Wearable Technology Reveals Gait Compensations, Unstable Walking Patterns and Fatigue in People with Multiple Sclerosis

Psarakis, M., *Greene, D., Cole, M. H., Lord, S. R., Hoang, P., & Brodie, M. A. (2018). Wearable technology reveals gait compensations, unstable walking patterns and fatigue in people with Multiple Sclerosis. Physiological Measurement.*

ABSTRACT

People with Multiple Sclerosis (PwMS) often experience a decline in gait performance, which can compromise their independence and increase falls. Ankle joint contractures in PwMS are common and often result in compensatory gait patterns to accommodate reduced ankle range of motion (ROM). Using advances in wearable technology, the aim of this study was to quantify head and pelvis movement patterns that occur in PwMS with disability and determine how these secondary gait compensations impact on gait stability.

Twelve healthy participants and twelve PwMS participated in the study. Head and pelvis movements were measured using two tri-axial accelerometers. Measures of gait compensation, mobility, variability, asymmetry, stability and fatigue were assessed during a six-minute walking test.

Compared to healthy controls, PwMS had greater vertical asymmetry in their head and pelvic movements (Cohen's *d*=1.85 & 1.60). Lower harmonic ratios indicated that PwMS were more unstable than controls (Cohen's *d*=-1.61 to -3.06), even after adjusting for their slower walking speeds. In the PwMS, increased compensatory movements were correlated with reduced ankle active ROM (*r*=-0.71), higher disability (EDSS) scores (*r*=0.58), unstable gait (*r*=-0.76), reduced mobility (*r*=-0.76) and increased variability (*r*=0.83).

Wearable device technology provides an efficient and reliable way to screen for excessive compensatory movements often present in PwMS and provides clinically-important information that impacts on mobility, stride time variability and gait stability. This information may help clinicians identify PwMS at high risk of falling and develop better rehabilitation interventions that, in addition to improving mobility, may help target the underlying causes of unstable gait.

Keywords: Harmonic Ratio, Accelerometer, Dynamic Stability, Compensations, Gait Screening

INTRODUCTION

Multiple sclerosis (MS) is a chronic neurodegenerative disease affecting over 2.3 million people worldwide [1]. People with Multiple Sclerosis (PwMS) often develop gait impairments that affect functional mobility, physical independence and quality of life [2, 3]. Gait impairments in PwMS are multifactorial in nature and often caused by a range of factors including; spasticity, sensory loss, fatigue, muscle weakness and joint contractures [4-6]. Joint contractures effect approximately 57% of those with MS and the ankle joint is the most common site for contractures [5]. Ankle contractures result in a significant reduction of dorsiflexion range of motion (ROM) and often require compensatory movements of the knee and hip to accommodate restricted ankle ROM [7, 8]. Compensatory gait patterns such as circumduction and vaulting assist with the reduced toe clearance during the swing phase of gait [9], while compensations such as knee hyperextension may be caused by the lack of passive dorsiflexion during the stance phase of gait [10]. Abnormal gait is a significant risk factor for falls with over 50% of PwMS falling at least once over a 3-month period [11].

Clinical gait analysis is often used to monitor disability and disease progression in neurological populations [12]. Gait impairments are commonly assessed using functional measures, such as the timed-up-and-go or the six-minute walk test (6MWT) to assess mobility, but these tests lack sensitivity to detect changes in gait quality [13]. Gait quality may be assessed by observational rating scales, however, the accuracy of this method is highly dependent on the observer's experience [14]. Optical motion capture laboratories can provide accurate assessments of compensatory movements that occur during gait [7, 8], but such resources are impractical in many clinical settings [13]. Therefore, an accurate and clinically-feasible method to assess compensatory movements and their effect on gait stability in PwMS would assist clinicians during rehabilitation to target the underlying causes of poor mobility and unstable gait.

Asymmetric spastic paraparesis is a common gait pattern in PwMS that results in uncoordinated movements of the lower limbs that affects trunk movements [6, 15]. Recent advances using wearable devices have enabled accurate assessments of pelvic, trunk and head movement patterns while walking in both healthy and neurological populations [9, 13, 16, 17]. Accelerometers have been used to assess dynamic gait stability using harmonic ratios (HR) for stroke survivors [18], people with cerebral

palsy [19], individuals with Parkinson's disease [20-22] and recently in PwMS [23] without disability. Previous research using wearable technology has shown PwMS have an increase in trunk variability [24], an increase in lateral trunk motion [13], poorer lower limb ROM [25], and have poorer gait smoothness [23].

Head and pelvis stabilisation play an important role in maintaining balance and postural stability during gait [26] yet few studies have focused on using wearable devices to quantify the compensatory movements that occur at both the head and the pelvis in PwMS with disability.

Extending this body of literature, the primary aim of this study is to (i) quantify the head and the pelvis movement patterns in people with and without MS and (ii) determine how these secondary gait compensations may impact on mobility and gait stability, symmetry and variability during unfatigued walking. Secondary analyses include fatigue and inter-lap reliability. New methods to assess these compensatory movements that occur in PwMS with disability are presented.

METHODS

SUBJECTS

Twelve participants with Multiple Sclerosis (three males and nine females) and twelve healthy participants (four males and eight females) participated in the study. Healthy participants were matched where possible for age, sex, height and body mass (Table 1). Characteristics of MS group are presented in Table 1. Inclusion criteria for eligible participants in the MS group included; i) a confirmed diagnosis of MS by a neurologist; ii) an Expanded Disability Status Scale (EDSS) of ≤ 6 (indicating the ability to walk at least 100 meters with or without a walking aid); iii) the ability to walk independently; iv) no relapses within the past 12 weeks; v) free from any other disease, injury or illness preventing them from completing 6MWT. All healthy controls were free from any diseases, injuries or illnesses that may have affected their gait at the time of testing. Informed consent was obtained from all participants prior to participation and the study was approved by the Human Studies Ethics Committee at the University of New South Wales

CLINICAL DISABILITY ASSESSMENT

Range of motion (ROM) at the ankle joint was measured on both sides and uses as the basis to determine the more affected leg in PwMS. Matching sides were assessed for control participants. The method for quantifying passive ankle ROM has been described previously [27, 28]. Briefly, 100N of pulling force was applied to the heads of the metatarsals, parallel to the shank and the ankle angle was measured using an inclinometer (or Plurimeter). Similarly, active ROM was measured using an inclinometer with participants actively dorsiflexing their ankle without assistance from the examiner.

Functional mobility was assessed using the 6MWT, which required participants to walk back and forth along a 20-meter walkway at a self-selected fast walking pace. Participants were given standard instructions to “walk as far as possible for six minutes” with standardized encouragement given at 1, 3 and 5 minutes [29]. The distance walked in the six-minute walk period was recorded.

EXPERIMENTAL PROTOCOL

Compensatory head and pelvis movement patterns were measured during the 6MWT using two tri-axial accelerometers (Opal™ by APDM, sampling frequency 128Hz). The sensors were fixed to the participant’s head and pelvis as detailed in previous studies [17]. Briefly, the first tri-axial accelerometer was incorporated into a light plastic helmet liner (total mass 67g) and secured to the participant’s head. The second tri-axial accelerometer was rigidly attached to the participant’s pelvis between the posterior superior iliac spines using double-sided tape and a thick Velcro belt to reduce soft tissue artefact. During the 6MWT, data were reported according to a global vertical, body-centred heading, coordinate system [9]. As such, movements of the head and pelvis in the vertical (VT) direction were independent of body position or sensor orientation and were expressed relative to the global vertical. The anterior / posterior (AP) axis of the tri-axial accelerometers pointed forwards and parallel to the floor, while the medial / lateral (ML) axes were directed right (-ve) to left (+ve) perpendicular to the direction of travel.

Data were recorded continuously for the 6WMT duration. Participants completed laps of a 20-meter walkway. The walkway was marked with 1-meter incremented scale fixed to the floor. Data collection was run through custom built graphic user interface in MATLAB. Gait parameters were calculated using the middle 18-meters of each lap. The start and end of each 18-meter segment were annotated using

push buttons each time the participants passed the 1-meter and 19-meter markers. At the completion the test an alarm sounded, participants were instructed to stop and the distance the last part-lap input into the research software by the clinician using the 1-meter walkway scale. Distance walked was calculated by multiplying the number of laps by 20-meters plus the last part-lap distance.

The middle 18-meters of each lap were used in order to limit the effect of end turns and changes in walking speed on our planned analysis of straight line and 'steady state' walking. For the primary aims of unfatigued walking gait parameters were calculated using the first 18-meter lap segment to minimise the effect fatigue has on gait in PwMS [30]. The secondary analysis of inter-lap reliability used data from the first and second laps and the analysis of fatigue used the first and last laps.

DATA ANALYSIS

Custom software was developed in MATLAB to record and analyse the data. Our software used APDM's development protocols to communicate directly with the devices and maintain synchronization with external events. Walks by participants were synchronized with video footage in case confirmation of any aspect of their performance was required.

Measures of mobility included speed ($m.s^{-1}$), cadence ($steps.min^{-1}$), and step length (cm). Measures of gait variability and asymmetry included, stride time variability (ms), step time asymmetry (%), pelvic and head sway variability (cm). Measures of gait compensations included pelvis sway area (cm^2), head sway area (cm^2), pelvis asymmetry (%) and head asymmetry (%). Gait stability measures included harmonic ratios of both the head and pelvis in the vertical, anterior-posterior and medial-lateral axes.

For each lap, walking speed was calculated as the distance travelled (i.e. 18-meters) divided by the time taken to complete the distance. Heel strikes were measured by detecting the peak AP acceleration of the pelvis sensor each step cycle [31]. Cadence, stride time variability, and step time asymmetry (between left and right steps) were then calculated from the measured heel strikes [32]. Step length was calculated from the distance travelled divided by the number of steps. Stride time variability was reported as the standard deviation of stride times (two consecutive steps equals one stride). Stride time variability was reported in milliseconds as this is a well-established risk factor for falls [33]. Step time

asymmetry was calculated as the percentage difference between the mean left and right step times (Equation 1). Step time asymmetry was reported as an absolute value to prevent group means being erroneously close zero in the subsequent statistical analyses [32].

Equation 1: Step time asymmetry was calculated as the absolute percentage difference each lap

$$StepTimeAsymmetry = abs\left(\frac{mean(StepTime_{left}) - mean(StepTime_{right})}{\min\left(mean(StepTime_{left}),\ mean(StepTime_{left})\right)}\right) * 100\%$$

Left and right steps were determined from the ML movements of the head sensor over consecutive strides. During each swing phase the participants head was observed to reside primarily over the stance foot. Therefore, (over multiple strides) if the mean ML position of the head sensor during odd steps was greater than the mean ML position of the head during even steps, then the first step of the walk segment was a left step. For steady state straight line walking the step assignment algorithm was confirmed by video to be 100% accurate for people with and without MS.

The head and pelvic excursions during each gait cycle (Figures 1 & 2) were measured by twice integrating (using MATLAB's cumulative sum function) the corrected linear accelerations from the first lap of the 6MWT and high-pass filtered (using filter thresholds scaled to 0.25 and 0.5 of the step frequency) to obtain an accurate measurement of the stride to stride movements [9]. Measurements were based on previously validated methods with low Normalized Root Mean Squared Errors (NRMSE ≤4%) reported between the gold standard VICON motion capture data and the wearable device data [9]. Movement patterns from multiple gait cycles (Figure 1, thin lines) were overlaid in 3D space, which allowed a mean trajectory for the both the head and pelvis to be calculated separately (Figure 1, thick lines) and three new gait parameters were calculated (Equations 2-4).

Equation 2: Sway area was the product of the AP and ML 95% sway ranges in the transverse plane.

$$SwayArea = 95\%rangeML * 95\%rangeAP$$

Equation 3: Vertical asymmetry was the absolute difference between left and right mean vertical trajectory ranges divided by the minimum vertical trajectory range and expressed as a percentage.

$$AsymmetryVT = abs\left(\frac{rangeVT_{left} - rangeVT_{right}}{\min(rangeVT_{left}, rangeVT_{right})}\right) * 100\%$$

Equation 4: Sway variability (variance) was the standard deviation of trajectory spread in 3D space. Each gait cycle (stride) was partitioned into 100 points. At each point, the variance of trajectories for all gait cycles about the mean for that point was calculated and the standard deviations of all axes combined.

$$SwayVariance = \sqrt{\sum_{100}^{n=1} \frac{var(SwayAP_n) + var(SwayML_n) + var(SwayVT_n)}{100}}$$

Gait stability was measured using Harmonic ratios. Harmonic ratios along each axis were calculated as a validated measure of dynamic stability. Lower values indicate more out of phase disturbances during the gait cycle, reduced stability and increased risk of falling [22, 26]. Briefly, data from each stride (two steps as defined by heel strikes) were transformed into the frequency domain using a Fast Fourier Transformation. Harmonic ratios for each lap were then calculated using the first 20 harmonics. For the AP and VT axes the in phase 'stabilizing' accelerations repeat in multiples of two each stride and therefore the sum of the even harmonic amplitudes were divided by the sum of the odd harmonic amplitudes. For the ML axis this ratio was inverted to account for the different movement period [22].

STATISTICAL ANALYSIS

Primary analyses

For the primary analysis of unfatigued walking; analysis of variance (ANOVA) was used to assess the differences in gait, demographics and clinical scores for people with and without MS. A Chi-Square test was used to assess for differences in gender distribution. Because the PwMS walked significantly slower than the healthy age-matched controls, the effects of walking speed on the other gait parameters were assessed using analysis of covariance (ANCOVA). Because of the small sample size, in PwMS conservative Spearman's rank correlations were used to assess how the participant demographics and clinical scores related to the gait compensations. Values (≥+0.7 or ≤-0.7) indicated a strong correlation; (≥+0.5 or ≤-0.5) a moderate correlation; and (≥+0.3 or ≤-0.3) a weak correlation. Spearman's

correlations were also used to investigate how gait compensations in PwMS related to their mobility, gait variability, gait asymmetry and gait stability. Significance was set at $p \leq 0.05$ for all statistical tests.

Sample size calculations were based on reported walking speeds for PwMS of 86cm.s^{-1} (standard deviation 27cm.s^{-1}) and healthy controls of 139cm.s^{-1} (standard deviation 21cm.s^{-1}) [34]. A power of 0.99 to detect the expected between group differences with a two-tailed significance of $\alpha=0.05$ was used to inform the size of the study comprising PwMS (n=12) and healthy controls (n=12).

Secondary analyses

Intraclass correlation coefficients (ICC) were used to assess the inter-lap agreement between the first and second laps of the 6MWT. These ICCs were used for the secondary evaluation of reliability. Criterion referenced reliability ICC (2,1) was used and 95% confidence intervals reported. ICC values greater than 0.70 indicate good agreement and gait parameters that are suitable for group comparisons. ICC values greater than 0.90 indicate excellent agreement and gait parameters that are suitable to inform individual patient care [35]. A two-way ANOVA with repeated measures in one factor (lap number) was used for the secondary evaluation of fatigue during the 6MWT. The gait parameters for the first and last laps from each participant were used. For each gait parameter, the main effects for group (PwMS vs healthy controls) and time (first lap vs last lap) and the group by time interaction were calculated. Significance was set at $p \leq 0.05$ for all statistical tests.

RESULTS

Primary analyses

PwMS were a similar height and mass compared to the healthy controls (Table 1) but had significantly reduced passive ankle range of motion (87.9º vs 96.6º), active ankle range of motion (65.5º vs 102.4º), and shorter six-minute walk distances (330m vs 506m). The median EDSS of PwMS was 4.25 (interquartile range 1.1), representing a moderate level of disability.

MS significantly affected all aspects of gait mobility, variability and asymmetry compensations and stability ($p \leq 0.05$, Table 2). PwMS walked slower with more variable and asymmetric gait patterns. For healthy controls, regular and symmetrical head and pelvic movement patterns were observed (Figure 2). For PwMS, head and pelvis compensatory movements during the swing phase of the affected leg

were greater than during the swing phase of the unaffected leg (Figure 2). PwMS also had reduced gait stability in all directions, as evidenced by lower harmonic ratios. The largest effect size was for gait stability (Cohen's *d* range = -1.61 to -3.06), followed by gait compensations (Cohen's *d* range = 1.14 to 1.85) and measures of mobility (Cohen's *d* range = -1.41 to -1.68).

After adjusting for differences in walking speed using ANCOVA (Table 2), PwMS still had significantly lower gait stability and greater VT asymmetry in their compensatory head and pelvic movements ($p \leq 0.05$). Furthermore, significant Group*Speed interactions were evident for cadence ($p=0.001$), stride time variability ($p=0.013$), head sway variability ($p=0.004$) and pelvis sway variability ($p=0.008$), head sway area ($p=0.011$) and pelvis sway area (p=0.006), which indicates that for PwMS quality of their gait is likely to respond differently to changes in walking speed compared to the quality of gait healthy controls (Figure 3).

Gait compensations in PwMS were significantly ($p \leq 0.05$) correlated with age and BMI (Table 3). Older PwMS and PwMS with higher BMI exhibited greater pelvic asymmetry ($r=0.57$) and less controlled head movements ($r=0.57$). Moderate to strong correlations were also observed between gait compensations and EDSS score and ankle active ROM, but not passive ROM. PwMS with higher EDSS scores had increased head sway area ($r=0.58$). PwMS with lower ankle active ROM had greater VT asymmetry of both the pelvis ($r=-0.71$) and head ($r=-0.58$). Gait compensations were also strongly correlated with reduced gait performances. Greater pelvic sway area was strongly correlated with reduced mobility (speed and cadence, $r=-0.76$). Greater sway area at both the head and pelvis was moderate to strongly correlated with increased stride time variability ($r=0.58$ to 0.83) and increased sway variability ($r=0.75$ to 0.82). Conversely, greater VT asymmetry was moderate to strongly correlated with increased step time asymmetry ($r=0.57$ to 0.72). Increased gait compensations were also moderate to strongly correlated with decreased gait stability as measured by decreased harmonic ratios along various axes ($r=-0.56$ to -0.76).

Secondary analyses

The inter-lap reliability of the gait parameters was good to excellent (Appendix 1). The reliability of the new parameters describing gait compensations (ICC 0.87 to 0.95) was similar to the reliability of the

established measures of mobility (ICC 0.82 to 0.98) and harmonic ratios (ICC 0.85 to 0.94). The lowest reliability was observed for stride time variability and sway variability (ICC 0.70 to 0.79).

The unadjusted group differences reported for the primary gait assessments of unfatigued walking (ANOVA, p-value, Table 2) remained significant after considering the secondary effects of fatigue (first lap vs last lap, two-way ANOVA, Group-p, Appendix 2). Two main effects of fatigue were observed. Both PwMS and healthy controls experienced a significant decline in walking speed and cadence with time (Lap-$p \leq 0.02$). A significant interaction was observed for head sway variability (Group-by-Lap-$p=0.03$). Comparing the first lap to the last lap – healthy controls reduced their variability with time while PwMS increased their variability with time.

DISCUSSION

Wearable technology reveals large gait compensations and reduced stability in PwMS

The primary aim of this study was to quantify the head and pelvic movement patterns that occur in PwMS using wearable devices during unfatigued walking and determine how these secondary gait compensations may impact on gait mobility and stability. Our results demonstrate that PwMS with disability had greater compensatory movements at both the head and the pelvis (Table 2) that were strongly correlated to reduced mobility and increased gait variability (Table 3). Compared to healthy controls, PwMS had greater VT asymmetry in their head and pelvic movements (Cohen's $d=1.85$ & 1.60) and reduced gait stability as measured by harmonic ratios (Cohen's $d=-1.61$ to -3.06). Importantly, these differences in gait asymmetry and gait stability were found to be independent of the slower walking speeds observed in the MS population.

Consistent with previous research, our results confirmed that PwMS had greater gait impairments characterized by lower cadences, greater stride time variability and greater step time asymmetry [3, 34]. While most previous research has used electronic walkways to quantify spatiotemporal gait impairments in PwMS, our data, supports recent advances [13, 23, 24], which suggest wearable technology provides an accurate and accessible tool that is capable of completing comparable clinical assessments. Furthermore, for PwMS with disability, our results demonstrate wearable devices can provide additional reliable information about the compensatory movements and stability at both the

head and the pelvis (Figure 2), which may provide a more sensitive way to measure gait quality that is independent of group differences in walking speed.

Gait compensations, active ankle ROM, disability level and the mobility/dynamic stability trade-off

The unstable head and pelvis movements observed in PwMS were assumed to largely reflect secondary gait compensations resulting from lower limb muscle weaknesses and joint contractures (the primary gait restriction) [8]. A systematic review of common compensatory mechanisms, however, suggests a more complex scenario [8]. Although common impairments such as ankle contracture and foot drop often result in adaptive compensation strategies that increase pelvic tilt, rotation, elevation and abduction during walking, in PwMS the relative importance of passive physical effects versus active gait compensations may be debated [8]; particularly for head movements, which may be mechanically linked with pelvic movements. In this discussion, "gait compensations" therefore refers to secondary gait restrictions that could be both passive and active in origin. In agreement with previous research [36, 37], limited ankle range of motion in PwMS and ankle contractures likely contributed to these gait compensations. While large head and pelvis movements may have been necessary to accommodate muscle weaknesses and joint restrictions our analysis of harmonic ratios shows that these secondary gait compensations also reduced gait stability in PwMS.

The gait compensations observed in PwMS most strongly correlated with poorer active ankle ROM and higher EDSS scores (Table 3). Our results are consistent with previous research that found mean ankle ROM to be less during walking and was correlated to greater motor impairment [25]. Our results suggest that for people with more severe MS, larger secondary gait compensations at the head and pelvis were necessary to maintain function and continue to ambulate. The significant group*speed interactions observed for the sway area (head sway area p=0.011 and pelvis sway area p=0.006, Table 2) indicates an important trade-off between mobility (gait speed) and dynamic stability (control of sway area). For healthy people, the positive slope (Figure 3) indicates faster walking speed was achieved by more energetic stepping, which caused greater pelvic movement. However, for PwMS we hypothesize the negative slope (Figure 3) indicates that walking speed may have been limited by their ability to maintain control of their sway area. Additional experiments measuring sway area at different walking speeds are

required to confirm this. Screening for excessive head and pelvis compensatory movements in PwMS may therefore provide clinicians with new tools to quantify disease progression within the clinical setting. In addition to existing assessments of mobility, clinicians may also use the wearable device assessments gait symmetry and stability to help assess the effectiveness of various treatment modalities.

Gait compensations were quantified by abnormal movements occurring in the transverse (AP*ML sway area) and frontal planes (VT asymmetric displacements) during the 6MWT. Sway area during gait may provide a novel way to assess dynamic postural control and balance deficits in clinical populations during activities. Our results demonstrated that the sway area for PwMS was approximately double at the pelvis (22.4cm^2 vs 10.7cm^2) and head (19.2cm^2 vs 10cm^2) when compared to healthy controls. Results are consistent with previous research that found PwMS had increased trunk movements during gait [13, 24]. Quantifying abnormal movements in the frontal plane revealed significant differences in VT asymmetric displacements between the groups. Our results highlighted that PwMS have an inter-limb imbalance of more than 65% in head and pelvic symmetry. This significant inter-limb compensation is attributed to the variety of gait patterns observed in our sample (often observed in patients with neurological involvement), which included circumduction (swinging leg around), vaulting (hip hiking on one side while pushing off on the other side) and steppage gait (lifting the leg higher to avoid tripping).

Gait stability, falls risk and rehabilitation

Gait stability was measured using harmonic ratios (HR) along the ML, AP and VT axes. Our findings are consistent with previous work that showed PwMS had reduced gait smoothness and margin of stability [23, 38]. Unstable and variable gait has been associated with an increased risk of falls in people with Parkinson's Disease and older people [22, 26] and may provide clinicians with insightful metrics that are useful for screening at-risk individuals in MS populations [39].

With respect to variability, we found significant differences in head and pelvic sway trajectories when compared to healthy controls. The greater variability of trajectories may be explained by the additional compensatory movements of the lower limbs. Previous research has shown that PwMS have greater variability of the lumbar spine when compared to the sternum during gait because of the dampening effect of the spine [24]; however, our analysis did not support this finding.

Our study builds on previous research into gait impairments in PwMS [13, 23, 24, 38]. Specifically, our analysis combines assessments of mobility, stride time variability and step time asymmetry with assessments of gait compensations, gait stability and sway variability at both the head and pelvis. For PwMS and increasing disability, the additional patient-specific information about head movements may be important because head is a platform for sensory organs and therefore plays a vital role in maintaining dynamic balance and preventing falls.

With respect to rehabilitation, previous research has demonstrated the need for an intervention to treat the primary cause and not the secondary gait compensation [40]. While greater gait compensations were correlated with participant demographics, it is our view that active ankle range of motion (combining flexibility, lower limb strength and motor control) is both a modifiable and an important primary cause of secondary gait compensations in PwMS. Inability to dorsi-flex the foot during the swing phase may result in large compensatory movements at the pelvis (required to help clear the toe of the affected limb during the swing phase of gait) and large compensatory movements at the head (to help maintain balance over the stance leg). Our data suggest these large and unstable head and pelvic movements are both inefficient and may increase falls risk.

Secondary analyses of reliability and fatigue

The analysis of inter-lap reliability during the 6MWT showed that for an 18-meter segment of straight-line walking, wearable devices can reliably assess gait compensations (Appendix 1). Similar to the established measures of gait mobility and gait stability, good to excellent reliability (ICC 0.87 to 0.95) was observed. Reliability for stride time variability and sway variability was slightly lower, but sufficient for group comparisons in research [35]. With respect to providing patient specific advice reliability (particularly for measures of gait variability) may be further improved by averaging values from several 18-meter segments.

Both PwMS and healthy controls experienced a significant decline in walking speed and cadence over the 6MWT (Appendix 2). In line with previous work on walking-related motor fatigue [30], in our study PwMS reduced their walking speed on average by 10.3% between the first and last laps. Furthermore, fatigue was also observed to affect PwMS differently to healthy controls. For the measures of gait variability, asymmetry, compensations and stability, PwMS deteriorated between the first and last laps

while healthy people improved. These group-by-lap interactions were small compared to the main and primary group effects and were therefore non-significant (with the exception of head sway variability, p=0.03) as our study was not powered to detect these changes. This indicates a larger sample size should be used to further investigate the effects of fatigue gait compensations, gait variability and stability and fall risk in PwMS.

Limitations and future research

We acknowledge certain study limitations. Our small sample included participants with a median EDSS score of 4.25 representing a moderate level of disability within the MS population. Care must be taken before generalizing our findings to PwMS with all levels of disability. The severity of the disease can influence gait patterns, PwMS have a range of disabilities and this may affect their compensatory movements differently. Larger studies are required for additional subgroup analyses in people with different levels of disability and to further investigate the effects of fatigue on gait compensations, gait stability and fall risk. Although muscle strength was indirectly assessed through active ankle range of motion, the direct contribution of lower limb muscle strength should be further examined in the future through additional strength testing. In this study, stride time variability and step time asymmetry were based on the step times derived from the pelvic sensor; accuracy may be improved by using additional sensors on each foot or shank.

Future research should also focus on understanding the mechanisms behind gait compensations, the relative importance of passive physical effects versus active gait compensations and the changes that occur with differences in walking speed, ankle range of motion and fatigue in PwMS. Additionally, future research should focus on understanding the complex interactions between ankle range of motion, lower limb muscle strength and fatigue, and how these influences may affect all other elements of the kinetic chain.

CONCLUSION

Wearable technologies provide a clinically feasible, reliable and accurate method to assess gait quality, screen PwMS for excessive and unstable compensatory movements at the head and pelvis and

increased falls risk. Early detection of gait abnormalities may help clinicians to identify PwMS who are at risk of falling and facilitate the earlier implementation of targeted rehabilitation interventions to address the underlying primary gait restrictions that cause gait impairments. Future research is warranted to determine whether novel interventions that aim to treat ankle contractures and improve active ankle range of motion can reduce secondary gait compensations, improve gait mobility and stability and prevent falls in people with MS. Future research should also examine how alterations in active ROM of other elements in the kinematic chain influence gait mobility, stability and the effects of fatigue on gait compensations and gait stability in PwMS.

Funding

This research is supported by NHMRC and MS Research Australia.

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Table 1 Participant characteristics, passive/active ankle range of motion and six-minute walking distance for people with MS and healthy controls. Data represent the mean and standard deviations except for gender which represents the number and percentage of males in each group. Test 1 = one-way ANOVA; Test 2 = Chi-Square test.

	People with MS		**Healthy Controls**		Test	p-value
	Mean	SD	Mean	SD		
Gender [male]	N=3	25%	N=4	33%	2	0.65
Age [years]	52.0	9.1	55.8	12.23	1	0.40
Height [m]	1.69	0.06	1.65	0.09	1	0.21
Mass [kg]	71.5	17.9	72.3	9.91	1	0.89
BMI [kg/m^2]	25.1	5.7	26.8	3.34	1	0.39
Passive Ankle ROM [º]	87.9	7.8	96.6	5.92	1	**0.006**
Active Ankle ROM [º]	65.5	15.8	102.4	5.95	1	**< 0.001**
6MWT [m]	330	112	506	82.64	1	**< 0.001**

Table 2 Unfatigued mobility, stability and symmetry measures assessed during the six-minute walk test for people with MS and healthy controls.

	People with MS		Healthy Controls		ANOVA	Effect Size	ANCOVA	
	Mean	SD	Mean	SD	p-value	d	Group p	Group*Speed p
Gait Mobility								
Speed [$m.s^{-1}$]	0.97	0.35	1.50	0.28	**<0.001**	-1.68	-	-
Cadence [$steps.min^{-1}$]	101.67	20.05	123.22	8.03	**0.002**	-1.41	0.862	**0.001**
Step length [cm]	55.72	10.50	72.62	10.09	**0.001**	-1.64	0.730	0.221
Gait Variability and Asymmetry								
Stride Time Variability [ms]	52.27	47.59	22.27	8.47	**0.043**	0.88	0.839	**0.013**
Step Time Asymmetry [%]	9.01	9.21	2.65	1.63	**0.028**	0.96	0.516	0.105
Pelvic Sway Variability [cm]	2.24	1.06	1.25	0.34	**0.006**	1.26	0.337	**0.008**
Head Sway Variability [cm]	2.70	1.26	1.90	0.33	**0.047**	0.86	0.927	**0.004**
Gait Compensations*								
Pelvis Sway Area AP x ML [cm^2]	22.45	11.01	10.7	3.7	**0.002**	1.43	0.140	**0.006**
Pelvis Asymmetry VT [%]	81.84	62.19	11.1	6.4	**0.001**	1.60	**0.049**	0.319
Head Sway Area AP x ML [cm^2]	19.24	11.14	10.0	3.0	**0.011**	1.14	0.677	**0.011**
Head Asymmetry VT [%]	75.86	51.00	8.6	5.5	**<0.001**	1.85	**0.008**	0.529
Gait Stability (harmonic ratio)**								
Pelvis - VT	1.50	0.33	2.14	0.21	**<0.001**	-2.31	**0.006**	0.0854
Pelvis - AP	1.43	0.19	1.91	0.19	**<0.001**	-2.47	**<0.001**	0.0830
Pelvis - ML	1.00	0.13	1.44	0.22	**<0.001**	-2.41	**0.002**	0.8822
Head - VT	1.53	0.26	2.36	0.28	**<0.001**	-3.06	**<0.001**	0.2129
Head - AP	1.22	0.15	1.62	0.15	**<0.001**	-2.65	**<0.001**	0.7949
Head - ML	1.05	0.20	1.33	0.15	**0.001**	-1.61	**0.042**	0.1127

ANCOVA – Analysis of covariance adjusting for walking speed (group) and interactions with group vs speed

***Gait Compensations** = AP x ML = total sway area, VT = Ratio of asymmetry between left and right displacement in the vertical axis*

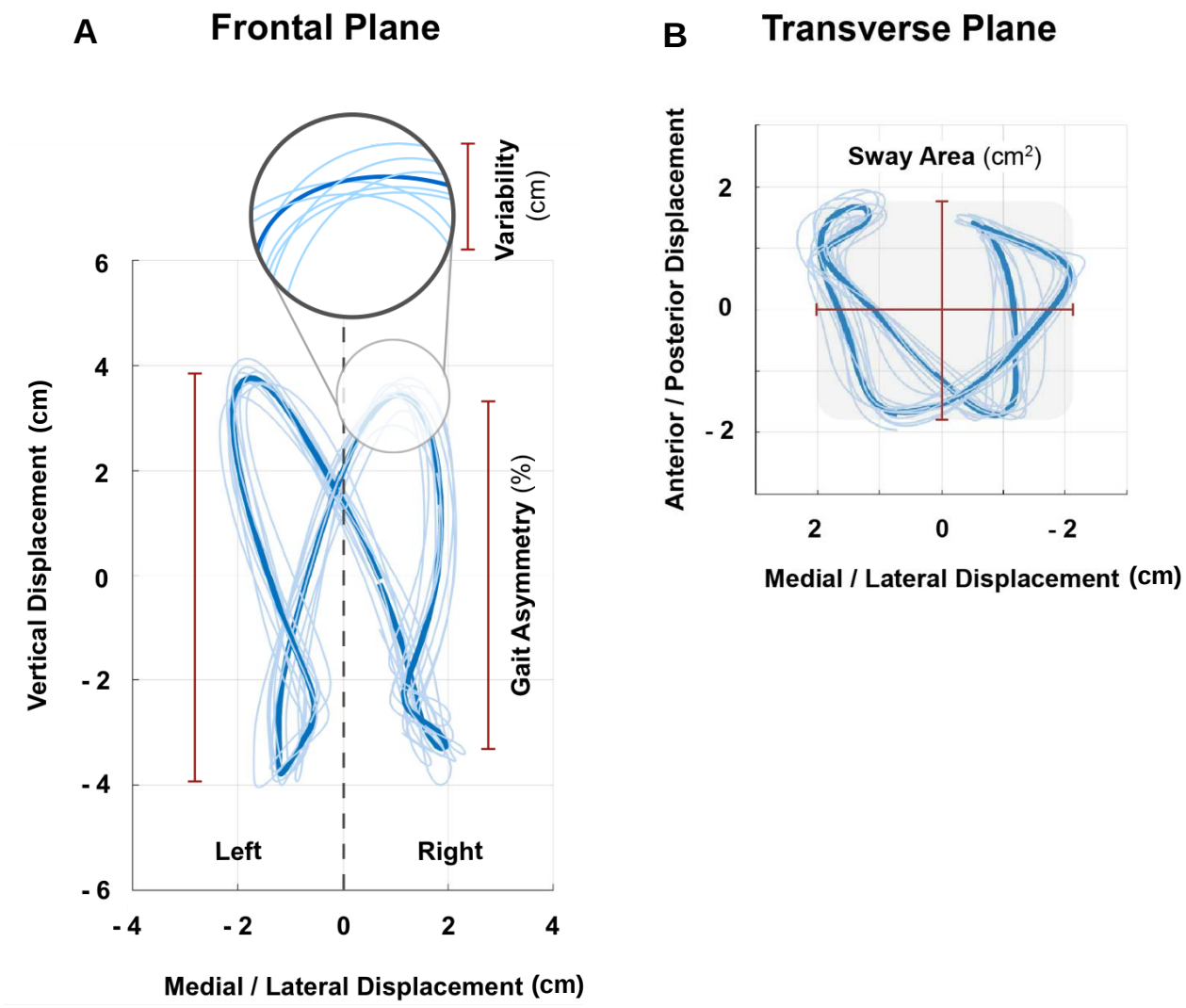
****Gait Stability** = Harmonic ratio VT - vertical axis, AP –anterior-posterior axis, ML – medial-lateral ax*

Table 3 Correlations with gait compensations in PwMS

	GAIT COMPENSATIONS			
	Pelvic Compensations		Head Compensations	
	Sway Area [cm^2]	Asymmetry VT [%]	Sway Area [cm^2]	Asymmetry VT [%]
Demographics				
Sex	0.08 (0.80)	0.03 (0.93)	-0.14 (0.67)	0.25 (0.43)
Age	-0.08 (0.81)	0.41 (0.19)	**0.57** (0.05)**	0.12 (0.71)
Height	-0.10 (0.77)	-0.24 (0.44)	0.11 (0.73)	0.18 (0.57)
Mass	-0.18 (0.57)	0.53 (0.08)	0.20 (0.54)	0.36 (0.25)
BMI	-0.03 (0.92)	**0.57** (0.05)**	0.16 (0.62)	0.31 (0.33)
MS severity				
EDSS	0.29 (0.36)	0.52 (0.09)	**0.58** (0.05)**	0.48 (0.12)
Years since diagnosis	0.09 (0.77)	-0.14 (0.67)	0.00 (0.99)	-0.02 (0.95)
Ankle ROM				
Passive ROM	0.25 (0.44)	-0.07 (0.83)	0.36 (0.25)	-0.37 (0.23)
Active ROM	-0.39 (0.21)	**-0.71*** (0.01)**	-0.21 (0.50)	**-0.58** (0.05)**
Gait Mobility				
Speed	**-0.76*** (0.01)**	-0.41 (0.19)	**-0.66** (0.02)**	-0.24 (0.44)
Cadence	**-0.76*** (0.01)**	-0.46 (0.13)	**-0.75*** (0.01)**	-0.24 (0.46)
Step length [cm]	**-0.69** (0.02)**	-0.39 (0.21)	-0.52 (0.09)	-0.34 (0.29)
Gait variability and Asymmetry				
Stride Time Variability	**0.83*** (0.001)**	-0.07 (0.83)	**0.58** (0.05)**	-0.21 (0.51)
Step Time Asymmetry	0.37 (0.24)	**0.72*** (0.01)**	0.38 (0.22)	**0.57** (0.05)**
Pelvic Sway Variability	**0.78*** (0.005)**	0.28 (0.38)	**0.76*** (0.01)**	0.27 (0.40)
Head Sway Variability	**0.82*** (0.002)**	0.30 (0.34)	**0.75*** (0.01)**	0.22 (0.48)
Gait Stability				
Pelvis HR VT	-0.44 (0.15)	-0.48 (0.12)	-0.51 (0.09)	-0.53 (0.08)
Pelvis HR AP	-0.35 (0.27)	**-0.76*** (0.01)**	**-0.62** (0.04)**	-0.47 (0.13)
Pelvis HR ML	0.03 (0.92)	**-0.76*** (0.01)**	-0.51 (0.09)	**-0.69** (0.02)**
Head HR VT	-0.41 (0.18)	-0.29 (0.35)	**-0.61** (0.04)**	-0.29 (0.25)
Head HR AP	0.15 (0.65)	-0.35 (0.27)	0.08 (0.82)	-0.47 (0.13)
Head HR ML	-0.37 (0.24)	**-0.56** (0.05)**	-0.24 (0.44)	-0.41 (0.19)

Spearman's rank correlations – *r*-values with **(*p*-values)** presented in brackets; significant correlations ($p \leq 0.05$) marked strong **(***)** moderate **(**)** or weak **(*)**. ***Gait Compensations –*** *Sway Area = AP x ML sway, Asymmetry VT = Ratio of asymmetry between left and right displacement in the vertical axis.* ***Gait Stability –*** *Harmonic ratio VT - vertical axis, AP –anterior-posterior axis, ML – medial-lateral axis.*

Figure 1 Calculation of gait Parameters from a health age-matched participant



(A) Front Plane - Gait asymmetry was calculated using the difference in vertical displacement between left and right sides and expressed a percentage. Gait variability was calculated as the distance or spread of data away from the mean in centimetres.

(B) Transverse Plane - Sway area was the product of the AP and ML (95%) sway ranges in the transverse plane.

Figure 2 Frontal Plane - Gait Asymmetry and Variance

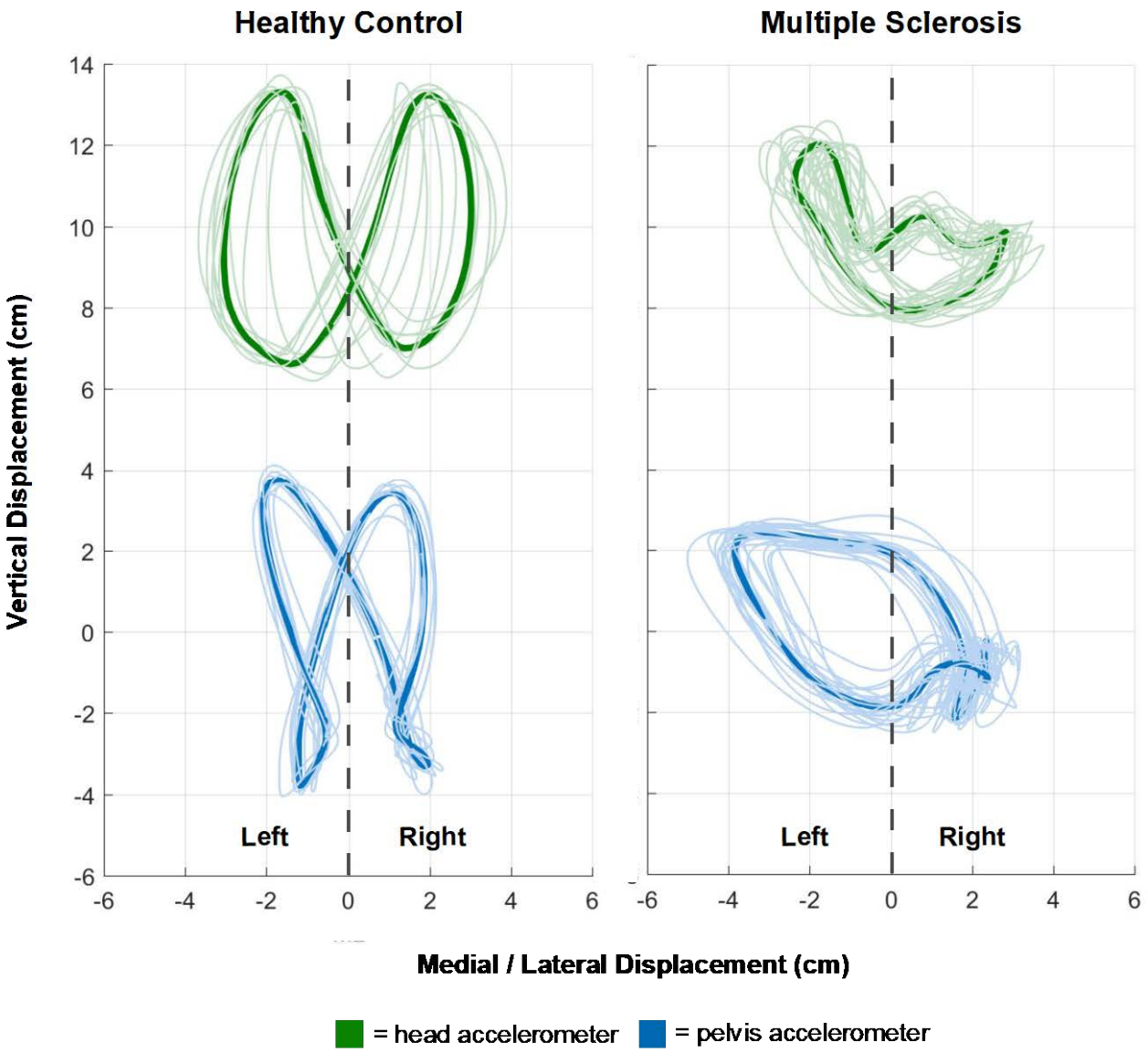


Figure 2 - Data from one lap of the 6-minute walk test by a person with MS (right panel) and their healthy age matched control are presented (left panel). The affected limb is the left leg for the PwMS. For this participant with MS, during the swing phase the left leg (affected limb) large compensatory movements at the pelvis (blue line) were observed that enabled greater toe clearance. During the swing phase of the left leg (affected limb) both the head (green line) and pelvis (blue line) moved to the right to counter balance the participant's center of mass over the stance leg.

Figure 3 Group by Speed Interactions – The walking speed vs control of sway area trade off.

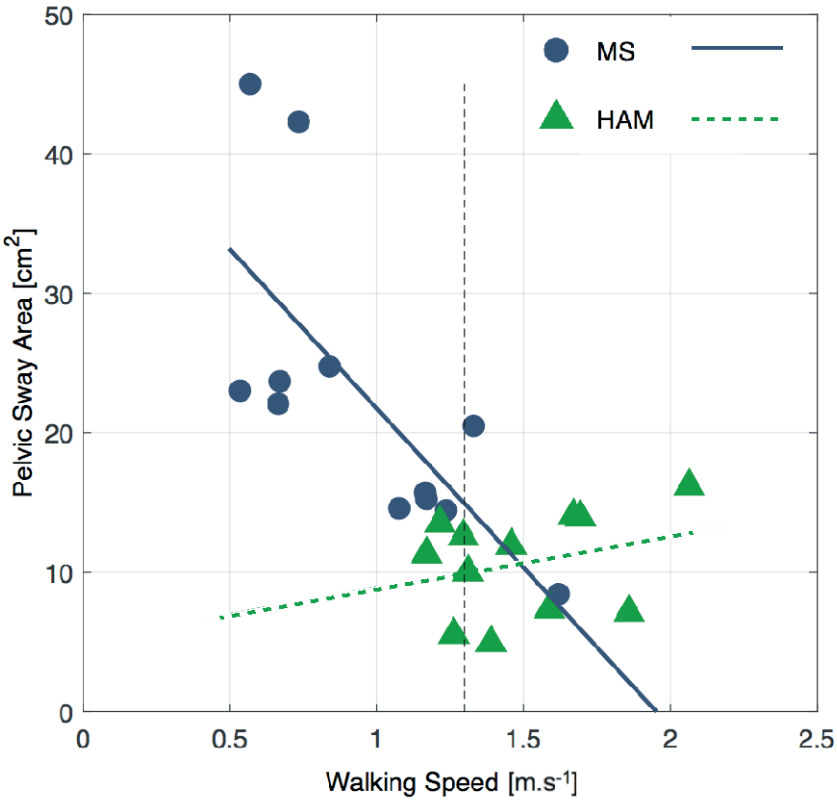


Figure 3: MS (circles) – people with multiple sclerosis. HAM (triangles) – health age matched controls. For pelvic sway area, a significant interaction was observed with walking speed (ANCOVA p-value 0.006). For people with MS, a strong negative correlation between walking speed at pelvic sway area (Spearman's *r*=-0.76, Table 3) was observed. Conversely, for the healthy controls a weak positive correlation (*r*=0.30) was observed. The existence of significant interactions indicates that the relationship between gait quality and walking speed may be different for people with and without MS.

Appendix 1 Inter-lap reliability of gait assessed between the first and second laps of the six-minute walk test for people with MS and healthy controls.

	ICC(2,1)	ICC 95% CI Lower bound	ICC 95% CI Upper bound
Gait Mobility			
Speed [$m.s^{-1}$]	**0.91***	0.81	0.96
Cadence [$steps.min^{-1}$]	**0.98***	0.94	0.99
Step length [cm]	0.82	0.63	0.92
Gait Variability and Asymmetry			
Stride Time Variability [ms]	0.70	0.41	0.86
Step Time Asymmetry [%]	0.84	0.67	0.93
Pelvic Sway Variability [cm]	0.76	0.51	0.89
Head Sway Variability [cm]	0.79	0.56	0.90
Pelvis Sway Area AP x ML [cm^2]	0.87	0.72	0.94
Pelvis Asymmetry VT [%]	**0.91***	0.80	0.96
Head Sway Area AP x ML [cm^2]	0.88	0.75	0.95
Head Asymmetry VT [%]	**0.95***	0.89	0.98
Gait Stability (harmonic ratio)**			
Pelvis - VT	**0.94***	0.87	0.97
Pelvis - AP	0.86	0.71	0.94
Pelvis - ML	**0.92***	0.83	0.96
Head - VT	**0.94***	0.86	0.97
Head - AP	0.85	0.69	0.93
Head - ML	**0.91***	0.80	0.96

ICC(2,1) – Intraclass correlation coefficient for criterion referenced reliability. **ICC 95% CI** – associated lower and upper bounds for the ICC(2,1) 95% confidence interval. Values greater than 0.70 indicate acceptable reliability for group research, values greater than 0.90 marked **(*)** indicate excellent agreement between laps.

Appendix 2 Analysis of fatigue during the six-minute walk test for people with MS and healthy controls

	People with MS First Lap		People with MS Last Lap		Healthy Controls First Lap		Healthy Controls Last Lap		Two-way ANOVA p-values		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Group	Lap	Group-by-Lap
Gait Mobility											
Speed [$m.s^{-1}$]	0.97	0.35	0.87	0.32	1.50	0.28	1.42	0.29	**<0.01***	**0.01***	0.80
Cadence [$steps.min^{-1}$]	101.82	19.91	96.37	23.39	123.30	8.02	121.94	8.04	**<0.01***	**0.02***	0.12
Step length [cm]	55.63	10.56	52.89	9.56	72.57	10.12	69.27	10.94	**<0.01***	0.06	0.86
Gait Variability and Asymmetry											
Stride Time Variability [ms]	51.00	47.06	56.09	44.79	21.56	8.69	16.44	8.62	**<0.01***	1.00	0.41
Step Time Asymmetry [%]	8.50	9.13	10.97	9.56	2.71	1.75	1.65	1.32	**<0.01***	0.57	0.15
Pelvic Sway Variability [cm]	0.72	0.28	0.89	0.70	0.45	0.11	0.44	0.14	**<0.01***	0.31	0.30
Head Sway Variability [cm]	0.90	0.37	1.11	0.65	0.75	0.16	0.65	0.18	**0.01***	0.43	**0.03***
Gait Compensations*											
Pelvis Sway Area AP x ML [cm^2]	27.17	14.59	35.01	32.32	11.68	4.09	11.70	3.19	**<0.01***	0.28	0.28
Pelvis Asymmetry VT [%]	81.85	61.67	83.92	47.70	11.42	7.18	9.99	6.89	**<0.01***	0.96	0.79
Head Sway Area AP x ML [cm^2]	29.67	18.89	46.62	52.17	12.68	3.95	12.21	4.73	**<0.01***	0.18	0.14
Head Asymmetry VT [%]	75.30	50.48	79.69	47.14	8.95	5.52	4.92	4.61	**<0.01***	0.98	0.48
Gait Stability (harmonic ratio)**											
Pelvis - VT	1.51	0.33	1.42	0.41	2.13	0.20	2.20	0.17	**<0.01***	0.93	0.11
Pelvis - AP	1.43	0.19	1.40	0.34	1.90	0.18	1.95	0.26	**<0.01***	0.84	0.53
Pelvis - ML	1.00	0.13	0.98	0.16	1.43	0.21	1.49	0.25	**<0.01***	0.42	0.13
Head - VT	1.54	0.27	1.46	0.32	2.36	0.27	2.39	0.28	**<0.01***	0.77	0.41
Head - AP	1.22	0.15	1.27	0.17	1.61	0.17	1.59	0.19	**<0.01***	0.74	0.21
Head - ML	1.05	0.20	0.99	0.14	1.34	0.15	1.44	0.26	**<0.01***	0.66	0.06

Two-way ANOVA – Analysis of variance with repeated measures in one factor; significance ($p \leq 0.05$) marked **(*)**; Group – PwMS vs Health Controls; Lap – First vs Last Lap (effect of fatigue); Group-by-Lap – tests if fatigue effect was different for PwMS vs Health Controls (interaction). ***Gait Compensations*** *= AP x ML = total sway area, VT = Ratio of asymmetry between left and right displacement in the vertical axis.* ***Gait Stability =*** *Harmonic ratio VT - vertical axis, AP –anterior-posterior axis, ML – medial-lateral axis*