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Altered visual and somatosensory feedback affects gait stability in persons with multiple sclerosis

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ABSTRACT

Persons with multiple sclerosis (PwMS) often report problems due to sensory loss and have an inability to appropriately reweight sensory information. Both of these issues can affect individual's ability to maintain stability when walking under challenging conditions. The purpose of the current study was to determine how gait stability is adapted when walking under challenging sensory conditions where vision and somatosensation at the feet is manipulated. 25 healthy adults and 40 PwMS (15 fallers, 25 non-fallers) walked on a treadmill at their preferred normal walking speed under 3 conditions: normal walking, altered vision using goggles that shifted visual field laterally, and altered somatosensation using shoes with compliant foam soles. Inertial measurement united recorded acceleration at the lumbar and right ankle, and acceleration variability measures were calculated including root mean square (RMS), range, sample entropy (SaEn), and Lyapunov exponents (LyE). A gait stability index (GSI) was calculated using each of the four variability measures as the ratio of lumbar acceleration variability divided by foot acceleration variability in the frontal and sagittal planes. The sagittal and frontal GSI_{RMS} were larger in the somatosensory condition compared to the normal and visual conditions ($p < 0.001$). The frontal GSI_{SaEn} was greater in the visual condition compared to the somatosensory condition ($p = 0.021$). The frontal and sagittal GSI_{LyE} was greater in the somatosensory condition compared to the normal and visual conditions ($p < 0.002$). The current study showed that HC, MS non-fallers and MS fallers largely adapted to altered sensory feedback during walking in a similar manner. However, MS faller subjects may be more reliant on visual feedback compared to MS non-fallers and HC subjects.

1. Introduction

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system which can result in a wide range of disability and disrupt signaling throughout the brain and spinal cord (Compston & Coles, 2008). Persons with MS (PwMS) often report functional deficits and disabilities related to any combination of cognition, somatosensation, vision, and gait and balance function (Frohman, Racke, & Raine, 2006; Noseworthy, Lucchinetti, Rodriguez, & Weinshenker, 2000). Gait and visual function have been identified as the two most valuable areas of physical function by MS patients (Heesen et al., 2008). Approximately 80% of PwMS report problems with walking and balance (Souza et al., 2010), and 50% of PwMS experience at least 1 fall per year (Ylva Nilsagard, Lundholm,

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Gunnarsson, & Denison, 2007). During walking, stability is maintained through constant interaction between the base of support and center of mass (Winter, 1995), driven by sensory feedback and motor output controlled by the sensorimotor system (Bauby & Kuo, 2000; Peterka & Loughlin, 2004). Vision, proprioception, and information from the vestibular system can be tuned and reweighted as necessary due to changes in environment in order to maintain balance (Cenciarini & Peterka, 2006; Peterka & Loughlin, 2004). For example, when standing or walking altered visual input, feedback from proprioception and the vestibular system becomes more relied upon (Adamcova & Hlavacka, 2007; Reynard & Terrier, 2014; Zhang & Deshpande, 2016). While sensory reweighting has been studied in PwMS during quiet standing (Cattaneo & Jonsdottir, 2009; Van Emmerik, Remelius, Johnson, Chung, & Kent-Braun, 2010), it is not clear how PwMS adapt their walking under challenging sensory conditions.

Visual disturbances occur in up to 85 percent of PwMS, often due to inflammation or demyelination of the optic nerve (Sakai, Feller, Galetta, Galetta, & Balcer, 2011). These disturbances in the optic nerve can cause symptoms such as dimmed or altered visual fields, loss of vision, abnormal eye movements, and double vision (Sakai et al., 2011). Previous studies have shown that impaired vision negatively influences balance in PwMS and is a risk factor for increased risk of falls (Nilsagard, Lundholm, Denison, & Gunnarsson, 2009). The Romberg ratio, a measure relating to reliance on visual feedback during standing sway, has been shown to be related to disability level and fall risk in PwMS (Kalron, 2017). Persons with moderate to severe MS demonstrate a greater reliance on visual feedback during standing compared to those with mild disability (Kalron, 2017). When visual information is removed or altered, the sensorimotor system must compensate using proprioceptive feedback and information from the vestibular system to maintain balance. This sensory reweighting is an important aspect of stability control, and PwMS may have a decreased ability to appropriately reweight sensory information between the visual, somatosensory, and vestibular systems compared to healthy adults (Cattaneo & Jonsdottir, 2009; Van Emmerik et al., 2010).

Altered or loss of sensory feedback from the lower extremity is common in PwMS and results in symptoms such as tingling or numbness (Kurtzke, 1983; Newsome, Wang, Kang, Calabresi, & Zackowski, 2011). Subjects who report such symptoms often present with altered walking mechanics in order to compensate for the altered sensation, which is typically characterized as a conservative gait strategy presenting with shorter and wider steps and resulting in an overall slower walking speed (Peebles, Bruetsch, Lynch, & Huisinga, 2017). Previous studies have tested the effects of altering lower extremity somatosensation during quiet standing by having subjects stand on a foam pad (Hlavackova & Vuillerme, 2012; Horlings et al., 2009) which reduces the pressure and proprioceptive feedback from the lower extremity, and altering this somatosensory information results in a larger sway area in PwMS (Alpini et al., 2012). While standing on a foam pad provides information about sensory reweighting during standing (Hlavackova & Vuillerme, 2012; Horlings et al., 2009; Peterka & Loughlin, 2004), it is not clear how PwMS adapt to altered sensory information during walking. However, since the majority of falls occur during walking (Berg, Alessio, Mills, & Tong, 1997; Tinetti, Speechley, & Ginter, 1988), and altered or diminished sensorimotor feedback can lead to increased fall risk, it is important to understand how PwMS adapt to walking under challenged sensory conditions.

Maintaining stability during walking involves a controlled relationship between the base of support and center of mass. Acceleration variability from the trunk and foot segments can provide information about how movement is being controlled at these individual segments (Harbourne & Stergiou, 2009; Huisinga, Mancini, St George, & Horak, 2013; Stergiou, Harbourne, & Cavanaugh, 2006). However, measuring how movement is controlled at only the trunk or the feet alone may not provide a full representation overall balance (Craig, Bruetsch, Lynch, & Huisinga, 2017). The current study uses an analysis of the relationship between trunk and foot acceleration variability called the gait stability index (Craig, Bruetsch, & Huisinga, 2018). The gait stability index quantifies acceleration variability at the trunk relative to acceleration variability at the feet, providing a more comprehensive measure of whole-body balance than a single body segment measurement.

The purpose of the current study was to determine how the relationships between trunk and foot acceleration variability are adapted when walking under challenging sensory conditions. Since healthy adults demonstrate optimal variability (Stergiou et al., 2006) and will optimally adapt their walking under challenging conditions, we hypothesized that healthy adults will adapt their GSI metrics under the challenging visual and somatosensory conditions, but PwMS with and without fall history may be less adaptable and therefore will not demonstrate similar adaptations.

2. Methods

Forty PwMS, and 25 age matched healthy controls (HC) participated in the current retrospective cross-sectional study. 15 MS fallers were selected as PwMS who self-reported 2 or more falls in the previous 12 months (Garcia, Dias, Silva, & Dias, 2015), the remaining 25 MS non-fallers had no more than 1 fall in the previous 12 months (Table 1). All participants gave informed written

Table 1
Summary of subject demographics.

	Healthy Controls N = 25	MS Non-fallers N = 25	MS Fallers N = 15
Age	41 (8.5) yrs	44 (9.9) yrs	48 (9.6) yrs
M/F	7/18	5/20	7/8
BMI	43.7 (8.3)	46.9 (8.7)	53.4 (6.5)
EDSS	N/A	3.3 (1.9)	4.4 (1.1)
Falls in previous 12 months	0	0	3.75 (1.7)

consent prior to testing, and all study protocols were approved by the University of Kansas Medical Center Human Research Committee. Subjects were excluded if they had any orthopedic or neuromuscular co-morbidities that could affect their walking or balance, history of vestibular disfunction, diabetes, women who were currently or recently pregnant, or any pre-existing conditions that could make exercise dangerous such as myocardial infarction, chest pain, unusual shortness of breath, etc. MS subjects were excluded if they were currently prescribed symptom specific medication (i.e. Fampridine) which can affect gait, if they were unable to walk at least 100 m without rest or use of a mobility aide, or if they self-reported significant problems with vision. Any PwMS with a Kurtzke Expanded Disability Status Scale (EDSS) greater that 5.5 (Kurtzke, 1983) were also excluded from the study.

Wireless inertial measurement units (Opal, APDM, Portland, OR, USA) were placed on the subjects' right ankle and lumbar spine. The right ankle inertial measurement unit was placed over the lateral surface of the distal shank, just superior to the ankle joint and the lumbar inertial measurement unit was placed over the posterior surface of the lumbar spine at the L4-L5 level. These sensor locations have been selected in previous studies as representative locations for upper and lower body movement during walking (Craig et al., 2018; Craig, Bruetsch, Horak, Lynch, & Huisinga, 2017). To determine subjects' preferred walking speed, subjects were timed while walking over a 10-meter walkway at their normal comfortable speed, and an average of three trials was used to calculate their preferred walking speed (Franz, Francis, Allen, O'Connor, & Thelen, 2015). Subjects were then asked to walk on a treadmill at this preferred walking speed for three individual trials of 90 s each, with the wireless inertial measurement units recording at 128 Hz for the duration of each trial. The first trial was the normal walking condition where subjects walked on the treadmill with no sensory manipulation. The second trial was the altered vision condition where subjects walked at their preferred speed while wearing glasses with a prism film (Press-On Prism, 30 degrees, 3 M Health Care, St. Paul, MN, USA) to shift gaze by approximately 30 degrees which has been shown to significantly alter spatial and temporal walking parameters during gait (Helbostad, Vereijken, Hesseberg, & Sletvold, 2009). The prism glasses were large enough to fit comfortably over any subjects' personal prescription glasses. The third and final walking trial was the altered somatosensory condition where subjects walked at the preferred speed while wearing shoes with 2″ of dense foam (Hlavackova & Vuillerme, 2012) (2.8 lbs/ft^3, Foam Factory Inc, Milford, MI, USA) affixed to their soles which deforms and does not significantly change subject height. Standing on dense foam has been shown to significantly alter somatosensory input and alter postural sway parameters (Hlavackova & Vuillerme, 2012; Horlings et al., 2009). The somatosensory condition trials and the vision condition trials were not randomized, but subjects took a required seated rest for a minimum of 3-minutes between each trial to prevent fatigue.

The acceleration time series from each sensor was translated from local Cartesian coordinates to resultant frontal and sagittal plane time series local to each sensor. The frontal and sagittal planes were analyzed individually since movement in each of these planes during walking may use different control strategies, with frontal plane using more active control and sagittal plane using more passive mechanisms (O'Connor & Kuo, 2009). To account for differences in number of strides across different walking speeds, the middle 60 strides of each trial were selected for analysis (Mehdizadeh & Sanjari, 2017; Terrier & Reynard, 2014). A custom Matlab program (Matlab version R2013b, The MathWorks Inc., Natick, MA, USA) was used to calculate all variability measures. All subsequent analyses were performed on the resultant sagittal and frontal plane time series, and data was left unfiltered for appropriate analysis of time series characteristics (Mees & Judd, 1993).

Root mean square was calculated as the square root of the mean of squares over all data points in the time series and was used to quantify the average dispersion of the acceleration traces (Craig et al., 2017). Range was calculated as the difference between the maximum and minimum acceleration values within the time series and was used to quantify the absolute spread of acceleration data across the entire time series (Craig et al., 2017). These linear variability measures overall quantified the magnitude or amount of acceleration variability present in the respective time series.

Nonlinear variability measures Sample entropy (SaEn) and Lyapunov exponents (LyE) were used to quantify the temporal structure of variability within the time series, providing information about how movement of the foot and trunk segments is controlled (Stergiou, 2016). The use of entropy analyses on these types of human movement datasets has been widely discussed in previous work (Kavanagh, 2009; Stergiou, 2016; Yentes et al., 2013). For our purposes, a more tightly controlled and repetitive walking pattern will be reflected in a more repetitive acceleration signal. The SaEn analysis is used in the current study to quantify the level of repeatability in these signals, while the LyE analysis determined the divergence of accelerations, and these types of analyses have been similarly used in previous work for this purpose (Kavanagh, 2009; Riva, Toebes, Pijnappels, Stagni, & van Dieen, 2013; Tochigi, Segal, Vaseenon, & Brown, 2012). A thorough explanation of SaEn and LyE and their calculation can be found in previous literature (Craig et al., 2017; Richman & Moorman, 2000; Stergiou, 2016; Wolf, Swift, Swinney, & Vastano, 1985; Yentes et al., 2013). For SaEn, a vector length of $m = 3$ was chosen after testing for relative consistency as explained by Yentes et al. (Craig et al., 2017, 2018; Yentes et al., 2013). Time series specific time delay and embedding dimension were calculated using the Average Mutual Information algorithm (Baker & Gollub, 1996; Gomez Garcia, Godino Llorente, & Castellanos Dominguez, 2012; Stergiou, 2016) and False Nearest Neighbors algorithm (Stergiou, 2016) respectively. Time delays ranged from 8 to 27. The median embedding dimension of 8 was used for the LyE analysis.

The gait stability index (GSI) metrics were calculated as the ratio of lumbar acceleration (ACC) variability divided by foot acceleration (ACC) variability, for each of the 4 variability metrics (RMS, range, SaEn, LyE) in the frontal and sagittal planes (Craig et al., 2017).

$$GSI = LumbarACCVariability_{FrontalorSagittal}/FootACCVariability_{FrontalorSagittal} \quad (1)$$

Four GSI metrics were calculated in each plane using each of the four variability measures: GSI_{RMS}, GSI_{Range}, GSI_{SaEn}, GSI_{LyE}, resulting in 8 GSI metrics total used in the statistical analysis. The GSI metrics are unitless and used to examine lumbar acceleration

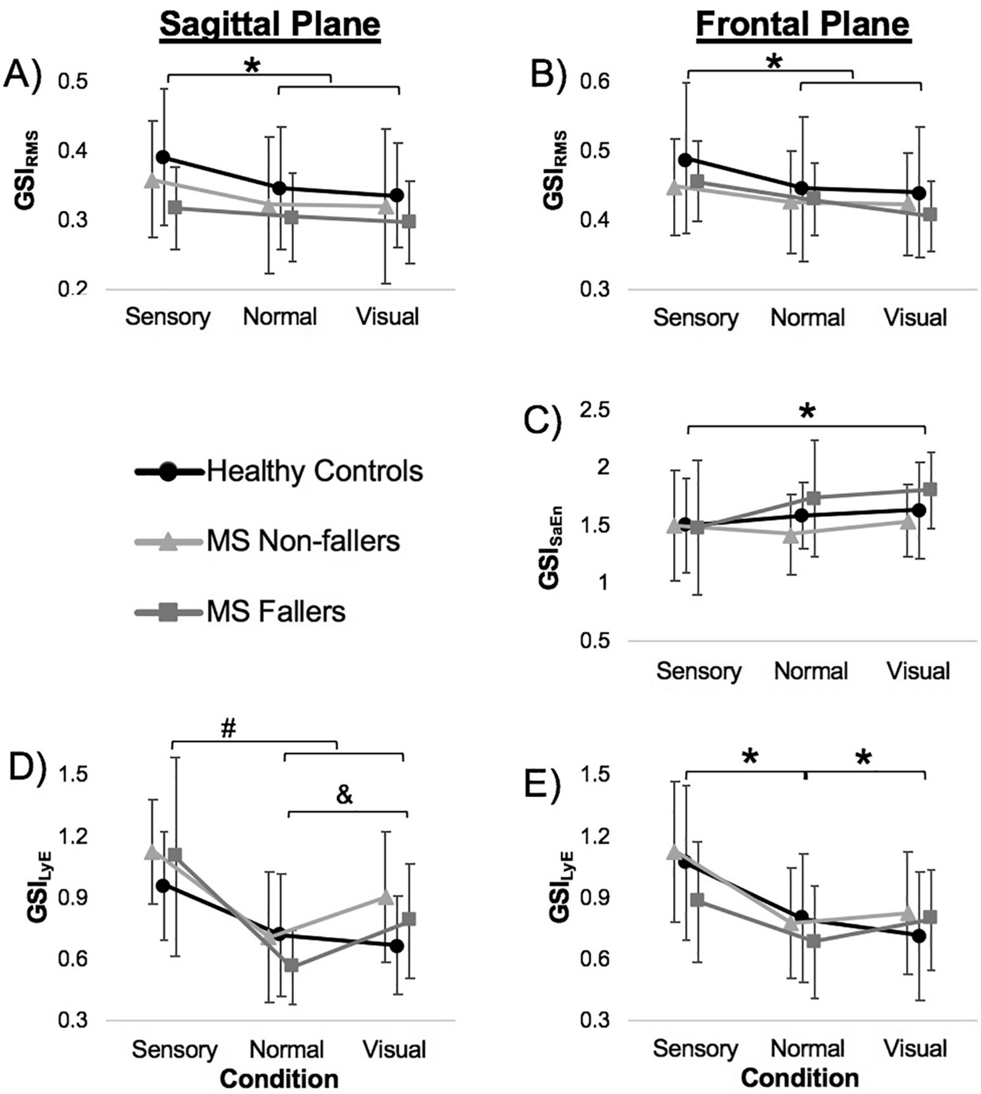

Fig. 1. Means and standard deviations for GSI metrics. A – Sagittal plane GSI_{RMS}, B – Frontal plane GSI_{RMS}, C – Frontal plane GSI_{SaEn}, D – Sagittal plane GSI_{LyE}, E – Frontal plane GSI_{LyE}. Effect of condition for: all groups *; healthy controls and MS Fallers #; MS Fallers only &.

variability relative to foot acceleration variability within an individual subject. A GSI equal to 1 indicates that acceleration variability at the trunk and foot segments are exactly equal, a GSI greater than one indicates more lumbar acceleration variability relative to foot acceleration variability, and a GSI of less than one indicates less lumbar acceleration variability relative to foot acceleration variability (Craig et al., 2017). In the current study, healthy adults are assumed to demonstrate optimal control and adaption of their upper and lower body control, which is represented in their respective gait stability indices (Stergiou & Decker, 2011; Stergiou et al., 2006). An altered gait stability index in MS subjects relative to healthy adults, either significantly higher or lower, would represent altered control of whole-body stability.

To assess the effect of altered sensory conditions on the GSI metrics across groups, a 3 Condition × 3 Group ANOVA was performed on each GSI metric. Post-hoc t-tests were used to explore significant main effects and interactions. Statistical significance was set at the $p < 0.05$ level for all analyses, and all analyses were completed in SPSS 2013 (version 22, IBM Corp., Armonk, NY).

3. Results

GSI_{RMS} showed a main effect of Condition in the frontal ($F = 17.982$, $p < 0.001$) and sagittal ($F = 26.635$, $p < 0.001$) planes, where the GSI_{RMS} in the somatosensory condition was greater than in the normal ($p < 0.001$) and visual ($p < 0.001$) conditions (Fig. 1A and 1B). GSI_{SaEn} showed a main effect of Condition in the frontal plane ($F = 4.344$, $p = 0.016$), where the GSI_{SaEn} in the visual condition was greater than in the somatosensory condition ($p = 0.021$) (Fig. 1C). GSI_{LyE} showed a main effect of Condition in the frontal ($F = 11.770$, $p < 0.001$) and sagittal ($F = 17.462$, $p < 0.001$) planes, where the GSI_{LyE} was greater in the somatosensory condition than in the normal condition ($p < 0.002$) and visual condition ($p < 0.001$) (Fig. 1D and 1E). GSI_{LyE} also showed a significant interaction between Group and Condition in the sagittal plane ($F = 3.188$, $p = 0.016$), where HC and MS fallers showed larger GSI_{LyE} in the somatosensory condition compared to the normal ($p < 0.008$) and visual ($p < 0.018$) conditions, and only MS fallers showed a larger sagittal plane GSI_{LyE} in the visual condition compared to the normal condition ($p = 0.001$) (Fig. 1D). There were no significant main effects of Group found for any GSI metrics.

4. Discussion

The purpose of the current study was to determine how the relationships between trunk and foot acceleration variability are adapted when walking under challenging sensory conditions. Our results show that there was an effect of Condition indicating that HC, MS non-fallers, and MS fallers all adapted to the challenging sensory conditions. Partially supporting our hypothesis, there was one GSI metric which revealed an adaptation during the visual condition which was made only by MS faller group in the sagittal plane. However, our hypothesis was not fully supported as there were no other interactions or main effects of Group found for any of the GSI metrics during any of the conditions which indicates that all three groups adapted relatively similarly to the changing sensory conditions.

The GSI_{RMS} results in the frontal and sagittal planes showed that accelerations were larger at the trunk relative to the feet during the altered somatosensation condition compared to the visual and normal conditions across the three groups. Previous studies have shown that individuals with loss of sensation in their lower extremity adapt their walking to maintain a more conservative gait strategy characterized by shorter and wider steps (Gehlsen et al., 1986; Peebles et al., 2017). The goal of a conservative gait strategy is to contain the center of mass more within the base of support in order to have a larger safety margin in case of a perturbation such as a trip of a slip, therefore it may be expected that the GSI_{RMS} would decrease with the adoption of a conservative gait. However, the results of the current study show that the trunk accelerations relative to the foot accelerations are larger in the somatosensory condition compared to the normal condition across all groups. A post-hoc analysis of the individual trunk and foot segment accelerations showed that the trunk and foot accelerations both showed an increased RMS in the somatosensory condition (Fig. 2). Together, these results demonstrate that while both upper and lower body accelerations increased during the somatosensory condition (Fig. 2), the trunk accelerations relative to the foot accelerations were still larger (larger GSI_{RMS}) in the somatosensory condition compared to the normal walking condition (Fig. 1). Altered somatosensory feedback likely results in an altered sense of the body center of mass position relative to the ground and surrounding environment, which has been previously shown to be related to worse dynamic stability and falls in PwMS (Kelleher, Spence, Solomonidis, & Apatsidis, 2009; Peebles et al., 2017). Healthy adults have been shown to walk with increased hip, knee, and trunk range of motion when walking on a compliant surface, increasing foot clearance during walking (Bárbara, Freitas, Bagesteiro, Perracini, & Alouche, 2012). While the need to raise the foot higher may partly be due to the physical demands of walking on a compliant surface, previous studies have shown similar adaptations made by individuals who have worse somatosensation (Hazari et al., 2016; Mustapa, Justine, Mohd Mustafah, Jamil, & Manaf, 2016), and individuals who have plantar sensation experimentally altered (Nurse & Nigg, 2001). It is also possible that these adaptations in the gait pattern serve to increase amplitudes of proprioceptive feedback in other areas such as the knees and hips to compensate for the altered plantar pressure and ankle proprioception feedback (Hudspeth, Jessell, Kandel, Schwartz, & Siegelbaum, 2013).

The GSI_{SaEn} results showed that in the frontal plane, trunk accelerations were more irregular relative to foot accelerations in the visual condition compared to the somatosensory condition. However, the GSI_{LyE} in the frontal and sagittal planes showed the trunk accelerations were more predictable compared to the foot accelerations in the visual condition compared to the somatosensory condition. Together these results indicate that when visual information is not reliable during walking, trunk accelerations may be actively constrained so that small perturbations can be quickly attenuated in order to minimize movement and provide a stable base for the neck and head. This attenuation could result in increased irregularity in trunk movement over repeating cycles as demonstrated by the altered GSI_{SaEn}. Previous studies have similarly shown that altering visual information can lead to constrained trunk movement in order to minimize motion of the trunk segment within the base of support and maintain a cautious gait (Helbostad et al., 2009; Saucedo & Yang, 2017). Additionally, the results for the MS faller group showed that across the three conditions, the sagittal GSI_{LyE} was smallest in the normal walking condition and significantly increased in both the visual condition and somatosensory condition. There were no differences for GSI_{SaEn} in the sagittal plane, which may reflect the fact that SaEn is a measure of repeatability, and therefore the motion in the sagittal plane maintains consistent repeatability, as it is dominated by the repetitive propulsive stepping patterns (Bauby & Kuo, 2000; O'Connor & Kuo, 2009). The MS faller group was the only group that demonstrated a larger sagittal GSI_{LyE} in the visual condition compared to the normal condition. This may highlight that the MS faller group is more reliant on their visual feedback to maintain stability and therefore is more affected by altered visual feedback than MS non-fallers and HC. This finding is in parallel to previous studies which have shown that fall-prone PwMS who have somatosensory loss become heavily reliant on their visual information during quiet stance, and become more unstable when vision is altered (Van Emmerik et al., 2010). The current results seem to indicate a similar reliance on visual information during walking in the MS faller group.

Since PwMS have been shown to have altered ability to reweight sensory information during quiet stance (Cattaneo & Jonsdottir, 2009; Van Emmerik et al., 2010), it was expected that the MS subjects would show different adaptations to challenging sensory conditions during walking compared to healthy adults. However, the GSI metrics in the current study largely showed no main effects of Group. One possible explanation is that the GSI metrics are designed to study whole body stability during walking and all subjects were fully ambulatory and able to maintain stable gait since there were no subjects who fell during testing. Therefore, since subjects remained stable in all three conditions, it can be expected that the GSI metrics would reflect similar adaptations across all groups. It is also possible that there may be differences between how these groups adapt to the challenging sensory conditions that were not able

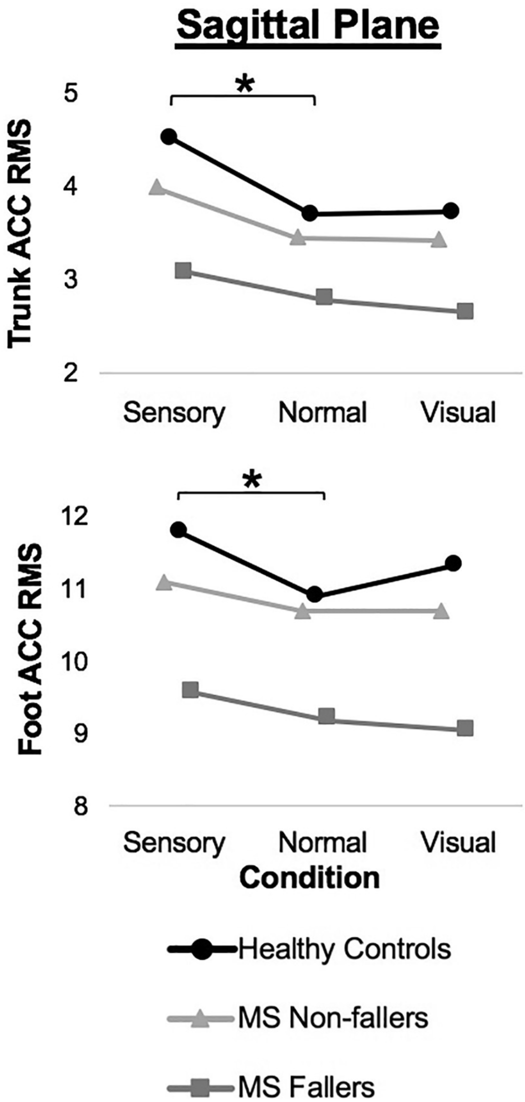

Fig. 2. Root mean square of individual trunk and foot accelerations during the three walking conditions. Effect of condition all groups *, $p < 0.01$.

to be observed using the GSI metrics. For example, Killeen et al. showed that altered visual feedback resulted in changes to minimal toe clearance in older adult subjects but not in healthy young subjects, where older adults increased their minimum toe clearance during the challenging condition (Killeen et al., 2017). Similar toe-clearance adaptations, for example, may occur in PwMS and future studies should examine other outcome measures to further determine if PwMS adapt to walking in challenging sensory conditions similar to healthy adults.

There are some limitations in the current study that should be noted. First, a treadmill was used in order to record sufficiently long time series for analysis, and while many previous studies have used treadmill gait for similar variability analyses (Craig et al., 2017; Dingwell & Marin, 2006; Owings & Grabiner, 2003; Rosenblatt & Grabiner, 2010), there have been few studies which introduced challenging sensory conditions on a treadmill. It is possible that the lack of visual flow, constrained walking speed, and constrained walking path on the treadmill masked some variability that may be observed in overground walking. However, it is expected that trends similar to those observed in the current study would be observed during overground as well. A second limitation is that while walking on compliant foam does alter sensory feedback, it may also alter some physical mechanics of walking which are not solely due to altered sensory information such as the need to raise the foot higher. However, these physical changes are minimal relative to the altered sensations of the foam shoes inducing altered gait characteristics. Finally, it is important to consider that all MS subjects in the current study were ambulatory without the need for an assistive device. Since MS can present in a wide range of symptoms which may or may not result in walking and balance deficits, it may be of interest in future studies to identify specific functional deficits in a larger cohort of MS subjects that may be linked with an inability to appropriately adapt in challenging conditions.

5. Conclusions

During walking, visual, vestibular, and somatosensory feedback is integrated and used to help monitor where the body is relative to the surrounding environment in order to maintain upright balance during standing and walking. When one of the three sensory modes is altered, more weight can be placed on the others to compensate and maintain reliable sensory feedback though the system may still demonstrate instability or changes in the walking pattern due to the altered sensory feedback. The current study showed that HC, MS non-faller and MS faller subjects largely adapted to altered sensory feedback during walking in a similar manner. However, MS faller subjects may be more reliant on visual feedback compared to MS non-fallers and HC subjects. Future studies should determine if specific symptomology or functional deficits in PwMS make adaptations more difficult when walking under altered sensory conditions and should further explore gait adaptations to challenging sensory conditions using other types of outcome measures.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humov.2019.05.018.

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