UHASSELT
KNOWLEDGE IN ACTION

Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Assessment of perceptive accuracy for detecting walking speed variations in persons with multiple sclerosis and healthy controls during overground walking at fastest speed

Freya Ramaekers
Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij neurologische aandoeningen

PROMOTOR :
Prof. dr. Peter FEYS

BEGELEIDER :
De heer Gianluca FLORIO

UHASSELT
KNOWLEDGE IN ACTION

www.uhasselt.be
Universiteit Hasselt
Campus Hasselt:
Martelarenlaan 42 | 3500 Hasselt
Campus Diepenbeek:
Agoralaan Gebouw D | 3590 Diepenbeek

2024
2025

Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Assessment of perceptive accuracy for detecting walking speed variations in persons with multiple sclerosis and healthy controls during overground walking at fastest speed

Freya Ramaekers

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij neurologische aandoeningen

PROMOTOR :

Prof. dr. Peter FEYS

BEGELEIDER :

De heer Gianluca FLORIO

Research context

The study investigates perceptual accuracy in overground walking, specifically the ability to detect variations in self-paced walking speed. This process relies on the integration of motor, cognitive, and interoceptive systems, which are often affected in people with multiple sclerosis (PwMS)(Feys et al., 2016; C. Gonzalez Campo et al., 2020; Stephan et al., 2016). Evidence from stroke populations suggests that walking performance in real-life contexts may not be fully captured by standard clinical gait assessments. Feld et al. (2018) demonstrated that dual-task gait speed, which simulates everyday walking under cognitive load, accounted for significantly more variance in daily walking activity than traditional single-task speed. This result highlights the relevance of attentional and perceptual demands in motor control and suggests that performance under realistic conditions offers better insight into ambulatory behaviour. Integrating such perspectives into MS research may improve our understanding of how PwMS perceive and regulate their walking.

PwMS frequently experience impairments in walking, cognitive functioning, and fatigue regulation. These symptoms are known to reduce quality of life and limit functional independence (Larocca, 2011; Sandroff et al., 2018). Interoceptive disturbances have been shown to relate to increased fatigue perception and altered activity regulation in PwMS (Cecilia Gonzalez Campo et al., 2020; Megan Ware et al., 2022). By exploring the perceptual accuracy of PwMS in monitoring their own gait performance, this study aims to gain insight into self-monitoring mechanisms.

How PwMS perceive changes in their own motor performance can inform individualised interventions, particularly in fatigue management, fall prevention, and self-regulation of physical activity. Deficits in interoception and performance monitoring may contribute to unsafe walking behaviour, increased fatigue perception, or under-overestimation of physical capabilities (McMorris et al., 2018; Van den Bergh et al., 2017).

Understanding how accurately PwMS detect fluctuations in their gait performance may provide insight into underlying deficits in interoception and cognitive-motor integration, thereby guiding the development of targeted interventions.

Moreover, investigating the role of individual differences (e.g., cognitive function, fatigue, pain) in perceptual accuracy may support the personalization of care in clinical rehabilitation settings (Behrens et al., 2023)

This thesis was conducted in the context of an experimental research study supervised by Prof. Dr Peter Feys and PhD student Gianluca Florio and took place within REVAL, the Rehabilitation Research Centre at Hasselt University. Although not linked to a predefined externally funded project, it is associated with the faculty-funded doctoral position of Gianluca Florio.

The research question was developed by the student in collaboration with the supervisor and co-supervisor. The student was responsible for conducting the literature review, processing the data, performing the statistical analyses, contributing to the design of the perceptual task, assisting with participant recruitment, and supporting the implementation of the testing procedures. All stages of the thesis, from conceptual design to final reporting, were independently managed by the student under supervision.
This master's thesis is an individual mono thesis. The work reflects the student’s capacity to integrate clinical knowledge, scientific reasoning, and practical skills in designing and executing a multidisciplinary research study.

Inhoudsopgave

Abstract

Background: PwMS often experience impaired gait, fatigue, and cognitive deficits that can influence their ability to monitor physical performance. Accurate perception of performance is crucial for safe mobility and self-regulation, yet little is known about perceptual accuracy during walking in PwMS.

Objective: To compare the detection accuracy of gait speed variations during overground walking between PwMS and healthy controls (HC), and to explore factors influencing this accuracy.

Methods: Twenty participants (10 PwMS, 10 HC) completed a 6-Minute Walk Test (6MWT) at maximal speed while wearing inertial measurement units. Participants reported perceived changes in walking speed using a handheld sensor. Detection accuracy, defined as the ratio of self-reported variations to objective gait speed variability, was used as the experimental outcome. Questionnaires and cognitive/motor tests assessed interoception, fatigue, and function.

Results: The average age of the PwMS group was 43 years, while the HC group had an average age of 35 years. The average distance covered in the 6MWT was 528.21 metres for PwMS and 659.29 metres for HC. Detection accuracy was significantly lower in PwMS compared to HC, with no interaction over time. Moderate, non-significant correlations were found between detection accuracy and cognitive function, interoceptive sensibility, and fatigue. Sex had a significant effect on detection accuracy, with females scoring lower overall.

Conclusion: Detection accuracy is reduced in PwMS compared to healthy controls, independent of time. Although moderate, non-significant correlations were found between detection accuracy and cognitive function, interoceptive sensibility, and fatigue, these trends suggest potential areas for future research.

Introduction

Multiple sclerosis (MS) is a chronic and progressive disease characterised by the demyelination of the central nervous system, leading to irreversible disability over time (Abril Oliva Ramirez et al., 2021). The condition is more commonly observed in females, with an average diagnosis age of 32 years (Walton et al., 2020).

The clinical presentation of MS varies significantly between patients but often includes symptoms like fatigue, motor and sensory impairments, and cognitive deficits, leading to an overall reduction in quality of life (Feys et al., 2016). Among these, walking impairments and fatigue are reported by most PwMS, contributing substantially to impairments in daily functioning and decline in quality of life (Larocca, 2011; A. Oliva Ramirez et al., 2021).

According to Larocca (2011), 41% of people with multiple sclerosis (PwMS) report difficulties with walking, and 70% identify it as the most challenging aspect of living with the condition (Larocca, 2011).

A 2017 study by Comber et al. highlighted gait impairments in PwMS, including those with low levels of disability, measured by the Expanded Disability Status Scale (EDSS). Gait impairments that PwMS commonly experience is reduced stride length, slower walking speed, prolonged double support duration, and shorter step length. When comparing PwMS to HC, these impairments become even more pronounced during rapid walking (Comber et al., 2017).

Walking is an activity that requires not only motor skills but also cognitive abilities for optimal performance. Both motor problems and cognitive impairments, which PwMS often experience, influence their walking. These cognitive impairments, particularly in memory, attention, processing speed, and executive functions, can significantly affect daily functioning: the ability to manage tasks, retain information, and maintain focus is often impacted (Sandroff et al., 2018).

In addition to cognitive deficits, fatigue and fatiguability make it challenging for PwMS to sustain prolonged walking performance. Fatigue, as a trait, is the “subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities” while its increased perception during a specific activity represents state fatigue. The phenomenon known as walking fatigability describes a person’s tendency to decline in walking performance over time (Santinelli et al., 2024; Van Geel et al., 2021).

Interoception is the awareness of one’s physiological state. We provide definitions for the different constructs in the appendix. Interoception is crucial for self-understanding and could play a key role in managing conditions such as MS. Recent observational studies indicate a relationship between interoceptive disturbances, or disruptions in the brain's processing of internal bodily signals, and fatigue in PwMS (C. Gonzalez Campo et al., 2020). Interoception involves a sophisticated interplay between neural mechanisms and cognitive functions: an inferential process where the brain constructs a "perception of the physiological condition of the entire body" through the processing of interoceptive sensory input and self-generated interoceptive predictions here referred as ‘prior beliefs’. The inferential process entails a continuous comparison between predicted and actual bodily states. (Stephan et al., 2016) This process is precision-weighted (see figure 1). This implies that the brain may rely more on prior beliefs and expectations when there is a physiological dysfunction contributing to more noisy sensory input and that subjective experience not only depends on physiological signals but also on the brain’s interpretations based on prior knowledge and expectations. (Van den Bergh et al., 2017)

PwMS frequently experience symptoms such as walking impairments, fatigue, and cognitive difficulties, which significantly affect daily functioning (Feys et al., 2016). Notably, even in cases where neurological dysfunction appears mild, often reflected by low Functional System (FS) scores within the EDSS, PwMS can still present with marked motor deficits (Dalgas et al., 2009)
Additionally, disruptions in interoceptive processing may play a key role in these early motor changes. Altered interoception, defined as the ability to perceive internal bodily sensations, has been linked to lower physical activity levels and heightened perceptions of fatigue (M. Ware et al., 2022). It is conceivable that diminished interoceptive accuracy compromises an individual's ability to monitor movement dynamics, such as gait speed or smoothness, thereby contributing to subtle but functionally significant mobility limitations.

These findings raise the possibility that deficits in bodily self-awareness may precede, and potentially exacerbate, overt clinical symptoms. Understanding the role of interoception in early motor dysfunction could therefore provide a novel explanatory framework and inform more sensitive diagnostic and rehabilitative strategies for PwMS.

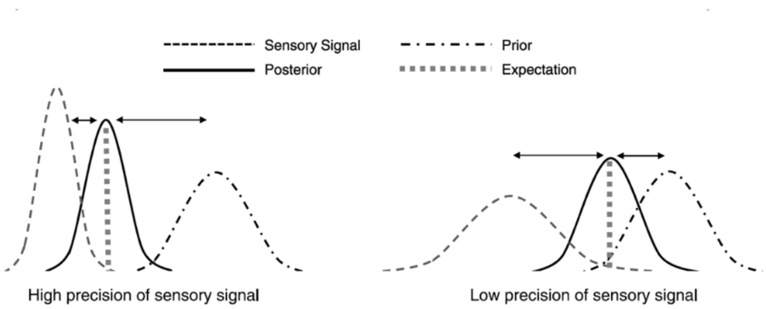
This master's thesis aims to investigate whether there is a difference in detection accuracy for detecting speed variations between PwMS and HC during an overground walking performance at the fastest speed.

The primary research question is, is there a significant difference in detection accuracy for walking speed variations during overground walking performance at maximal speed between PwMS and HC? The primary hypothesis states that PwMS will demonstrate reduced perceptual accuracy in estimating their walking speed compared to HC during 6 minutes of overground walking at fastest speed.

Secondarily, the study will explore factors that may influence perceptual accuracy for walking speed variations during overground walking. The secondary research question is: To what extent do factors such as interoceptive sensibility, cognitive impairments, motor impairments, pain, and fatigue influence perceptual accuracy for walking speed variations in PwMS compared to HC during overground walking? The secondary hypothesis suggests that reported interoceptive disturbances, cognitive impairments (visual memory, processing speed and executive functions), and increased levels of motor and cognitive fatigue will be linked to reduced detection accuracy during 6 minutes of overground walking at fastest speed.

Figure 1

Inferential process



(Van den Bergh et al., 2017)
The figure illustrates how the precision of sensory signals influences perception under predictive coding models.
Left side (High precision of sensory signal): *When sensory input is precise, the brain can update its prior knowledge (dashed-dot line) more accurately, resulting in a posterior distribution (solid line) that is closer to the actual sensory signal (dashed line).*

Right side (Low precision of sensory signal): *When sensory input is less precise (e.g., noisy or ambiguous), the brain relies more heavily on prior expectations. The posterior distribution remains closer to the prior, showing that the system is less influenced by the new, uncertain sensory information and more by pre-existing expectation*

Methods

Study

This study examined how accurately PwMS and HC can perceive changes in their walking performance by using a newly designed perceptive task performed during a prolonged walking test executed overground (6 minutes walking test - 6MWT, performed on 30 meters long walkway).

The central ethical committee of Uhasselt (Belgian number: B1152024000009) approved all study documents.

Participants

20 participants were recruited: 10 PwMS and 10 healthy controls (HC). The inclusion criteria for PwMS were age above 18 years old, diagnoses of MS, no relapses less then 1 month, ability to walk unassisted for 500 meters (without orthoses or walking aid) at the start of the study.

Participants in both groups were excluded in case of cognitive impairments limited understanding of the study instruction, pregnancy, musculoskeletal disorders in the lower limb (not MS related), cardiovascular red flags for exercise, or other diagnoses for neurological or metabolic diseases limiting the full execution of the test.

Procedure

Clinical assessment

By using a web-based secured digital survey (Castor® web application) demographic data and questionnaires were collected.

Several questionnaires served as tools for factors that potentially interfere with perceptive abilities. Self-reported symptom perception and functional limitations were evaluated using various tools. Pain severity and its interference with daily activities were measured using the Brief Pain Inventory (BPI) (Cleeland & Ryan, 1994). Fatigue was evaluated through the Modified Fatigue Impact Scale (MFIS) which captures the perceived impact of fatigue across physical, cognitive, and psychosocial domains (Fisk et al., 1994).

To explore participants' subjective beliefs about their perceptive abilities and to compare these beliefs between PwMS and the HC, a set of interoceptive and proprioceptive self-assessment instruments was administered. The Interoceptive Sensitivity and Attention Questionnaire (ISAQ) was used to evaluate beliefs about sensitivity to internal bodily states and attentional focus toward them (Bogaerts et al., 2022). The Postural Awareness Scale (PAS) provided a measure of participants' self-perceived proprioceptive awareness (Cramer et al., 2018).

The baseline assessments were divided into two categories: testing cognitive executive functions and evaluating motor performance. Cognitive executive functions were assessed using the Symbol Digit Modalities Test (SDMT), which measures information processing speed, attention, and working memory (Benedict et al., 2017).The Revised Brief Visuospatial Memory Test (BVMT-R) will assess speed processing. The BVMT-R is a visuospatial memory test such that participants view a stimulus page for 10 seconds and are asked to draw as many of the figures as possible in their correct location on a separate sheet of paper (Tam & Schmitter-Edgecombe, 2013).

For motor capacity, walking endurance will be assessed with the 6-Minute Walk Test (6MWT) ("ATS statement: guidelines for the six-minute walk test," 2002; Kalinowski et al., 2022). The 6MWT is complemented by fatigue ratings before and after the test using the visual analogue scale for fatigue (VAS-F 0-10) (Lee et al., 1991).

Experimental procedure: Familiarization

The familiarization procedure was conducted to ensure that participants understood how to use the instruments and methods for registering their subjective reports on motor performance. Participants were instructed to wear noise-cancelling headphones and use a hand-held force-sensing device (see figure 2) to indicate perceived changes in gait speed during the 6MWT. Each time the device was squeezed, it automatically recorded the timestamp, which served as a record of the self-perceived variations in walking speed.

Instructors explained that the device would be used during the overground walking task to capture the time point of any perceived changes in walking speed. The threshold sensitivity of the sensor, defined as the minimum input hand-grip force required to trigger a recording, was set at 25% of the participant's maximal hand-grip strength to make it effortless and easy to use, still allowing to clean the signal noise generated form holding the sensor in the palm while walking at maximal speed. This strength was determined through an average of three maximal isometric handgrip tests using the same sensor.

During the familiarization process, trials were conducted using simple perception tasks, such as reacting to visual stimuli while walking. Participants were informed that they would follow the same procedure to report their own perceptions of walking speed during the experimental phase of the study.

Figure 2

Hand-helf force-sensing device

Perception of performance variations

Participants were tested overground during a 6MWT to assess their ability to accurately perceive changes in their gait speed. They were instructed to walk for 6 minutes at their fastest speed that they could safely maintain and report any perceived variations in their speed by squeezing a handheld sensor. The sensor was chosen as a modality to acquire participant reports because holding it in the hand serves as a reminder for the ongoing perceptual task, helping maintain continuous attention on their speed. The action of holding the sensor, without squeezing it, confirmed that the participant did not perceive any change in speed during the corresponding span of time, in accordance with the standardized instructions they received.

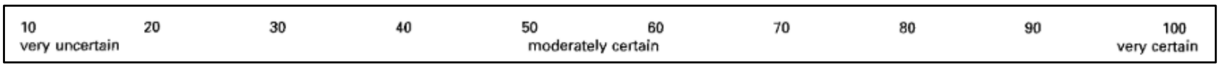
During the 6MWT, participants wore wearable inertial measurement unit (IMU) sensors strategically positioned on their bodies. Specifically, six Opal™ sensors developed by APDM, Inc. (Portland, OR, USA) were used to collect gait data. These sensors measured the parameter walking speed. They were placed as follows: two on the dorsal surfaces of the feet, two on the lower legs, one on the anterior aspect of the sternum, and one on the posterior aspect of the third or fourth lumbar vertebra.

The instructor followed a standardized script to ensure neutral instructions were consistent for each participant. For the 6MWT, a modified protocol was used; none of the verbal encouragements for each minute were provided, and the participants walked alone to avoid interfering with participants' perception of walking speed variations. ("ATS statement: guidelines for the six-minute walk test," 2002)

The level of perceived fatigue was asked just before and immediately after the test using the VAS-F. Furthermore, a short VAS (Figure 3) after the 6MWT assessed the participant's confidence in their accuracy for detecting speed variations during the test "On a scale from 0 to 100, how certain are you that you have been precise/accurate in detecting ongoing variations in your performance? Please mark your confidence level on the presented visual scale".

Figure 2

Visual scale for confidence rating



Subjective beliefs on their perceptive accuracy

<u>Data analysis</u>

Statistical analyses were conducted using JMP (JMP Pro 16, SAS Institute Inc., Cary, NC, USA). Prior to conducting inferential analyses, assumptions of normality and homogeneity of variances were assessed. The Shapiro–Wilk test and Q–Q plots indicated a non-normal distribution of key variables, and Levene's test revealed unequal variances across groups. As a result, non-parametric statistical methods were employed.The primary analysis assessed differences in perceptual accuracy among self-paced performance variations. Detection accuracy (DA), used as an outcome measure, was determined by dividing the number of perceptual reports by the coefficient of variation (CV) of measured performance (gait speed). The CV was calculated as the standard deviation divided by the mean, expressed as a percentage. DA served as a novel outcome measure reflecting perceptual accuracy. To assess group differences in DA over time, a non-parametric two-way ANOVA was conducted on rank-transformed DA values, with group (PwMS vs. HC) as the between-subjects factor and time (minutes 1–6 of the 6MWT) as the within-subjects factor. A secondary, exploratory analysis examined the relationship between DA and potential predictors, including interoceptive processing, cognitive impairments, motor impairments, and fatigue. Given the small sample size and the ordinal nature of some measures, Spearman's rank correlation coefficients (r) were calculated separately for each group (PwMS and HC) to identify potential monotonic associations between DA and clinical or subjective variables. Although none of the correlations reached statistical significance, correlations were interpreted to inform future hypothesis-driven research.

Outlier consideration was integrated qualitatively, with attention given to participants reporting extremely high or low frequencies of perceptual events. These individual differences were considered during interpretation but were not excluded from analysis to preserve the ecological validity of the dataset.

Results

Participants characteristics

The study included ten PwMS and ten HC. The PwMS group consisted of 9 females and 1 male, while the HC group included 8 females and 2 males. The average age of the PwMS group was 43 years (range: 29–67), compared to 35 years (range: 24–61) in the HC group. The mean number of years since disease onset in the PwMS group was 10.3 years.

Regarding physical performance, the average walking speed during the 6MWT was 1.47 m/s for PwMS and 1.83 m/s for HC. The average distance walked during the 6MWT was 528.21 metres for PwMS and 659.29 metres for HC. Independent samples t-tests revealed that these differences were statistically significant for both walking speed (p = 0.0011) and distance covered (p= 0.0010).

Table 1

Demographic and Functional Characteristics of HC and PwMS

Participant	Sex	Age	6MWT Distance (m)	6MWT Speed (m/s)
HC 1	Female	43	692.52	1.92
HC 2	Female	31	687.2	1.77
HC 3	Male	31	666.0	1.85
HC 4	Male	31	621.0	1.73
HC 5	Female	31	725.4	2.10
HC 6	Female	24	626.4	1.74
HC 7	Female	25	615.6	1.71
HC 8	Female	29	687.6	1.91
HC 9	Female	48	637.2	1.77
HC 10	Female	61	684.0	1.90
PwMS 1	Female	34	568.8	1.58
PwMS 2	Female	34	577.8	1.61
PwMS 3	Female	43	540.0	1.50
PwMS 4	Female	36	531.0	1.48
PwMS 5	Female	67	457.2	1.27
PwMS 6	Male	29	640.8	1.78
PwMS 7	Female	42	432.0	1.20
PwMS 8	Female	49	583.2	1.62
PwMS 9	Female	33	619.2	1.72
PwMS 10	Female	60	351.9	0.98

Note. *6MWT = Six-Minute Walk test.*

Detection accuracy

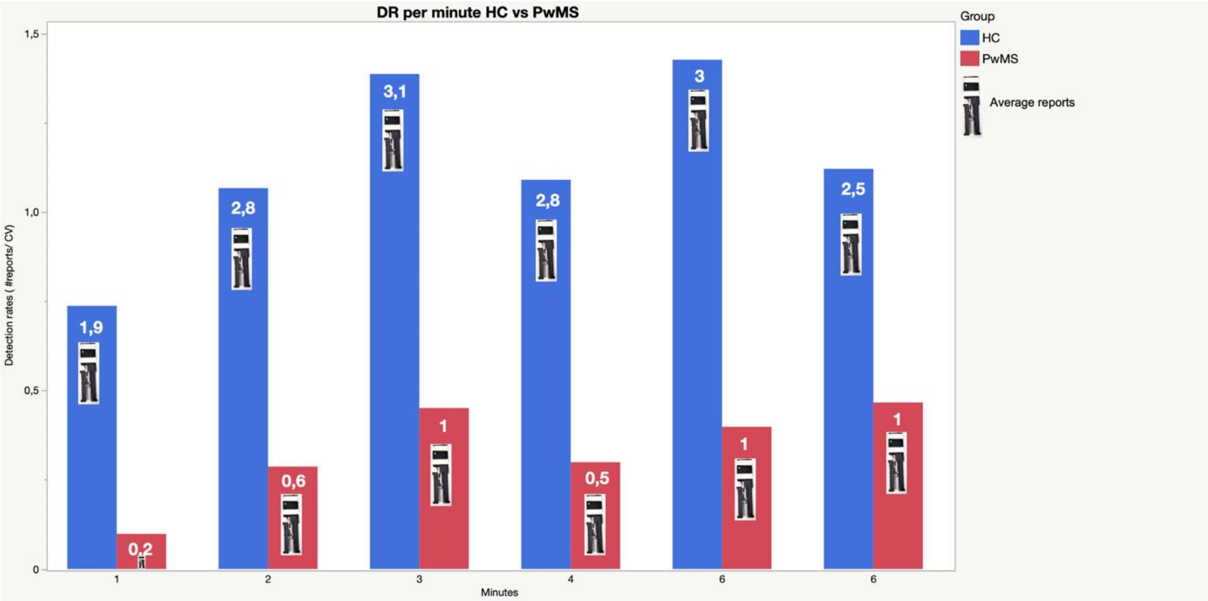
Figure 4 shows the DA for each minute during the 6MWT, comparing HC and PwMS. The HC group consistently demonstrated higher DAs across all six time points, whereas the PwMS group showed lower and relatively stable DAs over time. A non-parametric two-way ANOVA on rank-transformed data revealed a significant main effect of *group* (p = .0014), indicating that HC participants had significantly higher detection accuracy than PwMS across the test duration. No significant main effect of time was observed (p = .1654), nor was there a significant group × time interaction (p = .8863). The detection accuracy did not change significantly over the course of the test, and the difference between the two groups remained consistent over time.

Figure 5 presents the raw number of reports during the 6MWT for each participant, while Figure 6 shows the corresponding CV% for each minute. These figures highlight substantial inter-individual differences, particularly among PwMS, where report counts were generally low and more variable. In contrast, many HC participants maintained consistently high report rates across the 6 minutes.

Table 3 summarises the number of reports, CV%, self-reported fatigue (pre and post 6MWT), and confidence ratings for each participant. HC participants generally reported a higher number of correct detections and exhibited smaller increases in fatigue. In contrast, PwMS showed greater increases in fatigue after the test, but in some cases, they reported high confidence levels despite lower detection accuracy. This suggests a possible mismatch between their actual performance and self-awareness.

Figure 3

Detection accuracy for each minute.



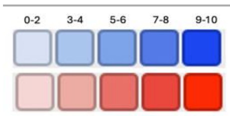
Note: *HC participants achieved significantly higher detection accuracy than PwMS participants across all time points, with no significant effect of time or interaction between group and time.*

Table 2

Detection performance, fatigue levels, and confidence ratings across 6 minutes

		Minute 1	*Minute 2*	*Minute 3*	*Minute 4*	*Minute 5*	*Minute 6*	*6MWT*	*Pre-Fatigue (0-10)*	*Post-Fatigue (0-10)*	*confidence (%)*
HC 1	*Report*	5	8	10	8	8	7	46	0	4	60
	CV%	2.93	3.84	2.95	2.93	2.41	2.38	3.39			
HC 2	*Report*	3	2	1	1	1	1	9	0	2	30
	CV%	1.90	2.51	2.14	1.94	1.61	2.16	2.16			
HC 3	*Report*	3	6	5	7	5	5	31	0	1	60
	CV%	3.51	3.52	3.61	5.14	2.68	4.79	4.67			
HC 4	*Report*	6	7	6	4	6	6	35	2	3	65
	CV%	2.45	4.01	1.45	1.43	1.41	1.57	1.81			
HC 5	*Report*	0	0	3	3	3	2	11	1	5	75
	CV%	2.40	1.80	2.80	3.43	2.83	2.96	3.07			
HC 6	*Report*	1	2	2	1	2	6	14	1	1	60
	CV%	2.08	1.71	1.99	1.65	1.27	1.55	1.93			
HC 7	*Report*	0	0	1	2	1	0	4	0	1	80
	CV%	2.24	1.92	2.00	2.79	2.79	2.28	3.05			
HC 8	*Report*	0	0	0	1	2	0	3	1	3	75
	CV%	3.02	2.47	1.94	2.05	2.73	2.14	3.29			
HC 9	*Report*	1	2	3	1	1	2	10	4	7	50
	CV%	3.35	2.22	1.58	1.24	1.74	2.80	3.97			

HC 10	*Report*	0	0	0	0	1	0	1	1	6	65
	CV%	4.22	2.75	3.03	3.24	4.59	2.76	3.83			
PwMS 1	*Report*	0	1	1	0	1	0	3	1	3	70
	CV%	3.03	1.72	2.02	2.13	1.41	2.18	2.72			
PwMS 2	*Report*	1	2	1	2	2	3	11	1	1	90
	CV%	2.34	1.96	1.55	2.15	2.81	2.54	2.49			
PwMS 3	*Report*	0	0	0	0	0	0	0	2	3	100
	CV%	2.29	1.42	1.59	1.74	2.08	2.05	2.44			
PwMS 4	*Report*	0	0	1	0	0	0	1	1	2	20
	CV%	2.61	1.50	1.17	1.65	1.83	1.71	2.86			
PwMS 5	*Report*	0	0	2	0	1	1	4	2	6	90
	CV%	3.12	2.09	3.73	2.27	2.37	2.09	2.96			
PwMS 6	*Report*	0	0	0	0	0	1	1	1	2	70
	CV%	2.51	4.33	1.99	2.49	2.17	3.00	6.21			
PwMS 7	*Report*	1	2	1	2	1	2	9	2	8	40
	CV%	1.79	2.37	1.31	1.14	1.37	1.47	2.99			
PwMS 8	*Report*	0	0	3	0	2	0	5	2	5	100
	CV%	3.09	3.84	3.85	3.53	4.05	3.03	3.86			
PwMS 9	*Report*	0	1	1	1	3	2	8	0	5	100
	CV%	4.42	2.37	2.31	3.38	3.27	2.79	6.70			
PwMS 10	*Report*	0	0	0	0	0	1	1	1	6	60
	CV%	1.97	1.91	1.66	2.01	1.50	1.68	1.91			



Note. *HC consistently showed higher DA compared to PwMS. Fatigue increased post-task in both groups but was more pronounced in PwMS. Confidence levels varied widely, with several PwMS reporting high confidence despite low performance.*

Figure 5

Reports during 6MWT for each participant.

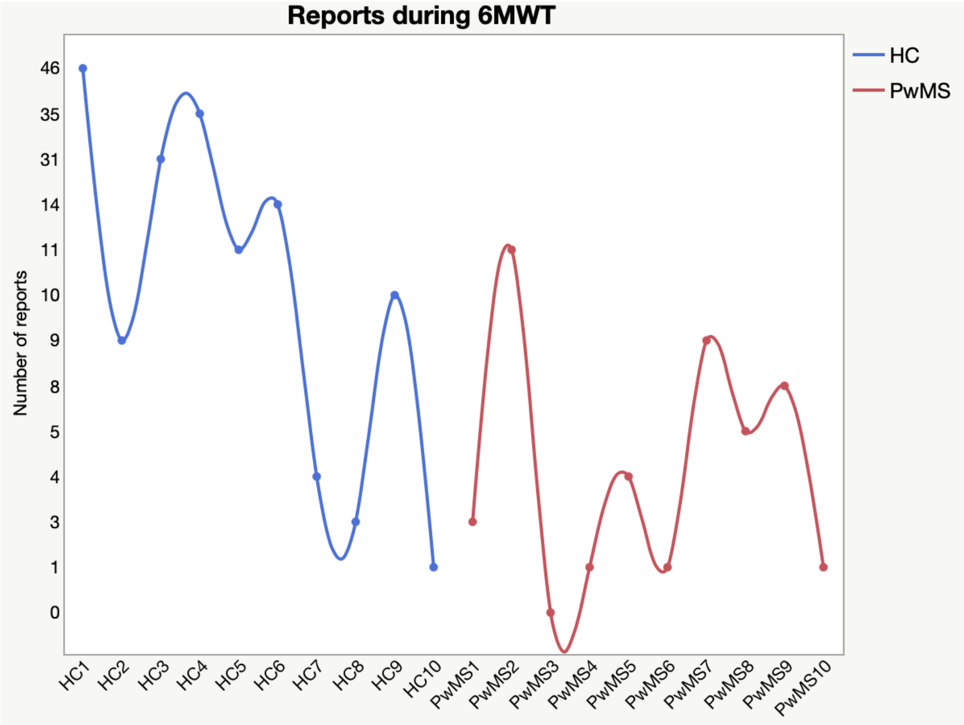
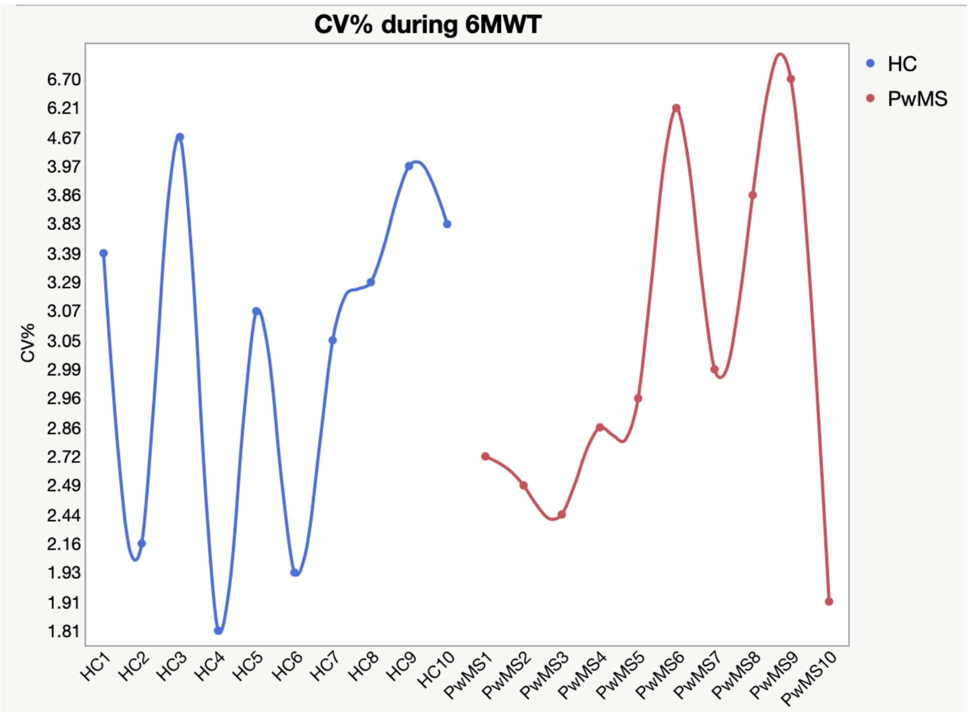


Figure 6

CV% during 6MWT for each participant.



Correlation analysis of detection accuracy and clinical characteristics

No statistically significant correlations were found between DA and any clinical or cognitive variable in either the HC group or PwMS (all $p > 0.05$). However, several small to moderate, non-significant correlations were observed. These varied in strength and direction across groups, suggesting the possibility of group-specific trends.

In terms of cognitive performance, the SDMT showed a small negative association in HC (r=–0.13, p=0.73) and a moderate one in PwMS (r=–0.45, p=0.19), neither of which reached significance. Similarly, for the BVMT, the association was negative in PwMS (r = –0.52, p = 0.13), while in HC the correlation was negligible (r = 0.03, p = 0.93).). Although not statistically significant, these patterns may point toward an association between lower cognitive performance and reduced detection accuracy, with more consistent trends observed in the MS group.

For interoceptive sensibility, assessed via the sensory subscale of the ISAQ, PWMS showed a moderate negative association with DA. (r = –0.50, p = 0.14), while in HC a small positive correlation was found (r = 0.24, p = 0.50). While these associations did not reach significance, they suggest that lower interoceptive sensitivity might relate to poorer detection accuracy, especially in PwMS.

In terms of physical performance, In the HC group, DA showed a small negative correlation with 6MWT performance (r = –.25, p = .53). A similar correlation was observed in the group with PwMS, where the correlation was moderate (r = –.36, p = .31). These correlations were not statistically significant.

The most notable divergence between groups was observed in the relationship between DA and pain, as measured by the BPI. Among the HC group, a small-to-moderate negative correlation was found (r = –0.42, p = 0.23), whereas in PWMS, a small positive correlation was observed (r = 0.17, p = 0.64). Although not statistically significant, the relationship between detection accuracy and pain appeared to differ between groups.

MFIS was not meaningfully associated with DA in either group (HC: r = 0.09, p = 0.80; PWMS: r = 0.18, p = 0.63). Similarly, no meaningful correlations were found between DA and the

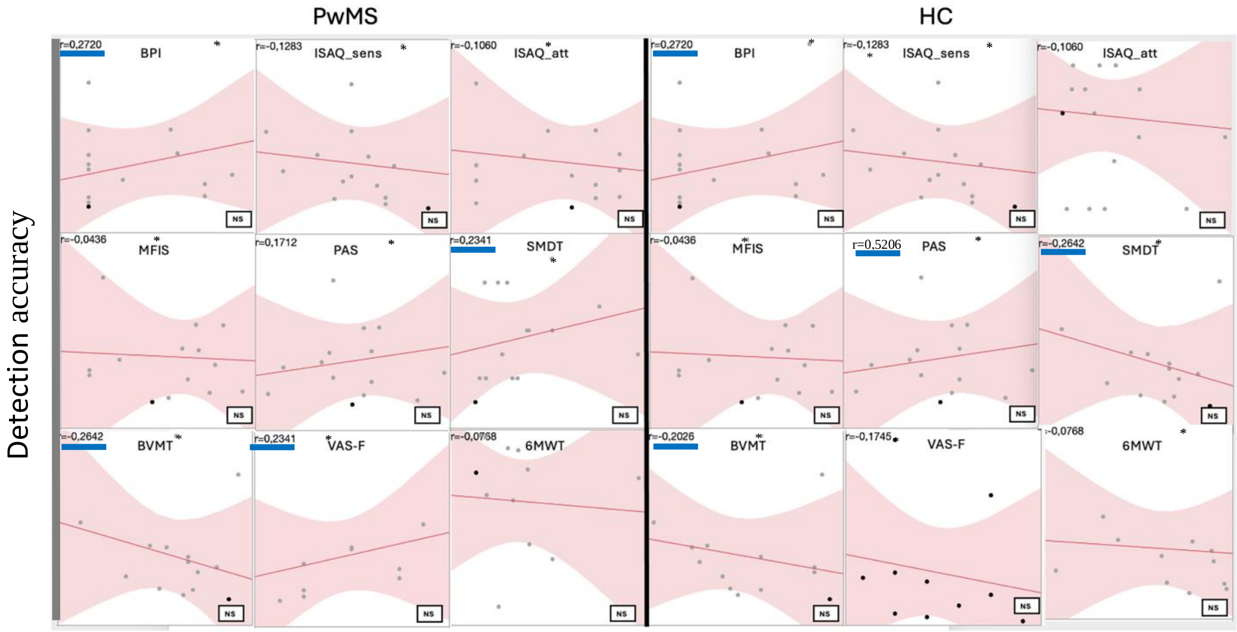
PAS in PWMS (r = 0.10, p = 0.78), while in HC, a moderate positive correlation emerged (r = 0.61, p = 0.06).

The ISAQ, attional subscale showed a small-to-moderate positive correlation in HC (r = 0.34, p = 0.33), but this correlation was absent in PWMS (r = –0.07, p = 0.84).

When looking specifically at fatigue, HC showed a small, non-significant negative correlation between DR and fatigue (r = –0.389, p = 0.267). In contrast, PwMS demonstrated a moderate positive monotonic association (r = 0.5618), suggesting a potential difference in how fatigue influences detection rate across groups.

Figure 7

Correlations Between Detection Accuracy and Clinical/Cognitive Measures in Patients.



*Note: * = outliers; PAS = Pain Anxiety Symptoms; BPI = Brief Pain Inventory; ISAQ_SENS = Sensory subscale of the Impact on Self-Assessment Questionnaire; MFIS = Modified Fatigue Impact Scale; SMDT = Symbol Digit Modalities Test; BVMT = Brief Visuospatial Memory Test; ISAQ_ATT = Attention subscale of the ISAQ. VAS-F = Visual analogue scale – fatigue; 6MWT = 6-Minute Walk Test. Correlations with a moderate magnitude (|r| > 0.2) are highlighted in blue.*

Discussion

This master's thesis aimed to investigate detection accuracy during overground walking at maximal speed over a six-minute period (6MWT), comparing PwMS to HC. The findings confirmed the primary hypothesis: PwMS exhibited significantly lower DA for self-perceived variations in walking speed compared to HC. This suggests a reduced ability in PwMS to monitor changes in their own motor performance, supporting existing literature that points to altered interoceptive processing in this population (Stephan et al., 2016; M. Ware et al., 2022).

Importantly, no significant effect of time or group × time interaction was found, indicating that the perceptual deficit observed in PwMS remained stable throughout the six-minute test rather than increasing over time due to fatigue. This stability suggests that the diminished detection ability may reflect a baseline impairment in interoceptive-motor integration rather than a fatigue-induced decline.

Although exploratory correlation analyses did not reveal statistically significant associations between detection accuracy s accuracy and clinical measures (e.g., fatigue, pain, cognitive function, or interoceptive sensibility), several moderate correlations were observed. Most notably, negative correlations emerged between DA and visuospatial memory (BVMT), processing speed (SDMT), and interoceptive sensibility (ISAQ_sensory). These correlations may reflect the cognitive demands involved in accurately perceiving internal states, particularly when attentional resources or memory functions are compromised.

Importantly, the associations between DA and interoceptive measures appeared to differ across groups, indicating a potentially altered role of body awareness in multiple sclerosis. PwMS showed a moderate negative correlation between interoceptive sensibility (ISAQ_sensory) and DA, in contrast to the small positive trend in HC.

Although these findings did not reach statistical significance, they suggest a potential influence of cognitive load and disrupted bodily awareness on self-monitoring performance. Interestingly, the relationship between DA and fatigue showed divergent trends across groups. In healthy controls (HC), a small negative correlation was observed, aligning with the conventional view of fatigue as a factor that reduces perceptual performance. However, in PwMS, a moderate positive association emerged. This finding may indicate that, in the context of multiple sclerosis, fatigue does not solely act as a depleting influence but could also function as a compensatory signal.

However, due to the small sample size and limited statistical power, we interpret these relationships as hypothesis-generating rather than conclusive.

One methodological consideration is the presence of potential outliers in the DA. Specifically, one participant submitted an unusually high number of perceptual reports, while another submitted very few. These individuals may have interpreted the task differently or experienced unique difficulties in attentional control or understanding. Such outliers can substantially influence correlation analyses by inflating or masking relationships between variables. In reviewing our results, the influence of these outliers appears plausible, particularly given the small sample size and the exploratory nature of the correlations. The observed variability in detection behaviour could have contributed to the lack of statistically significant associations, despite moderate effect sizes in several instances. Importantly, the statistical methods employed did not explicitly account for outliers.

Conclusion

This study contributes to a growing understanding of perceptual deficits in PwMS, suggesting that impairments in detecting moment-to-moment variations in performance may stem from disrupted interoceptive and cognitive-motor integration. These insights call attention to the need for a multidimensional approach to rehabilitation that includes assessment and training of performance awareness. Future research should aim to replicate these findings in larger, sex-balanced samples and evaluate the effects of interventions targeting interoceptive and cognitive functioning on perceptual accuracy during physical activity.

Reference list

ATS statement: guidelines for the six-minute walk test. (2002). *Am J Respir Crit Care Med*, *166*(1), 111-117. https://doi.org/10.1164/ajrccm.166.1.at1102

Barrett, L. F., & Simmons, W. K. (2015). Interoceptive predictions in the brain. *Nat Rev Neurosci*, *16*(7), 419-429. https://doi.org/10.1038/nrn3950

Behrens, M., Gube, M., Chaabene, H., Prieske, O., Zenon, A., Broscheid, K. C., Schega, L., Husmann, F., & Weippert, M. (2023). Fatigue and Human Performance: An Updated Framework. *Sports Med*, *53*(1), 7-31. https://doi.org/10.1007/s40279-022-01748-2

Benedict, R. H., DeLuca, J., Phillips, G., LaRocca, N., Hudson, L. D., & Rudick, R. (2017). Validity of the Symbol Digit Modalities Test as a cognition performance outcome measure for multiple sclerosis. *Multiple Sclerosis Journal*, *23*(5), 721-733. https://doi.org/10.1177/1352458517690821

Bogaerts, K., Walentynowicz, M., Van Den Houte, M., Constantinou, E., & Van den Bergh, O. (2022). The Interoceptive Sensitivity and Attention Questionnaire: Evaluating Aspects of Self-Reported Interoception in Patients With Persistent Somatic Symptoms, Stress-Related Syndromes, and Healthy Controls. *Psychosom Med*, *84*(2), 251-260. https://doi.org/10.1097/psy.0000000000001038

Cleeland, C. S., & Ryan, K. M. (1994). Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singap*, *23*(2), 129-138.

Comber, L., Galvin, R., & Coote, S. (2017). Gait deficits in people with multiple sclerosis: A systematic review and meta-analysis. *Gait Posture*, *51*, 25-35. https://doi.org/10.1016/j.gaitpost.2016.09.026

Cramer, H., Mehling, W. E., Saha, F. J., Dobos, G., & Lauche, R. (2018). Postural awareness and its relation to pain: validation of an innovative instrument measuring awareness of body posture in patients with chronic pain. *BMC Musculoskelet Disord*, *19*(1), 109. https://doi.org/10.1186/s12891-018-2031-9

Cullen, K. E. (2023). Vestibular motor control. *Handb Clin Neurol*, *195*, 31-54. https://doi.org/10.1016/B978-0-323-98818-6.00022-4

Dalgas, U., Stenager, E., Jakobsen, J., Petersen, T., Hansen, H. J., Knudsen, C., Overgaard, K., & Ingemann-Hansen, T. (2009). Resistance training improves muscle strength and functional capacity in multiple sclerosis. *Neurology*, *73*(18), 1478-1484. https://doi.org/10.1212/WNL.0b013e3181bf98b4

Enoka, R. M., & Duchateau, J. (2016). Translating Fatigue to Human Performance. *Med Sci Sports Exerc*, *48*(11), 2228-2238. https://doi.org/10.1249/MSS.0000000000000929

Feld, J. A., Zukowski, L. A., Howard, A. G., Giuliani, C. A., Altmann, L. J. P., Najafi, B., & Plummer, P. (2018). Relationship Between Dual-Task Gait Speed and Walking Activity Poststroke. *Stroke*, *49*(5), 1296-1298. https://doi.org/10.1161/strokeaha.117.019694

Feys, P., Giovannoni, G., Dijsselbloem, N., Centonze, D., Eelen, P., & Lykke Andersen, S. (2016). The importance of a multi-disciplinary perspective and patient activation programmes in MS management. *Mult Scler*, *22*(2 Suppl), 34-46. https://doi.org/10.1177/1352458516650741

Fisk, J. D., Ritvo, P. G., Ross, L., Haase, D. A., Marrie, T. J., & Schlech, W. F. (1994). Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. *Clin Infect Dis*, *18 Suppl 1*, S79-83. https://doi.org/10.1093/clinids/18.supplement_1.s79

Gonzalez Campo, C., Salamone, P. C., Rodríguez-Arriagada, N., Richter, F., Herrera, E., Bruno, D., Pagani Cassara, F., Sinay, V., García, A. M., Ibáñez, A., & Sedeño, L. (2020). Fatigue in multiple sclerosis is associated with multimodal interoceptive abnormalities.

Multiple Sclerosis Journal, *26*(14), 1845-1853. https://doi.org/10.1177/1352458519888881
Gonzalez Campo, C., Salamone, P. C., Rodríguez-Arriagada, N., Richter, F., Herrera, E., Bruno, D., Pagani Cassara, F., Sinay, V., García, A. M., Ibáñez, A., & Sedeño, L. (2020). Fatigue in multiple sclerosis is associated with multimodal interoceptive abnormalities. *Mult Scler*, *26*(14), 1845-1853. https://doi.org/10.1177/1352458519888881
Hillier, S., Immink, M., & Thewlis, D. (2015). Assessing Proprioception: A Systematic Review of Possibilities. *Neurorehabil Neural Repair*, *29*(10), 933-949. https://doi.org/10.1177/1545968315573055
Kalinowski, A., Cutter, G., Bozinov, N., Hinman, J. A., Hittle, M., Motl, R., Odden, M., & Nelson, L. M. (2022). The timed 25-foot walk in a large cohort of multiple sclerosis patients. *Mult Scler*, *28*(2), 289-299. https://doi.org/10.1177/13524585211017013
Khalsa, S. S., Adolphs, R., Cameron, O. G., Critchley, H. D., Davenport, P. W., Feinstein, J. S., Feusner, J. D., Garfinkel, S. N., Lane, R. D., Mehling, W. E., Meuret, A. E., Nemeroff, C. B., Oppenheimer, S., Petzschner, F. H., Pollatos, O., Rhudy, J. L., Schramm, L. P., Simmons, W. K., Stein, M. B., . . . Zucker, N. (2018). Interoception and Mental Health: A Roadmap. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *3*(6), 501-513. https://doi.org/10.1016/j.bpsc.2017.12.004
Larocca, N. G. (2011). Impact of walking impairment in multiple sclerosis: perspectives of patients and care partners. *Patient*, *4*(3), 189-201. https://doi.org/10.2165/11591150-000000000-00000
Lee, K. A., Hicks, G., & Nino-Murcia, G. (1991). Validity and reliability of a scale to assess fatigue. *Psychiatry Res*, *36*(3), 291-298. https://doi.org/10.1016/0165-1781(91)90027-m
Manjaly, Z. M., Harrison, N. A., Critchley, H. D., Do, C. T., Stefanics, G., Wenderoth, N., Lutterotti, A., Muller, A., & Stephan, K. E. (2019). Pathophysiological and cognitive mechanisms of fatigue in multiple sclerosis. *J Neurol Neurosurg Psychiatry*, *90*(6), 642-651. https://doi.org/10.1136/jnnp-2018-320050
McMorris, T., Barwood, M., & Corbett, J. (2018). Central fatigue theory and endurance exercise: Toward an interoceptive model. *Neurosci Biobehav Rev*, *93*, 93-107. https://doi.org/10.1016/j.neubiorev.2018.03.024
Murphy, J. (2022). Propensity to use interoceptive signals: An important individual difference. *Biol Psychol*, *171*, 108326. https://doi.org/10.1016/j.biopsycho.2022.108326
Murphy, J., Catmur, C., & Bird, G. (2019). Classifying individual differences in interoception: Implications for the measurement of interoceptive awareness. *Psychon Bull Rev*, *26*(5), 1467-1471. https://doi.org/10.3758/s13423-019-01632-7
Oliva Ramirez, A., Keenan, A., Kalau, O., Worthington, E., Cohen, L., & Singh, S. (2021). Prevalence and burden of multiple sclerosis-related fatigue: a systematic literature review. *BMC Neurol*, *21*(1), 468. https://doi.org/10.1186/s12883-021-02396-1
Oliva Ramirez, A., Keenan, A., Kalau, O., Worthington, E., Cohen, L., & Singh, S. (2021). Prevalence and burden of multiple sclerosis-related fatigue: a systematic literature review. *BMC Neurology*, *21*(1), 468. https://doi.org/10.1186/s12883-021-02396-1
Quadt, L., Critchley, H. D., & Garfinkel, S. N. (2018). The neurobiology of interoception in health and disease. *Annals of the New York Academy of Sciences*, *1428*(1), 112-128. https://doi.org/10.1111/nyas.13915

Riemann, B. L., & Lephart, S. M. (2002). The Sensorimotor System, Part II: The Role of Proprioception in Motor Control and Functional Joint Stability. *J Athl Train*, *37*(1), 80-84.

Sandroff, B. M., Motl, R. W., Reed, W. R., Barbey, A. K., Benedict, R. H. B., & DeLuca, J. (2018). Integrative CNS Plasticity With Exercise in MS: The PRIMERS (PRocessing, Integration of Multisensory Exercise-Related Stimuli) Conceptual Framework. *Neurorehabil Neural Repair*, *32*(10), 847-862. https://doi.org/10.1177/1545968318798938

Santinelli, F. B., Abasiyanik, Z., Ramari, C., Gysemberg, G., Kos, D., Pau, M., Kalron, A., Meyns, P., Ozakbas, S., & Feys, P. (2024). Manifestations of walking fatigability in people with multiple sclerosis based on gait quality and distance walked during the six minutes walking test. *Mult Scler Relat Disord*, *91*, 105909. https://doi.org/10.1016/j.msard.2024.105909

Stephan, K. E., Manjaly, Z. M., Mathys, C. D., Weber, L. A., Paliwal, S., Gard, T., Tittgemeyer, M., Fleming, S. M., Haker, H., Seth, A. K., & Petzschner, F. H. (2016). Allostatic Self-efficacy: A Metacognitive Theory of Dyshomeostasis-Induced Fatigue and Depression. *Front Hum Neurosci*, *10*, 550. https://doi.org/10.3389/fnhum.2016.00550

Suksasilp, C., & Garfinkel, S. N. (2022). Towards a comprehensive assessment of interoception in a multi-dimensional framework. *Biol Psychol*, *168*, 108262. https://doi.org/10.1016/j.biopsycho.2022.108262

Tam, J. W., & Schmitter-Edgecombe, M. (2013). The Role of Processing Speed in the Brief Visuospatial Memory Test – Revised. *The Clinical Neuropsychologist*, *27*(6), 962-972. https://doi.org/10.1080/13854046.2013.797500

Van den Bergh, O., Witthoft, M., Petersen, S., & Brown, R. J. (2017). Symptoms and the body: Taking the inferential leap. *Neurosci Biobehav Rev*, *74*(Pt A), 185-203. https://doi.org/10.1016/j.neubiorev.2017.01.015

Van Geel, F., Bielen, H., Theunissen, K., Moumdjian, L., Van Nieuwenhoven, J., Van Wijmeersch, B., Meesen, R., Ramari, C., & Feys, P. (2021). Clinical manifestation and perceived symptoms of walking-related performance fatigability in persons with multiple sclerosis. *Int J Rehabil Res*, *44*(2), 118-125. https://doi.org/10.1097/MRR.0000000000000457

Walton, C., King, R., Rechtman, L., Kaye, W., Leray, E., Marrie, R. A., Robertson, N., La Rocca, N., Uitdehaag, B., van der Mei, I., Wallin, M., Helme, A., Angood Napier, C., Rijke, N., & Baneke, P. (2020). Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. *Mult Scler*, *26*(14), 1816-1821. https://doi.org/10.1177/1352458520970841

Ware, M., O'Connor, P., Bub, K., Backus, D., & McCully, K. (2022). The role of worry in exercise and physical activity behavior of people with multiple sclerosis. *Health Psychol Behav Med*, *10*(1), 786-805. https://doi.org/10.1080/21642850.2022.2112197

Ware, M., O’Connor, P., Bub, K., Backus, D., & McCully, K. (2022). The role of worry in exercise and physical activity behavior of people with multiple sclerosis. *Health Psychology and Behavioral Medicine*, *10*(1), 786-805. https://doi.org/10.1080/21642850.2022.2112197

* Chatgpt was used for checking grammar, searching for synonyms, rephrasing sentences.

Appendix A

Perception[1,4]	The process by which sensory information is interpreted by the brain to form an understanding of the environment or the body's condition. This includes integrating interoceptive and exteroceptive cues**.**
Sensory input [5,11]	Information received by sensory receptors, which is then processed by the nervous system to form perceptions. Proprioceptors and mechanoreceptors in the vestibular system provide crucial sensory inputs for motor control.
Prior beliefs [1]	Pre-existing expectations and experiences that influence how sensory information is interpreted and how perceptions are formed. These are part of the inferential process that shapes interoceptive awareness.
Accuracy[11]	Accuracy in the context of perception refers to the degree of truthfulness or correctness of the perception. For example, proprioceptive accuracy involves how accurately one can perceive the position and movement of body parts.
Sensibility[6,12]	Sensibility in interoception refers to self-beliefs about one's own interoceptive accuracy and attention. It represents how individuals perceive their own capacity to sense and interpret bodily signals.
Attention[8,9]	The level of focus or cognitive resources allocated to processing and monitoring sensory cues, affecting awareness and responsiveness to sensory input.
Interoception[1,6]	The ability to sense, interpret, and integrate signals originating from within the body. This involves understanding physiological conditions and is critical for self-efficacy judgments during physical activity, as it enhances the awareness of one's internal state and informs decision-making related to movement and effort.
Exteroception[11]	The process of perceiving external stimuli, contributing to an individual's awareness of their environment. This integrates sensory inputs from outside the body to build performance awareness.
Proprioception[3,11]	The awareness of the position and movement of body parts, relying on receptors in muscles, tendons, and joints. It is essential for optimal motor control and forms a link between interoception and exteroception.
Fatigue[7,10]	In the context of MS refers to a subjective feeling of tiredness or exhaustion that is disproportionate to the level of activity performed. It is a common and often debilitating symptom that can affect physical, cognitive, and emotional functioning. Fatigue in MS can be persistent (chronic) or can occur in episodes (acute), and it significantly impacts the quality of life.
Fatiguability[2,7]	The susceptibility to fatigue, specifically referring to the rate at which an individual becomes fatigued during a physical or cognitive task. In MS, fatiguability often manifests as a rapid decline in performance, such as reduced walking distance or increased perceived exertion during activities over time. It is an objective measure of the decline in performance capability.
Trait[9]	A trait refers to a stable and enduring characteristic or disposition of an individual that is consistent over time and across situations. Traits are aspects of personality or habitual patterns of behavior, thought, and emotion. In the context of fatigue, trait fatigue would refer to a person's general tendency to experience fatigue, independent of situational factors.
State [12]	A state refers to a temporary condition or status that can change over short periods. In psychological and physiological terms, it represents the transient characteristics or conditions of an individual that can fluctuate, such as current levels of fatigue, mood, or cognitive functioning. State-related measures capture these dynamic changes in response to internal and external stimuli.
Awareness [1,6,12]	Refers to the state or ability to consciously perceive, feel, or be cognizant of events, objects, thoughts, emotions, or sensory patterns. It is a broader concept that encompasses attention, interoception, exteroception, and the recognition of both internal and external stimuli. Awareness is foundational to self-efficacy, decision-making, and adaptive behaviors in response to environmental demands

References (Barrett & Simmons, 2015; Behrens et al., 2023; Cullen, 2023; Enoka & Duchateau, 2016; Hillier et al., 2015; Khalsa et al., 2018; Manjaly et al., 2019; McMorris et al., 2018; Murphy, 2022; Murphy et al., 2019; Quadt et al., 2018; Riemann & Lephart, 2002; Suksasilp & Garfinkel, 2022)