Gait & Posture 71 (2019) 289–295

Contents lists available at ScienceDirect

Gait & Posture

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

Full length article

Upper body accelerations as a biomarker of gait impairment in the early stages of Parkinson's disease

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ARTICLE INFO

Keywords:
Gait analysis
Accelerometers
Harmonic ratio
Balance
Head and pelvis
Human movement

ABSTRACT

Background: Changes in upper body (UB) motion during gait may be a marker of incipient pathology, intervention response and disease progression in Parkinson's disease (PD), which if independent from the lower body motion, might provide an improved assessment of gait.

Research question: This study aimed to test this hypothesis and establish whether variables calculated from accelerations measured on the UB are unique from spatiotemporal characteristics and can contribute to an improved classification of PD gait.

Methods: Data was obtained from 70 people with PD (69.2 ± 9.9 y.o., UPDRS III: 36.9 ± 12.3) and 64 age-matched controls (71.6 ± 6.8 y.o.). Spatiotemporal characteristics were measured using a pressure sensitive mat (GAITRite). Head and pelvis accelerations were synchronously measured with wearable inertial sensors (Opal, APDM). Pearson's product-moment correlations were calculated between 49 selected variables from UB accelerations (representing magnitude, smoothness, regularity, symmetry and attenuation) and 16 traditional spatiotemporal characteristics (representing pace, variability, rhythm, asymmetry and postural control). Univariate and multivariate regression analysis was used to test the variables ability to classify PD gait.

Results: The variables were mostly unique from each other (67% of variables recorded an $r < 0.3$). Univariate and multivariate analysis showed that UB variables were moderately better at classifying PD gait than the spatiotemporal characteristics (Univariate: 0.70 to 0.81, Multivariate: 0.88 to 0.91 AUC).

Significance: This study showed for the first time that, if aiming at objective and optimal sensitive biomarkers for PD, UB variables should be measured in conjunction with spatiotemporal characteristics to obtain a more holistic assessment of PD gait for use in a clinical or free-living environment.

1. Introduction

Neurodegenerative diseases such as Parkinson's disease (PD) impair the ability to walk safely and efficiently [1]. Consequently, gait has been introduced as a biomarker to identify incipient pathology, contribute towards diagnostic algorithms, and quantify disease progression and response to intervention [2]. A majority of research and clinical analysis of PD gait has been performed in research laboratory settings and is primarily focused on movement of the lower limbs, especially end point trajectories of the feet which are expressed by standard spatiotemporal measures (such as step length and cadence). The emergence of small, lightweight inertial measurement units (IMUs) has facilitated measurement of upper body motion, which is known to be impaired in PD due to increased axial rigidity, asymmetrical arm swing and flexed posture. [3,4]. Therefore, its measurement may be further indicative of a reduced postural control and highlight disease specific impairments. Consequently, new gait variables calculated using IMUs have been developed and are proposed to describe magnitude, smoothness, attenuation, regularity and symmetry [5]. If these upper body variables highlight different aspects of motion, they may capture important clinical features of PD gait that are not already described by spatiotemporal measurements and are more indicative of impaired control [6,7]. Being able to measure gait using body worn sensors such as the IMUs might be more easily applied to clinics and free-living

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https://doi.org/10.1016/j.gaitpost.2018.06.166
Received 4 October 2017; Received in revised form 12 April 2018; Accepted 24 June 2018
0966-6362/

environments [8,9].

Although certain upper body variables can indicate a reduced quality of gait in PD [10–12], previous studies have typically assessed few variables using small sample sizes or focused upon other promising measures such as arm swing (not considered here due to a singular focus on the trunk's movements) [5]. Furthermore, as movements of the upper and lower body are rarely assessed in conjunction with each other [7], it is unknown whether upper body movements describe unique information or are merely a reflection of impaired lower body gait mechanics. If measuring movements of the upper body in PD can provide unique information, their inclusion to current gait models may improve objective measurement of gait impairments symptomatic of PD. It is hypothesised that because the aforementioned symptoms are specific to the upper body, its measurement will better characterise PD gait. Our aims in this study were therefore, to establish whether: i) upper body accelerations during gait are merely a reflection of lower body mechanics and are correlated with spatiotemporal characteristics; and ii) if upper body accelerations can discriminate between people with PD and age-matched controls independently and in combination with standard spatiotemporal characteristics with the potential to better characterise PD gait.

2. Methods

2.1. Subjects

Seventy participants with early stage PD (Age: 69.2 ± 9.9 yr, 23 females, Height: 1.68 ± 0.01 cm, Mass: 76.94 ± 16.16 kg, UPDRS III: 36.9 ± 12.3) and 64 age-matched controls (Age: 71.6 ± 6.8 yr, 29 females, Height 1.70 ± 0.10 cm, Mass: 80.12 ± 13.20 kg) were recruited into ICICLE-GAIT, a collaborative study within ICICLE-PD, an incident cohort study (Incidence of Cognitive Impairment in Cohorts with Longitudinal Evaluation – Parkinson's disease) within 4 months of diagnosis. Participants were excluded from ICICLE-GAIT if they had any neurological (other than PD), orthopedic, or cardiothoracic conditions that may have markedly affected their walking or safety during the testing sessions. People with PD had to be diagnosed with idiopathic PD according to the UK Parkinson's Disease Brain Bank criteria and were excluded if they presented with significant memory impairment (Mini Mental State Exam (MMSE) ≤24 [13]), dementia with Lewy bodies, drug induced parkinsonism, "vascular" parkinsonism, progressive supranuclear palsy, multiple system atrophy, corticobasal degeneration or poor command of English. None of the participants demonstrated severe tremor or dyskinesia. This study was conducted according to the Declaration of Helsinki and had ethical approval from the Newcastle and North Tyneside research ethics committee. All participants signed an informed consent form.

2.2. Measurement protocol

All participants were tested on medication and walked at their preferred pace for two minutes around a 25 m circuit containing a 7 m long pressure sensitive electronic walkway (Platinum model GAITRite, software version 4.5, CIR systems, United States of America) [14]. Accelerations were measured using two IMUs (128 Hz, Opal™, APDM Inc, Portland, OR, USA) located at 5th lumbar vertebra, to represent movement of the pelvis, and upon the back of the head. The sensor's X axis pointed downwards representing the vertical direction (V), the Y axis pointed to the right representing the medio-lateral direction (ML) and the Z axis pointed backwards representing the anterior-posterior direction (AP). The instrumented walkway and the IMUs were synchronised (± 1 sample) using a custom-made cable and the data was collected at 128 Hz using the same A/D converter. The acceleration data was segmented based upon the timing values obtained from the instrumented walkway meaning only straight line walking while in contact with the walkway was analysed.

2.3. Variables

Sixteen clinically relevant spatiotemporal variables were selected a priori according to a five-domain (pace, rhythm, variability, asymmetry and postural control) model of gait developed in older adults and validated in people with PD [2].

A broad range of upper body acceleration variables were selected for their applicability to be calculated in a clinical environment (e.g. using a limited enclosed space) and their ability to describe different domains of movement. Acceleration signals were realigned to the earth's gravitational constant [15,16], and a low-pass Butterworth filter with a cut-off frequency of 20 Hz was applied using MATLAB (version 8.4.0, R2014b) [7]. All variables were calculated on a single stride basis except the autocorrelation variables (collected during each pass of the GAITRite mat). Each variable was calculated in the AP, ML and V direction. Upper body acceleration variables were grouped into five domains: Magnitude, represented from the acceleration RMS (RMS) [15,17]; Smoothness, represented by jerk RMS (jerk) [18,19] and the jerk ratio [20]; Attenuation, represented by the coefficient of attenuation (CoA) [17]; Regularity, represented by the step and stride output from calculating the unbiased autocorrelation [21]; and Symmetry, represented by both the symmetry output from the autocorrelation (Auto sym) [21] and the harmonic ratio (HR) [12].

2.4. Statistical analysis

Group means and standard deviations of all variables were calculated to provide reference values for each group. To answer whether the upper body accelerations were correlated with the spatiotemporal characteristics (aim 1), Pearson's correlations were calculated. Following checking for normality and ensuring a normal distribution in all parameters, to address the second aim, a univariate analysis (receiver operator characteristic (ROC) curve) was first used to quantify how well each upper body acceleration variable could discriminate between people with PD and age-matched controls. Variables with an area under the curve (AUC) below 0.6 were removed to refine the models, to avoid multicolinearity and overfitting each model in the subsequent multivariate analysis. A multivariate analysis (binary logistic regression followed by ROC) was then performed using variables from the head, pelvis and the spatiotemporal model independently and in combination with each other. For the independent analysis, participant descriptors (e.g. age, sex, height and mass) were controlled for by force entering them into the analysis as an initial block. Block two was performed in a forward stepwise fashion. To test whether additional classification could be achieved using the acceleration variables in combination to the spatiotemporal model's variables, a three-block model was also used. For this 3 block analysis, the spatiotemporal variables were first entered in block two (forward stepwise) and the upper body acceleration variables were then subsequently added in a forward stepwise fashion in the third block to determine if they could add any significant additional classification.

3. Results

Table 1 shows all variable values and their corresponding univariate AUC values.

Most variables only mildly correlated with the variables within the spatiotemporal model (< 0.3: 59% and 67%, > 0.3 and < 0.5: 20% and 19%, > 0.5 and < 0.7: 15% and 9%, > 0.7: 6% and 6% for the control and PD group, respectively) (Fig. 1). Spatiotemporal variables describing Pace were correlated with all upper body domains, although strong correlations were only seen between with step regularity. Bar a few exceptions, the absolute difference between the PD and control group *r* values was similar between both groups therefore highlighting similar coupling between upper body accelerations and lower body spatiotemporal characteristics in both groups.

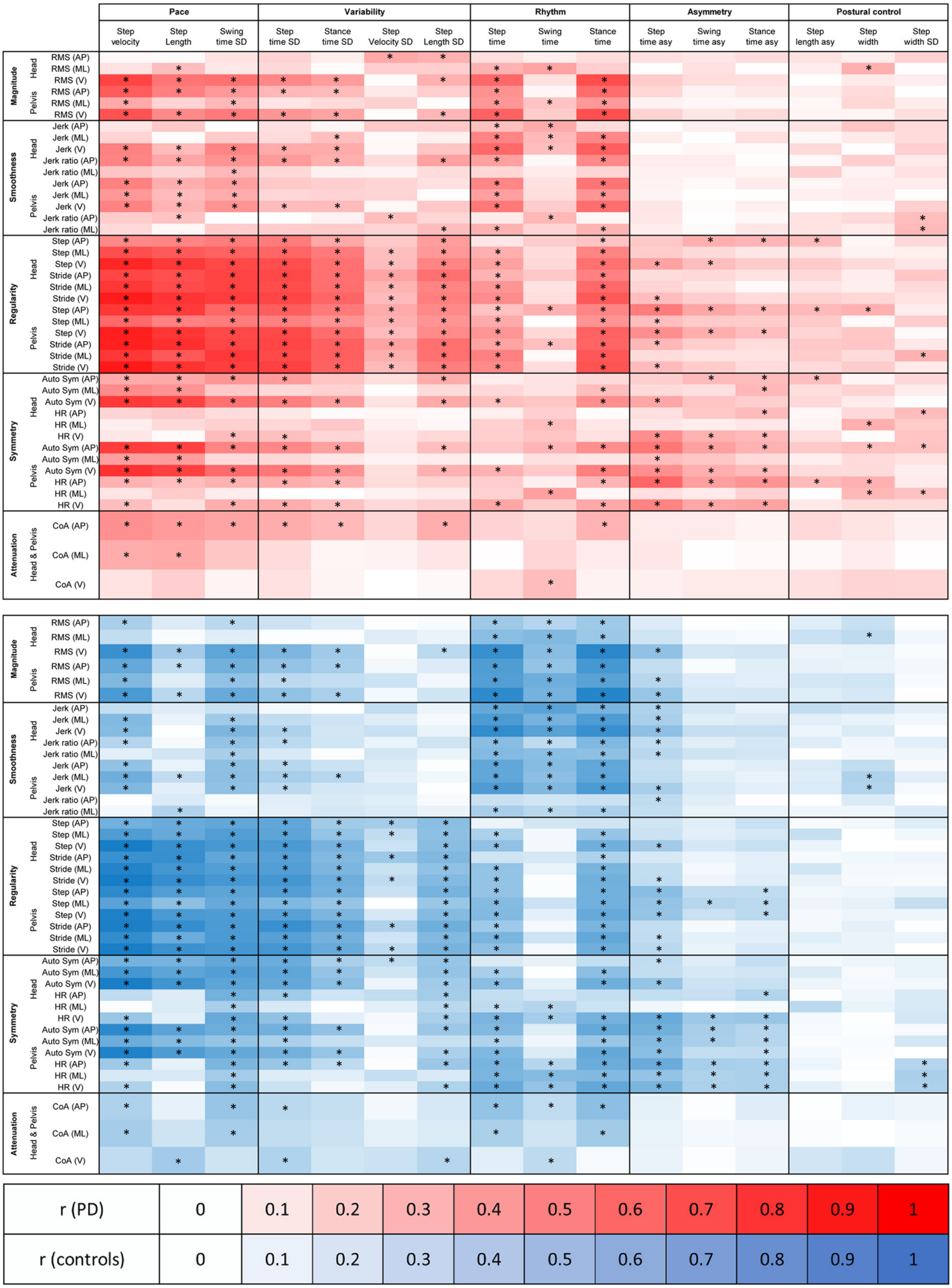
Table 1
Mean, standard deviation and univariate AUC values of all spatiotemporal and upper body acceleration variables for people with PD and controls.

Variable type	Domains		Variable	Control Mean (SD)	PD Mean (SD)	AUC
Spatiotemporal characteristics	Pace		Step velocity (ms^{-1})	1.28 ± 0.19	1.13 ± 0.22	0.687
			Step Length (m)	0.68 ± 0.08	0.61 ± 0.11	0.674
			Swing time SD (ms)	13.68 ± 3.86	18.08 ± 8.27	0.698
	Variability		Step time SD (ms)	14.94 ± 5.54	19.23 ± 9.30	0.667
			Stance time SD (ms)	23.03 ± 9.66	27.11 ± 12.60	0.59
			Step velocity SD (ms^{-1})	0.05 ± 0.01	0.05 ± 0.01	0.556
			Step length SD (m)	0.02 ± 0.00	0.02 ± 0.01	0.662
	Rhythm		Step time (ms)	0.53 ± 0.04	0.54 ± 0.04	0.566
			Swing time (ms)	0.38 ± 0.03	0.38 ± 0.03	0.51
			Stance time (ms)	0.68 ± 0.06	0.71 ± 0.06	0.595
	Asymmetry		Step time asymmetry (ms)	12.6 ± 11.14	20.42 ± 16.76	0.64
			Swing time asymmetry (ms)	8.19 ± 8.30	15.01 ± 11.74	0.673
			Stance time asymmetry (ms)	8.62 ± 8.86	15.37 ± 11.94	0.688
	Postural control		Step length asymmetry (m)	0.01 ± 0.01	0.02 ± 0.02	0.65
			Step width (m)	0.09 ± 0.02	0.09 ± 0.03	0.514
			Step width SD (m)	0.02 ± 0.00	0.02 ± 0.00	0.678
Upper body accelerations	Magnitude	Head	RMS (AP) (ms^{-2})	0.66 ± 0.16	0.69 ± 0.25	0.505
			RMS (ML) (ms^{-2})	0.86 ± 0.24	0.82 ± 0.27	0.547
			RMS (V) (ms^{-2})	1.75 ± 0.55	1.40 ± 0.47	0.696
		Pelvis	RMS (AP) (ms^{-2})	1.12 ± 0.31	0.92 ± 0.33	0.689
			RMS (ML) (ms^{-2})	1.03 ± 0.37	0.83 ± 0.30	0.655
			RMS (V) (ms^{-2})	1.82 ± 0.56	1.51 ± 0.52	0.671
	Smoothness	Head	Jerk (AP) (ms^{-3})	17.27 ± 6.39	19.51 ± 7.26	0.592
			Jerk (ML) (ms^{-3})	16.07 ± 5.16	16.84 ± 6.02	0.532
			Jerk (V) (ms^{-3})	47.01 ± 18.95	39.66 ± 14.05	0.609
			Jerk ratio (AP) (dB)	-3.12 ± 1.10	-2.18 ± 1.35	0.727
			Jerk ratio (ML) (dB)	-3.26 ± 1.07	-2.57 ± 1.07	0.668
		Pelvis	Jerk (AP) (ms^{-3})	46.38 ± 20.81	39.23 ± 20.64	0.625
			Jerk (ML) (ms^{-3})	43.19 ± 17.54	36.60 ± 14.78	0.615
			Jerk (V) (ms^{-3})	62.48 ± 29.00	52.76 ± 23.38	0.604
			Jerk ratio (AP) (dB)	-0.92 ± 0.77	-0.97 ± 0.66	0.53
			Jerk ratio (ML) (dB)	-1.13 ± 0.76	-1.06 ± 1.05	0.515
	Regularity	Head	Step (AP)	0.33 ± 0.20	0.28 ± 0.15	0.61
			Step (ML)	-0.55 ± 0.10	-0.43 ± 0.12	0.757
			Step (V)	0.60 ± 0.12	0.46 ± 0.14	0.763
			Stride (AP)	0.47 ± 0.12	0.39 ± 0.14	0.659
			Stride (ML)	0.58 ± 0.10	0.47 ± 0.13	0.729
			Stride (V)	0.60 ± 0.12	0.48 ± 0.15	0.732
		Pelvis	Step (AP)	0.51 ± 0.12	0.38 ± 0.13	0.76
			Step (ML)	-0.42 ± 0.13	-0.26 ± 0.11	0.81
			Step (V)	0.57 ± 0.12	0.44 ± 0.14	0.747
			Stride (AP)	0.57 ± 0.12	0.45 ± 0.14	0.741
			Stride (ML)	0.49 ± 0.13	0.36 ± 0.14	0.739
			Stride (V)	0.59 ± 0.12	0.47 ± 0.14	0.724
	Symmetry	Head	Auto symmetry (AP)	0.46 ± 0.27	0.40 ± 0.18	0.629
			Auto symmetry (ML)	-0.64 ± 0.11	-0.54 ± 0.15	0.748
			Auto symmetry (V)	0.67 ± 0.11	0.55 ± 0.13	0.776
			HR (AP)	1.19 ± 0.33	1.18 ± 0.33	0.513
			HR (ML)	2.17 ± 0.60	1.93 ± 0.56	0.621
			HR (V)	2.49 ± 0.63	1.96 ± 0.51	0.739
		Pelvis	Auto symmetry (AP)	0.61 ± 0.12	0.49 ± 0.13	0.749
			Auto symmetry (ML)	-0.59 ± 0.14	-0.44 ± 0.15	0.77
			Auto symmetry (V)	0.66 ± 0.11	0.54 ± 0.13	0.749
			HR (AP)	1.96 ± 0.54	1.54 ± 0.37	0.724
			HR (ML)	1.63 ± 0.50	1.27 ± 0.40	0.729
			HR (V)	2.36 ± 0.63	1.89 ± 0.50	0.72
	Attenuation	Head & Pelvis	CoA (AP) (%)	26.82 ± 15.76	12.43 ± 23.65	0.702
			CoA (ML) (%)	5.86 ± 22.86	-5.35 ± 27.10	0.62
			CoA (V) (%)	2.82 ± 6.13	4.37 ± 8.25	0.531

a. AP = anterior-posterior. ML = medio-lateral. V = vertical.
b. SD = standard deviation.

The univariate ROC curve analysis showed that 62% (10 out of 16) of the spatiotemporal variables and 75% (37 out of 49) of the upper body variables significantly discriminated between the two groups ($AUC > 0.6$; $p < 0.05$). The single best discriminating variable of PD gait was step regularity obtained from calculating the autocorrelation from ML pelvis acceleration (AUC = 0.81). The highest AUC for the spatiotemporal values was swing time variability (AUC = 0.70). The top ten classifiers for the spatiotemporal model and the upper body acceleration variables are shown in Fig. 2. Fig. 3, shows the spatiotemporal model [2] and the conceptual acceleration based models following the univariate variable reduction. Each model shows the deviation of the Z score as calculated using the age matched controls mean and standard deviation values as a reference.

The AUC values and variables in the multivariate models are shown in Table 2 for both the two and three block methods. The force entered patient demographic information in Block 1 recorded an AUC of 0.729



a. *indicates a significant correlation at the 0.05 significance level
b. AP = anterior-posterior. ML = medio-lateral. V = vertical
c. SD = standard deviation Asy = asymmetry

Fig. 1. Heat map displaying the Pearson's product-moment correlation coefficients (r) between the variables representing spatiotemporal and upper body acceleration domains for both the PD (Red) and control group (Blue) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

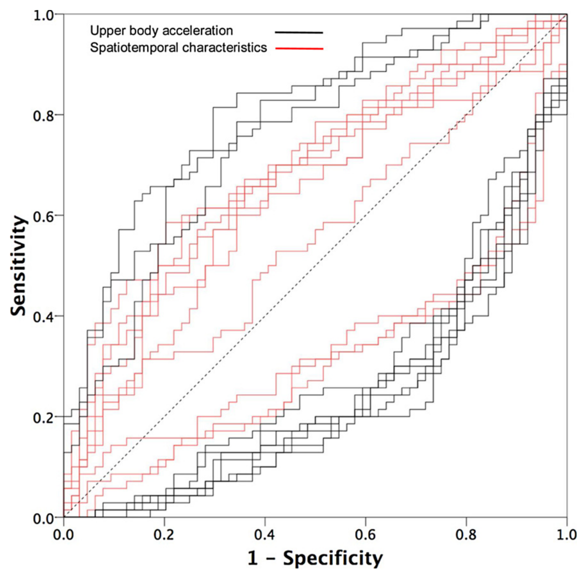


Fig. 2. ROC for the top ten classifiers from the spatiotemporal model and the top ten from the upper body acceleration variables.

($CI_{95\%}$: 0.64–0.81). When the gait variables were then entered in a forward stepwise fashion, all model's AUCs were greater than 0.88, confirming the importance of looking at a gait in a multi-facet way when using it as a biomarker in PD. With the two block method there was only a difference of 0.025 AUC between the poorest (spatiotemporal model, AUC: 0.88, $CI_{95\%}$: 0.83–0.94) and best (head model, AUC: 0.91, $CI_{95\%}$: 0.86–0.96) model. The 3 block analysis was performed to discover if measuring upper body movement provided additional classification ability. Therefore, the spatiotemporal variables were entered in block 2 (forward stepwise) and the acceleration based variables where subsequently entered in block 3 (also forward stepwise). This additional block achieved a significant improvement to the spatiotemporal model, however, the AUC only increased by 0.01, 0.02 and 0.02 for the head model, pelvis model and the combined information from the head and pelvis model, respectively.

4. Discussion

This study showed that, not all information about impaired PD gait can be captured through measuring spatiotemporal information and as such upper body accelerations provide novel information about gait. For the purpose of discriminating between the two groups, this information was as good, if not better, than standard spatiotemporal gait characteristics. The upper body is therefore not merely a passenger unit during gait and its motion may be a useful biomarker for PD. When combined with the spatiotemporal information, upper body acceleration variables contributed to a better description PD gait, however, the improved discrimination ability was negligible.

Surprisingly, none of the upper body variables were highly correlated with the variables within the postural control domain within the spatiotemporal model, despite often being defined as a direct measure [5]. This lack of correlation may suggest that the different variables measure different aspects of postural control. Previous studies that focused on the movement of the head during gait for people with PD concluded that a lack of correlation between acceleration based gait stability measures and lower body mechanics suggest they are distinct and can provide separate targets for therapy [10]. The fact that unique and favorable information was obtained through measuring upper body accelerations supports the idea that new and useful information is gained relative to just spatiotemporal characteristics and that a multidimensional analysis of gait may help to further understand the complexity of gait impairment and progression in PD [22]. Therefore, this

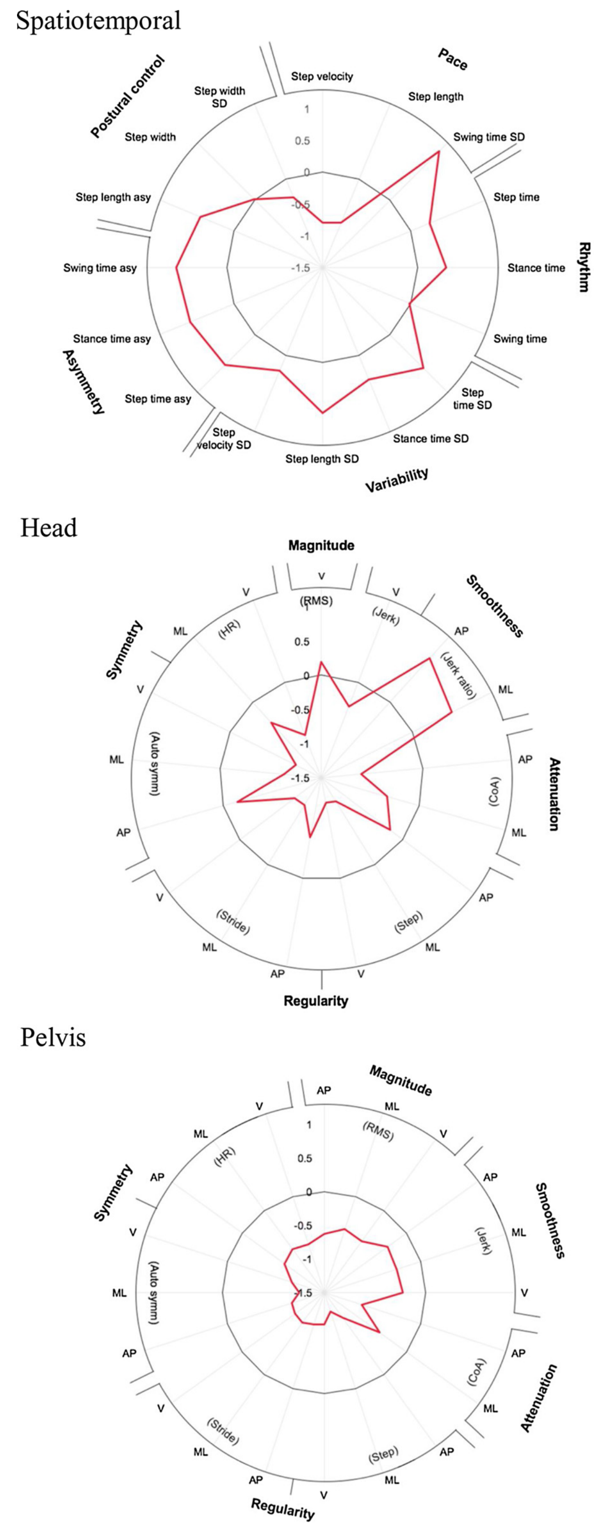


Fig. 3. Radar plot illustrating each variable from the spatiotemporal, head and the pelvis model. The central line represents the control data. Deviation from zero along the X axis radiating from the center of the plot represents how many standard deviations (based upon the control means and standard deviations) the PD differ from the controls.

a. AP = anterior-posterior. ML = medio-lateral. V = vertical

b. SD = standard deviation Asy = asymmetry.

uncorrelated and additional information supports that this information should be assessed in conjunction and potentially provide separate targets for therapy.

Table 2
Results of the two block and three block multivariate analysis including area under the curve (AUC and 95 CI) values and list of the variables included in the model.

Block number	Variables added	AUC	95% CI Lower Bound	95% CI Upper Bound	Variables in the model
Two block method					
Block 1 (force entered)	Demographic information	0.729	0.644	0.814	Age Sex Height Mass
Block 2 (stepwise entered)	Spatiotemporal model	0.887	0.83	0.943	Step length Swing time SD Step width SD
	Head	0.912	0.863	0.961	Jerk RMS (V) Jerk ratio (ML) Step regularity (ML) Step regularity (V) Auto symmetry (AP)
	Pelvis	0.896	0.842	0.951	Step regularity (ML) Stride regularity (AP)
Three block method					
Block 1 (force entered)	Demographic information	0.729	0.644	0.814	Age Sex Height Mass
Block 2 (stepwise entered)	Spatiotemporal model	0.887	0.83	0.943	Step length Swing time SD Step width SD
Block 3 (stepwise entered)	Head	0.898	0.846	0.95	Jerk ratio (AP/V)
	Pelvis	0.904	0.853	0.955	Step regularity (ML)
	Head & Pelvis	0.904	0.853	0.955	Step regularity (ML PV)

a. AP = anterior-posterior. ML = medio-lateral. V = vertical.
b. SD = standard deviation.

Regarding the variables that did correlate, such as the variables within the regularity and pace domains, the acceleration regularity variables achieved higher AUC variables than the pace domain spatiotemporal variables (one exception). As pace provides very useful information about disease progression [23], the potential of obtaining a proxy measure outside a controlled environment may be advantageous. Previous work stated that the relationship between walking speed, regularity and symmetry needs further analysis to discover if they are the same or separate constructs of gait [21]. Although this was not the focus of the investigation, the fact that regularity and symmetry variables correlated with the variables from the pace domain but were better capable to classify PD gait, opens the opportunity for acceleration based measures to replace or be combined with more traditionally used variables within multivariate gait models. One example where this may be beneficial is within the recent emphasis of trying to obtain relevant gait measures from participants in a free living environment [8,24]. For example, when recently attempting to replicate the spatiotemporal model using a single accelerometer located on the pelvis [8], step width and step width variability could not be calculated and the postural control domain in the model could not be replicated. Future research is therefore warranted to determine if the accelerations variables shown to be effective to characterise PD gait in the current investigation can be reliably obtained in a variety of environments and add to the free-living spatiotemporal model as a new representation of the postural control domain.

Negligible differences in the ability to classify the PD group based on their gait were found between the spatiotemporal model and those from the head or pelvis accelerations models. Therefore, if physical and economical resources are limited, models created from upper body accelerations could equally be used to classify PD gait. For this purpose, a sensor placed upon the pelvis may be the most applicable due to its methodically preferable location and ability to detect stride timing information in a variety of environments [16,25]. Furthermore if placed at the pelvis, the variables in the current investigations can potentially be combined with further variables such as stability measures [26] and turning characteristics [27], which were not included in this study due to methodological limitations. However prior to this, each variable needs to have their reliability assessed and to determine their efficacy to detect longitudinal and intervention outcomes.

The reported results showed that movements and multiple variables from the upper body can classify PD gait and as such this study represents an important step toward their adoption as useful biomarkers in the clinic or free-living environment. Nonetheless, discovering which of these variables (or even variables from other movements such as those calculated from arm swing movements) are sensitive and specific to the underlying disease process in PD [18], is a next essential step. However to achieve this step, longitudinal assessments are needed to examine how well upper body accelerations can track changes to gait due to disease progression and response to intervention [5,18], particularly in free-living and clinical settings where it is often impractical to measure gait using traditional methods of three-dimensional motion capture or instrumented walkways.

5. Conclusion

Most upper body acceleration variables provided additional and unique information about PD gait with respect to a traditional spatiotemporal gait model. The current results show promise for using acceleration based variables to highlight movements symptomatic of PD gait either alone or in addition to spatiotemporal characteristics. Until it is known exactly which variables are best for the desired purpose of using gait as a biomarker and the causality of the connection between the upper and lower body during gait is better understood, we recommend acceleration variables should still be assessed in conjunction to spatiotemporal variables in an attempt to record a holistic characterisation of PD gait. The results of this investigation warrants continued research to refine the best characterisation of PD gait using multiple techniques and different domains of gait in order to provide a more objective assessment of gait and improve the observation of people with PD in a clinical, or potentially, free-living environment.

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Acknowledgements

This work was supported by the MRC and Arthritis Research UK as part of the MRC-Arthritis Research UK Centre for Integrated research into Musculoskeletal Ageing (CIMA), Department of Mechanical Engineering, University of Sheffield, and Institute of Neuroscience, Newcastle University. ICICLE-GAIT is supported by the National Institute for Health Research (NIHR) Newcastle Biomedical Research Centre and Unit based at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University. ICICLE-PD is supported by Parkinson's UK. The research was also supported by NIHR Newcastle CRF Infrastructure funding and by the NIHR Sheffield Biomedical Research Centre. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

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