing session, a small, light-weight, water-proof, tri-axial accelerometer (Axivity AX3, York, UK; 23.0×32.5×7.6 mm; weight: 11 grams; 100 Hz sampling rate) was placed on each subject's lower back at the level of the fifth lumbar vertebrae, as previously described[11] . The device was attached with a hydrogel adhesive and covered with a Hypafix bandage. Participants were asked to wear the device continuously for one week and to continue their daily activities as usual. Upon completion of the one-week recording, participants removed the device and sent it back to the local clinical site.

Daily-living activity metrics

As previously described [9], an algorithm automatically identified the different activities (walking, lying, standing, and sitting) and each bout of walking throughout the week-long recording and then extracted measures that reflect the quantity and quality of walking. To focus on steady-state walking and to compare in-lab walking with community ambulation, we evaluated walking bouts that were at least 60 seconds long[9]. However, when focusing on gait quantity, we used walking bouts of all lengths. The extracted measures are defined in

Supplementary Material Table 1; these include measures of gait quantity (e.g., number of steps, number of walking bouts) and gait quality. Gait quality measures included those that reflect pace (e.g., step length), gait symmetry (e.g., .step regularity) gait variability (e.g., the amplitude of dominant frequency) and variability across walking bouts (e.g., SD of the peaks amplitude CV). To describe the overall level and distribution of physical activity intensity, we averaged the vector magnitude value over fifteen-second epoch, similar to Doherty et al [27]. Then, we generated the signal vector magnitude, SVM, measurement, an empirical cumulative distribution function from all available fifteen-second epochs (for further information on how SVM reflects daily-living physical activity, see Supplementary Material Methods). Data was included in the analysis if the recording was longer than three days.

Statistical Analyses

A series of multivariable linear regression analyses were performed to identify independent predictors associated with the two dependent measures of interest: 1) motor symptom severity as expressed by the MDS-UPDRS-part III; and, in separate analyses, 2) total daily-living physical activity level, as expressed by the SVM of the acceleration signal, summed over the week. Normality of data was assessed using Shapiro-Wilk tests. To avoid colinearity, we first examined the relationships among metrics within daily-living and within laboratory subcategories using Pearson's correlations. If two metrics were strongly correlated with one another ($r>0.7$), only the one most strongly associated with the dependent variable (e.g., MDS-UPDRS-part III) was retained. Subsequently, we carried out a series of backward regression models to identify the relationship between the dependent outcome and independent factors associated with the dependent variable by examining each family of measures first (e.g., balance and functional tests, gait quantity, gait pace, gait symmetry, gait variability, day and night activity, and variability across walking bouts, demographics and subject's characteristics and MDS-UPDRS I-III) and then generating a single, parsimonious model. The process is summarized in Supplementary Material Figure 1. A variable was entered into the model if the significance level of its F value of the ANOVA was less than 0.05 and was removed if the significance level is greater than 0.10. All analyses were adjusted for age, sex and disease duration. All of the independent predictors that were identified within each set were then entered into another backward regression model to identify the laboratory and daily-living predictors. Finally,

the predictors that remained in those models were entered into a final regression model. We report the beta and p-values for the predictors. SPSS version 24 was used for the statistical analyses.

RESULTS

The subjects had moderate disease severity (Hoehn & Yahr 1-3) and were multiple fallers (at least two falls in 6 months prior to assessment). They were generally well-educated, did not have major cognitive impairments, and had approximately 10 years of motor symptoms (Table 1). The univariate relationships between the MDS-UPDRS-parts I-III (and the total score), two selected laboratory-based gait and balance measures, and total daily-living physical activity are summarized in Figure 1. Total daily-living physical activity was not strongly correlated with the scores on any of the MDS-UPDRS tests or with the lab-based assessment of balance or gait. Gait speed and MiniBest scores were moderately correlated with MDS-UPDRS-part III scores.

The multivariate associations between each laboratory and daily-living family of metrics and PD motor symptom, i.e., MDS-UPDRS-part III, are summarized in Supplementary Material Table 2. Age, sex and disease duration explained 6.0%, laboratory-based measures of gait and balance explained 27.1%, and daily-living measures explained 37.8% of the variance of the MDS-UPDRS-part III scores. When considered together in a final block-wise regression model, the predictors explained 46.2% of the variance in the MDS-UPDRS-part III (see Table 2a). As shown in Figure 2a, daily-living measures accounted for 62.0% of the explained variance, laboratory measures for 30.1%, demographics and subject characteristics for 7.7% of the explained variance of PD motor symptom severity as assessed in the clinic using the MDS-UPDRS-part III.

Examining these relationships from a different perspective, Supplementary Material Table 3 summarizes the contribution of demographics and subject characteristics, MDS-UPDRS (parts I-III) scores and laboratory gait and balance measures to the variance in total daily-living physical activity (i.e., SVM). Age, sex and disease duration explained 12.4% of the variance, as shown in Model A. Since women had significantly fewer years of disease duration and significantly higher SVM, we added a disease duration and sex interaction term to the model. As shown in Model B, MDS-UPDRS-part III had the strongest association with total daily-living physical activity among the three UPDRS tests, predicting 15.8% of its variance when considered together with

demographics and subject characteristics. However, the MDS-UPDRS-part III alone accounted for only 5.8%. Laboratory-based balance and gait measures explained 27.6% of the SVM variance, as summarized in Model C.

When considered together in a final block-wise regression model, 27.1% of the variance of total daily-living physical activity was explained (see Table 2b). Laboratory gait simmetry measures accounted for 44.0%, demographics and subject characteristics for 42.7%, and the MDS-UPDRS-part III for 13.3% of the explained variance of the total daily-living physical activity (see Figure 2b); in other words, the MDS-UPDRS explained less than 4% (0.13 x 0.27=) of the variance in total daily-living physical activity. Scores on the MDS-UPDRS parts I and II were not independently associated with total daily-living physical activity.

DISCUSSION

The results of this cross-sectional analysis indicate that daily-living physical activity, laboratory-based measures of dynamic balance, demographics and subject characteristics are related to PD motor symptom severity, as expected, and that they explain almost 50% of the variance of motor symptom severity (recall Figure 2a). On the flip side, demographics and subject characteristics, laboratory-based gait and balance tests, and disease severity (i.e., MDS-UPDRS I-III) explained less than a third of the total daily-living physical activity (recall Figure 2b). Taken together, these findings suggest that home-based, 7 days continuous daily-living-based measures of mobility and function are related to traditional measures of disease severity, specifically MDS-UPDRS part III. In addition, daily-living measures also apparently provide additional information that is not strongly reflected by conventional standardized, one-time measures conducted in the clinic (e.g., MDS-UPDRS I-III, Mini-BESTest).

The contribution of laboratory-based and daily-living physical activity measurements to the variance of PD motor symptom severity

Our results suggest that daily-living mobility monitoring adds considerable explanatory value to the severity of motor symptoms in PD. We found that daily-living activity measures independently explain 37.8% of the

variance of the severity of motor symptoms, as reflected by the MDS-UPDRS-part III (see Supplementary Material Table 2). This relatively high value is somewhat surprising when considering that the MDS-UPDRS-part III score is composed of items that evaluate a wide range of PD non-gait related symptoms including tremor, speech, facial expressions, rigidity, and bradykinesia. The MDS-UPDRS-part III items related to gait, balance and lower extremity movements account for approximately one-third of the total possible score. This demonstrates a noticeable advantage of assessing PD mobility using objective tools of home-based, continuous daily function when compared to laboratory-based assessment (mobility capacity) which may be influenced by the clinician's subjectivity and the patient's extra effort during a short term examination. Supported by other recent studies[19,28], our findings demonstrate the importance of the emerging approach of assessing PD motor disability in daily-living conditions based on continuous recordings, in addition to a conventional one-time, laboratory assessment. Our analysis revealed important associations between specific measures of daily-living activity (daily-living gait variability and the number of longer and shorter walking bouts) and severity of the motor symptoms in PD (recall Supplementary Material Table 2). Interestingly, the participants mainly used short 5-10 second walking bouts, whereas long bouts (> 120 sec) were rare (recall Supplementary Material Table 1). A possible explanation for these findings may be that daily-living activities, mostly at home, were composed of a large number of short walking bouts. Perhaps, people with PD with worst disease severity prefer to get up for a "good reason" twice a day (the mean of large bouts in our analysis, recall Supplementary Material Table 1) instead of making more frequent short movements. Conceivably, improving strength and fitness in treatment sessions along with balance training may lengthen PD patients' walking bouts, might positively influence their motor disability and even reduce future fall risk.

The contribution of PD motor symptom severity and other laboratory-based assessment of mobility to the variance of total daily-living physical activity

When trying to explain total daily-living activity, all laboratory tests together (including gait, balance and the severity of motor symptom) accounted for less than 30% of its variance (recall Table 2b). These findings, supported in part by previous studies[4,28], are likely related to the influence of environmental conditions, motor and non-motor fluctuations, comorbidities and other putative mediators of daily-living physical activity that cannot be accounted for by one-time laboratory or clinic testing. The best predictors of total daily-living

activity were demographics and subject characteristics (which were retained in all models), followed by gait symmetry measured in the laboratory (see Table 2b). Unexpectedly, balance tests, walking speed and step length measured in the lab did not contribute to the variance of the total daily-living physical activity, nor did cognitive function (as represented by the Montreal Cognitive Assessment). Somewhat counter-intuitively, we found that only the MDS-UPDRS-part III score remained as a predictor (explaining approximately 16% of the variance in SVM, together with age, sex and disease duration), while the other two parts of the MDS-UPDRS (ADL and non-motor symptoms) did not remain as predictors (see Supplementary Material Table 3). Yet, our results seem to be consistent with other research which found that higher age, gender and greater severity of motor symptoms are associated with less time spent walking[21] and total energy expenditure (kcal/day)[16]. As previously demonstrated, greater total daily-living physical activity is known to protect against a range of diseases and negative outcomes [22,23] and is negatively associated with mortality in old age[29]. Moreover, recent studies showed that physical activity plays a role in improving a multitude of global and specific motor and non-motor symptom in PD patients[17,18]. Thus, in PD, daily physical activity may be considered as a form of non-pharmacological therapy[17]. Finally, the role of daily-living physical activity as an important predictor of many adverse health outcomes suggests that one needs to measure it to gain a more complete estimate of the impact of disease and treatments[30].

In conclusion, to the best of our knowledge, this is the first systematic examination of the relationship between daily-living physical activity and motor symptom severity in patients with PD. On the one hand, our findings revealed that standardized measures such as clinic-based MDS-UPDRS-part III along with other laboratory gait measures are relatively weak predictors of how patients actually function at home and in the community (i.e., outside of the clinic) (recall Table 2b and Figures 1 and 2). On the other hand, specific daily-living activity measures apparently are relatively strong predictors of motor symptom severity (recall Table 2a and Figure 2a). These findings emphasize the difference between clinical or laboratory testing and real-life activity of patients. Thus, the present results underscore the importance of monitoring daily-living activity for understanding disability and disease progression as well as potentially monitoring the effects of interventions and treatments.

Limitations and Future Work

The present work has several limitations. The cross-sectional nature of this analysis limits our ability to identify cause and effect and changes over time. The participants who were analyzed here were all, by definition, fallers. In the future, it will be important to see if similar associations are observed among PD subjects who are not fallers and among less severely impaired patients. Potential new metrics resulting from more advanced analytical approaches (and additional sensing technologies such as gyroscopes) could provide even greater input into the functional motor performance of patients during daily-living. Furthermore, it is not possible to fully separate passive and active acceleration from the measurement of a tri-axial accelerometer placed on the lower back alone. Nonetheless, the present findings suggest that measuring daily-living physical activity has strong potential to more fully and optimally assess patients with PD and to explore functional decline and changes over time in response to therapeutic interventions and potential deterioration. Prospective studies are needed to further evaluate the degree to which long-term, 24/7 monitoring of gait and physical activity adds new levels of granularity and additional relevant information, above and beyond more conventional, one-time assessments.

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TABLES

Table 1: Participant characteristics (entries are mean ± SD, median (range) or %).

Variable	PD (n = 125)
Age (yrs)	71.49 ± 6.38
Gender (% men)	60.52%
Education (yrs)	13.34 ± 4.39
Body-mass-index (kg/m2)	25.91 ± 3.67
Disease Duration (yrs)	9.13 ± 6.42
Levodopa Equivalent Daily Dose (mg/kg)	970 ± 608
Hoehn and Yahr Stage	2.5 (1–3)
Montreal Cognitive Assessment	23.87 ± 4.21
Mini Mental State Examination	28.02 ± 1.69
UPDRS Total score	63.47 ± 21.53
UPDRS Part III (Motor)	30.43 ± 13.04
Falls in 6 month prior to assessment	3 (2–50)

Table 2a: Multivariable model of joint contributions of lab-based and daily-living measures to the variance in motor symptom severity, as evaluated by the MDSUPDRS part III.

	R^2 within block	R^2 Change	Total R^2
Demographics and subject characteristics Age (β = 0.193) Disease Duration (β = 0.177)	0.061	0.061	**0.462**
Laboratory Gait and Balance Measures** Age (β = 0.017) Disease Duration (β = 0.081) Mini-BESTest (β = −0.506)	0.281	0.220	
Daily-Living Measures ** Age (β = −0.051) Disease Duration (β = 0.075) Mini-BESTest (β = −0.490) Gait Quantity: number of walking bouts above 120 s long (β = 0.348) number of walking bouts 5–10 s long (β = −0.186) Gait Variability: ampML (β = 0.256) frqML (β = 0.217)	0.462	0.182	

** this block of analyses builds on the previous block. Initial steps leading to these results are shown in a supplementary material table.

Table 2b: Multivariable model of joint contributions of lab-based measures and motor symptom severity to the variance in total daily-living physical activity, as measured by the SVM.

	R^2 within block	R^2 change	Total R^2
Demographics and subject characteristics Age (β = −0.187) Sex (β = −0.004) Disease Duration (β = −0.178)*	0.113	0.113	**0.271**
Motor Symptom Severity** Age (β = −0.139) Sex (β = 0.001) Disease Duration (β = −0.152)* MDS-UPDRS-part III (β = −0.214)	0.155	0.042	
Laboratory Gait and Balance Measures** Age (β = −0.127) Sex (β = −0.066) Disease Duration (β = −0.237)* MDS-UPDRS-part III (β = −0.134) Gait Symmetry: StpRegV (β = 0.268) HRv (β = −0.174)	0.270	0.116	

* Adjusted to sex-disease duration interaction.

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FIGURES

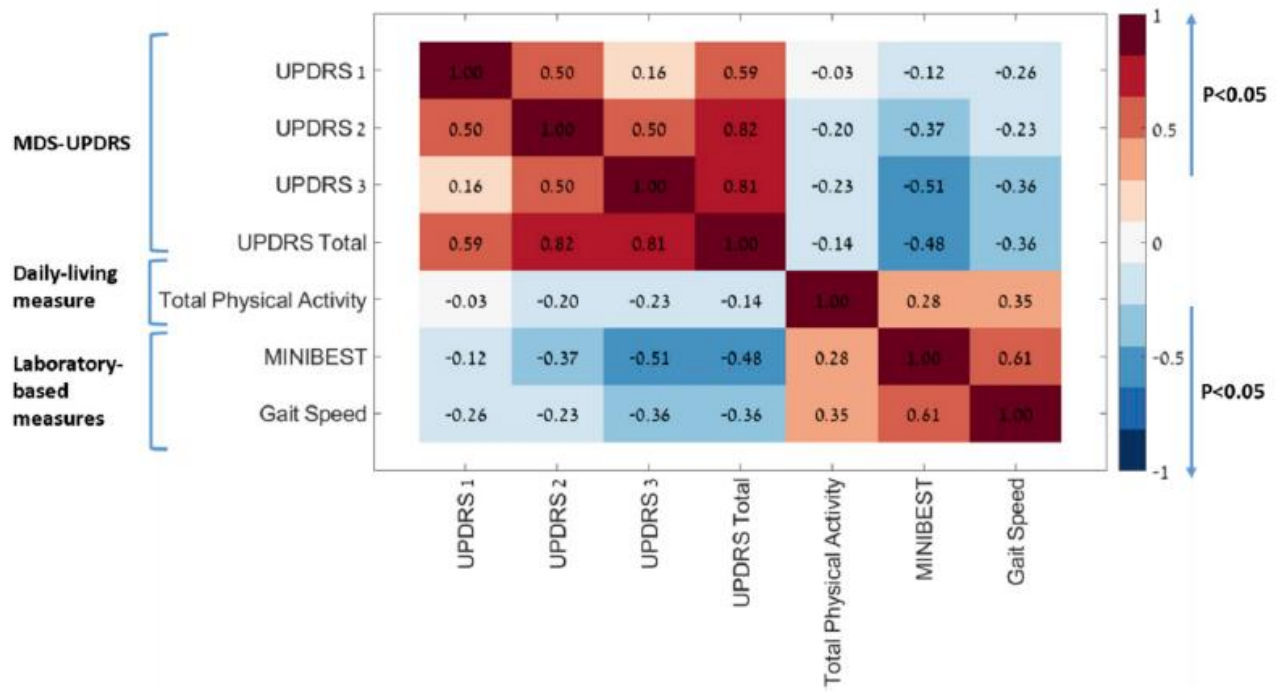


Figure 1: Heat map showing the univariate Pearson correlation coefficients between MDS-UPDRS, daily living activity, specifically, total daily-living physical activity (SVM), and lab-based measures of gait and balance. Darker pixels reflect higher correlation values. Note that MDS-UPDRS parts I-III and total scores are only moderately correlated to total daily-living physical activity. Gait speed and the MiniBest were chosen as representatives of lab-based representatives because of their widespread use and because of their relatively strong association with MDS-UPDRS 3. Similar results were obtained using Spearman's correlation instead of Pearson's.

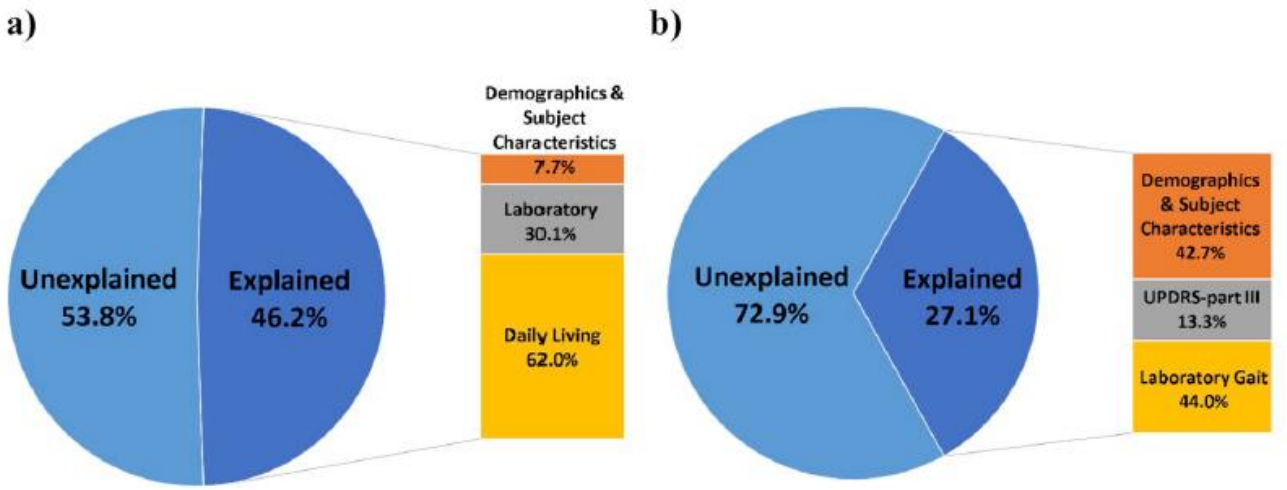


Figure 2: Variance of the two dependent outcome measures. a) Variance in MDS-UPDRS-part III as explained by laboratory and daily-living metrics. Daily-living measures accounted for 62.0%, laboratory measures for 30.1% demographics and subject characteristics for 7.7% of the explained variance in the MDS-UPDRS part III: motor part of the Unified Parkinson's Disease Rating Scale; b) Variance in total physical daily-living physical activity, SVM, as explained by subject demographics, the MDS-UPDRS, and laboratory measures of gait and balance. Demographics and subject characteristics accounted for 42.7%, MDS-UPDRS-part III 13.3% and laboratory gait measures for 44.0% proportion of the explained variance. Note that MDS-UPDRS parts I and II were included as potential predictors, but they were not significant independent predictors and hence were not included in the final model. (MDS-UPDRS part III: motor part of the Unified Parkinson's Disease Rating Scale).

Supplementary Material Methods

The use of accelerometer-based technology as a tool for assessing daily-living physical activity

Physical activity that occurs during daily-living is a modifiable behavior that has numerous known health benefits[1,2]. It is not surprising, therefore, that many public health efforts have focused on promoting a more active lifestyle to improve the health of older adults and patients with disease[3]. Traditionally, community-based studies used self-report and questionnaires to assess physical activity[4]. More recently, with the advance of technology, activity monitoring (also referred to by some as actigraphy) has been used to quantify daily-living activity. Activity monitoring is a non-invasive method that is widely used in epidemiologic and other studies to objectively measure how active (or inactive and sedentary) an individual is. With activity monitoring, an unobtrusive, body-fixed sensor captures movement continuously over the course of several days using a small accelerometer to measure total daily-living physical activity; this approach mitigates the problems of self-report like recall bias and other sources of subjectivity[5]. Previous work using an accelerometers to measure activity has shown that measures of total daily-living physical activity are related to and predictive of many important health outcomes such as obesity, death[6,7], disability[8,9], cognitive decline[10], mild cognitive impairment[11,12], and dementia[10,13,14]. Moreover, recent studies showed that physical activity plays a role in improving a multitude of global and specific motor and non-motor symptom in patients with Parkinson's disease[15,16].

Typically, a small sensor is worn for a week or more to measure gross motor activity. Older activity monitoring sensors that were based on an accelerometer stored and reported activity counts as measured in 15 second windows and then summed the results over days or a week. Newer devices measure and record the acceleration (and hence movement) in 3 dimensions and can be also be used to quantify total daily-living physical activity as well as gait quantity and quality, as done in the present study. To obtain the amount of physical activity, the movement in all three acceleration axes are accounted for by determining the signal vector magnitude, SVM, essentially, the sum of the acceleration signal across each of the 3 orthogonal directions (vertical, v, aneterior-posterior, ap, and medial-lateral, ml) , at every sample point:

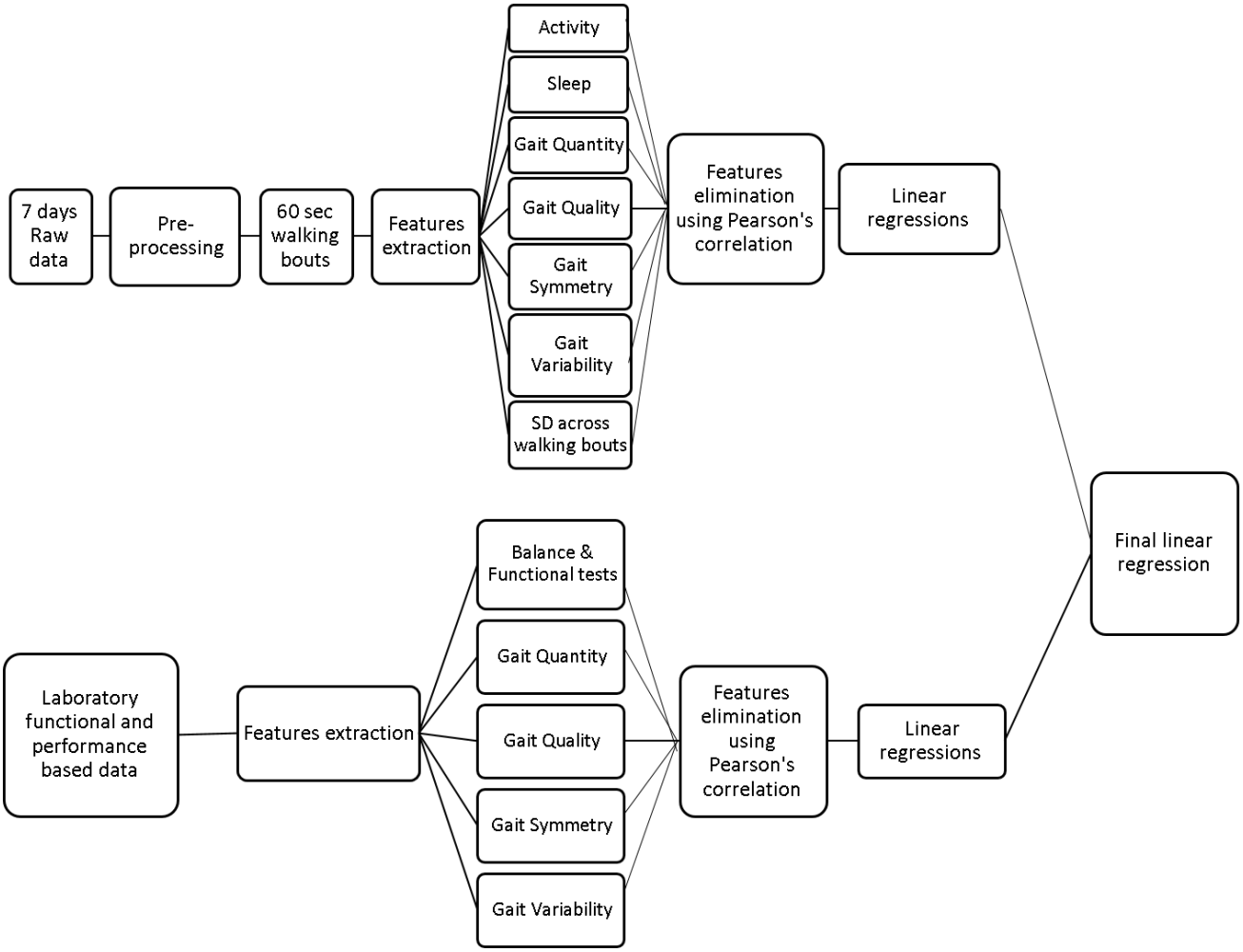
$$SVM = \sqrt{acc_v^2 + acc_{ap}^2 + acc_{ml}^2}$$

Once the SVM is determined at each time point, it can be summed over 15-second blocks and then summed over the day to produce actigraphy-like measures of daily-living. In the present analyses, SVM refers to the total daily-living physical activity as the activity measure is summed over the day (and averaged over each day of the recording). In addition, the raw acceleration can be used to quantify gait and other movement features.

Daily-living physical activity may be influenced by factors such as exercise, cognition, affect, and social interactions. Therefore, objective monitoring putatively captures activity features that are not reflected in a single test in a laboratory or by self-report questionnaires. Due to developments in the technology, accelerometers and related devices have become one of the most widely used method for objective assessment of physical activity in large scale studies[17-21]. For example, the recent UK Biobank study assessed daily-living activity in more than 10,000 subjects using an accelerometer (the same one used in the present study)[22] and NIH-sponsored study of mobility in older adults also used a similar device[23].

The selection of the wearable device and its location

The Axivity 3-D accelerometer sensor used in the present work has been used as the basis for assessing activity in more than 150 publications. It is the same device that is used in the large UK Biobank study and is very similar to other devices used to measure daily-living activity[24-28], using the same principles and concepts applied in the present analyses. In order to evaluate 'whole body' movement, we choose to place the accelerometer close to the center of mass, as previously described by Mathie et al. [29] and used in other studies [30-33] (among many others).



Supplementary Material Figure 1. Block diagram summarizing the analysis process

Supplementary Material Table 1: Daily-living and laboratory based measures

	Variable	Mean ± SD
Laboratory functional and performance based variables		
Balance & Functional Tests	Mini-Balance Evaluation Systems Tests (Mini-BESTest)	21.48±5.38
	Four Square Step Test (FSST)	13.40±5.51
Gait Quantity	Two Minute Walk Distance [m] (2MinWalk)	123±30
Gait Pace	Step length [cm] (GMstepLength)	55.42±11.25
Gait Rhythm	Cadence [steps/min]	110.91±11.77
Gait Symmetry	Step symmetry V axis [unitless] (StpSymV)	0.99±0.20
	Step regularity V axis [unitless] (StpRegV)	0.58±0.15
	Harmonic ratio V Axis [unitless] (HRv)	0.86±0.18
	Harmonic ratio ML Axis [unitless] (HRml)	0.63±0.16
Gait Variability	Stride regularity V axis [unitless] (StrRegV)	0.59±0.14
	Dominant frequency V axis [Hz] (FrqV)	1.82±0.18
Daily-living based variables*		
Activity	Sum SVM at day time [g] (SVMDay)	1844±701
	Percent Active at Night [%] (PrcActiveNight)	2.99±1.86

Sleep	Mean nap bout at day time [minutes] (MeanNapBout)	43.05±28.55
Gait Quantity	Number of walking bouts 5-10 sec [#]	98.52±48.73
	Number of walking bouts >120 sec [#]	2.30±2.35
Gait Pace	Mean step length [cm] (MeanStepLength)	54.48±7.87
Gait Symmetry	Step regularity ML axis [unitless] (stpRegML)	0.28±0.10
Gait Variability	Dominant frequency ML axis [Hz] (frqML)	0.90±0.09
	Amplitude of the dominant frequency ML axis [g^2/Hz] (ampML)	0.28±0.14
SD across walking bouts	SD of step length [cm] (SD_StepLength)	4.12±2.11
	SD of the peaks amplitude CV [g^2/Hz] (SD_CVAMPPeaks)	0.14±0.06
	SD of width of the dominant frequency ML axis [Hz] (SD_wdML)	0.16±0.11
	SD cadence of V axis [Hz] (SD_Cadence)	5.18±2.15

*In the case of daily-living measures, only those that remained significant in each sub-category after the backwards elimination process are presented here.

Supplementary Material Table 1: Contributions of lab-based and daily-living based measures to the variance in the severity of motor symptoms (MDS-UPDRS Part III)

Models				**R^2**
Model A – Demographics and Subject Characteristics	Age (β=.215)*			**0.060**
	Sex (β=0.140)			
	Disease Duration (β=.174)*			
Model B – Laboratory Gait and Balance Measures	Sub-category	Predictors within each sub-category	R^2	**0.271**
	Balance &Functional tests**	Mini-BESTest (β=-0.532)*	0.283	
	Gait Quantity	2MinWalk (β=-0.408)	0.179	
	Gait Pace	GMstepLength (β=-0.351)	0.193	
	Gait Symmetry	StepSymV (β=0.223)	0.140	
	Gait Variability	StrRegV (β=-0.224)	0.124	
	Demographics	(β=NS)		
Model C – Daily-Living Measures	Sub-category	Predictors within each sub-category	R^2	**0.378**
	Activity	PrcActiveNight (β=-0.163) SVMDay (β=-0.222)	0.114	
	Sleep	MeanNapBout (β=0.182)	0.033	
	Gait Quantity**	Number of Walking bouts 5-10 sec (β=-0.451)* Number of Walking bouts >120 sec (β=0.261)*	0.228	
	Gait Pace	MeanStepLength (β=-0.314)	0.099	
	Gait Symmetry	StpRegML (β=0.189)*	0.092	
	Gait Variability**	frqML (β=0.355)* ampML (β=0.355)*	0.264	
	SD across walking bouts	STD_StepLength (β=-0.165)* STD_wdML (β=-0.263)* STD_Cadence (β=-0.157)* STD_CVAMPPeaks (β=0.198)*	0.224	

	Demographics	(β=NS)		

* Features that remained following backwards regression within each category.

** Categories remained in the final backwards regression with both laboratory gait and balance and daily-living measures.

β=NS: This feature did not survive following backwards regression within its subcategory.

Supplementary Material Table 3: Contributions of Lab-based Measures, UPDRS-part I-III to Variance in total daily-living physical activity as measured by the SVM

Models				**R^2**
Model A - Demographics and Subject Characteristics[f]	Age (β=-0.208)*			**0.124**
	Sex (β=-0.053)*			
	Disease Duration (β=-0.219)*			
	Sex-Disease Duration interaction (β=0.455)*			
Model B – Disease Severity Scores	UPDRS part I (β=NS)			**0.158**
	UPDRS part II (β=NS)			
	UPDRS part III (β=-0.286)*			
	Demographics (β=0.499)*			
Model C – Laboratory Gait and Balance Measures			R^2	**0.276**
	Function Performance Based Balance Measurements	FSST (β=NS) Mini-BESTest (β=0.215)* Sex (β=0.222) Disease Duration (β=-0.212) Age (β=-0.217) Sex-Disease Duration interaction (β=0.461)*	0.205	
	Gait Quantity	2MinWalk (β=0.377)* Sex (β=0.222) Disease Duration (β=-0.192)	0.212	
	Gait Rhythm	Cadence* (β=0.170) Sex (β=0.187) Disease Duration (β=0.178) Age (β=-0.157) StrideTimeV (β=NS)	0.139	

Gait Symmetry**	HRv (β=-0.192) * StpSymV (β=NS) StpRegV (β=0.297)* HRml (β=0.170)* Sex (β=0.233) Disease Duration (β=0.233) Age (β=-0.178)	0.273
Gait Variability	StrRegV (β=0.387)* FrqV (β=NS) Sex-Disease Duration interaction (β=0.314)	0.236

*Features remained following backwards regression within subcategory.

** Categories remained in the final backwards regression.

[!]MoCA score as a representor of cognitive abilities was included as potential predictor in this model but did not remain after backwards elimination.

β=NS: This feature did not survive following backwards regression within this subcategory.

SUPPLEMENTARY MATERIAL REFERENCES

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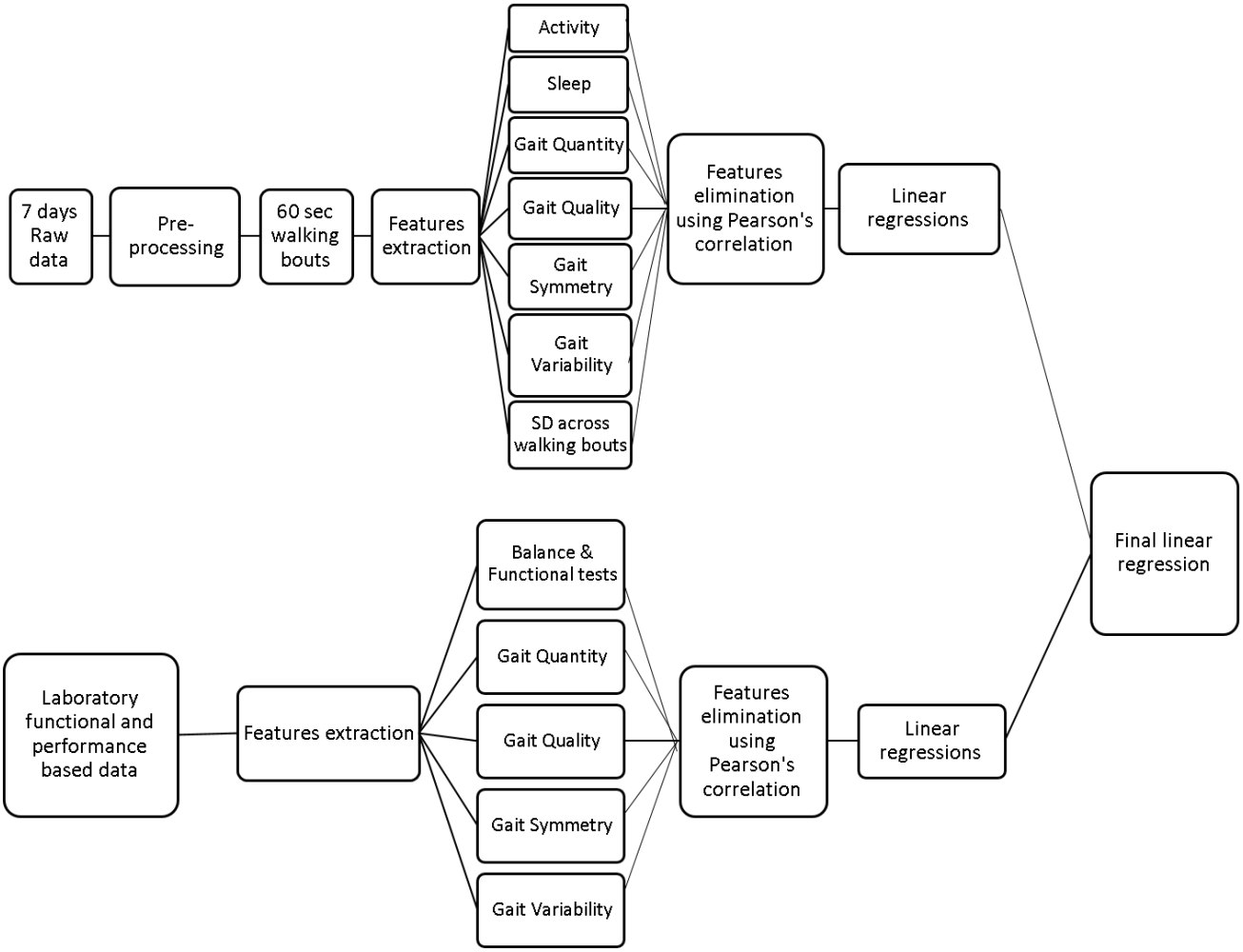

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Gait Quantity	Number of walking bouts 5-10 sec [#]	98.52±48.73
	Number of walking bouts >120 sec [#]	2.30±2.35
Gait Pace	Mean step length [cm] (MeanStepLength)	54.48±7.87
Gait Symmetry	Step regularity ML axis [unitless] (stpRegML)	0.28±0.10
Gait Variability	Dominant frequency ML axis [Hz] (frqML)	0.90±0.09
	Amplitude of the dominant frequency ML axis [g^2/Hz] (ampML)	0.28±0.14
SD across walking bouts	SD of step length [cm] (SD_StepLength)	4.12±2.11
	SD of the peaks amplitude CV [g^2/Hz] (SD_CVAMPPeaks)	0.14±0.06
	SD of width of the dominant frequency ML axis [Hz] (SD_wdML)	0.16±0.11
	SD cadence of V axis [Hz] (SD_Cadence)	5.18±2.15

*In the case of daily-living measures, only those that remained significant in each sub-category after the backwards elimination process are presented here.

Supplementary Material Table 2: Contributions of lab-based and daily-living based measures to the variance in the severity of motor symptoms (MDS-UPDRS Part III)

Models				**R^2**
Model A – Demographics and Subject Characteristics	Age (β=.215)*			**0.060**
	Sex (β=0.140)			
	Disease Duration (β=.174)*			
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	Balance &Functional tests**	Mini-BESTest (β=-0.532)*	0.283	
	Gait Quantity	2MinWalk (β=-0.408)	0.179	
	Gait Pace	GMstepLength (β=-0.351)	0.193	
	Gait Symmetry	StepSymV (β=0.223)	0.140	
	Gait Variability	StrRegV (β=-0.224)	0.124	
	Demographics	(β=NS)		
Model C – Daily-Living Measures	Sub-category	Predictors within each sub-category	R^2	**0.378**
	Activity	PrcActiveNight (β=-0.163) SVMDay (β=-0.222)	0.114	
	Sleep	MeanNapBout (β=0.182)	0.033	
	Gait Quantity**	Number of Walking bouts 5-10 sec (β=-0.451)* Number of Walking bouts >120 sec (β=0.261)*	0.228	
	Gait Pace	MeanStepLength (β=-0.314)	0.099	
	Gait Symmetry	StpRegML (β=0.189)*	0.092	
	Gait Variability**	frqML (β=0.355)* ampML (β=0.355)*	0.264	
	SD across walking bouts	STD_StepLength (β=-0.165)* STD_wdML (β=-0.263)* STD_Cadence (β=-0.157)* STD_CVAMPPeaks (β=0.198)*	0.224	

Demographics	(β=NS)		

* Features that remained following backwards regression within each category.

** Categories remained in the final backwards regression with both laboratory gait and balance and daily-living measures.

β=NS: This feature did not survive following backwards regression within its subcategory.

Supplementary Material Table 3: Contributions of Lab-based Measures, UPDRS-part I-III to Variance in total daily-living physical activity as measured by the SVM

Models				$\mathbf{R^2}$
Model A - Demographics and Subject Characteristics[f]	Age (β=-0.208)*			**0.124**
	Sex (β=-0.053)*			
	Disease Duration (β=-0.219)*			
	Sex-Disease Duration interaction (β=0.455)*			
Model B – Disease Severity Scores	UPDRS part I (β=NS)			**0.158**
	UPDRS part II (β=NS)			
	UPDRS part III (β=-0.286)*			
	Demographics (β=0.499)*			
Model C – Laboratory Gait and Balance Measures			R^2	**0.276**
	Function Performance Based Balance Measurements	FSST (β=NS) Mini-BESTest (β=0.215)* Sex (β=0.222) Disease Duration (β=-0.212) Age (β=-0.217) Sex-Disease Duration interaction (β=0.461)*	0.205	
	Gait Quantity	2MinWalk (β=0.377)* Sex (β=0.222) Disease Duration (β=-0.192)	0.212	
	Gait Rhythm	Cadence* (β=0.170) Sex (β=0.187) Disease Duration (β=0.178) Age (β=-0.157) StrideTimeV (β=NS)	0.139	

Gait Symmetry**	HRv (β=-0.192) * StpSymV (β=NS) StpRegV (β=0.297)* HRml (β=0.170)* Sex (β=0.233) Disease Duration (β=0.233) Age (β=-0.178)	0.273
Gait Variability	StrRegV (β=0.387)* FrqV (β=NS) Sex-Disease Duration interaction (β=0.314)	0.236

*Features remained following backwards regression within subcategory.

** Categories remained in the final backwards regression.

[!]MoCA score as a representor of cognitive abilities was included as potential predictor in this model but did not remain after backwards elimination.

β=NS: This feature did not survive following backwards regression within this subcategory.

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