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Exploring Fatigue in Multiple Sclerosis: "Investigating objective metrics of ambulation and activity (biomarkers) alongside the patient's perspective."- A Naturalised Phenomenological approach

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Abstract

Multiple sclerosis (MS) fatigue is a multifaceted phenomenon that is difficult to describe, portray and monitor. The correspondence between fatigue and fatigability remains problematic; investigating and bridging different domains of fatigue will assist in the overall measurement and management of fatigue in MS.

This study used an interdisciplinary, naturalised phenomenological approach guided by Varela [1996] and Gallagher [2015]. Twelve people with MS (pwMS) and 11 older healthy volunteers were recruited. The timed 25-foot walk (T25FW) was repeated before and after the six-minute walk (6MW) with wearable sensors attached to the ankle, thigh and sternum. A descriptive phenomenological interview and analysis [Giorgi et al., 2017] was used to determine the overarching phenomenon of fatigue. The mean, median, standard deviation were calculated with parametric (unpaired t-test, ANOVA and Spearman's correlation coefficient) and non-parametric (rank-sum, Mann-Whitney U and Kruskal-Wallis) tests to investigate the velocity and peak angular velocity (ω) of each T25FW and minute of the 6MW.

Nonsignificant and variable results were detected in ambulatory measurements in pwMS in the 6MW. However, sensor-derived measurements of average ankle and thigh peak ω were higher in healthy participants (447.17 ± 63.88, 194.64 ± 72.68 degrees/second) when compared to pwMS (350.37 ± 85.72, 359.87 ± 93.91, 145.53 ± 54.09, 121.43 ± 57.44 degrees/second) in the 6MW of the dominant and weak leg, respectively. Walking velocity of pwMS post-6MW in the T25FW was significantly slower compared to the healthy group (5.83 ± 1.69, 4.19 ± 0.75) and pwMS displayed only a 0.08-second difference pre- to post-6MW in the T25FW. Fatigue was revealed as an all-engrossing phenomenon that took captive unconscious facets of emotion, bodily and perceptive aspects of an individual's everydayness and caused deep disruption to daily rhythm. Four constituents were established highlighting fatigue on a continuum of sensation: (1) familiar body falling away, (2) sweeping sudden fatigue towards stasis, (3) cloudiness of consciousness, and (4) managing the everydayness. A continuum was drawn up that began to reveal the confluence between fatigue and fatigability. Although the direct relationship remains unclear, this naturalised phenomenological study highlights the interwoven nature of fatigue, fatigability and the potential role stigma and dignity play part to. Results suggest fatigue is a global and complex phenomenon. This is an attempt to use a naturalised phenomenological approach and to assess its usefulness in this area of research. Phenomenological insights could provide useful insight for further measurement of fatigue. The findings from this research may support, guide and tailor management interventions for MS fatigue in multiple fields of healthcare.

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List of abbreviations

Abbreviation	**Full description**
10MW:	Ten-metre walk
10MWf:	Ten-metre walk fast
10MWu:	Ten-metre walk usual
2MW:	Two-minute walk
6MW:	Six-minute walk
ATS:	American Thoracic Society
BDI:	Beck Depression Inventory
BSN:	Body sensor networks
CIS:	Checklist Individual Strength
CNS:	Central nervous system
DTW:	Dynamic time warp
EDSS:	Expanded Disability Status Scale
EDSS-S:	Self-administered Expanded Disability Status Scale
EMG:	Electromyography
EPP:	Empirical phenomenological psychological
FAI:	Fatigue assessment instrument
FAMS:	Functional Assessment of Multiple Sclerosis
FDS:	Fatigue Descriptive Scale
FIS:	Fatigue Impact Scale
fMRI:	Functional magnetic resonance imaging
FSS:	Fatigue Severity Scale
GNDS:	Guy’s Neurological Disability Scale

IIRS:	Illness Intrusiveness Ratings Scale
IMU:	Inertial measurement unit
IPA:	Interpretative phenomenological analysis
MFIS:	Modified Fatigue Impact Scale
MIMUs:	Magneto-inertial measurement units
MMR:	Mixed-methods research
MRI:	Magnetic resonance imaging
MS:	Multiple sclerosis
MSWS-12:	Multiple Sclerosis Walking Scale
MVC:	Maximal voluntary contractions
NARCOMS:	North American Research Committee on Multiple Sclerosis
NGIMU:	Next generation inertial measurement unit
NMSS:	National Multiple Sclerosis Society
NP:	Neurophenomenology
PASAT:	Paced Auditory Serial Addition Test
Peak ω:	Peak angular velocity
PHE:	Public Health England
PPMS:	Primary progressive multiple sclerosis
PRMS:	Progressive-relapsing multiple sclerosis
PwMS:	Person/people with multiple sclerosis
QOL:	Quality of life
ROI:	Region of Interest
ROM:	Range of movement
RRMS:	Relapsing-remitting multiple sclerosis

SDMT:	Signal Digit Modalities Test
SF-36:	Short Form (36) Health Survey
SPMS:	Secondary progressive multiple sclerosis
T25FW:	Timed 25-foot walk
TAP:	Test battery for attentional performance
TD:	Turn detection
THIN:	The Health Improvement Network
TUG:	Timed Up and Go Test
U3A:	University of the Third Age
uT:	Unit tesla
ω:	Angular velocity

Preface and acknowledgements

The basis for this research stemmed from my interest in human sciences and my passion for developing research in healthcare in chronic conditions, such as Multiple Sclerosis. The human body is a complex yet magnificent structure of systems, it is a single structure that is made up of billions of smaller structures that all coordinate to maintain function. In this thesis, I embarked on the exploration of Multiple Sclerosis related fatigue and its multidimensional nature to some of these systems in terms of measurement. Fatigue is a symptom that has far-reaching impacts and can affect an individual's physical, emotional and intellectual states of being. To delve into the intricate nature of fatigue, it was observed from multiple approaches (physiological and phenomenological). As the world moves forward, clear comprehension and precise measurement are needed.

In truth, I could not have accomplished this without a strong support group. First of all, my supervisors, Professor Kathleen Galvin and Doctor Harry Witchel, who have guided me gracefully through each stage of my PhD. I have learnt a great deal from both of you, which I have thoroughly enjoyed. Secondly, my close family and friends, each of whom have provided patience and support. A special acknowledgement to my sister, Leanne, for your wise counsel and boundless support, and to Kyle, for the immeasurable moral support and constant supply of pizza as a motive. Lastly, my gratitude to MS Sussex Centre and Eastbourne MS Society for your kind cooperation and participation.

I would like to dedicate this thesis to the late Nicolette Richardson, friend, and wonderful osteopath, without you, I would not be where I am today.

Thank you all for your unwavering support, I am forever grateful.

Author Declaration

I declare that the research contained in this thesis, unless otherwise formally indicated within the text, is the original work of the author. The thesis has not been previously submitted to this or any other university for a degree, and does not incorporate any material already submitted for a degree.

Signed:

[redacted]

Dated: 28/04/2021

"We know not through our intellect but through our experience… I will never know how you see red and you will never know how I see it. But this separation of consciousness is recognised only after a failure of communication, and our first movement is to believe in an undivided being between us."

— Maurice Merleau-Ponty, The Primacy of Perception: And Other Essays on Phenomenological Psychology, the Philosophy of Art, History and Politics [1964].

Chapter One: Introduction: The current understanding and characteristics of Multiple Sclerosis related fatigue

1.1. General background

Multiple sclerosis (MS) is a chronic, inflammatory, neurodegenerative disease affecting an estimated 2.5 million people worldwide [Dua & Rompani, 2008]. It is the leading cause of disability in young adults in Western Europe and North America with an estimated incidence of 11.52 and 4.84 per 100,000 in women and men, respectively [Mackenzie et al., 2013]. The disease involves genetic, environmental, and immunological factors and is characterised by demyelinated lesions throughout the central nervous system (CNS) [Due & Rompani, 2008]. In this respect, physical, psychological, and emotional factors impact people with MS (pwMS) and cause considerable interference to daily activities. Alongside depression and disability, fatigue is reported to be one of the most debilitating symptoms for pwMS, with approximately 75-90% of individuals reported to suffer from MS-related fatigue [Dua & Rompani, 2008]. It is a physical, psychological, social, and even existential dimension of a person's life; it is a multi-faceted symptom that is often difficult to describe and portray as it remains poorly understood within the literature [Kos et al., 2004].

Fatigue is a ubiquitous phenomenon that has been fundamentally problematic to identify, illustrate, and monitor. It has many definitions and is comprised of several physiological and psychological aspects [Kos et al., 2004]. Prior to 1984, fatigue within MS was not recognised as a dominant symptom and rarely listed in clinical or research settings. Freal et al. [1984] published an article that demonstrated 78% of pwMS listed fatigue as one of their most common symptoms. It was the single most common symptom reported as interfering with activities of daily living. Nevertheless, further investigation found many individuals were unable to distinguish between fatigue and other symptoms, possibly due to a lack of understanding.

Since the work of Freal et al. [1984], research on MS fatigue has expanded and continues to attract scientists and the research community. In 1998, the Multiple Sclerosis Council for Clinical Practice published a definition of fatigue, describing it as "*a subjective lack of physical or mental ability that is perceived by the individual or the caregiver to interfere with usual or desired activities*." [Multiple Sclerosis Council for Clinical Practice Guidelines, 1998]. Nonetheless, for a symptom that has been repeatedly described as a complex construct, this clinical definition may not reflect and fully describe the phenomenon [Multiple Sclerosis International Federation, 2012].

Regardless of the MS Council for Clinical Practice's definition raising awareness and guidance for the MS community, Beckerman et al. [2020] identified a lack of consensus regarding the ideal core measurement and classification of MS-related fatigue. Before something can be measured, it must be defined, and before a definition can be approved, there must be an appropriate instrument/s for assessing the phenomenon under investigation [Beckerman et al., 2020]. According to Dittner et al. [2004], there are more than 250 measures to assess all aspects of fatigue, which ultimately produces a wide range of definitions [Dittner, Wessely, & Brown, 2004]. This was recognised as a "*catch-22*" situation that generates uncertainty with aetiology and classification. This has caused many researchers to struggle with assessment [Dittner, Wessely, & Brown, 2004].

Fatigue has been categorised into physical, cognitive, and psychosocial constructs with different assessments suggested approaching distinct aspects of fatigue [Beckerman et al., 2020]. In the literature, experiences and perceived fatigue are reported as complex, due to its non-objective character and multifaceted nature [Braley and Chervin, 2010]. Typically, subjective fatigue is usually measured using self-reported questionnaires and surveys, as the majority of questionnaires are considered a valid and reliable approach to understand and measure fatigue [Beckerman et al., 2020]. Nevertheless, in multidimensional scales, the total scores can result in a loss of information on underlying individual dimensions [Christensen & Piper-Terry, 2004]. Krupp [2003] emphasised the need for a clear definition of the dimensions of fatigue and appropriate instruments of assessment and reported the current limitation in research by the lack of well validated definition of fatigue.

Fatigue is understood to be a subjective experience. However, researchers argue that fatigue must be measurable to accurately monitor it accordingly. Numerous studies have acknowledged this in an attempt to deepen the understanding of the foundations of fatigue and explore its characteristics, classifications, patterns, and relation to sociodemographic information [Lerdal et al., 2007; Pittion-Vouyovitch et al., 2006; Ghajarzadeh et al., 2013; Razazian et al., 2014; Mills & Young, 2008; Forwell et al., 2008].

The use of single measurements in MS fatigue (namely in the clinic and out of context) continues to be problematic because of the day-to-day variations in MS disability and fatigue. The addition of context (namely qualitative analysis) to quantifiable measurement may provide a unique opportunity to integrate divergent individual perspectives, while also presenting novel sensor metrics.

The following introductory subsections outline the current understanding on the characteristics and associations identified with MS fatigue, including the types of fatigue, sociodemographic associations, and the current measurement of fatigue. An overview of the MS and fatigue literature is presented, providing comprehensive rationale for the proposed research objectives, namely to deepen current understanding of how fatigue is experienced measured.

1.2. Commonplace groupings of fatigue

Fatigue has previously been divided into numerous categories within the literature. However, the common categories are primary and secondary fatigue, and physical and cognitive fatigue. In the following section, the definition and associations within each category are discussed, to illustrate a foundational comprehension of fatigue within MS.

1.2.1. Primary and secondary fatigue

Two recognised types of fatigue can affect pwMS. These are dependent on whether fatigue is directly caused by damage to the CNS or other associated MS symptoms [Dalgas et al., 2018]. Primary fatigue relates directly to the underlying pathophysiologic processes of the disease that cause immune dysregulation, inflammation, neuronal dysfunction, and demyelination [Forwell et al., 2008]. Although the results remain inconclusive in the literature, it is hypothesised that three potential mechanisms cause primary fatigue: changes to the CNS (axonal loss and cortical reorganisation), changes in the immune system, and endocrine influences [Braley & Chervin, 2010]. Kos et al. [2008] found greater levels of fatigue in pwMS that had direct demyelination and axon functional deterioration in comparison to non-fatigued individuals. Additionally, Colombo et al. [2000] suggested that individuals who experienced fatigue had significantly higher lesion loads[1] in certain areas of the brain, including the parietal lobe and periventricular trigone, compared to individuals who did not experience fatigue. These structural changes to the brain can affect the patterns of cerebral activation and demand higher energy in the brain which can cause and affect an individual's fatigue level [Roelcke et al., 1997; Filippi et al., 2002].

Perceived fatigue has been associated with greater lesion loads. However, it is highly contentious whether these are strong associations or not [Giovannoni, 2006]. Findings from other studies suggest that increased levels of immune markers are associated with fatigue; for example, proinflammatory cytokines have been associated with daytime sleepiness [Heesen et al., 2006]. Fatigue was linked to immune activation in one study, where cytokines such as interferon-y and TNF-α were raised [Iriarte, Subira & Castro, 2000]. Although the current literature is limited, disturbances in the neuroendocrine system may potentially cause primary fatigue [Gottschalk et al., 2005; Téllez et al., 2006; Rammohan et al., 2002; Zifko, et al., 2002; Zellini, Niepel, Tench, & Constantinescu, 2009]. Lower levels of the hormones cortisol and dehydroepiandrosterone have been associated with other conditions that are affected by fatigue, such as chronic fatigue syndrome, lupus, and rheumatoid arthritis. However, specific MS fatigue research remains inconclusive [Gottschalk et al., 2005; Téllez et al., 2006; Rammohan et al., 2002; Zifko et al., 2002; Zellini, Niepel, Tench, & Constantinescu, 2009].

Secondary (or non-primary) fatigue encompasses MS-related factors from environmental or emotional stress, such as pain, poor sleep and agents used to treat symptoms of MS (muscle relaxants, anticonvulsants, and interferon betas) [Coote et al., 2017]. Secondary fatigue is not directly caused by the disease process, but can be affected by external factors such as diet and lifestyle. Secondary fatigue has been explored in studies to aid the management of sleep deprivation, depression, and lifestyle [Coote et al., 2017]. Sleeping problems in pwMS were rated two to three times higher than healthy individuals [Bamer, Johnson, Amtmann, & Kraft, 2008; Lobentanz, Asenbaum, Vass, & Sauter, 2004; Merlino et al., 2009]. In agreement with previous studies, Strober [2015] found sleeping problems to be a significant contributor to fatigue [Kaminska et al., 2012; Kaynak et al., 2006; Moreira et al., 2008; Strober, 2015]. Over 50% of pwMS report chronic sleeping problems that result in worsening fatigue and daytime sleepiness [Fleming & Pollak, 2005]. Mills & Young [2010] found 85% of pwMS reported

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[1] Lesions (also called plaques) indicate damage to the myelin, known as demyelination, of the CNS, specifically the brain matter and the spinal cord. The volume of lesions is called the "lesion load."

between five and ten hours of nocturnal sleep a night, however, only 63.7% of them reported higher levels of fatigue alongside broken nocturnal sleep. The authors found no linear relationship between duration of sleep and fatigue, instead, a ‘V-shaped’ relationship was revealed. The results indicated those who slept between seven to eight hours a night reported the lowest levels of fatigue compared to individuals who slept fewer or more hours [Mills & Young, 2010].

Researchers have investigated the association between mood and fatigue in pwMS, in particular depressive mood and fatigue [Bakshi, 2003; Patrick, Christodoulou, Krupp & York, 2009; Pittion-Vouyovitch et al., 2006]. The relationship between fatigue and depression remains problematic in research due to fatigue and depression sharing symptomology [Pittion-Vouyovitch et al., 2006]. Fatigue has been reported to increase depressive mood and vice versa. Therefore, it is not always obvious which one causes the other [Pittion-Vouyovitch et al., 2006]. Research suggests that high levels of depression are related to all dimensions of fatigue subscales and there are significant positive correlations between Becks Depression Inventory (BDI) and Fatigue Severity Scale (FSS) [Skerrett & Moss-Morris, 2006; Ghajarzadeh et al., 2013; Pittion-Vouyovitch et al., 2006]. Bol et al. [2009] found fatigue to be highly sensitive to a clinically significant depressive symptom and recommend screening for depression in individuals who suffer from disabling fatigue. Although Bol et al. [2009] found depressed and anxious participants reported greater levels of fatigue, the authors only found a weak linear correlation between fatigue with both depression and anxiety. Additionally, consideration of psychological and personality factors may interfere with the relationship between fatigue and depression (for example avoidance, coping, motivation, and so forth) [Bol et al., 2009]. Many medications prescribed to pwMS can cause fatigue as a side effect, therefore awareness of the type of medication and its possible side effects is important [Gottberg, Gardulf, & Fredrikson, 2000].

In summary, both primary and secondary fatigue can be present in pwMS and may interact with one another [Kos et al., 2008]. The interaction between the two types makes it difficult to rule out one pathogenesis from another [Finlayson, 2012].

1.2.2. Physical and cognitive fatigue

Physical or motor fatigue can be defined as a loss of force during sustained muscle activity [Edwards et al., 1977]. In MS, fatigue is likely to be accompanied by a reduction of walking speed or distance, paresis, ataxia, or spasticity [Sehle et al., 2011]. It can often be related to performance fatigability[2], which ultimately affects an individual's exercise and movement capacity [Rudroff, Kendred & Ketelhut, 2016]. Mills & Young [2008] explored the definition of all domains of fatigue via semi-structured interviews and a cross-sectional survey. Fatigue experienced in motor features were largely reported in paresis with common descriptions of foot-dragging and maintaining an erect posture after prolonged standing or walking [Mills & Young, 2008]. Such phenomena of bodily and extremity experiences were often paired with the description of the feeling of "heaviness" and increased difficulty executing complex movements [Mills & Young, 2008]. Basic motor functions like walking were described as involving a higher level of concentration ("having to think of putting one foot in front of the other") [Mills & Young, 2008].

Motor weakness and spasticity have been reported to correlate consistently with fatigue and other secondary causes of fatigue in MS [Motl, Mcauley, Wynn & Suh, 2011]. A variety of abnormalities in muscle force generation and muscle metabolism differ distinctly between pwMS and the general population [Kent-Braun, Sharma, Miller & Weiner, 1994]. Such motor problems affect ambulation. PwMS state walking dysfunction to be one of the most challenging aspects of their condition, and highly prioritise walking as it gives independence and enables them to maintain their quality of life [La Rocca, 2011].

Van der Linden et al. [2018] reported people who are mild to moderately disabled, but without fatigability, may initially demonstrate a similar gait pattern to the healthy general population. However, when fatigue is present, the gait pattern may distinctly differ. Gait changes have been reported in a variety of kinematics and kinetic parameters concerning fatigue. A deterioration of velocity, lower extremity joint range of movement (ROM), cadence, and step length in pwMS have been researched to identify motor impairment with fatigability in ambulation [Filli et al., 2018; Motta et al., 2016; Shema-Shiratzky et al., 2019; Taborri et al., 2019; Van der Linden et al., 2018]. Gait deterioration is explored further Chapter Three.

Benedict et al. [2005] investigated the prediction of quality of life (QOL) in pwMS, concerning fatigue, physical disability, and cognitive impairments. The authors found that physical activity (measured using the FSS) correlated with physical disability (measured using the Expanded Disability Status Scale (EDSS)). Fatigue was inversely correlated to physical QOL, alongside physical disability and depression [Benedict et al., 2005]. PwMS have reported motor fatigue following physical activity, leading to an exacerbation of symptoms that they may not have

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[2] Fatigability is the magnitude or rate of change of motor performance on an objectively measured reference criterion after any type of voluntary activity or exercise [Kluger et al., 2013].

experienced at rest [Smith, Adeney-Steel, Fulcher, & Longley, 2006]. Conversely, participating in regular physical activity has a positive influence on the QOL in pwMS who have developed gait abnormalities [Stroud & Minahan, 2009]. Due to fear of worsening symptoms, physical activity can deter pwMS from engaging in any form of exercise [Stroud & Minaham, 2009]. There appears to be a limit to the level and intensity of physical activity pwMS can perform without interference of fatigue. In Chapter Two, the approach and form of exercise that pwMS can perform is explored through individuals' experiences.

Cognitive dysfunction is apparent in MS fatigue. Measurable cognitive deficits are reported in an estimated 45-65% of pwMS [Desousa & Albert, 2002; Bagert, Camplair, & Bourdette, 2002; Mills & Young, 2008; Newland, Starkweather, & Sorenson, 2016; Fernández-Muñoz et al., 2015]. Cognitive fatigue can be defined as a failure to sustain attention, and decline in alertness, orientation, and executive attention during a continuous task or performance [Holtzer et al., 2011]. The most recognised cognitive dysfunctions in pwMS are inability to sustain cognitive function, speed, flexibility, and alertness whilst performing mental and physical activities [Mills & Young, 2008; Rotstein, O'Connor, Lee, & Murray, 2012].

PwMS believed there was an increased mental effort, poor attention, energy expenditure, and a decrease in motivation levels accompanied with fatigue [Mills & Young, 2008; Bol et al., 2009]. To avoid exacerbating cognitive fatigue, many pwMS report pre-planning and increased levels of organisation to prepare and reserve their energy accordingly [Bol et al., 2009]. Commonly, pwMS report difficulties participating in daily activities when they perceived their energy as depleted [Mills & Young, 2008].

Skerrett & Moss-Morris [2006] explored individuals' interpretations of their fatigue and social impairment. The authors reported changes in participants' everyday activities, employment, relationships, and recreational activities. Interestingly, although anxiety and depression explained some alterations to physical, mental, and social adjustment, cognitive-behavioural variables significantly affected fatigue levels [Skerrett & Moss-Morris, 2006]. The findings suggest behavioural patterns and mood may be particularly imperative when addressing pwMS management of fatigue and illness-related impairment. Other psychological factors that affect the way patients perceive their disease may also contribute to fatigue levels [Skerrett & Moss-Morris, 2006].

Blaney & Lowe-Strong [2009] found that pwMS have difficulties speaking, such as carrying out sentences and multitasking whilst feeling fatigued. Fatigue was reported to increase the frequency and severity of communication symptoms (memory, thinking, and speech dysarthria) [Blaney & Lowe-Strong, 2009].

Claros-Salinas et al. [2013] investigated whether cognitive fatigue is a spontaneous phenomenon or whether it could be provoked through cognitive effort and motor exercise. Participants in this study performed attention tasks before and after treadmill training and completed a standardised cognitive load of battery neuropsychological tests [Claros-Salina et al., 2013]. The authors found that cognitive fatigue was provoked by physical and cognitive load, favouring the concept that subjective and objective levels of cognitive fatigue were much higher when induced through exertion in comparison to spontaneous changes of fatigue during the course of the day [Claros-Salinas et al., 2013].

In another study, a decline in cognitive function with measures of verbal and visual memory and conceptual planning was demonstrated [Krupp & Elkins, 2000]. Although there was no significant difference in pwMS compared to healthy controls, there was a degree of change in the pattern of cognitive performance with an increase in cognitive fatigue across the duration of the tests [Krupp & Elkins, 2000]. Generally, researchers agree that self-reported fatigue is independent of objective cognitive functioning [Krupp & Elkins, 2000; Paul, Beatty, Schneider, Blanco, & Hames, 1998; Claros-Salinas et al., 2013]. Krupp [2003] found neither the FSS or the self-reported ratings of mental and physical fatigue corresponded with changes in cognitive functioning.

According to Newland et al. [2016], subjective experiences of fatigue are related to psychological factors, whereas cognitive dysfunction and deficits are likely the result of a neurodegenerative process (for example, cognitive impairment is associated with decreased heart rate activity) [Newland, Starkweather, & Sorenson, 2016; Bol, Duits, Hupperts, Verlinden, & Verhey, 2010]. This may explain the lack of relationship between fatigue and cognitive performance in most studies of pwMS. Cognitive features rarely present alone without motor features: Mills & Young [2008] stated as little as 1% of pwMS reported this. However, 10.2% reported motor features without cognitive features of fatigue.

In summary, the vast majority of pwMS present with a variety of cognitive and motor impairments simultaneously, dependent on the individuals' daily activities and tasks. As suggested above, the majority of pwMS experience a degree of motor dysfunction throughout their disease, which can commonly manifest into peripheral and bodily weakness, stability, and spasticity. Cognitive dysfunction has been reported to provoke and affect an individual's alertness, attention and memory, and can significantly affect thought processes and retention, and how they go about their daily activities. Physical and cognitive fatigue can both be investigated through subjective and objective lenses – these have both been briefly highlighted in this section and the significance of both viewpoints has been identified.

1.3. Associations with MS fatigue

Numerous associations have been explored in MS fatigue. The overview of associations discussed in the following section covers the phenotypes of fatigue, the patterns of fatigue regarding daily fluctuations and disease duration, neurological disability severity, and heat sensitivity.

1.3.1. Phenotypes of MS and its relationship to fatigue

Phenotypes are clinical course descriptions of specific classifications of disease types within MS [Lublin et al., 2014]. There are four phenotypes within MS: primary progressive (PPMS), secondary progressive (SPMS), relapsing-remitting (RRMS), and progressive-relapsing (PRMS) [Lublin et al., 2014]. The association of disease type with the severity and impact of fatigue is highlighted in previous research [Braley & Chervin, 2010]. Some degree of fatigue is reported in all phenotypes, however, the association between the type of MS and the level of fatigue varies [Kronecke, 2000]. Overall, findings are consistent in considering disease pattern as one of the parameters related to fatigue [Lerdal, 2003].

Fatigue is most commonly reported to be greater in progressive MS rather than relapsing MS [Kaya Aygunoglu, Celebi, Vardar, & Gursoy, 2015; Pittion-Vouyovitch et al., 2006, Kroencke, 2000; Razazian, Shokrian, Bostani, Moradian, & Tahmasebi, 2014; Ghajarzadeh et al., 2013; Mills & Young, 2010]. Razazian et al. [2014] reported fatigue in 100% of individuals with progressive subtypes, but only 58% in RRMS [Razazian, Shokrian, Bostani, Moradian, & Tahmasebi, 2014].

Patient-reported outcomes for fatigue were reportedly worse in persons with progressive MS, alongside depression, pain, and balance [Zhang, Taylor, Simpson, Blizzard & Van der mei, 2018]. Kroencke [2000] and Ghajarzadeh et al. [2013] reported progressive MS to have virtually no difference in covariate-adjusted means to RRMS after controlling certain variables. The association between the phenotypes and fatigue may differ depending on the method of analysis and the variables controlled in each study. However, a trend of worsening subjective fatigue is more apparent in people with progressive MS.

Only a few studies have explored the fatigue levels between PPMS and SPMS, but findings are inconsistent. Mainero et al. [1999] reported higher levels of fatigue in SPMS, despite both groups having similar disability ratings. In a more recent study, people with SPMS scored significantly higher in the questionnaires such as FSS and QOL [Kaya Aygunoglu, Celebi, Vardar, & Gursoy, 2015]. Additionally, Mills & Young [2010] conducted a large cross-sectional study that confirmed greater levels of fatigue in those with progressive MS compared to those with relapsing MS, yet there was no significant difference between the two. Overall, for the most part, it is agreed that individuals with progressive MS suffer from greater levels of fatigue. However, it remains unclear which types of progressive MS are more strongly associated with fatigue.

1.3.2. Patterns of daily fatigue

Fatigue is a known early symptom in the onset of MS and is reported throughout the disease [Vries, Dorpel, & Mescheriakova, 2017]. The recognised daily and disease patterns of MS fatigue has been discussed, and it is debated whether this follows a sporadic or circadian pattern [Newland, Starkweather, & Sorenson, 2016]. Mostly, fatigue severity has been reported to spike at certain times of day. However, individual experiences are unique and fatigue levels can reportedly occur at any given time during the day [Newland, Starkweather, & Sorenson, 2016].

Streckis et al. [2014] examined fatigue by measuring a two-minute continuous voluntary contraction of the quadriceps muscle at different intervals throughout the day. The authors found significantly higher level fatigue severity in females in the evening, compared to any other time of day [Streckis et al., 2014]. In a similar study, Kim et al. [2010] examined pwMS over three weeks using wrist-worn devices, FSS and MFIS. The Real Digital Fatigue Score captured circadian variations of fatigue scores increasing in the mean: 3.4 at 9am, 4.0 at 1pm, 4.5 at 5pm, and 5.0 at 9pm [Kim et al., 2010]. Even though specific phenotypes of MS were not described (which could alter the findings), the Real Digital Fatigue Score significantly correlated with FSS and MFIS, implying fatigue may potentially be associated with a circadian pattern [Kim et al., 2010].

Newland et al. [2016] suggested that pwMS who are moderately disabled, along with a progressive course type, will experience an increase in persistent fatigue in combination with 10-years since diagnosis. Johansson et al. [2009] conducted a longitudinal study exploring the variation of fatigue over two years. Participants’ FSS scores varied significantly, with 54%

changing FSS category one or several times, 27% were persistently fatigued, and 19% persistently non-fatigued [Johansson et al., 2009].

Powell et al. [2017] tracked the daily fluctuations of individuals with RRMS to assess their perception of fatigue throughout the day. Fatigue was reportedly highest in late afternoon, when fatigue noticeably increased with physical exertion, compared to healthy controls [Powell, Liossi, Schlotz & Moss-Morris, 2017]. Most of the research into the impact of circadian rhythm and fatigue timing indicated that fatigue may worsen over the course of the day [Iriarte, Subirá & Castro, 2000]. Individuals with long-standing MS are more likely to suffer from higher levels of fatigue than those of new diagnosis [Ghajarzadeh et al., 2013]. Currently, the literature indicates that fatigue exists early on and can remain present either intermittently or consistently throughout the disease course [Fisk, Pontefract, Ritvo, Archibald, & Murray, 1994; Pittion-Vouyovitch et al., 2006].

1.3.3. Neurological disability and its association to fatigue

Most research indicates that the greater the disability severity, the higher the level of fatigue experienced by pwMS. Researchers have reported a positive correlation between neurological disability measures from the EDSS and the level of fatigue (measured using self-reported questionnaires) [Kaya Aygunoglu, Celebi, Vardar, & Gursoy, 2015; Mills & Young, 2010, Pittion-Vouyovitch et al., 2006, Ghajarzadeh et al., 2013, Kroencke, Lynch, & Denney, 2000; Gupta, Nagaraj, Prasad, Taly, & Christopher, 2013; Rotstein, O'Connor, Lee, & Murray, 2012].

Lerdal et al. [2007] investigated the patterns of fatigue longitudinally, over the course of two years. Sporadic and persistent patterns of fatigue were explored and found to be equally prevalent. Persistent fatigue was significantly related to reduced capacity of work, whereas both persistent and sporadic fatigue had a negative impact on disability, depression, and heat sensitivity [Lerdal et al., 2007]. Other researchers have corroborated the findings of Lerdal et al. [2007], concluding that pwMS who experience a greater degree of fatigue have significantly higher levels of disability, even after controlling cofounding factors of depression, age, and duration of illness [Colosimo et al., 1995; Kroencke, Lynch, & Denney, 2000].

Fernandez-Monuz et al. [2015] suggested that psychological/cognitive variables play a more complex role in the relationship between the two. Fatigue may contribute to depression by reducing physical function as the result of a lack of energy. Fernandez-Monuz et al. [2015] observed no association between self-reported fatigue and level of disability in a cohort of 108 pwMS. Pittion-Vouyovitch et al. [2006] discovered a relationship between an increase in physical and social aspects of fatigue, and an increase in EDSS score. However, there was a lack of correlation between aspects of cognitive fatigue and disability severity. This may indicate that EDSS assesses physical deficiencies and social disruption, rather than cognitive measures of fatigue, related to disability.

Hohol & Weiner [1995] conducted a large survey based on the registry of the North American Research Committee on MS (NARCOMS) and found a non-linear relationship between disability and fatigue. Self-reported fatigue has previously been associated with a variety of physical and psychological functional impairment, although the direct relationship between specific variables of physical and psychological impairment remains unclear [Motl et al., 2009]. However, NARCOMS and Mills & Young [2010] found a specific level of disability was significant concerning an increase in self-reported fatigue [Hohol & Weiner, 1995]. Once ambulation was affected and ambulation impairment became more prominent (EDSS 5.5), a significant increase in fatigue was experienced in pwMS [Mills & Young, 2010]. Fatigue remained stable after this level of disability, until pwMS felt a further decline in disease, scoring higher in the EDSS [Mills & Young, 2010]. A decline in physical function was associated with self-perceived fatigue, where the greater the fatigue, the poorer the physical quality of life [Turpin, Carroll, Cassidy, & Hader, 2007].

In summary, a degree of association between disability severity and self-reported fatigue in pwMS was found in the literature. The degree of perceived fatigue is somewhat correlated with the function of ambulation. Once ambulation impairment is prominent, elevated levels of fatigue are reported. Different aspects of fatigue, physical, and social components are more likely to be associated with an increase in disability.

1.3.4. Ambient temperature and heat

Environmental factors, such as temperature and heat sensitivity, have been considered to affect fatigue [Rudroff, Kindred, & Ketelhut, 2016]. In other medical conditions and in the general population, individuals report tiredness or fatigue in the afternoon. However, ambient temperature and the physiological effects of heat are distinct and uniquely exacerbate fatigue in pwMS [Krupp, 2003; Kos, Kerckhofs, Nagels, D'hooghe, & Ilsbroukx, 2008]. This is known as Uhthoff's phenomenon, and it is often described as the worsening of neurological symptoms from bodily overheat from weather, exercise, or illness [Gupta, Nagaraj, Prasad, Taly, & Christopher, 2013]. Authors of previous studies have often reported this phenomenon with individual perceptions of heat sensitivity worsening with fatigue [Pittion-Vouyovitch et al., 2006; Krupp, 2003]. Bergamaschi et al. [1997] found that worsening fatigue was magnified by heat in participants who experienced severe fatigue and a higher disability (measured using EDSS). In addition, Forwell et al. [2008] reported that 80% of participants perceived fatigue to be exacerbated by heat. However, the results indicated no difference between those reporting fatigue to be worsened by heat and those stating heat was not a factor. Lerdal et al. [2007] collected data on heat sensitivity using a Likert scale to assess the degree of heat from the weather to the degree of fatigue experienced in 267 individuals. The results indicated that heat sensitivity scores correlated significantly with fatigue of sporadic and persistent nature.

Few studies indicate a relationship between the mechanisms and the physiological state of heat sensitivity. However, Flensner & Lindencrona [1999; 2002] did investigate the use of cooling suits or therapy on pwMS and its influence on heat sensitivity and fatigue. All eight participants described a reduction in muscle strain, cognitive fatigue, and social problems related to fatigue [Flensner & Lindencrona, 2002]. Using the Fatigue Impact Scale (FIS), the authors found a decrease in all physical, cognitive, and psycho-social aspects of daily living whilst pwMS were wearing cooling suits [Flensner & Lindencrona, 2002].

In another study, researchers examined the effects of cooling garments on participants with mild to moderate disability [Schwid et al., 2003]. Participants wore a cooling shirt for an hour a day for one month, alongside either: sham treatments, low dose, or high dose cooling shirts. There were modest improvements in self-reported fatigue, with the greatest reduction in body temperature reported in the group trialling the high dose cooling shirts [Schwid et al., 2003]. In this group, improvements in walking velocity, visual acuity, and the Multiple Sclerosis Functional Composite (MSFC) were observed [Schwid et al., 2003].

Physiologically, core temperature during simulated work activity is elevated in pwMS compared to healthy controls [Lerdal, Gulowsen Celius, Krupp, & Dahl, 2007]. However, research is limited, and the literature related to fatigue and heat sensitivity in pwMS is problematic. Overall, international research indicates adjusted and control of body temperature would decrease the likelihood of subjective fatigue [Lerdal, Gulowsen Celius, Krupp, & Dahl, 2007; [Flensner & Lindencrona, 2002; Schwid et al., 2003].

1.4. Sociodemographic associations

Sociodemographic associations concerning the impact of fatigue on pwMS have been explored. Factors including employment, education, age, and gender are discussed in the subsequent sections.

1.4.1. Employment status and fatigue factors impacting employment

In pwMS, the influence which symptom manifestation has on employment status has been highlighted [Raggi et al., 2016]. Fatigue has an adverse effect on employment outcomes and is commonly reported as affecting pwMS' ability to remain in work [Green, Todd & Pevalin, 2007]. Unemployment rates for pwMS vary between studies and internationally, but it is clear that it is much higher than in the general population [Julian et al., 2008].

Vijayasingham & Mairami [2018] reported that more pwMS with fatigue focus on managing emotions that accompany work, rather than managing the work or task itself. PwMS with mild disability and a lower EDSS score are much more likely to work and be employed, whereas unemployed pwMS experience greater and more persistent levels of fatigue [Sweetland, Howse, & Playford, 2012; Mills & Young, 2010; Lerdal, 2003]. Although some pwMS with milder symptoms and disability decide to change their work habits and hours early on in their diagnosis, their occupation can still be affected by events or factors that trigger their fatigue [Vijayasingham, Jogulu, & Allotey, 2017].

The incidence of exacerbated fatigue has been reported in hot working environments and open-plan offices that can disrupt temperature and noise levels. These interferences cause a decrease in sustained concentration, cognitive impairment, slurred speech, and reduced dexterity that considerably impacts work functionality and productivity [Vijayasingham, Jogulu, & Allotey, 2017]. Occupations with inflexible work environments which are highly stressful, physically demanding, or involve long shift pattern work are much more likely to cause pwMS to become unemployed [Vijayasingham & Mairami, 2018]. Consequently, some individuals consider reducing their exposure to such environments through a partial or a complete reduction in work hour, thereby gaining a work-life-illness balance [Vijayasingham, Jogulu, & Allotey, 2017].

There is a significant association between MS, loss of employment, and a lower quality of life [Weiland et al., 2015]. Coping strategies for pwMS in the workplace have been described in the literature, including goal-setting and positive cognitive reframing to help address some negative impacts [Blaney & Lowe-Strong, 2009; van der Hiele et al., 2016]. However, even with these strategies, the concern of access and infrastructure cannot always be addressed, which can limit employment for pwMS [Vijayasingham & Mairami, 2018].

In summary, pwMS have a significantly higher rate of unemployment than the general population [Julian et al., 2008]. The small percentage of pwMS who remain in employment generally report lower levels of fatigue and incorporate coping mechanisms to sustain work ethic and ability in the workplace [Blaney & Lowe-Strong, 2009].

1.4.2. Level of education and the significance of fatigue

Educational level may potentially affect fatigue and an individual's perception of fatigue [Kroencke, Lynch, & Denney, 2000; Lerdal, 2003; Razazian, Shokrian, Bostani, Moradian, & Tahmasebi, 2014]. Although it is difficult to consider the direct relationship between the two, a few researchers have proposed an association between education level and the significance of fatigue through self-reported questionnaires.

Studies have been primarily focused on coping mechanisms and management concerning the effect and level of fatigue experienced [Weiland et al., 2015; Lerdal, 2003]. On average, pwMS who scored lower on self-reported fatigue questionnaires, such as the FSS, were more likely to have a higher level of education [Kaya Aygunoglu, Celebi, Vardar, & Gursoy, 2015]. Supporting this, Lerdal [2003] found a significant inverse association between fatigue and education when controlling for age, gender, and time since MS diagnosis. The findings from other studies corroborate this, and indicate an increase in self-reported fatigue is congruent with a lower educational status [Tedeschi et al., 2007; Weiland et al., 2015]. Although, interestingly, when controlling for phenotypes of MS, PPMS did not significantly negatively correlate with education level [Lerdal, 2003]. Lerdal [2003] suggested that individuals with a higher level of education may potentially be more familiar with coping mechanisms or have the flexibility to adapt psychologically. This may allow them to reflect on their experiences of fatigue and ultimately manage their fatigue more effectively. Weiland et al. [2015] hypothesised that individuals with a higher level of education were more likely to be pro-active and engage in self-care and lifestyle management.

Despite this, some authors have reported no significant association between the degree of fatigue and education status. There are conflicting views on the variables related to fatigue and whether this has a direct impact on the association between education and fatigue [Mills & Young, 2010; Razazian et al., 2014].

1.4.3. Association with age and gender to perceived fatigue

Public Health England (PHE) released new data from general practitioner records in 2018 which indicated an increase in both incidence and prevalence rates of MS in England [PHE, 2020]. MS was most prevalent in the age category 60-69 years old however, generally fatigue and age are topics less well established in the literature [PHE, 2020; Sanai et al., 2016]. Some researchers have found fatigue to be a common and persistent symptom in older pwMS, observing a positive correlation between fatigue and age [Wood et al., 2013; Weiland et al., 2015; Lerdal, 2003]. Nevertheless, Lerdal [2003] hypothesised that individuals with a diagnosis of PPMS may have affected the overall results. This is because individuals with PPMS are often diagnosed at an older age, compared to those diagnosed with RRMS [Lerdal, 2003]. As such, individuals may be susceptible to fatigue as they age, irrespective of illness type. However, it has been suggested that fatigue may possibly be experiences throughout the disease, irrespective of age [Morrison & Stuifbergen, 2016; Flachenecker et al., 2004; Ghajarzadeh et al., 2013].

According to the Health Improvement Network (THIN), 72% of pwMS in the UK are female [PHE, 2000]. Existing literature on the relationship between gender and fatigue is mixed [Mills & Young, 2010; Kaya Aygunoglu, Celebi, Vardar, & Gursoy, 2015; Razazian et al., 2014; Fjeldstad, Brittain, Fjeldstad & Pardo, 2010; Fazili & Shayesteh-Azar, 2012]. In a few studies, authors describe females with MS as experiencing greater levels of self-reported fatigue. Fatigue can cause some females to not participate in the surrounding world and acts as a barrier in relation to their physical, cognitive, and social activities [Weiland et al., 2015; Tedeschi et al., 2007; Olsson et al., 2005]. Nonetheless, other researchers have reported higher ratings of the impact of fatigue in daily life in males in comparison to females, noting a significant correlation between men and increased levels of self-reported fatigue [Razazian et al., 2014; Fazili & Shayesteh-Azar, 2012; Fjeldstad, Brittain, Fjeldstad & Pardo, 2010]. Lerdal [2003] found the gender differences for self-reported fatigue in the general population were not observed in the MS population.

Considering the current literature, mixed findings indicate that all ages and both genders experience a degree of fatigue. It is unclear which gender suffers from greater levels of fatigue and whether fatigue is significantly associated with a specific age group.

1.5. The current measurement of fatigue

Fatigue is not typically described as a simple continuum from “no fatigue” to “severe fatigue”. The evaluation of fatigue remains a difficult task, that has been identified and assessed in multiple ways. Although it is complicated due to the multidimensional nature of fatigue, there are a wide variety of fatigue measures with “subjective” measures of self-reported questionnaires and interviews, and “objective” measures, to assess physical fatigue over a given time period [Chipchase, Lincoln, & Radford, 2003]. In the following section, both subjective and objective measures and the types of measures used are briefly discussed.

1.5.1. Self-reported measures of fatigue

Self-reported measures are specifically designed to incorporate an individual’s viewpoint, and are suggested as more practical for use in clinical settings [MacAllister & Krupp, 2005]. Self-reported measures are frequently used and they are believed to be the most suitable measures for fatigue, as they provide insight into the individual’s perception and experience of the symptom [Schwartz, Jandorf & Krupp, 1993].

To appropriately monitor fatigue, scales are used to assess a current or previous experience of fatigue. A single-item scale can be used to gather an opinion about an experience or feeling on a single dimension. It can be an uncomplicated and intuitive measure, but it is often viewed as generating impulsive responses from participants, which can compromise reliability [Multiple Sclerosis International Federation, 2012].

Multi-item scales are used to assess broader experiences of fatigue, including different domains of fatigue. These are reported to be more reliable measures [Mills et al., 2010]. There are a variety of self-reported measures used for fatigue within MS. Kos et al. [2004] identified eight self-reported measurements they believed to be most appropriate for the MS population, based on clinical and scientific criteria (see Table 1.1). Five fatigue-specific scales and four subscales of quality of life instruments were selected and evaluated [Kos et al., 2004].

Within the MS literature, the Fatigue Impact Scale (FIS) and the MFIS are the most widely recognised scales used to measure fatigue [Kos et al., 2004]. Both the FIS and MFIS use Likert scales ranging from 0, indicating “no problem”, to 4, indicating “extreme problem” [Larson, 2013]. The MFIS evolved from the FIS through the elimination and refinement of items that appeared both content-redundant and/or had a high inter-item correlation [Ritvo et al., 1997].

Table 1.1.: Self-reported scales of fatigue in Multiple Sclerosis (arrow up = the higher the level of self-reported fatigue).

Scale	***Number of items***	***Score range***	***Maximum total score***	***Scoring direction***	***Dimensions***
Fatigue Severity Scale [Krupp, LaRocca, Muir-Nash, &Steinberg, 1989].	*9*	*1-7 (Likert)*	*63*	↑	*Modality, severity, frequency, impact on daily life.*
Fatigue Impact Scale [Fisk, Pontefract et al., 1994].	*40*	*0-4 (Likert)*	*160*	↑	*Cognitive, psychosocial, physical impact.*
Modified Fatigue Impact Scale [Multiple Sclerosis Council for Clinical Practice Guidelines, 1998].	*21*	*0-4 (Likert)*	*84*	↑	*Cognitive, psychosocial, physical impact.*
Fatigue Descriptive Scale [Iriarte et al., 1999].	*5*	*0-3*	*17*	↑	*Modality, spontaneity, severity, frequency and Uhthoff phenomenon.*
Fatigue Assessment Instrument = Multiple Sclerosis Specific-Fatigue Scale [Schwartz, Jandorf, & Krupp, 1993].	*29*	*1-7 (Likert)*	*203*	↑	*Fatigue severity, situation, consequences, responsiveness to rest/sleep.*
Short Form-36, vitality scale [Ware & Sherbourne, 1992].	*4*	*1-6 (Likert)*	*24*	↓	*Frequency of vitality.*
Guy's Neurological Disability Scale, fatigue subscale [Sharrack & Hughes, 1999].	*5*	*0-1*	*5*	↑	*Frequency, impact on daily activities.*
Illness Intrusiveness Ratings Scale [Devins et al., 1993].	*13*	*1-7 (Likert)*	*91*	↑	*Interference of illness with 13 domains of life.*
Functional Assessment of Multiple Sclerosis, subscale thinking/fatigue [Cella et al., 1996].	*9 (5 fatigue items)*	*0-4 (Likert)*	*36 (fatigue items only: 20)*	↑	*Modality, consequences.*

MFIS contains nine physical, 10 cognitive, and two psychosocial items. Higher scores indicate greater self-reported impact on the quality of life from fatigue [Larson, 2013]. The MFIS is recommended for use as a comprehensive (total score) and multidimensional (separate subscales) assessment for the impact of fatigue in MS [Larson, 2013]. As both scales are used to assess the impact of fatigue, the MFIS has moderate to strong correlations with the FSS

[Flachenecker et al., 2002; Kos et al., 2004; Telléz et al., 2013]. However, the MFIS primarily only assesses the impact of fatigue, whilst the FSS measures the severity and frequency of fatigue.

Kos et al. [2004] conducted a study to evaluate self-reported fatigue measures used specifically in the MS population. They explored the clinical usefulness, availability, ease of administration, scientific properties, level of measurement, reliability, validity, and applicability to patients, with variation in the symptom, and responsiveness. Nine scales were assessed to explore their usefulness in an occupational therapy setting. Due to the occupational therapy context of the evaluation, the predominant area of interest was the impact of fatigue on daily living [Kos et al., 2004]. Hence, scales such as the FIS and MFIS were highlighted as useful tools. However, the FIS could provoke fatigue (40-items), therefore the MFIS was suggested as a good alternative [Kos et al., 2004].

Kos et al. [2004] reported that the scales varied in usefulness, depending on the information desired. Where the nature of fatigue is of interest, scales such as FSS, FDS, and FAI can be useful. FSS has reportedly good scientific properties and, like the FAI, is self-administered. Although the FDS requires an interview, which is more time-consuming, it is highly correlated with the FSS [Kos et al., 2004]. The four sub-scales of questionnaires – SF-36, GNDS, IIRS, and FAMS – are all reliable and valid scales. However, Kos et al. [2004] reported that they provide limited information concerning fatigue and only the GNDS has demonstrated responsiveness. Nevertheless, these sub-scales could be valuable for screening fatigue in pwMS and should not be completely discarded. Overall, the authors concluded that the majority of fatigue-specific scales are reliable and valid instruments. However, some scales fail to demonstrate stability and responsiveness [Kos et al., 2004].

The MFIS was proposed by the US National Multiple Sclerosis Society (NMSS) as a good tool for assessing the impact of fatigue across multiple dimensions, including physical, cognitive, and psychosocial aspects of fatigue [NMSS, 1998]. However, until Flachenecker et al. [2002] and Telléz et al. [2005], the MFIS had never been used in large trials and assessed for clinical relevance for fatigue in MS. Telléz et al. [2005] investigated whether the MFIS offered a more comprehensive assessment of fatigue in pwMS. The authors found that fatigue needs to be addressed in a more comprehensive manner and the MFIS could offer a more detailed understanding of its psychosocial and cognitive aspects of fatigue, with the physical subscale demonstrating the strongest correlation with the FSS [Téllez et al., 2005].

Iriarte et al. [1999] developed the FDS to evaluate the severity and quality of fatigue, including symptom characteristics. In the development of this scale, Iriarte et al. [1999] performed a study to explore its usefulness in evaluating fatigue in MS. It proved useful in characterising the existence and quality of fatigue and informed researchers on the repercussions of fatigue on daily living [Iriarte et al., 1999]. The scale highlighted patterns of fatigue, with a large percentage of pwMS experiencing fatigue on a daily basis or every other day. Nonetheless, only preliminary work has been done, and further work to explore the psychometric properties is required [Iriarte et al., 1999; Whitehead, 2009].

Another fatigue-specific scale is the FAI. It is a 29-item scale that was designed to evaluate severity, pervasiveness, associated consequences, and response to sleep [Schwartz, Jandorf, & Krupp, 1993]. Schwartz et al. [1993] developed the instrument in attempt to yield a global fatigue severity scale and differentiate normal fatigue from other fatigue-related medical disorders. They conducted a study on pwMS and other fatigue-related conditions (including Lyme disease, chronic fatigue syndrome, systematic lupus erythematosus, and dysthymia) to assess the reproducibility and convergent validity of other measures of sleep [Schwartz, Jandorf, & Krupp, 1993]. Although the instrument clearly distinguished fatigue in the normal population from fatigue in chronic illnesses, the test-retest correlations for the FAI subscales were only moderate and failed to significantly correlate with other measures of fatigue and sleep components [Schwartz, Jandorf, & Krupp, 1993].

Self-reported questionnaires are easily administered measures that can be reliable and valid in a clinical or research setting [Multiple Sclerosis International Federation, 2012]. Nevertheless, due to the lack of validated objective measures of fatigue, the validation of self-reported measures is performed by comparison of other self-reported measures [Kroencke, Lynch, & Denney, 2000]. Scales are also limited when taken at one point in time, as this could affect an individual’s memory of an experience or event when they felt fatigued [Telléz et al., 2005]. Fatigue can impair and alter an individual’s introspection and thought process on what they experience [Kroencke, Lynch, & Denney, 2000]. This could potentially skew an individual’s reflection on their experiences of fatigue.

There are numerous scales that focus on fatigue from a uni- or multidimensional perspective. The variety of scales demonstrate the complexity and vast symptomatology fatigue exhibits. The assessment of fatigue remains difficult due to its subjectivity and its multidimensionality. Although there are more than 250 measures to assess all aspects of fatigue, MFIS and FIS remain the most widely recognised. They also appear to be the most responsive to change in fatigue due to disease progression [Multiple Sclerosis International Federation, 2012].

Although experiences of fatigue are reported in Chapter Three, interview-based studies are established within the literature which highlight the facets of fatigue as experienced by pwMS. Thematic analyses and phenomenological studies have been conducted to explore individuals' perspectives and the different components of the everydayness of fatigue with MS [Blaney & Lowe-Strong, 2009; Flensner et al., 2003; Holberg & Finlayson, 2007; Lohne et al., 2010; Mezini & Soundy, 2019; Moriya & Kutsumi, 2010; Newton et al., 2016; Olsson et al., 2005; C. Smith et al., 2011; C. M. Smith et al., 2015; Stuifbergen & Rogers, 1997; Turpin et al., 2018; Yorkston et al., 2003]. Different approaches and methodologies have been used to comprehend an individual's experience, including phenomenological methods of hermeneutic and empirical phenomenological psychological, inductive and existential analyses, and more general in-depth qualitative exploratory designs [Blaney & Lowe-Strong, 2009; Flensner et al., 2003; Lohne et al., 2010; Mezini & Soundy, 2019; Newton et al., 2016; Olsson et al., 2005; C. Smith et al., 2011; C. M. Smith et al., 2015; Turpin et al., 2018; Yorkston et al., 2003].

Fatigue has been described as unpredictable, and an overwhelming feeling that affects cognitive, motor, and social functions. The unpredictable nature of fatigue can restrict mental and physical tasks, and worry around uncertainty can heighten the level of anxiety in pwMS. Overall, fatigue is described as having a negative impact on pwMS' lives, as it creates social distance and feelings of isolation, without appropriate and efficient understanding and management. Moreover, fatigue has been described in a multitude of manners through interviews and self-reported questionnaires. Researchers have also used objective measures in an attempt to quantify fatigue, but this remains difficult and is less well established in the literature.

1.5.2. Objective measures of fatigue

Objective measures of MS fatigue are designed to assess performance fatigability to support the investigation of performance change over time due to physical fatigue. Objective measures cover a variety of different domains, but the most common of these are motor and cognitive fatigue [Severijns et al., 2017]. Although there are many performance fatigability tests, in the following section, only the most common tests for each domain will be discussed. The effectiveness of measuring fatigue in pwMS will also be explored, for the purposes of setting the background context to the present study.

Cognitive fatigue[3] can be measured through performance decrements in cognitive demanding tasks over time [Linnhoff, Fiene, Heinze, & Zaehle, 2019]. The objective of cognitive assessment is to assess the behavioural consequences that ultimately cause failure in the maintenance of optimal performance over an acute but sustained time period [Holtzer, Shuman, Mahoney, Lipton, & Verghese, 2011]. Cognitive fatigue can be assessed through changes in reaction time, accuracy, and proceeding speed in vigilance tests over time. The most commonly used tests include the Test Battery for Attentional Performance (TAP), the Paced Auditory Serial Addition Test (PASAT), and the Signal Digit Modalities Test (SDMT) [Linnhoff, Fiene, Heinze, & Zaehle, 2019].

In the majority of studies, researchers have demonstrated an increased reaction time and decreased accuracy with timed tasks such as administering the TAP test when exploring alertness levels [Fiene et al., 2018; Claros-Salinas et al., 2010; Krupp, & Elkins, 2000; Neumann et al., 2014; Kujala, Portin, Revonsuo, & Ruutiainen, 1995; Heesen et al., 2010; Bailey, Channon, & Beaumont, 2007; Chinnadurai, Venkatesan, Shankar, Samivel, & Ranganathan, 2016]. Claros-Salinas et al. [2010] used the TAP test to explore the diurnal variations of cognitive performance in pwMS at three different times of the day on two consecutive days. Findings from self-reported measures indicated an increase in cognitive fatigue throughout the day, which corresponded with a objective cognitive measure of decline in pwMS, compared to healthy controls. Neumann et al. [2014] conducted a similar study, investigating the cognitive alertness of pwMS compared to healthy participants. As expected, the reaction times after cognitive load only increased in pwMS, whilst the reaction time in healthy participants remained unchanged.

Cognitive speed and working memory, which can also be a sign of cognitive decline and fatigue, are commonly assessed using the PASAT or the SDMT [Linnhoff, Fiene, Heinze, & Zaehle, 2019]. The PASAT has demonstrated sensitivity and validity for measuring cognitive fatigue. It has been used in studies to explore sustained attention over a given time period by comparing metrics between early and late performance [Berard, Smith & Walker, 2018; Walker et al., 2012; Morrow, Rosehart, & Johnson, 2015]. Schwid et al. [2003] conducted a pilot study to objectively measure cognitive fatigue as a decline in performance during tests requiring sustained attention. The authors reported a 5.3-5.8% decline in PASAT performance;

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[3] Cognitive fatigue can be defined as an executive failure to maintain and optimize performance over acute but sustained mental effort resulting in performance that is lower and more variable than the individual's optimal ability [Holtzer, Shuman, Mahoney, Lipton & Verghese, 2011].

pwMS scored a mean of 18.7/20 of correct items in the first phase of the test and 17.8/20 correct items on the last phase [Schwid et al., 2003]. Although all pwMS demonstrated a decline in cognition, no significant difference was found compared to healthy controls [Schwid et al., 2003]. Likewise, Berard et al. [2018] conducted a study using the PASAT to examine cognitive fatigue after a three-year interval in individuals with RRMS. There was no significant difference between the MS and healthy control group, although there was a recognised trend of a decreased performance in the MS group compared to the healthy controls at all times [Berard, Smith & Walker, 2018].

Following Schwid et al. [2003], Kos et al. [2004] conducted a pilot study in which they described a significant, 21.1% performance decline in pwMS, compared to a 9.6% decline in healthy controls. Although a pilot study, these results indicate that the PASAT can detect change in cognition by fatigue in both pwMS and healthy control groups [Kos et al., 2004]. Despite this, the sensitivity of the test has been queried as there are two approaches to the scoring method, which ultimately affects the overall scoring and test. Typically, PASAT scoring is assessed by counting all the correct responses together. However, the “chunking method” can be used whereby the first two numbers are added then the next number is skipped [Fisk, & Archibald, 2001; Snyder, Aniskiewicz & Synder, 1993]. This reportedly reduces the overall difficulty of the task, by decreasing the need to perform a simultaneous cognitive process [Berard, Smith & Walker, 2018].

Kluger et al. [2013] describe motor fatigue using the following definition: “motor fatigability is the magnitude or rate of change of motor performance on an objectively measured reference criterion after any type of voluntary activity or exercise”. Motor fatigability can occur in all populations and has been measured in multiple ways. Severjins et al. [2017] conducted a systematic review to detect the most optimal assessment to quantify motor fatigue in pwMS and to summarise the available information on psychometric properties. For the healthy population, it is known that motor fatigability is task-specific: protocols most likely to challenge the CNS with high-intensity exercise to the peripheral neuromuscular system can cause motor fatigability [Vøllestad, 1997; Taylor & Gandevia, 1985]. For pwMS, there is no gold standard available to determine motor fatigability, as it is not known if pwMS experience motor fatigability during the same tasks, or whether they can be compared to the healthy population due to the unknown pathophysiological mechanisms [Severijns et al., 2017]. Thus, researchers have attempted to identify motor fatigability in pwMS to establish a protocol that can appropriately monitor the changes of motor fatigue.

Through their systematic review, Severijns et al. [2017] found that 30 out of 38 studies incorporated repeated isometric contractions in the lower or upper extremities to assess the rate of declined strength in pwMS. In most of the studies, researchers opted to assess maximal voluntary contractions (MVC) that included the greatest amount of tension a muscle can generate and hold at that specific time. However, in some of the other studies, researchers used submaximal isometric tasks of 10-50% of MVC or nonisometric protocols, where isokinetic protocols were used by assessing muscle contractions at different joint angles [Liepert, Mingers, Heesen, Baumer & Weiller, 2006; Wolkorte, Heersema & Zijdewind, 2015; Perretti, Balbi & Orefice, 2004]. Muscle contractions are commonly assessed using dynamometry either hand-held or biodex isokinetic to measure strength, endurance, and power of specific muscle or muscle groups. Isometric contractions have the advantage that they can be highly standardised and easily interpreted [Severjiins et al., 2017]. However, results can sometimes be difficult to compare due to the different protocols and methods of application across different studies [Severijns et al., 2017]. There is a mixture of studies in relation to accuracy and the body location that is best to assess the rate of declined strength and rate of change [Severijns et al., 2017]. The assessment of lower extremity strength has been explored due to ambulation and the considerable effect on daily activities that use locomotion [McLoughlin, Barr, Crotty, Sturnieks & Lord, 2014]. However, upper extremity strength has been frequently explored due to neurophysiological investigations for the mechanisms of fatigability [Severijns et al., 2017].

Although more thoroughly discussed in Chapter Three, fatigability has also been investigated regarding ambulation [Schwid et al., 1999; Surraka et al., 2004; Burschka et al., 2012]. Walking impairments are highly prevalent in pwMS, with up to 75% of individuals reported to have difficulties and a degree of ambulatory dysfunction throughout the disease [Hobart et al., 2001]. Walking is an essential part of independence and is the most highly prioritised bodily function that can impact a person's daily activities, functional status, quality of life and employment [Paltamaa, Sarasoja, Leskinen, Wikström & Mälkiä, 2007; La Rocca, 2011]. Observing walking velocity and gait dynamics can be useful in evaluating treatment interventions and assist in rehabilitation programmes. However, the interpretation of changes in gait kinetics and kinematics can be difficult as an increase in motor fatigability may be identified, and other underlying impairments like spasticity[4] and ataxia[5] can be detected [Severijns et al., 2017].

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[4] Spasticity is a condition in which muscles stiffen or tighten, preventing normal fluid movement.

[5] Ataxia is a term for a group of disorders that affect co-ordination, balance and speech including walking.

Researchers have explored different tests in an attempt to measure ambulatory fatigue, the most frequently used of which is the six-minute walk (6MW) [Goldman et al., 2008]. Mcloughin et al. [2014] assessed strength and balance in pwMS before and after walking the 6MW, and found greater loss of strength and balance in pwMS after the 6MW compared to the healthy controls. In a systematic review by Severijns et al. [2017], walking for a fixed time or distance on a treadmill or free overground walking was observed in 10 studies. The studies varied in duration and instruction of walking (at a comfortable or fast walking pace). The indices of walking were examined based on walking velocity, distance, and/or specific gait kinematics [Engelhard, Dandu, Patek, Lach, & Goldman, 2016; Sehle et al., 2011].

Sehle et al. [2011] investigated kinematic gait analysis and attempted to objectively quantify and assess ambulatory motor fatigue by observing pwMS treadmill walking for six minutes. The authors found that fatigue in pwMS manifests as changes in gait pattern. Some pwMS were more affected by the gait parameters including step length, width and height, followed by hip circumduction and knee flexion angle. Others demonstrated more variability in their gait movement [Sehle et al., 2011]. The authors suggested that fatigue had a tendency to amplify changes in gait patterns that were already present, and the extent of gait changes was associated with the severity of symptoms. Gait patterns typically become more variable with fatigue which could generate problems with perception, instability and increased risk of falling, therefore affecting their overall daily functioning [Sehle et al., 2011].

Overall, there is some evidence of motor fatigability in pwMS in comparison to healthy controls. However, the type of exertion task performed, as well as the type of MS and the level of disability, can significantly impact motor fatigability results [Severjins et al., 2017]. Most motor fatigability assessments are based on isometric maximal contractions and functional activity performance changes over time [Multiple Sclerosis Council for Clinical Practice Guidelines, 1998; Kluger, Krupp, & Enoka, 2013]. There is limited information about psychometric protocols for motor fatigability in pwMS as there is still no clear consensus on the method of assessment to best detect motor fatigability in pwMS. Detecting motor and gait changes in pwMS will enable subtle detection of the rate of change in temporal, kinetic, and kinematic parameters. Ambulatory fatigue may increase the risk of tripping or falling during locomotion, as physiological and biomechanical factors, along with environmental demands, may exacerbate and further accentuate walking impairment and disability in pwMS.

It would be useful to comprehensively understand how ambulation-induced fatigue influences overall gait patterns and behaviours as this would further assist the development of appropriate management and treatment interventions. It would also improve individual functioning in terms of gait and motor functionality for pwMS. This is of significance for this study, as understanding the effects of fatigue on different characteristics of gait and function will provide a clearer understanding of pwMS' actual fatigue. Fatigue is regarded as one of the most prominent symptoms experienced by pwMS, and its negative impact on quality of life has been repeatedly documented [Forbes et al., 2006; Pittion-Vouyovitch et al., 2006]. Therefore, a thorough assessment of subjective and objective measures is needed as part of fatigue management.

1.5.3. Phases of a gait cycle

To comprehend an individual's walk and the dynamics of gait, understanding the gait cycle is essential. Walking is a natural mode of locomotion for a human to travel from one place to another. It requires placing each foot in turn to allow repeated movement, otherwise known as the gait cycle [Dormans, 2015]. The gait cycle starts and finishes when the same foot strikes the ground. It is composed of a stance (60%) and a swing (40%) phase, which are further subdivided into eight gait terms (see Figure 1.1.).

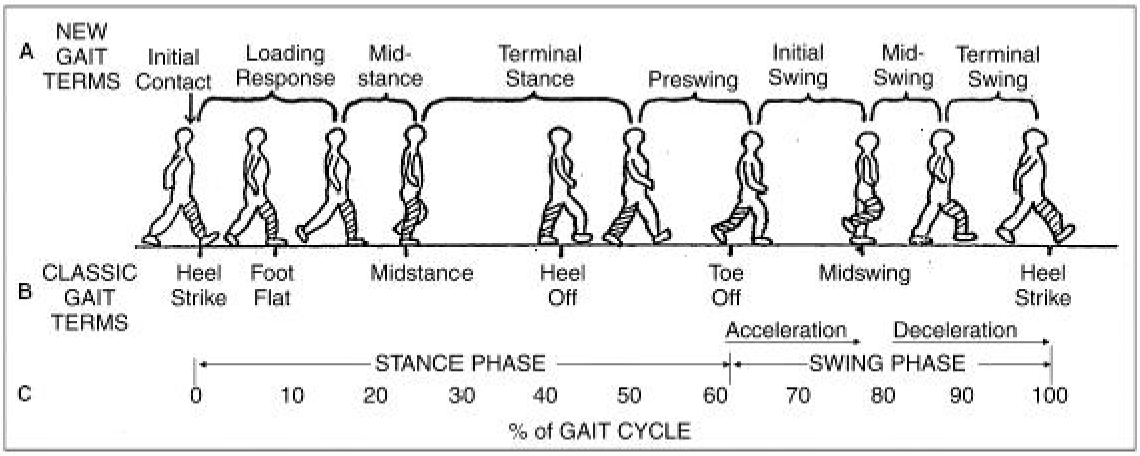

Figure 1.1. Gait cycle terms.

The gait terms consist of five functional stance subphases and three functional swing subphases. The stance subphases are: initial contact, loading response, midstance, terminal stance, pre-swing. The swing subphases are: initial swing, mid-swing, and terminal swing [Burnfield, 2010]. The stance phase starts at heel strike, with both feet on the ground (more commonly known as double support) which consumes on average 10% of a gait cycle. However, this reduces in percentage as gait velocity increases and disappears completely with running [Delisa, 1998; Umberger, 2010]. Commonly, the slower an individual's gait speed, the greater the percentage of time in double support [Delisa, 1998]. The remaining time consists of one limb on the ground (known as single support), where one limb swings forward to begin the next step [Umberger, 2010].

The swing phase occurs as the acceleration of one foot is lifted and the hip, knee, and foot are flexed to mid-swing, before deacceleration occurs as the foot prepares to strike the ground [Delisa, 1998]. One gait cycle takes approximately 0.9-1 seconds in a healthy adult. However, this can vary and lengthen with certain neurological conditions such as MS and Parkinson's [McGrath, Howard & Baker, 2015].

The phases are described by Kharb et al. [2011]:

1- "Initial contact (heel strike): the hip is flexed, the knee is extended, the ankle is dorsiflexed[6] to neutral and the heel is in contact with the floor.
2- Loading Response (foot flat): the body weight is transferred onto the forward leg. Using the heel as a rocker, the knee is flexed for shock absorption. Ankle plantar flexion[7] limits the heel rocker by forefoot contact with the floor. This is the initial double stance period.
3- Mid stance (heel off): the first half of single limb support, the limb advances over the stationary foot by ankle dorsiflexion (ankle rocker) while the knee and hip extend. This is the first half of the single limb support interval.
4- Terminal stance: the heel rises and the limb advances over the forefoot rocker. The knee increases its extension and then just begins to f1ex slightly. Increased hip extension puts the limb in a more trailing position. Throughout this phase body weight moves ahead of the forefoot.
5- Pre-swing (toe off): This phase is also known as weight release and weight transfer phase. While the abrupt transfer of body weight promptly unloads the limb, this extremity makes no active contribution to the event.
6- Initial swing: The foot is lifted, and limb advanced by hip flexion and increased knee flexion. The ankle only partially dorsiflexes. It begins with lift of the foot from the floor and ends when the swinging foot is opposite the stance foot.
7- Mid-swing: Advancement of the limb anterior to the body weight line is gained by further hip flexion. The knee is allowed to extend in response to gravity while the ankle continues dorsiflexing to neutral. This second phase of the swing period

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[6] Dorsiflexion is the movement of raising the foot upwards towards the shin (flexion of the foot).
[7] Plantarflexion is the movement of pointing the foot downwards, away from the shin (extension of the foot).

begins as the swinging limb is opposite the stance limb. The phase ends when the swinging limb is forward, and the tibia is vertical.

8- Terminal swing (heel strike): Limb advancement is completed by knee flexion. The hip maintains its earlier flexion, the ankle remains dorsiflexed to neutral. This final phase of swing begins with a vertical tibia and ends when the foot strikes the floor."

[Kharb, Saini, Jain & Dhiman, 2011].

An abnormal gait has been previously reported in pwMS. However, walking abnormalities are poorly characterised, due to widely disseminated lesions throughout the brain and spinal cord [Filli et al., 2018]. Unlike in other neurological diseases, there is no textbook or typical gait pattern in MS that has been clearly identified for diagnoses. However, a few characteristics have been recognised, and MS gait impairment can result from imbalance, fatigue, muscle weakness, spasticity, reduced coordination, and other associated symptoms [Roeing, Wajda, Motl & Sosnoff, 2015]. In a normal gait, the gait cycle should be regular with successive cycles of a similar length. Nevertheless, as pwMS tire and slow down after walking continuously (dependent on their disability level), their gait parameters are impacted and there is gait variability [Qureshi, Brandt-Pearce, & Goldman, 2016]. Deterioration of gait, such as step length, cadence, and reduced lower extremity joint ROM, has been identified in the fatigue literature [Motta et al., 2016; Moon et al., 2017; Engelhard, Dandu, Patek, Lach & Goldman, 2016]. For this reason, assessment of specific gait characteristics in pwMS is imperative in this study, as this will confirm the effects of fatigue on ambulation and gait and support the identification of an objective biomarker for fatigability. Gait characteristics of fatigue as identified by wearable sensors are further discussed in Chapter Three.

1.6. Introduction to inertial sensors

Until recent decades, rigorous measurements of gait kinematics and function required the use of laboratory-based equipment involving motion capture [Colyer, Evans, Cosker, & Salo, 2018]. The use of motion capture systems in detecting accurate spatiotemporal gait parameters and joint kinematics in a variety of populations, including sporting activities, rehabilitation interventions, and chronic health conditions, is well established. However, the cost, time consumption, and accessibility of motion capture can be a great limitation to many researchers [Tao, Liu, Zheng & Feng, 2012].

An alternative method to measure gait kinematics is the use of wearable sensors to detect changes in movement. Wearable sensors have been used in sports, rehabilitation, and health diagnostics research. They have become a powerful tool to perform gait analysis, in particular, the assessment of gait characteristics in neurological conditions such as MS [Motta et al., 2016; Tao, Liu, Zheng & Feng, 2012]. There are numerous types of motion sensors, including accelerometers, gyroscopes, magneto-resistive sensors, goniometers, electromagnetic tracking systems, force sensors, and sensors for electromyography (EMG) [Tao, Liu, Zheng & Feng, 2012]. However, in this thesis, only accelerometry[8], gyroscopy[9] , and magnetometry[10] will be used and described.

Recently, wearable sensors have been incorporated within neurological gait research to explore gait dynamics in Parkinson's, MS, Alzheimer disease, and cerebral palsy [Vienne-Jumeau, Quijoux, Vidal & Ricard, 2019; Brognara, Palumbo, Grimm & Palmerini, 2019; Vienne, Barrois, Buffat, Ricard & Vidal, 2017]. The next generation inertial measurement units (NGIMU) are compact inertial measurement units (IMU), a subclass of wireless sensors that include a triple-axis gyroscope, accelerometer, and magnetometer. NGIMUs have been used to assess and quantify ambulation in multiple studies [Tong, 2018]. IMUs have been used to investigate conditions such as MS to obtain meaningful data on an individual's physical function. This has been valuable in assessing an individual's ability to conduct daily activities [Sehle et al., 2011].

An accelerometer measures acceleration to determine the body's position and monitor the body's movement in relation to gravity [Vahdatpour, Amini, Xu & Majid Sarrafzadeh, 2011]. Acceleration in triple-axis inertial sensors in the X, Y, and Z direction is measured in metres per second squared (m/s^2). Accelerometers are the most widely used universal sensor to monitor physical movement and ambulation because they are low powered, durable, inexpensive, and readily available [Kavanagh & Menz, 2008].

A gyroscope measures the rate of change in orientation over time with reference to an inertial frame of reference (the angular velocity) [Guo & Hong, 2019; Reze & Osajda, 2013]. It measures degrees per second (°/s) and has onboard temperature sensors and accurate calibration to correct thermo-mechanical noise and bias drift [Lowe & Olaighin, 2014].

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[8] Accelerometers are an instrument for measuring the acceleration of a moving or vibrating body.

[9] Gyroscopes are an instrument that measures the rate of velocity at which an object rotates around a specific point or axis in a given time period.

[10] Magnetometers are an instrument used for measuring magnetic forces.

Lastly, magnetometers are magnetic field sensors that detect nearby magnetic forces as well as the Earth's magnetic field. Magnetometers measure the magnetic force in unit tesla (uT) and can be used to isolate gravity if the readings are stable enough. Magnetometry in wearable sensors can be used to detect the strength and change in the magnetic field, namely a change of direction (especially when the wearer makes a 180-degree turn). The use of inertial sensors has been highlighted in recent MS research, with growing literature on sensor-derived measurements of ambulatory function by clinically established tasks, including studies detecting gait deterioration [Goldman, Motl & Rudick, 2010; Engelhard, Dandu, Patek, Lach & Goldman, 2010].

1.6.1. The use of inertial sensors in this research

The use of a singular measure, such as a stopwatch, can be used to identify global changes in a clinical and research setting. For example, a physiotherapy intervention could measure a change in walking velocity to explore the significance of a rehabilitation programme before and after a rehabilitation programme. However, singular measurements with a stopwatch do not have sufficient resolution to classify patients and estimate prognosis [Cohen, Reingold, Polman, & Wolinsky, 2012].

In MS, inertial sensors can be worn to detect subtle changes in gait that standard stop-watch measurements are unable to record [Spain et al., 2012]. Inertial sensors have the power to detect the specificity of the subtle gait changes that increase the possibilities of detailed spatiotemporal and kinematic measurements. The use of sensors can also reduce floor and ceiling effects[11] of stopwatch measurements. Given fatigue can be difficult to measure, new measures going beyond traditional kinematics may be required. Coordination decrement, as well as velocity decreases, may reflect fatigue. A breakthrough application is to use multiple sensors to classify ambulatory patterns reflecting gait kinematics [Needham et al., 2014]. Analysing multiple sensors concurrently will reflect healthy and pathological patterns of ambulation.

In summary, MS fatigue is a varying and complex phenomenon with physical and cognitive functions of impairment in ambulation, strength, memory, concentration, and alertness. Individuals who have progressive MS, are unemployed, and have a lower educational status

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[11] A ceiling effect is a measurement limitation that occurs when the highest or almost the highest possible score on a measurement or instrument is reached. This decreases the likelihood that the measurement has accurately measured the intended phenomenon. The floor effect is the opposite, when a measurement limitation occurs at the lowest or almost the lowest possible score on a measurement or instrument is reached.

typically report higher incidences of self-reported fatigue. The MS population has a considerably higher unemployment rate in comparison to the general population. Associations of age and gender are less well established in the literature, with mixed results. However, older pwMS commonly describe more fatigue.

The degree of disability is somewhat correlated with ambulatory ability: once ambulation dysfunction is prominent, a greater level of fatigue is reported. Additionally, self-reported fatigue is worsened by heat from the weather, exercise, and illness, and often exacerbates as the day progresses. Although there is a wide variety of self-reported measures, the MFIS and FIS are more well-established and commonly recognised for specific MS fatigue. Objective measures of cognitive and motor fatigue have been described in the literature, although clear biomarkers remain difficult to identify as there is still no clear consensus on the best method of assessment of fatigability. Comprehension of ambulation and fatigue through perceived and palpable viewpoints is imperative in this study to understand fatigue globally. In the following section, the facets of an individual’s experience of fatigue, how movement and fatigue affect them, and how pwMS feel this affects others, are explored. A narrative literature review was done to explore the current qualitative literature on fatigue within MS.

Chapter Two: Scoping the literature: Experiences of MS-related fatigue

The following two chapters scope the current literature on different aspects of fatigue in MS. In Chapter Two, a scope of the qualitative literature on the experiences of MS fatigue is described. This is not typical in a phenomenological orientated study to front with the literature. However, with a phenomenon like fatigue and its complexity, and the nature of the interdisciplinary study, it was necessary to scope the current understanding in both fields to grasp what is known about fatigue, its experiences and gait characteristics. As a PhD researcher, I aimed for guidance in regard to the process of orientating, articulating, and delineating fatigue from multiple facets. To study fatigue from a phenomenological and physiological perspective in a naturalised phenomenological study, and to conduct original and rigorous research, I considered scoping the literature to best orientate my understanding on the phenomenon under investigation. In this chapter, the facets of an individual's fatigue of bodily and cognitive features are explored, as well as how they feel their experiences affect others. This narrative review was intended to gain an insider's perspective on understanding the everydayness of fatigue, to delineate the tenants of fatigue and the sensations it brings to pwMS.

Most of the literature highlights the unpredictable nature of fatigue. Individuals often experience different levels of fatigue depending on their activity. However, pwMS describe a degree of fatigue as always present. Overall, a physical presence of fatigue, that altered their perception and bodily appearance, was found through this review. Fatigue was described as a barrier in many bodily, cognitive, and psychosocial aspects for pwMS. The sensation of fatigue was debilitating, pwMS felt visibly weaker as embodiment changed lifeworld aspects, such as selfhood and sociality. For pwMS, their bodily construct and bodily perception to others were significant to them, therefore it valuable for a researcher and clinician to understand.

2.0. Introduction

MS-related fatigue is considered to impair individuals' daily activities and affect many components of their life [Flensner, Ek, & Söderhamn, 2003; Garcia-Jalon, Lennon, Peoples, Murphy & Lowe-Strong, 2012]. Fatigue is a distinct impairment reported to be one of the most debilitating symptoms for pwMS [Smith, Hale, Olson, Baxter, & Schneiders, 2013]. Physical, psychosocial and cognitive symptoms can be exacerbated by fatigue and, when coupled with loss of neurological function, fatigue plays a significant role in all components of a pwMS' life [Fisk et al., 1994]. To understand the effects of these facets in pwMS and others around them, direct and rich descriptive experiences of fatigue in their everydayness, more specifically the bodily and embodiment changes from fatigue, need to be fruitfully understood.

Fatigue has been explored in the qualitative literature and described as an all-absorbing phenomenon that causes unpleasant and disruptive experiences for pwMS. It has also been described as overbearing cognitive function. Nevertheless, a description of the physicality of fatigue and how pwMS feel others perceive their fatigue remains incomplete in the literature. Embodiment has been established in relation to how it affects physical activity and exercise. However, it has not been determined how bodily changes in their everydayness and how this impacts all constructs of their life.

To understand the lived experiences[12] of MS fatigue, a first-person insider's perspective will permit a greater and more global understanding of the phenomenon [Bonner & Tolhurst,2002]. The observation and rich descriptions of an individual's lived experiences allow insight into events, experiences, or structures that entail discovery and valuable information of the phenomenon under investigation. Furthermore, an investigation into the MS fatigue literature on embodiment, will enable a grounded understanding for future fatigue-tailored management programmes.

Considering this, a literature review was conducted in March 2020 to scope the current literature about understanding the "everydayness", lived experiences, and embodiment of fatigue for pwMS. Researchers have previously investigated the lived experiences of pwMS with fatigue, including the most common experiences, and the impacts fatigue has on pwMS and those close to them. However, the characterisation of embodiment of fatigue, how it affects an individual's everydayness, and its experiential features, is less established within the literature. The research questions guiding this review are as follows:

1) Self – what facets does an individual experience through physical movement and activity when fatigued during their everydayness?
2) Others – how does an individual's fatigue affect others and how does the fatigue experience of the person with MS impact others during their everydayness?

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[12] In phenomenological research, a lived experience is a representation of the experiences and choices of a given person.

2.1. Methods

The methods and search strategy were guided by Petticrew & Roberts [2006], using a range of databases including CINAHL Plus, PsycNFO, Web of Science, PubMed, Ovid MEDLINE (including EMBASE) and Psychology Database (ProQuest). The search strategy and terms were developed in consultation with a specialist librarian and a supervisor. This enabled the appropriate conduct of an accurate review scoping the literature on the experiences of MS fatigue. The search terms included “experiences”, “multiple sclerosis”, “fatigue”, and “qualitative”, with articles dating from 1996 to February 2020. There was a high number of duplicates found which affected and narrowed the overall number of articles reviewed.

Articles accepted included the descriptions and experiences of MS fatigue, lived experiences, and experiences of physical activity and movement with fatigue. The meaning of fatigue to pwMS and the impact it has on their daily lives were all included in the review. Articles excluded from the review compromised of non-English reports, articles investigating specific interventions or rehabilitation strategies for MS fatigue, paediatric MS research, and articles not directly exploring fatigue. Only qualitative articles were included, therefore all experimental research papers were excluded. Table 2.1 outlines the search terms for each database and the number of papers initially yielded.

Table 2.1 Search terms for narrative qualitative review.

Database	Search terms	Yielded	Actual included
CINAHL Plus	Experienc* AND Multiple Sclerosis AND fatigue AND qualitative	17	2
PsycINFO	Experienc* AND Multiple Sclerosis AND fatigue AND qualitative	19	3
Web of Science	Experienc* AND Multiple Sclerosis AND fatigue AND qualitative	14	2
PubMed	Experienc* AND ti(Multiple Sclerosis) AND ti(fatigue) AND qualitative	19	2
Ovid MEDLINE (including EMBASE)	Experienc* AND ti(Multiple Sclerosis) AND ti(fatigue) AND qualitative	39	4
Psychology Database (ProQuest)	Experienc* AND ti(Multiple Sclerosis) AND ti(fatigue) AND qualitative	12	1

Total	**120**	**14**

Table 2.2.: Summary of qualitative articles for narrative review.

Author/s	Article title	Methodology	Publication date	Key findings
Smith, Olson, Hale, Baxter & Schneiders	How does fatigue influence community-based exercise participation in pwMS?	An inductive thematic approach.	2011	Perceived control over MS-related fatigue influenced exercise choices in our participants with seven factors: wellness philosophy, a related goal, belief that control was possible, feeling safe and supported, ability to manage limits, being satisfied with trade-offs and positive definition of self.
Moriya & Kutsumi	Fatigue in Japanese people with multiple sclerosis.	An exploratory, descriptive, and contextual design.	2010	The participants made efforts to live with fatigue on their own terms. Fatigue was found to affect the lifestyle of people with MS and their ability to be true to themselves. As a result, the participants devised their own way of coping with fatigue.
Olsson, Lexell & Soderberg	The meaning of fatigue for women with multiple sclerosis.	Hermeneutic phenomenological approach.	2004	Two major themes were described in the study. PwMS experienced their body as a barrier and absent. The feeling of being an outsider was expressed as the body had become an enemy of survival.
Stuifbergen & Rogers	The Experience of Fatigue and Strategies of Self-Care among pwMS.	An exploratory, descriptive design with semi structured interviews.	1997	Categories of self-care strategies were established, including energy conservation, recharge efforts, enhancing resistance to fatigue, and temperature control.
Blaney & Lowe-Strong	The impact of fatigue on communication in MS: The insider's perspective.	A phenomenological approach.	2007	Fatigue had an impact on communication impairment, activity and participation. The authors concluded that self-reported studies have an important role to play in the clinical assessment of fatigue and communication in MS.

Table 2.2. (continued).

Mezini & Soundy	A Thematic Synthesis Considering the Factors which Influence Multiple Sclerosis Related Fatigue during Physical Activity.	Thematic analysis	2019	The authors described three key themes during physical activity: fatigue-related consequences, exercise related barriers and factors that make fatigue bearable for pwMS.
Smith, Fitzgerald & Whitehead	How Fatigue Influences Exercise Participation in Men with Multiple Sclerosis.	An interpretive description method with an inductive analysis approach.	2015	The participants described a process of goal readjustment with regards to exercise that helped them stay engaged in meaningful physical activity despite the effects of fatigue.
Yorkston, Johnson, Klasner, Amtmann, Kuehn & Dudgeon	Getting the work done: a qualitative study of individuals with multiple sclerosis.	A phenomenological approach.	2003	The participants developed strategies in order to get work done and be productive. The authors found participants utilised resources by prioritising, planning, constructing and evaluating strategies.
Holberg & Finlayson	Factors Influencing the Use of Energy Conservation Strategies by Persons with Multiple Sclerosis	An in-depth qualitative interview: A transtheoretical approach	2007	The authors described three themes relating to how participants enhanced or hindered their use of energy conservation strategies: experience with the disease, sense of self, and environmental factors. Education was highlighted as giving participants a new ability to manage their MS.
Lohne, Aasgaard, Caspari, Slettebø & Naden	The lonely battle for dignity: Individuals struggling with multiple sclerosis.	A phenomenological-hermeneutic approach.	2010	The findings indicated that participants believed dignity required time and is experienced only in a context of empathy and mutual confidence. The participants highlighted the struggle of fatigue.

Table 2.2. (continued).

Newland	The use of Focus Groups to Characterize Symptoms in Persons with Multiple Sclerosis.	Qualitative analysis followed the method of Krippendorff (2004).	2012	The findings indicated the importance of capturing single and co-occurring symptoms in participants' own words. Fatigue and loss of cognition was identified as a co-occurring symptom alongside heat intolerance, vision loss and fatigue.
Newton, Griffiths & Soundy	The Experience of Fatigue in Neurological Patients with Multiple Sclerosis: A Thematic Synthesis.	Thematic synthesis of qualitative and mixed methods studies.	2016	Biopsychosocial experiences of fatigue challenged participants and may have altered the impact of fatigue, including the strategies individuals employ to help manage fatigue.
Turpin, Kerr, Gullo, Bennett, Asano & Finlayson	Understanding and living with multiple sclerosis fatigue.	Existential approach to thematic analysis.	2018	PwMS Participants gained an understanding of the effect of MS fatigue over time by performing and adapting their daily activities and knowing the stories of others.
Flesner, Ek & Soderhamn	Lived experience of MS-related fatigue—a phenomenological interview study.	An empirical phenomenological psychological approach (EPP)	2003	Fatigue was concluded to be a comprehensive phenomenon. It is a time-consuming and all absorbing phenomenon, involving the body and the whole human being.

2.2. Results

Fatigue is a symptom that has been described, portrayed, and studied in multiple modes in attempt to provide a deeper and more complete understanding. In this literature review, fatigue is discussed in four sub-sections in attempt to summarise the current understanding of the experiences of fatigue as described by pwMS in the qualitative literature. The four sections are as follows: (1) Visual physicality, heaviness, powerlessness; (2) A tangible form of cognitive complaints, emotion, sense of identity deriving from fatigue; (3) Anxiety, worry, depression as a consequence from fatigue; (4) Social aspects of living with fatigue; (5) Embodiment changes from environmental factors.

2.2.1. Visual physicality, heaviness and powerlessness

Predominantly, pwMS described their fatigue as experienced through actions and feelings in their body. Embodied descriptions included: “heavy limbed”, “unable to have the strength” or “will to move” once the “energy had depleted” and “the heaviness in my legs is like little bitty cement bags on my ankles” [Newland, Thomas, Riley, Flick, & Fearing, 2012; Newton, Griffiths, & Soundy, 2016; Olsson, Lexell, & Söderberg, 2005]. Participants who described their bodily experience as a “heaviness”, outlined basic motor functions like walking as involving foot dragging, the limitation of physical functioning and, at a higher described severity, of the inability and restriction to move [Newton et al., 2016]. A common experience was feeling overwhelmed, almost paralysed by the sudden onset of fatigue, as if their body was shutting down. This made individuals feel powerless, with the desire to rest becoming their only priority [Newton et al., 2016; Stuifbergen & Rogers, 1997]. Stuifbergen & Rogers [1997] captured the portrayal of this helplessness sensation from a few accounts: “I just have to lay anywhere, and it could be so bad that it’s laying on glass”.

The experience of fatigue is characterised by energy impoverishment: “being hit by a tidal wave…it literally feels like someone cut off my left arm…and just feels like the blood and all the energy that I have in my body is kind of going out at the same time” [Stuifbergen & Rogers, 1997]. This heaviness of fatigue was occasionally associated with pain in some studies, as well as physical weakness and loss of balance [Flensner et al., 2003; Stuifbergen & Rogers, 1997]. PwMS described having a reduction of body control, sometimes perceived as like being drunk due to instability or swaying. This fatigue was expressed as a novel sensation, dissimilar from common fatigue, and they felt unable to fully recover or get rid of it. One participant reported it felt like fatigue was stuck fast to their body “…it’s stuck to my skin and can’t be peeled off.

It's there all the time" [Flensner et al., 2003; Mezini & Soundy, 2019; Moriya & Kutsumi, 2010]. This analogy could insinuate the feeling of fatigue, its consistency, and being never fully able to abandon fatigue. The feeling of complete energy restoration prior to diagnosis may never be experienced again due to a degree of fatigue always feeling present. Fatigue was often described as an on-going sensation of different severities that affected different physical functions, dependent on the severity of fatigue. Nevertheless, the existence of fatigue, mild or severe, was unfailingly present [Flensner et al., 2003; Mezini & Soundy, 2019; Moriya & Kutsumi, 2010].

Olsson et al. [2005] conducted a hermeneutic-phenomenological analysis and developed the theme "body as a barrier". This was as a result of the unpredictability of fatigue that caused pwMS to feel uncertain and insecure about participating in certain spontaneous activities. Complex fatigue reduced their control over their lives, including their ability to engage in physical activity [Smith, Fitzgerald, & Whitehead, 2015]. The sense of the unpredictability of the symptom produced a significant barrier for participation in physical activity, and individuals felt the benefits were unclear, reporting negative beliefs about the efficiency of exercising. This prevented some individuals from making an effort to become more active [Mezini & Soundy, 2019]. In Mezini & Soundy's thematic review, all pwMS exhibited a lack of understanding about fatigue, and there was a degree of unconfirming guidance from healthcare professionals regarding their communication or knowledge of fatigue. An interprofessional conflict was occasionally reported between instructions on physical activity regarding the type of activity and how beneficial it was. This generated confusion and uncertainty that often led to a heightened level of anxiety and worry [Mezini & Soundy, 2019; Olsson et al., 2005; Smith et al., 2015].

Smith et al. [2011] found that individuals who did exercise regularly perceived physical improvements in energy levels, with a reduction in heavy legs and improved sleep quality. Conversely, pwMS who performed lower levels of exercise experienced an increase in self-reported fatigue, especially with confounding variables such as stress, which exacerbates fatigue [Smith et al., 2011]. Mezini & Soundy [2019] found that more active individuals encompassed exercise to reduce their levels of stress, which subjectively decreased their levels of fatigue. Although exercise reportedly facilitated control on pwMS' perception of fatigue, they emphasised listening to their body was emphasised as a way to manage fatigue. Recognising bodily limitations was described as vital and identifying what their body could endure was frequently found through trial and error over a long period of time [Mezini &

Soundy, 2019]. The anxiety of physically pushing themselves to the limit was often expressed as a fine line between being beneficial and experiencing adverse effects [Mezini & Soundy, 2019]. Some of the symptoms in recognising these limits were: increasing head pressure, signs of muscular fatigue through lower extremity heaviness, and the increased tendency to trip [Smith, Olson, Hale, Baxter, & Schneiders, 2011]. Mezini & Soundy [2019] identified 16 studies in which participants describe an increase in perceived fatigue during or immediately after too much physical activity. The compilation of bodily symptoms was expressed through fatigability of functional decline, lack of balance, raised body temperature, increased likelihood to trip, lower extremity heaviness, knee-buckling, and a pins and needles sensation in the legs [Mezini & Soundy, 2019]. One participant described the heaviness of the muscles after physical activity as “wearing a trench coat that goes down to your ankles and it’s made of lead”. This often led to the loss of enjoyment and pleasure in physical engagement [Mezini & Soundy, 2019].

For rehabilitation interventions, there was a difference in approach regarding the strategy and management of fatigue [Moriya & Kutsumi, 2010]. Instead of focussing on reducing impairments as a result of fatigue directly (such as foot drop interventions), pwMS focussed on reducing the “load” by simplifying tasks and activities [Moriya & Kutsumi, 2010]. The reduction of “load” was intentionally achieved by planning and conserving physical strength and controlling the amount of times pwMS “go out” a month [Moriya & Kutsumi, 2010]. The maintenance of a balance between activity and rest has been reported as effective [Moriya & Kutsumi, 2010].

Holberg & Finlayson [2007] explored energy conservation strategies by examining the factors which were believed to influence those strategies. Simplifying activities or asking for help was part of the participants’ energy reservation strategy and delegation of tasks was identified as the best approach as it allowed participants to retain control over the situation, especially in a work environment [Holberg & Finlayson, 2007]. Some examples of ways participants saved energy included the use of motorised carts or reachers whilst food shopping [Holberg & Finlayson, 2007].

Most men took a flexible, problem-solving approach to managing their fatigue, by scaling back the intensity of certain activities and learning to compromise in situations [Smith et al., 2015]. A participant in a study by Smith et al. [2015] cited “dog power” as a fatigue management strategy, explaining that merely having to walk his dog aided the maintenance of his exercise routine and kept him engaged in walking.

Moriya & Kutsumi [2010] found that pwMS had unique measures for handling fatigue, a tendency to reserve their energy, and took measures to predict and control activity by resting when necessary. Adapting their lifestyle, such as by sleeping through a lunch break, allowed some individuals to switch off, and avoid rigorous thinking and unnecessary tasks. This would often lessen their level of fatigue [Moriya & Kutsumi, 2010]. Nonetheless, this would not completely alleviate fatigue, but simply create a method to continue through the working day [Moriya & Kutsumi, 2010]. Alternative methods for recharging energy levels included stretching, rest, medication, nutritional strategies, and avoiding certain physical activities [Stuifbergen & Rogers, 1997; Holberg & Finlayson, 2007]. Participants stated that different forms of movement and exercise gave them an increased sense of well-being and believed this suppressed fatigue. The correct amount and type of exercise, which was unique to the individual, was believed to control an individual's fatigue [Flensner et al., 2003; Smith et al., 2011, 2015].

In summary, pwMS expressed fatigue as affecting their perception and the functionality of their body. The level of severity fluctuated which resulted in limitations to an individual's capability and participation in physical activity. An ever-growing hesitancy to participate in exercise caused a loss of enjoyment and engagement due to fatigue. Self-motivated approaches, such as physical aid and energy conservation strategies, are described to benefit pwMS and are the most effective ways to manage fatigue. However, it is well established that fatigue is always present and impacts a pwMS' bodily functions.

2.2.2. A tangible range of cognitive complaints, emotion and sense of identity deriving from fatigue

Cognitive complaints refer to an individual having difficulty with concentration, decision-making, memory, and learning new skills. In the MS population, cognitive complaints are commonly reported and described in different ways [Blaney & Lowe-Strong, 2009; Newland et al., 2012; Newton et al., 2016; Stuifbergen & Rogers, 1997]. Within this review, cognitive impairments were commonly reported by pwMS, with variability in concentration levels, memory, and judgement/perception [Blaney & Lowe-Strong, 2009; Newland et al., 2012; Newton et al., 2016; Stuifbergen & Rogers, 1997]. The inability to think when an individual felt fatigued was described in numerous ways; a degree of cloudiness often affected an individual’s awareness and consciousness [Blaney & Lowe-Strong, 2002; Newland et al., 2012].

Blaney & Lowe-Strong [2009] explored the perspective of pwMS on the impact of fatigue on communication. The authors explored pwMS’ common experiences of sentence execution difficulties and multitasking, communication changes, and strategies used to conceal these impairments. The authors found an increase in the frequency and severity of communication impairments whilst fatigued (memory, thinking, and speech dysarthria), “sometimes I can slur my words…I’ll sound like I’ve had a few to drink and I haven’t” [Blaney & Lowe-Strong, 2009].

Newland et al. [2012] observed that some pwMS would forget what they were saying halfway through a sentence. Levels of concentration characteristically declined as pwMS struggled to stay actively engaged in conversation [Stuifbergen & Rogers, 1997]. This was described by pwMS as “if they were in a dream”; the mental fogginess created a haze over their cognitive ability to function [Stuifbergen & Rogers, 1997; Mezini & Soundy, 2019]. Newland et al. [2012] used focus groups to explore symptom clusters in pwMS. A common symptom expressed was fatigue and its association to cognitive loss, heat intolerance, and vision loss. Descriptions of “feeling drained” or “wiped out” were mentioned, with many participants expressing uncertainty about when fatigue would affect them [Newland et al., 2012]. PwMS also described the consequences of a noisy environment: static noise from a loud restaurant or numerous people talking at once would often exacerbate an individual’s fatigue and interfere with their ability to clearly think and retain information [Newton et al., 2016].

Frustration is a prevalent negative emotion amongst pwMS that can be defined as irritable distress after unresolved problems [Jeronimus & Laceulle, 2017]. Cognitive dysfunction from external impacting factors often led to a level of frustration in pwMS [Blaney & Lowe-Strong, 2009; Stuifbergen & Rogers, 1997]. The decline in cognitive ability was somewhat unpredictable, and the incapability to perform such cognitive functions and communicate efficiently would cause irascibility: “is it like a drunken slur you get when you’re tired? I remember one night, I was really quite angry…and she was only joking, and she said ‘have you been on the bottle?’, and I mean, she was only having a laugh with me but I thought, only if you knew!” [Blaney & Lowe-Strong, 2009]. Frustration was typically accompanied by emotional irritability and a lack of patience was directed towards themselves: “I am just emotionally exhausted… I want things to be short, a single response. I don’t want to interact”

[Stuifbergen & Rogers, 1997]. This left an emotional affliction and negative feeling related to fatigue. Individual's found everyday activities grinding, which would lead to more restriction and dependency on others [Stuifbergen & Rogers, 1997; Flensner et al., 2003].

Some pwMS revealed feelings of worthlessness and sadness, perceiving fatigue as a threat to their self-identity as they were forced to disengage with activities they used to enjoy: "give up my painting was a temporary sort of grieving time. It is a loss" [Mezini & Soundy, 2019]. These feelings were often associated with failure, fear, anxiety, anger, depression, and helplessness as an element of feeling trapped, as there was a dependency on others for help [Newton et al., 2016; Flensner et al., 2003]. PwMS often described more than one state of fatigue, which would often influence one another [Smith et al. 2011]. Smith et al. [2011] found this with one participant who described a depressive state and a fear for the future that often led to an unclear cognitive state that ultimately affected bodily strength, balance and ability to walk: "everything goes to pot". Smith et al. [2015] found fatigue made male pwMS feel "old before my time" and "not being a man" for losing their strength and energy.

In their thematic analysis, Turpin et al. [2018] explored the recognition and accommodation of fatigue in the context of the daily lives of pwMS. The theme of identity was central to the with participants initially struggling to identify a specific occurrence of fatigue or other contributing factors. Awareness of fatigue through the understanding of onset, trigger, severity, and presentation of fatigue were factors individuals considered in order to manage their fatigue accordingly [Turpin et al., 2018]. After the acceptance of fatigue, pwMS described how their capabilities and everyday activities had to coincide with fatigue. They had learnt to pay attention to their daily activity levels, and lowered expectations of their capacity to accomplish tasks.

Acceptance of fatigue was explored in several studies. In a study by Flesner et al. [2003], participants desired acceptance of their condition. They described the desire to face up to the facts and accept the limitations fatigue inflicts [Flensner et al., 2003; Moriya & Kutsumi, 2010]. With this acceptance, individuals chose not push themselves to their limits, and this made them feel more in control [Flensner et al., 2003]. This was seen as part of them, incorporated into their bodies, and they could feel like real human beings, perceiving themselves as living a more normal life.

In a study by Holberg & Finlayson [2007], sense of self was a predominant theme. The majority of participants reported they had adopted a "no worries attitude" by setting limitations and boundaries, accepting what they could and couldn't do [Holberg & Finlayson, 2007]. A lack of ability to complete a task or activity was part of their acceptance, as they would no longer "beat themselves up" over it. However, with this acceptance came a sense of loss of opportunity and choice in what they could do [Turpin et al., 2018].

The invisibility of fatigue often generated worry in pwMS. They described worry about how others perceived them and how fatigue may be seen as an excuse or a nuisance to others [Turpin et al., 2018]. Some pwMS chose to use the aid of a physical stick to make others understand that the disability is accompanied by fatigue. As pwMS felt the need to convince others of their disability, the physical and visible use of a walking stick would indicate a level of disability more noticeable to others around them [Turpin et al., 2018]. Conversely, other pwMS felt the need to hide the difficulties fatigue came with, to avoid the stigma and unnecessary attention [Turpin et al., 2018]. A change of attitude towards fatigue over time created a constant adjustment to their self-identity and their association with social roles [Fortenberry, Janson & Clark, 2013]. According to Kralik et al. [2003], a change of occupation, lifestyle and interpersonal relationships would be a narrative reconstruction of self-identity. Adapting to life with fatigue requires pwMS to embrace and accept a change in self-image, both to themselves and to others [Turpin et al., 2018].

In summary, cognitive impairment is apparent in pwMS who experience fatigue. Communication difficulties included difficulties with speech and executing sentences, as well as difficulties with memory retention, the ability to concentrate on the delivery of a speech, and remaining engaged in conversation. Cognitive dysfunction could lead to frustration, as cognitive activity tends to be more problematic following an MS diagnosis. Unpredictable cognitive performance can raise questions about self-identity, as others (or they themselves) could portray them differently. The process of understanding fatigue and adapting to the accompanying change is unique to each pwMS and is dependent on their perception of fatigue and self-identity.

2.2.3. Anxiety, worry and depression as a consequence of fatigue

Feelings of anxiety and depression were frequently reported as contributing to fatigue, with depressive symptoms amongst the strongest influences in cognitive fatigue [Morita & Kutsumi, 2010; Olsson et al., 2005; Mezini & Soundy, 2019]. The disruption of daily activities can cause pwMS to feel unable to lead a "normal" life [Moriya & Kutsumi, 2010; Olsson et al., 2005]. Disruption from fatigue can also cause individuals to completely stop their activity and reduce their senses by lying down the floor or standing still. One participant reported they used diapers due to the exhausting nature of walking back and forth to the toilet [Moriya & Kutsumi, 2010].

Some pwMS held an incomplete sense of self, as they struggled to try new or spontaneous activities due to anxiety about the challenges fatigue brought. Fatigue is uncertain and unpredictable in nature, and pwMS can be challenged by not being able to fully relying on their body as they could before diagnosis [Moriya & Kutsumi, 2010]. Individuals felt a temporary or permanent loss of control over their body that was exacerbated by fatigue, as the nature of their disease progression remained unknown [Mezini & Soundy, 2019]. The apprehension of fatigue was rooted in the fear of the unknown, cognitive ability, and function, but also the unpredictability of specific surroundings, both bodily and socially [Mezini & Soundy, 2019]. This negative feeling affected individuals' perceptions of fatigue and ability to continuously perform daily activities. A vicious cycle of anxiety, uncertainty and inability was often reported [Mezini & Soundy, 2019]. A description of the distress of fatigue experience was common rooted in psychological stress related to family, work or emotional issues, and the uncertainty of relapsing [Soundy & Elder, 2016; Smith et al., 2015; Smith, Hale, Olson, Baxter & Schneider, 2013].

Depressive feelings can often be triggered by the uncertainty of the future: there is a downward spiral effect of unclear thought, deterioration of bodily function, and ambulatory function [Smith et al., 2011]. As highlighted above, a major concern for pwMS is the invisibility of fatigue and the unexpected attacks. Lohne et al. [2010] highlighted a lonely battle of fighting fatigue which is rooted in the illness, as well as the hopeless battle of fighting for help and support with their fatigue. One individual described fatigue as an overwhelming experience, almost prison-like: "being inadequate, that's one's feeling with this illness… because I have no control, I am so exhausted just when I walk around my house . . . so I am not capable of doing it… What I can no longer do gives me continual sorrow… but I have no energy, though I understand that I must accept this, because I know how many… have to do that" [Lohne et al., 2010].

Like Smith et al. [2011], Flesnser et al. [2003] found participants experienced a heightened awareness of fatigue that brought about a sense of uneasiness, but also a sharpened awareness of their body, as fatigue did not feel natural to them. Although understanding their fatigue was of importance to pwMS, they often expressed a focus on bodily sensations and being more aware of these sensations were likely to exacerbate the feeling of fatigue [Smith et al., 2011].

Participants aimed to have a sense of control over their body, which reportedly lessened their perceived fatigue [Smith et al., 2015]. Similar to depression, an increase in stress could increase an individual's perception of fatigue: "well, it tends to… my frame of mind as well, you know if I can sink into a quite deep depression as well and when I feel really low I tend to not have a lot of energy" [Smith, Hale, Olson & Schneiders, 2009]. This may indicate that the degree of self-perceived fatigue has an important bearing on the overall mental health of the individual and cognitive implications should be considered when addressing fatigue in pwMS.

Frustration, if ongoing, can lead to depression in some individuals. Carver & Scheier [2000] reported that a state of depression is likely to occur when a frustrated goal is deeply rooted in the core of the self. Such a goal is not easily abandoned or even scaled back [Carver & Scheier, 2000]. The damage that frustration causes may lead to depressive symptoms, which could in turn prevent an individual from reaching their goal. Therefore, understanding their emotional and cognitive sensations and responses may aid an individual in accepting and understanding their fatigue more rapidly [Smith et al., 2015]. Mezini & Soundy [2019] discussed the association between the lack of control over fatigue and the increase in depressive symptoms due to the realisation of not achieving goals like they did before their diagnosis [Kayes, McPherson, Taylor, Schluter & Kolt, 2011; Smith, Hale, Olson & Schneiders, 2009].

2.2.4. Social aspects of living with fatigue

In numerous studies, researchers have recognised the social aspects of living with MS fatigue, concerning communication and self-care impairments [Blaney & Lowe-Strong, 2009; Mezini & Soundy, 2019; Moriya & Kutsumi, 2010; Newton et al., 2016; Stuifbergen & Rogers, 1997; Turpin et al., 2018]. As briefly stated in the previously section, pwMS have expressed that they have trouble interacting with others whilst fatigued due the increased difficulty of articulating themselves and lack of common understanding by others [Moriya & Kutsumi, 2010]. The struggle of word and sentence articulation creates a decrease in social interaction. Participants felt healthcare professionals were insufficiently involved or supportive, but thought this was caused by a lack of understanding and the invisibility of fatigue.

Although pwMS adopted certain self-care strategies to strategically manage their fatigue, barriers to participation in their social circles remained as some tasks, such as multitasking, ("walking and talking"), was not possible [Blaney & Lowe-Strong, 2009]. This loss of autonomy and dependency generated the sensation of not being understood by others in social situations that precipitated anxiety on how others perceive them [Newton et al., 2016; Turpin et al., 2018]. Stuifbergen & Rogers [1997] captured the overpowering impact fatigue had on one female participant. She was no longer able to enjoy her favourite social activities: "fatigue just rules my life". Fatigue imposed upon daily planning, dependence, personal relationships, and employment. Pre-planning, and more importantly, prioritising activities to prevent fatigue from impacting on their lives, were highlighted by participants [Mezini & Soundy, 2019]. An emphasis on organisation was important to pwMS, as this helped them feel more in control in a given situation [Mezini & Soundy, 2019]. Fatigue placed a strain on personal relationships, from completing simple day to day tasks and their dependency on others, and this caused a loss of a sense of independence.

Male pwMS were more likely to struggle with their self-identity, as changes to their employment status and potential dependency on their wife's income was challenging for them [Smith et al., 2015]. The feeling of isolation from a decline in social activities made pwMS feel more vulnerable and limited in what they could achieve [Stuke et al., 2009]. Feelings of embarrassment from their bodily limitations and constant need to justify themselves were often described [Stuke et al., 2009]. Mostly, pwMS preferred not to use mobility devices to manage their fatigue, in order to maintain their independence and be visually similar to the general population [Stuke et al., 2009; Induruwa, Constantinescu & Gran, 2012]. Nevertheless, some individuals felt the need to demonstrate some level of disability through the use of a walking stick [Turpin et al., 2018]. PwMS tended to compare themselves to the general population, especially regarding exercise and social activities [Stuke et al., 2009; Induruwa, Constantinescu & Gran, 2012; Soundy & Elder, 2016]. These psychological and physical restrictions generated the feeling of unacceptable behaviour, which ultimately caused a disengagement in their social activities [Stuke et al., 2009; Soundy & Elder, 2016; Stuifbergen & Rogers, 1997].

2.2.5. Embodiment changes from environmental factors

Ambient temperature is known to impact pwMS. Some pwMS reported a feeling of sluggishness and exacerbated fatigue with an increase in temperature [Mezini & Soundy, 2019; Newland et al., 2012; Newton et al., 2016; Stuifbergen & Rogers, 1997]. Newland et al. [2012] used focus groups to explore and identify symptoms in pwMS. Within the groups, a common symptom expressed was the association between fatigue, cognitive loss and heat intolerance. The higher temperatures from hot and humid weather caused an exaggeration of fatigue and a clear lack of energy for physical activity [Mezini & Soundy, 2019]. Some individuals stated that any increase in temperature would exacerbate their fatigue, whether from weather, direct sunlight or even extremely hot drinks [Mezini & Soundy, 2019]. A coping strategy for reducing the level of fatigue was to stay cool, and a few participants described how swimming several times a week enabled them to stay cool [Smith et al., 2015]. In a study by Stuifbergen & Rogers [1997], participants discussed methods of cooling by gauging the house temperature frequently or physically keeping certain body parts cool, such as the head: “I need my head to be cool, if it’s real hot weather, I’ll come in and put water on my head”. Colder weather also affected some pwMS; an increase in spasticity, muscle stiffness and pain levels would have a knock-on effect on their energy levels and other motor functions, such as balance [Newton et al., 2016; Mezini & Soundy, 2019; Stuifbergen & Rogers, 1997]. Conversely, Smith et al. [2015] found most male pwMS reported to like the colder weather. One male participant described his enjoyment of walking on frosty days because he did not tire as quickly as on warm days.

The unpredictability of specific surroundings tended to heighten individuals’ perceived fatigue [Mezini & Soundy, 2019]. Uneven walking surfaces and types of equipment (most gym equipment) that gave them a sense of unsafety often increased their levels of fatigue through anxious thoughts [Stuke et al., 2009]. Most individuals chose to not participate in particular activities due to these physical surroundings. For example, individuals with poor balance reported feeling unsupported and anxious to exercise in swimming pools, therefore, would stop attending swimming classes [Stuke et al., 2009]. Overall, external variables of extreme temperatures and features that generated anxious thoughts would increase levels of self-reported fatigue.

2.3. Summary

Many pwMS reported experiencing a degree of fatigue. Its unpredictable nature impacted their daily activities in many cognitive and motor aspects. PwMS often described an overwhelming feeling of defeat, as the body became intensely heavy and powerless. The decline in motor function with limb heaviness and muscle weakness, directly related to fatigue, was prominent in the majority of pwMS.

Alongside bodily impairment, cognitive dysfunction was described, including the inability to sustain mental function, speed and flexibility. The uncertainty of fatigue and their disease progression caused a heightened level of anxiety and depression in most pwMS. Numerous symptoms common to both fatigue and depression are clearly reported in the literature, and the relationship between the two remains problematic. Fatigue is known to increase a depressive mood and vice versa. Therefore, it is not always obvious which one is the consequence of the other. However, it is commonly reported that persistent fatigue directly impacts a depressive mood.

The uneasiness and lack of control over fatigue generated an increase in stress levels that consequently increased levels of perceived fatigue in pwMS. The nature of fatigue often left individuals hampered by anxiety and worry, due to the uncertainty of knowing their limits in cognitive, physical, and social activities. Consequently, this limited their participation in physical and social engagement, due to embarrassment and how they felt they were perceived by others. This created social distance and feelings of isolation that impacted professional and personal relationships. Basic functions that involved any degree of multitasking whilst fatigued, such as walking and talking, were reported to be of great difficulty for pwMS.

The physical presence of fatigue was described as debilitating. PwMS believed they felt and looked weaker as embodiment changed lifeworld aspects such as selfhood and sociality. Fatigue altered how individuals perceived themselves and how they felt others perceived them. The physicality of fatigue caused the body to become a barrier not only in physical activity, but all movement, activities and social engagements. PwMS experienced a bodily change and dysmorphia as other lifeworld aspects are all impacted by embodiment implications of their life.

Perceived fatigue was significant: there was a conscious sensation of fatigue that pwMS reported as negatively affecting emotional and motor complaints. The experience of energy impoverishment was predominantly experienced through bodily sensation and lack of control. PwMS described an overpowering, almost paralysing feeling taking control of their bodies, which made a variety of basic motor functions challenging, including engaging in physical activity. Regarding the most effective approach to managing fatigue, exercise and physical movement, advice from healthcare professionals was conflicted. This heightened anxiety, as pwMS feared it would worsen their condition.

The battle of establishing self-identity and how others perceived them was continuous, as some individuals wanted to keep the imagery and identity before their diagnosis, but others did not. Others' perceptions were important to pwMS in most social situations, which often caused individuals to reduce their attendance at social events. Bodily dysfunction from fatigue was often visible to them and to others; different states of fatigue were described as impacting or being portrayed through the body. Overall, significant bodily changes impacted their everydayness, and caused a degree of heightened awareness on how they believe others perceive them. Fatigue had become a part of their self-identity, and it had to be accepted in order to be managed.

The uncertainty of fatigue and its array of manifestation and behaviour was associated with increased levels of anxiety and depressive moods. The literature repeatedly reports the feeling of uneasiness of fatigue and how it can increase levels of stress which consequently affects their perception and overall outlook of fatigue. Clinically, these cognitive and emotional aspects should be highlighted and explored in more depth by therapists and practitioners; the interconnectivity of fatigue, anxiety, stress and depression can all be affected by their perception of MS and their fatigue. Addressing their perception of fatigue in relation to their management, behaviour and attitude could ultimately benefit pwMS and assist in enhancing their quality of life and how to live to the best of their ability with MS and fatigue.

In the following chapter, fatigue from the viewpoint of gait and ambulation is discussed. The current literature on gait kinematics and MS fatigue more specifically is investigated, and how inertial sensors can objectively identify fatigability in gait kinematics in pwMS is explored.

Chapter Three: Scoping the literature: The use of wearable inertial sensors for the detection of fatigability and gait characterisation.

In the following chapter, the usefulness of wearable sensor technology for the detection of ambulatory fatigue in pwMS through a variety of different parameters is explored. In this review, gait parameters have been identified in association with ambulatory fatigue. Researchers have highlighted the usefulness of wearable sensor technology to extract characteristics of fatigability. Nevertheless, most of the research consists of weak to moderate findings. In addition, there is currently no gold standard for the measurement of ambulatory fatigue that could provide consistency and reliability within a research and clinical setting.

3.0. Introduction

MS is an autoimmune chronic inflammatory disease that affects a variety of motor and cognitive functions due to damage of central nerve cells and myelin [Browne et al., 2014]. Gait impairment is a reported motor dysfunction, with an estimated 75% of individuals expressing a degree of ambulatory dysfunction throughout the course of their disease [Hobart et al., 2001]. Due to widely disseminated lesions throughout the CNS, gait abnormalities are poorly characterised in pwMS [Filli et al., 2018]. Unlike other neurological diseases, there is no textbook or typical gait pattern that has been clearly identified for diagnoses, due to the large gait variability. Although the exact patterns of gait impairment are still inconclusive in the literature, agreeance in other observations such as reduced gait speed, smaller cadence and increased duration in double support of the gait cycle has been reported [Motl et al., 2017]. It is recognised that pwMS are more likely to experience jerky movements in the trunk and lower extremities, with irregular foot placements and lack of trunk control whilst walking [Filli et al., 2018].

Impairment can result directly from physiological factors such as CNS lesions. However, psychological factors and an individual’s perception and gait can be affected too. Alongside factors such as motivation and depression, fatigue is thought to highly impact physical and psychological functions in pwMS [Khan et al., 2014]. Fatigue is clinically defined subjectively and has been explored in many diverse disciplines, revealing the multifaceted nature of the symptom. One facet includes ambulatory fatigue and its components concerning the nature of gait changes and patterns. Ambulatory fatigue has been considered more difficult to quantify, as there is no clear consensus regarding the most appropriate tool to measure walking disability and fatigue in pwMS [Goldman et al., 2008]. The most acknowledged walking test for ambulatory fatigue is the 6MW. However, other tests such as the two-minute walk (2MW) have also been used [Scalzitti et al., 2018; Goldman et al., 2008].

Typically, detailed measurements of gait parameters are conducted in a specialist biomechanics laboratory, with the use of the gold standard measurement of motion capture systems. However, these systems require access to such laboratories, and the expense of equipment and software can be prohibitive for small research grants or teams [Spain et al., 2012].

IMUs are small, portable systems that measure linear and angular motion and magnetism [Vienne-Jumeau et al., 2019]. Inertial sensors are a cost-effective type of wearable sensor that has been used in attempt to characterise gait in MS [Greene et al., 2015; Motta et al., 2016]. Wearable devices have been used in a variety of populations, including Parkinson's disease [Zampieri et al., 2011], stroke survivors [Janssen et al., 2008], knee arthroplasty [Shanahan et al., 2018], spinocerebellar ataxia [Matsushima et al., 2015; Shirai et al., 2019], geriatric individuals and those at risk of falling [Ganea et al., 2011], and pwMS [Spain et al., 2012]. Although IMUs have been used for the detection of balance and gait deficits in pwMS, their use for establishing clear biomarkers of ambulatory fatigue in pwMS is still inconclusive in the literature [Shema-Shiratkzy et al., 2019].

To comprehensively understand ambulatory fatigue, the aim of this review was to explore objective kinematic gait pattern changes in pwMS using wearable inertial sensor technology. The following research questions guiding this review were as follows:

1) What gait parameters have been used to assess ambulatory fatigue in pwMS with the use of wearable inertial sensor technology?
2) Have these gait parameters been used to objectively identify ambulatory fatigue?

The aim of this review was to concisely grasp the current use of inertial sensors to detect ambulatory fatigue in pwMS, to further understand how gait characteristics can be used to detect fatigability in MS.

3.1. Methods

The methods and search strategy were guided by Petticrew & Roberts [2006] using a range of databases, including PubMed, Ovid MEDLINE, and grey literature from Google Scholar. The search terms used and included are stated in Table 3.1., alongside the number of papers initially yielded.

A high level of duplicates found and removed, which reduced the overall number of articles included in the final review. The inclusion criteria comprised of a clinical diagnosis of MS, any gait parameters using wearable sensors for fatigue and fatigability, and assessment and tasks that investigated ambulation and fatigue. The type of studies included were randomised control trials, non-randomised control trials, and observational studies. Studies which involved non-MS population cohorts, rehabilitation or pharmacology trials, physiologically measured sensors, pressure pad walkways, and motion capture systems, and any qualitative studies, were excluded from the review.

A total of 10 papers was included in the review, comprising nine research articles and one systematic review. The research articles involved spatial-temporal kinematics parameters, gait features of dynamic time warp (DTW), and joint angle ROM with the use of wearable sensors.

Table 3.1.: Summary of search for quantitative review

Database	**Search terms**	**Yielded**	**Actual included**
PubMed	((((((((multiple sclerosis[Title]) OR (MS[Title])) AND (wearable[Title/Abstract])) OR (sensor[Title/Abstract])) OR (inertial[Title/Abstract])) OR (gyroscope[Title/Abstract])) OR (accelerometer[Title/Abstract])) AND (fati*[Title/Abstract])) AND (gait[Title/Abstract])	53	4
Ovid MEDLINE (including EMBASE)	(((multiple sclerosis or MS).ti. and sensor.kw.) or wearable.kw. or inertial.kw. or gyroscope.kw. or accelerometer.kw.) and fati*.kw. and gait.kw.	8	1
Grey literature – Google Scholar	“multiple sclerosis”, “fatigue”, “fatigability”, “wearable sensors”, “gait analysis”, “characteristics” ,“quantification”, “kinematics”.	64	5
Total		**125**	**10**

Table 3.2.: Summary of quantitative review articles

Author/s	**Article title**	**Methodology**	**Publication date**	**Key findings**
Engelhard, Dandu, Patek, Lach & Goldman	Quantifying Six-Minute Walk Induced Gait Deterioration with Inertial Sensors in Multiple Sclerosis Subjects.	An ActiGraph GT3X accelerometer on one hip. Gait cycles based on DTW. Cycles from later minutes were compared to baseline cycles to measure gait deterioration using a warp score.	2016	Correlations to MSWS-12 and MFIS validate the warp score. Warp scores (measures the stretch needed to align gait cycles to baseline gait cycles) rose in mild and moderate disabled pwMS between minutes three to six. Moderately disabled pwMS appeared to have gait deterioration with high warp scores throughout the walk and steadily increased with variance.
Dandu, Engelhard, Goldman & Lach	Determining physiological significance of inertial gait features in multiple sclerosis.	An ActiGraph accelerometer on each hip. The DTW score based on warp score and DTW distance.	2016	Walking speed, DTW distance score and warp score were closely related to several patient-reported outcome measures. They indicated the DTW score can primarily be a measure of physical fatigue and the warp scores measure balance and physical fatigue.
Qureshi, Brandt-Pearce & Goldman	Relationship between gait variables and domains of neurologic dysfunction in multiple sclerosis using six-minute walk test.	Wearable body sensor networks (BSNs) on the wrists, ankles and sacrum that detected angular acceleration to calculate gait cycle length variance and gait speed.	2016	PwMS who scored higher on the MFIS were more likely to reduce in gait velocity and take unequal length of gait cycles during the 6MW. However, the gait variable of individuals who scored under the median score of MFIS did not significantly change in gait parameters.

Table 3.2. (continued).

Motta, Palermo, Studer, Germanotta, Germani, Centonze, Cappa, Rossi & Rossi	Disability and Fatigue can be objectively measured in Multiple Sclerosis.	Seven wireless MIMUs (Xsens) placed on the pelvic, thigh, shank and foot of both legs. For each gait trial and each leg, means and standard deviations of ROM of hip (mROMH, sROMH), knee (mROMK, sROMK) and ankle (mROMA, sROMA) were evaluated.	2016	ROM in the hip, knee and ankle reduced compared to the control group. Findings indicated the hip ROM and motor performance index together could identify motor impairment and classify pwMS into fatigue and non-fatigue groups better than validated questionnaires.
Taborri, Studer, Grossi, Brambilla, Ferrò, Mantegazza & Rossi	Measuring changes in gait kinematics due to walking-related fatigue in patients with Multiple Sclerosis.	Seven wireless MIMUs (Xsens) placed on the pelvis, thigh, shank and foot of both legs. 6MW was performed to explore the ROM of the joint curve angles of throughout each minute of the 6MW.	2019	During the 6MW, ROM decrement was recognised from the second minute in the ankle, third minute from the knee and only the last minute from the hip compared to the control group. The authors concluded ROM in the lower extremity can provide a useful index for fatigability.
Shema-Shiratzky, Gazit. Sun, Regev, Karni, Sosnoff, Herman, Mirelman & Hausdorf	Deterioration of specific aspects of gait during the instrumented 6-min walk test among people with multiple sclerosis.	Wearable sensors, including accelerometer and gyroscope, were placed on the lower back and ankles (Opal, APDM). Gait parameters of speed, cadence, stride time variability, stride regularity and swing asymmetry were performed.	2019	Step and stride regularity were significantly diminished throughout the duration of the 6MW. There were changes in deterioration of cadence and sample entropy (complexity of the gait acceleration signal) that could indicate changes to walking instability may be generated by fatigue, although this is dependent on the level of disability.

Table 3.2. (continued).

Vienne-Jumeau, Quijoux, Vidal & Ricard	Wearable inertial sensors provide reliable biomarkers of disease severity in multiple sclerosis: A systematic review and meta-analysis.	Systematic and meta-analysis review.	2020	Wearable sensors have potential to increase detection of gait patterns and changes. Gait parameters of speed, step length and step duration can assist in disease severity monitoring in pwMS (EDSS 1-4.5).
Psarakis, Greene, Cole, Lord, Hoang & Brodie	Wearable technology reveals gait compensations, unstable walking patterns and fatigue in people with Multiple Sclerosis.	Two tri-axial accelerometers (Opal by APDM) placed on the pelvis and head to measure gait mobility, variability and asymmetry.	2018	Wearable sensors can provide accurate results to assess gait quality and screen for movements at the head and pelvis. PwMS had greater compensatory movements at the head and pelvis that were strongly correlated to reduced mobility and increased gait variability.
Morris, Cantwell, Vowels & Dodd	Changes in gait and fatigue from morning to afternoon in people with multiple sclerosis.	A clinical stride analyser to investigate gait speed, stride length, cadence and the percentage of the gait cycle spent in double limb support.	2002	Findings indicated little change in any of the gait variables in pwMS, with only a small increase in speed, stride length and cadence compared from the morning to the afternoon.
Moon, McGinnis, Seagers, Motl, Sheth, Wright, Ghaffari & Sosnoff	Monitoring gait in multiple sclerosis with novel wearable motion sensors.	Three types of sensors were used: BioStampRC skin mounted sensor on the tibia tuberosity bilaterally, inertial sensors (Xsens) placed on the medial surface of the tibia, and an ActiGraph activity tracker on the nondominant hip.	2017	Significant findings in duration and distance in the T25FW, Timed Up and Go Test (TUG) and 6MW were demonstrated in moderate and severe groups of MS. Additionally, Biostamp sensors accurately measured step and stride time when compared to Xsens sensors, while swing time was less accurate.

3.2. Results

The direct impact of fatigue on gait pathology and deterioration in pwMS using wearable sensor technology has been investigated in a limited number of studies. In the 10 papers in this review, measures of ambulatory fatigue with the following sub-sections were explored. These measures included spatial-temporal parameters, joint ROM, and the use of DTW for the detection of gait fatigability.

3.2.1. Spatial and temporal gait parameters and its relationship to ambulatory fatigue

Spatial (distance covered) and temporal (time) parameters are the most common measurements of gait that typically include walking speed, stride time and length, step time and length, and durations of stance and swing phase [Al-Obaidi et al., 2003]. In pwMS, spatiotemporal parameters have been investigated to understand patterns and changes in gait with fatigability. Although dependent on the degree of disability [Shema-Shiratzky et al., 2019], gait deterioration increased stride time and decreased step time throughout the 6MW [Moon et al., 2017; Shema-Shiratzky et al., 2019].

Moon et al. [2017] used three types of wearable sensors to calculate step count, temporal parameters, and the angular velocity (ω) of the shank in four groups (mild, moderate, and severe MS, plus a control group). Findings indicated that participants with EDSS scores of 2.5 and above were more likely to experience fatigue that influenced ambulatory dysfunction [Moon et al., 2017]. Participants in the mild group showed no significant differences in gait compared to the control group. However, the duration and distance in the T25FW, TUG, and 6MW were significant in the moderate and severe groups (at a comfortable, slow, and fast speed of walking). It should be noted that a treadmill was used to assess ambulation in this study, which may have resulted in miscellaneous data, compared to overground walking experiments.

Shema-Shiratzky et al. [2019] found only aspects of gait parameters significantly changed over the course of the 6MW. Distinct gait patterns of deterioration in cadence and sample entropy (complexity of the gait acceleration signal) were identified in both mildly and moderately disabled pwMS. Furthermore, step and stride regularity were significantly diminished throughout the 6MW in the moderately disabled, compared to the mild group. Step and stride regularity variability was most significant in minute five, while gait asymmetry became significantly worse during the last minute of the test [Shema-Shiratzky et al., 2019]. This could indicate changes to walking instability that may be generated by fatigue. However, this was not observed by the researchers [Shema-Shiratzkty et al., 2019]. Although Shema-Shiratzky et al. [2019] noted a significant change in cadence, this was inconsistent with previous literature. Motl et al. [2017] detected no changes of cadence through the 6MW in a cohort of 96 pwMS ranging from mild to severely disabled whereas, agreeing with Shema-Shiratzky et al. [2019], a pilot study found a significant reduction between the first and last ten gait cycles during the 6MW [van der Linden et al., 2018].

In a normal gait, individuals are expected to complete regular and successive gait cycles that are similar in length [Qureshi et al., 2016]. In pwMS, sustained walking often causes fatigue that creates a slower walking velocity, which ultimately influences gait variables. Qureshi et al. [2016] studied the relationship of gait speed and cycle length variability during the 6MW with wearable BSN nodes. Gait cycle length and speed were higher in participants who reported perceived fatigue, compared to those who reported minimal fatigue. The authors identified that participants who scored higher in MFIS were more likely to reduce in gait velocity and complete an unequal length of gait cycles during the 6MW [Qureshi et al., 2016]. Nonetheless, the gait variables of participants who scored under the median score of MFIS did not significantly change in gait parameters [Qureshi et al., 2016].

In one study, the secondary gait compensations of unfatigued and fatigued individuals were explored, to determine whether head and pelvis movements of stride and step time, sway area, and asymmetry of both areas were affected differently [Psarakis et al., 2018]. The researchers observed a significant decline in walking speed and cadence during the 6MW, with an average 10.3% reduction in speed between the first and last laps. Although the findings were not significant (except head sway variability), there was a deterioration in measures of gait variability, asymmetry, compensations, and stability in the pwMS during execution of the 6MW, whilst the control group improved. For pwMS, the affected leg emphasised greater compensatory movements in the head and pelvis during the swing phase in comparison to the unaffected leg [Psarakis et al., 2018]. These unstable movements of the head and pelvis were assumed to be caused by lower limb muscle weaknesses and joint contractures. Although currently still debated, common dysfunction from foot and ankle ROM is more likely to result in compensation strategies that increase pelvic tilt and head sway variability [Brodie et al., 2015; Schmid et al., 2013]. Such gait compensations could generate and increase gait energy output in pwMS, which ultimately could cause or contribute to fatigability in ambulation.

Morris et al. [2002] researched the changes to temporal and spatial variables of gait and fatigue over a five-hour period using a clinical stride analyser placed on the foot. Participants were instructed to walk along a 10m walkway four times in the morning, then again in the afternoon, to identify any gait changes. This was based on the assumption that fatigue is more present in the afternoon than in the morning. The findings showed little change in any of the gait variables in pwMS, with only a small increase in speed, stride length, and cadence. The patterns of gait showed little variability from morning to afternoon with symmetric, short-stepped, and slow footsteps [Morris et al., 2002]. The nonsignificant changes could be a characteristic of practice effects that have been seen in other gait studies, although the type of walking task used should also be considered for measuring ambulatory fatigue [Morris et al., 2002; Schubert et al., 1998]. Footstep patterns did not significantly change, even though perceived fatigue significantly increased from the morning to the afternoon [Morris et al., 2002]. Similarly, Krupp et al. [1988] and Schwartz et al. [1996] found no direct relationship between ambulation and subjective fatigue. Although participants perceived fatigue to increase in the afternoon, the findings indicated that the mechanisms regulating perceived fatigue are different from the motor control mechanisms regulating human locomotion [Morris et al., 2002]. Furthermore, the use of self-reported fatigue measures relating to motor performance could confuse judgments regarding pwMS' actual physical ability.

In studies by Qureshi et al. [2016], Shema-Shiratsky et al. [2019] and Moon et al. [2017], speed, step length, and step time were significantly associated with EDSS score. This may indicate simple biomarkers of gait severity in pwMS [Vienne-Jumeau et al., 2019]. However, improved gait algorithm detection is needed to provide consistent results throughout [Vienne-Jumeau et al., 2019]. Gait changes in spatial and temporal parameters from the morning to the afternoon seem unapparent. However, the perception of fatigue does significantly change, suggesting either the type of objective measurement used was inappropriate, or the perception of fatigue is a different construct to fatigability [Morris et al., 2002]. Gait mechanics and compensations should be further be explored so that the mechanisms behind gait compensations and the changes that are caused by fatigue can be understood [Psarakis et al., 2018].

3.2.2. Range of motions (ROM) and its association with ambulatory fatigue

It has been reported that a decrease in joint ROM in the lower extremity is likely to occur as ambulatory fatigue arises throughout the execution of the 6MW [McLoughlin et al., 2016]. In a few studies, authors have identified this through the use of wearable sensors [Motta et al., 2016; Taborri et al., 2019].

Motta et al. [2016] investigated lower limb gait kinematics during a one-minute walk to assess disability and fatigue in pwMS. The data was interpreted by capturing the angle curves related to each stride in the sagittal plane of magneto-inertial measurement units (MIMUs) placed on the pelvis, thigh, shank, and ankle to calculate the ROM of hip, knee and ankle in each leg. Calculations of ROMs, gait variability, and asymmetry were performed, and correlations were explored in attempt to find an independent measure for disability. The overall gait variability was calculated by the sum of all ROMs related to each joint of both legs: the higher the gait variability value – the motor performance index (labelled E in the study) – the higher the variability of gait. A reduction in ROM at the hip, knee, and ankle was found in pwMS, compared to a control group. Notably, gait variability (E) and hip ROM were the most significant from the MS compared to control group. ROM in the hip was significantly correlated with walking speed and the pyramidal functional score (as part of the EDSS). The E value was correlated to EDSS and self-reported measures that were suggested to likely assess overall disability [Motta et al., 2016]. The authors suggested that hip ROM and motor performance index (E) together could be used to identify motor impairment and classify patients with MS into fatigue and non-fatigued groups better than validated questionnaires [Motta et al., 2016]. If confirmed in a larger cohort and over the course of a longer walking task (2MW or 6MW), the measurement could be used for monitoring disease course and disability in RRMS.

In a 2019 study, Taborri et al. investigated lower limb kinematic changes throughout the 6MW, evaluating ROM decrements between the first and remaining five minutes. They assessed nine participants with RRMS who were able to walk unaided, and compared gait kinematics to a control group. Similarly to Motta et al. [2016], the sagittal angular velocity of each sensor was used to identify the first minimum value followed by the first maximum value of the filtered signal of stride. These were then divided into each minute to explore the change of ROM of the joint curve angles and any changes throughout the 6MW [Taborri et al., 2019]. All but one participant in the RRMS group displayed a lower ROM value throughout the execution of the task in the hip, knee, and ankle. There was a larger range of maximal difference in RRMS participants (2.8-3.5 degrees) compared to the control group (1.5-1.6 degrees). The average knee joint ROM values were significantly different from minute one to minutes three, four, five, and six, with all ankle ROM values significantly different compared to control participants

[Taborri et al., 2019]. However, the hip joint only showed a significant difference from minute one to six. The results highlight a difference in ROM compared to the healthy population, and the ankle joint illustrates significant decrement as early as the second minute of continuously walking [Taborri et al., 2019]. The significant results of the ankle were anticipated, as the effects of the tibialis anterior muscle have previously been reported as susceptible to activity reduced fatigue in pwMS [Kelleher et al., 2010]. As highlighted by Motta et al. [2016], the ROM for all lower limb joints can be considered a useful parameter for assessing fatigability in walking. However, this research should be reproduced using a larger sample size to produce accurate and consistent results.

3.2.3. Dynamic time warp (DTW) and its relation to ambulatory fatigue

Engelhard et al. [2016] explored the deterioration of a fatigued gait during the 6MW by calculating the warp score. The DTW is an algorithm used to measure two time-related sequences which may vary in speed [Keogh & Ratanamahatana, 2005]. Typically, it is used to overcome signal distortions. However, the distortions for Engelhard et al. [2016] in their study were measured to calculate the stretch and the warp score, which were manifested as gait pathology, instead of signal distortions. Gait cycles from the first and second minutes were used as a baseline to then compare to later minutes of the 6MW [Engelhard et al., 2016]. Measurable gait deterioration emerged in minutes three to six, demonstrated by the warp score and strong correlations to MSWS-12 and MFIS physical sub-scores. Moderately disabled participants followed a pattern of increasing warp scores after minute three, with a corresponding correlation with the MSWS-12. PwMS in the mild group were more likely to exhibit similar results to the control group, except for a sharp increase in warp score in minute six [Engelhard et al., 2016]. Gait deterioration appeared earlier in the moderate and severe group compared to the mild group [Engelhard et al., 2016].

Additionally, Dandu et al. [2016] sought to understand the physiological significance of the DTW distance and warp score for the assessment of gait pathology in pwMS. The DTW and warp score were used to assess correlation with gait features with linear and stepwise regression models. Six models were examined to explore gait features and walking speed in relation to clinical measures of EDSS, MSWS-12, and MFIS. Both physiological features improved the prediction of MSWS-12, MFIS, and EDSS scores, and showed a distinct physiologic significance compared to walking speed [Dandu et al., 2016]. DTW distance and warp score were shown to measure physical fatigue, with the warp score also measuring balance.

In their articles, Dandu et al. [2016] suggested their model, and Engelhard et al. [2016] their objective measure, as means to develop gait pathology and assist in determining ambulatory fatigue. Although the DTW is typically not used for gait pathology, Engelhard et al. [2016] and Dandu et al. [2016] propose promising alternative approaches in the detection of ambulatory deterioration which, with further study, could facilitate other measures and the overall monitoring and identification of MS gait characteristics in fatigue.

3.3. Discussion

In this review, the use of wearable sensors for the assessment of fatigability in gait parameters for pwMS was explored. Overall, there was agreement between authors that the higher the disability level in MS, the poorer their gait performance [Shema-Shiratzky et al., 2019; Motta et al., 2016; Psarakis et al., 2018; Vienne-Jumeau et al., 2019; Engelhardet al., 2016]. Nonetheless, not all gait parameters responded to fatigability walking tasks; this was dependent on the disability level.

Individuals with a mild disability typically demonstrated little to no significant changes in gait behaviour, mostly showing similar results to control groups in spatial-temporal and ROM parameters [Motta et al., 2016; Moon et al., 2017; Engelhard et al., 2016]. However, in one study, a sharp increase in warp score in the DTW in minute six of the 6MW in the mild group was detected, indicating a small degree of gait deterioration. Moderate and severe groups demonstrated a significant difference in walking velocity, distance, cadence, and warp and DTW distance scores, compared to mild and control groups [Motta et al., 2016; Moon et al., 2017; Engelhard et al., 2016]. Gait deterioration in both moderate and severe groups appeared early in the 6MW, compared to the mild group [Engelhard et al., 2016]. The categorisation for disability severity measured by the EDSS did vary across studies: mild (< 2.5, 2-3.5), moderate (3-4.5, 4-6), and severe (5-6.5). This could impact the accuracy of comparison between studies, influence the interpretation of data, and lead to unreliable results.

Only Morris et al. [2002] explored changes in ambulatory fatigue from the morning to the afternoon, involving a repeated 10m walkway task. The nonsignificant results of objective fatigue could indicate that fatigue has multiple constructs; subjective and objective fatigue may have different mechanisms, that of locomotion and regulating perceived fatigue [Morris et al., 2002]. Alternatively, this may highlight that only perceived fatigue displays an increase in fatigue in the afternoon, whereas motor performance is unaffected. However, as the authors state, the results could have been from practice effects or the type of measurement used. If a longer walking task was conducted, the results may have differed.

The most widely used measure of fatigability in gait was the 6MW [Goldman et al., 2008], however other tasks such as the 2MW, one-minute walk, and repeated measures of the TUG and T25FW were also used [Motta et al., 2016; Moon et al., 2017; Scalzitti et al., 2018]. Minute-by-minute assessment of gait parameters seems to be a promising approach to observe changes of gait features of fatigability over a sustained time; however, few studies have performed this [Qureshi et al., 2016]. A few studies highlight the correlation of the 6MW and 2MW, however, question the appropriate nature of assessing fatigue with only 2MW of walking for all gait parameters [Engelhard et al., 2016; Taborri et al., 2016]. As Taborri et al. [2016] demonstrated, only the ankle joint displayed ROM decrement in the second minute of walking, therefore it might not be useful to evaluate other gait changes in higher areas of the body. Even so, for pwMS with highly ambulatory impairment (EDSS > 5), the 6MW may be considered burdensome, therefore, the 2MW may be more appropriate for evaluating gait changes. However, this is dependent on disability level: Engelhard et al. [2016] observed a change in warp score and indication of gait deterioration only in the last minute of the 6MW in individuals with a mild disability. This raises the question: would walking tasks even longer than the 6MW elicit fatigue in individuals with a mild disability and enable a fuller understanding of fatigability for that severity group?

Researchers have highlighted that individuals who take six to eight seconds to complete the T25FW are more likely to need assistance with daily activities and use a cane. This provides useful information on the ambulatory and occupational status of pwMS. Likewise, individuals who take eight seconds or longer experience additional difficulties with ambulation dysfunction, occupation, and social activities [Goldman et al., 2013]. Short, simple walking tasks can provide valuable information about walking speed and functional ability. These should be used in conjunction with longer walking tasks, such as the 6MW, to fully comprehend the effects of fatigue.

The type of environment/surface used to perform these tasks on differed between the studies. Moon et al. [2017] used a treadmill that offered additional support through handrails, which allowed a degree of perceptive and physical support. However, a treadmill uses controlled speeds and may not be an ideal representation of real-life walking [Moon et al., 2017]. Other tests used overground walking in corridors and laboratories with a designated walkway [Morris et al., 2002; Engelhard et al., 2016; Psaraskis et al., 2018; Taborri et al., 2019; Shema-Shiratzky et al., 2019; Dandu et al., 2016]. Although this represented real-time walking, walkway lengths varied, and in some studies, involved turns. This made comparison between studies more difficult and additional analysis was required to deduct turns.

Moon et al. [2017] compared the accuracy and precision of temporal gait parameters of two sensors. BioStampRC was compared to MTx Xsens sensors in the T25FW, TUG, and 6MW and Bland-Altman plots were produced for graphical comparison [Moon et al., 2017]. The skin mounted sensor (BioStampRC) demonstrated highly accurate calculations of stride and step time when compared to inertial sensors (Xsens). However, swing time calculations were less accurate. Considerations were made regarding the detection of heel strike and toe-off in the algorithms, as the discrepancy of sensor thresholds may differ in the choice of sensor and therefore might affect the results and precision of gait parameters for the detection of fatigue. This further highlights the importance of the type of technology and measurement used for assessing fatigue in pwMS, as different technologies can produce different outcomes. Although finding the most reliable and accurate technology and measurement will provide a more granular assessment of fatigue and gait, a common or gold standard must be established for all levels of disability to reduce variable results. This will allow for greater sensitivity in detecting gait deterioration and meaningful comparison between studies.

3.3.1. Limitations

Most studies had a small sample size which can increase bias and decrease generalisability. Although there were attempts to follow standard protocol and procedure, in a few studies there was variation in the way tests were conducted (for example, using a walkway compared to a treadmill). As stated previously, this may have impacted results, as different walking surfaces may alter gait characteristics; increases in cadence and reduced knee angle motion compared to overground walking have previously been reported [Riley et al., 2007; Spain et al., 2012]. This impacts the sensitivity of direct comparisons between studies and should be considered when performing gait analysis in any population.

Another limitation is the positioning of the sensor. This can be crucial in human kinematic observation in relation to sensitivity and reliability on the specific body part, as well as the specific angle and positioning of the sensor on that body part. Lower back signals provide different readings to a sensor located on the ankle, due to the biomechanical movement and locomotion of an individual wearer. Furthermore, the specific positioning of a sensor in relation to gyroscope signals could be affected by noise and artefact [Greene et al., 2010].

Lastly, the phenotype of MS was not disclosed in all studies. Considering fatigue is reported to be greater in progressive MS, this could impact the significance of results and cause bias in studies [Ghajarzadeh et al., 2013; Kaya Aygunoglu et al., 2015; Kroencke et al., 2000; Mills & Young, 2010; Pittion-Vouyovitch et al., 2006; Razazian et al., 2014].

3.4. Conclusion

Researchers have identified deterioration of gait through DTW warp score, step length, cadence, and ROM of lower extremity joints with wearable sensor technology. However, there is currently no widely recognised or gold standard for the measurement and assessment of ambulatory fatigue. Additionally, different disability severities exhibit fatigue through different durations of sustained walking. Experimental tasks which take this into account should be conducted: individuals with an EDSS score below three may need to perform longer sustained walking tasks to elicit fatigue, in comparison to individuals who have an EDSS score of five and over.

Research highlights the usefulness and potential for wearable sensor data in the extraction of gait parameters as biomarkers of fatigability in the MS population [Qureshi et al., 2016]. However, it is still unclear from the literature which specific gait parameters measure fatigue in pwMS most rigorously. Reliability, validity, and sensitivity tests should be performed to validate clear and widely used objective markers of ambulatory fatigue.

It should be noted, although studies aim and should aim towards statistical significance in research, clinical significance should be considered and highlighted in ambulatory fatigue studies also. To clarify, statistical significance is ruled by the p-value and confidence intervals where typically $p<0.05$ means there is a statistical significance between comparisons. This indicates the results are unlikely to have occurred by chance, however, it doesn't necessarily indicate the importance of the difference or how meaningful it is for patients, the clinical significance. A clinical significance is the practical importance of an assessment or treatment, and whether it has a real, palpable effect on daily life. For example, if a study finds a safe treatment that could reduce foot drop in pwMS that makes a difference to their gait and how long they could walk for, this would be clinically significant as it makes a positive and noticeable improvement to pwMS. However, it doesn't necessarily have to be statistically significant. Clinical significance should be reiterated in all patient-orientated studies as it is demonstrates equal importance to statistical significance for palpable impact.

A set of objective tools for the assessment of ambulatory fatigue in MS is important, as the most widely used assessment in a clinical setting is currently based on an individual's self-assessment [Krupp et al., 1989; Motta et al., 2016]. It has been suggested that self-reported measures of physical fatigue potentially confound awareness of an individual's walking ability. Identifying ambulatory biomarkers with objective measurement would help us discover the "how" and "why" pwMS fatigue whilst walking. Validated objective measurements could assist in monitoring ambulatory fatigue and further contribute to and support management interventions of fatigue and gait impairment in clinical and physiotherapy settings.

To explore ambulatory fatigue through multiple facets, subjective and objective aspects should be used to incorporate a multi-disciplinary approach and understanding. This will improve the measurement and monitoring of MS fatigue, and support interventions designed to improve fatigue and ambulation for pwMS, helping with everyday living. In the following chapter, the current understanding of subjective and objective fatigue is explored.

Chapter Four: The current understanding of, and relationship between, physiological measures and experiential views of MS fatigue

Capturing fatigue parameters of MS can be difficult, considering the multifaceted nature of the phenomenon. In this chapter, an overview of literature highlighting the relationship between physiological measures and experiential views of fatigue is presented. The wide array, descriptions, subjective and objective manners of fatigue cause measurement to be problematic. It is argued that the current clinical measurements cannot always capture fatigue as a whole with the day-to-day variations of fatigue, and therefore, can be misused and misinterpreted in the assessment and monitoring of MS fatigue [Beckerman et al., 2020; Dittner, Wessely, & Brown, 2004]. Although the investigation on the direct relationship, and the similarities and differences of both viewpoints are limited, this chapter will establish and outline the current relationship.

The chapter is separated into the following sections: fatigue as experienced and reported, and its relationship to longer ambulatory tasks; feelings of fatigue and their association to shorter ambulatory tasks; self-reported measures of fatigue and their association with gait parameters. The literature indicated a degree of congruity between descriptions of fatigue and ambulatory fatigue; however, they remain weak and inconsistent. Fatigue is an unstable phenomenon and still relies heavily on the perceptions of fatigue for measurement. It is unclear whether fatigue directly affects walking or vice versa. The chapter further illustrates the uncertain congruence between fatigue and fatigability and further addresses the significance and rationale for this PhD (see section 5.1.).

4.1. Introduction

From a pathophysiology outlook, MS fatigue is a complex phenomenon that is suspected to involve immune, endocrine, axonal loss, and cytokine factors in the body [MacAllister & Krupp, 2005]. Its complexity is demonstrated through the existence of over 250 instruments developed to measure fatigue [Hjollund et al., 2007]. In numerous studies, researchers have highlighted the complexity of fatigue and the challenge in explaining it through the use of one scale or measurement.

There is currently no “gold standard” for the measurement of fatigue in MS. Nevertheless, the most widely used and recognised measurement is typically expressed in patient-reported outcome measures of a physical, cognitive and psychosocial domain that rely on the descriptions of fatigue [Beckerman et al., 2020]. The FSS and the MFIS are the most frequently used in research to measure how fatigue is experienced [Krupp & Elkins, 2000].

As outlined in Chapter One, fatigue is predominantly described as a “subjective” symptom that impacts an individual’s awareness of physical and/or mental energy to perform desired tasks and activities [Mills & Young, 2008]. Throughout the years, researchers have attempted to measure fatigue through the lens of pwMS and quantify it effectively [Wolkorte et al., 2015; Krupp & Elkins, 2000; Engelhard et al., 2016; Dalgas et al., 2018].

In some disciplines, researchers express the need to quantify fatigue and establish physiological measurements to efficiently assess and monitor fatigue in MS. Researchers have attempted to measure fatigue using tests with single-joint isometric muscle contractions [Wolkorte et al., 2015], repeated quadricep contractions [Andreasen et al., 2009], and the 6MW with gait analysis technology [Engelhard et al., 2016]. However, results are varied.

Physiological measurements of fatigue and fatigability performance are intended to provide an accurate index of an individual’s functional status [Bertrand & Willis, 1999]. According to Goverover et al. [2005], physiological measurement can be justified, as obtaining an accurate evaluation of pwMS’ everyday competency through self-reported or real-time measures of fatigue can be challenging. Nevertheless, there are issues related to the significance, reliability, and validity of physiological measures of fatigue. Fatigability can be divided into ambulatory or muscle contraction tasks that measure fatigue through continuous and sustained exertion. In numerous studies, researchers have investigated fatigability in MS to assess changes to motor function [Dalgas et al., 2018; Goverover et al., 2005; Severijns et al., 2017; Surakka et al., 2004]. Nonetheless, there is no clear consensus on which measurement/s accurately capture fatigability, and existing measures often fail to distinguish between the facets of fatigue as there is no direct comparison between the different protocols of motor fatigability [Severijins et al., 2017].

Ambulatory impairment is highly prevalent and is commonly experienced by pwMS [Hobart et al., 2001]. According to Weinshenker et al. [1989], two-thirds of pwMS progressively decline in ambulatory ability and do not retain the ability to walk 20 years after diagnosis. As reported in Chapter Three, ambulation remains considerably important for pwMS, as it provides a sense of independence and autonomy. Understanding the relationship between fatigue and ambulation, and how fatigue and fatigability are presented and affect an individual's gait, will assist in clinical management and rehabilitation [Kalron, 2015]. Furthermore, the congruence between fatigue as experienced and physiological fatigue remains unclear in the literature. Fatigue has been operationalised and broken down into constructs that only provide a partial view of fatigue. Thus, the whole phenomenon of fatigue has often been buried and not given due consideration. In this chapter, previous studies that have explored multiple aspects of fatigue will be discussed, in an attempt to illuminate fatigue and to figure out how to monitor the whole phenomenon of fatigue.

4.2. Fatigue as experienced and reported, and its relationship to longer ambulatory capacity tasks

Walking capacity tests employ the 6MW or the 2MW to exert pwMS and assess their ambulatory fatigue. However, the association between fatigability performance in ambulation and the descriptions of fatigue through self-reported measures have reported only weak to moderate associations [Dalgas et al., 2014, 2018; Hebert & Corboy, 2013; Kempen et al., 2012; Motl et al., 2012, 2013; Nogueira et al., 2013; Sacco et al., 2011].

In a recent study, Dalgas et al. [2018] explored the relationship between the “subjective impact of fatigue” and walking capacity, as well as the “perceived walking ability” from self-reported measures in a cohort of 189 mild to moderately disabled pwMS. There were significant but weak negative correlations between the 6MW distance walked and both the MFIS total score and MFIS physical sub-score (r = -0.14 and r = -0.30, respectively). This suggests that the higher the score of self-reported fatigue, the less distance covered during the 6MW. However, the authors concluded that the self-reported fatigue impact measure does not explain the variance in walking capacity tests due to weak correlations [Dalgas et al., 2018]. Similarly, in a small sample (n = 17) study, Hebert & Corboy [2013] reported a moderate negative correlation between the 6MW and MFIS physical sub-scores (r = -0.53) whilst investigating the association between fatigue and balance as a function of central sensory integration. There was also a moderate negative correlation between 6MW and MFIS psychosocial sub-scores (r = -0.51), which suggests that the further participants walked, the less social and behaviour factors influenced their walking ability.

Interestingly, Goldman et al. [2008] found moderate positive correlations between the 6MW and both MFIS total scores (r = 0.59) and MFIS physical sub-scores (r = 0.66) in 40 participants. These findings differ from other studies that determined weak associations between fatigue as reported by pwMS, and fatigue as measured. The experimental design may be one likely explanation for this. Participants in the Goldman et al. [2008] study were required to complete the questionnaires in between several 6MW tasks. The time of completion could have caused biased results due to the increased likelihood of real-time sensations of fatigue after performing a 6MW.Conversely, participants in the Dalgas et al. [2018] completed the questionnaires before the 6MW. This may affect the extent to which the two studies can be compared, with some participants completing questionnaires from memory, and others under the real-time sensations of fatigue.

Alvarenga-Folho et al. [2014] conducted a study that used 6MW to evaluate multiple aspects of fatigue in individuals with RRMS without disability (EDSS scores of 0-1.5). In the study, pwMS exhibited a decline in total distance walked compared to the control group. However, no relationship between MFIS scores and 6MW distance was observed. A univariate analysis highlighted no relationship between the subjective outlooks of fatigue of physical, cognitive, and social sub-domains of 6MW, or between the distance covered in the last minute of 6MW and descriptions of fatigue. The authors determined that descriptions of fatigue rose independently from disability. Alvarenga-Folho et al. [2014] concluded that the 6MW does not demonstrate motor fatigue in pwMS without neurological disability (EDSS scores of 0-1.5).

The MFIS, FIS, and 6MW are established within the literature as measures of MS fatigue. Nonetheless, there are variations between studies in the correlation and association of self-reported measures with 6MW metrics. Inconsistencies could be due to experimental design, level of disability, and/or phenotype. This highlights the need to adapt these methods, develop consistent measures, and establish a clear relationship between the descriptions of fatigue and fatigue as experienced.

4.3. Feelings of fatigue and their association with shorter ambulatory tasks

Researchers have also explored the relationship between subjective outlooks of fatigue and walking capacity tests of shorter distances such as the T25FW, 10MW, and TUG [Dalgas et al., 2018; Huisinga et al., 2011; Kalron, 2015; Nogueria et al., 2013]. In a study by Nogueira et al. [2013], pwMS walked at a comfortable speed for the 10MW, and there was a significant negative correlation between distance walked and MFIS total scores (r = 0.42). Similarly, authors of similar studies have reported a significant relationship between walking velocity and descriptions of fatigue measures from self-reported questionnaires. This highlights a decline in walking speed when pwMS experience greater fatigue [Huisinga et al., 2011; Kalron, 2015]. Huisinga et al. [2011] also observed associations between QOL measures and walking. The authors hypothesised the central neural drive affects both gait and fatigue, and this may influence an individual's subjective outlook of fatigue on walking speed. However, the mechanisms involved are not clearly understood [Huisinga et al., 2011].

Dalgas et al. [2018] found significant correlations between all walking tasks (6MW, 2MW, 10MW at a usual and fast speed (10MWf and 10MWu), T25FW and TUG) and MFIS physical sub-scores, after adjusting for sex, age, weight, and height. A weak but significant association between the TUG test and MFUS psychosocial properties was also observed [Dalgas et al., 2018]. Measures of balance, coordination, and lower extremity muscle strength are also incorporated in the TUG. Therefore, it is not a true measure of walking and may not be relevant for the direct assessment of walking capacity [Dalgas et al., 2018; Podsiadlo & Richardson, 1991]. From multivariate regression analyses, Dalgas et al. [2018] determined that age impacted both general fatigue, physical fatigue impact, and walking ability. Age is a considerable factor in fatigue, and in other factors influencing the management of MS. Nevertheless, Dalgas et al. [2018] suggested that some studies could be influenced by age, as it is seen as a dimension that can substantially affect fatigue, and should be more carefully considered in research [Dalgas et al., 2018; Podsiadlo & Richardson, 1991].

Overall, decreased walking velocity and the maintenance of walking could result in increased energy expenditure and would likely affect performance in everyday activities causing increased overall fatigue. Shorter walking tests, including the T25FW and 10MW, measure neurological impairment in relation to gait speed, which does not directly measure fatigability [Kempen et al., 2011; Rossier & Wade, 2001]. Considering this, shorter walking capacity measurements can provide interesting and valuable information for fatigue and ambulation. However, this will not drive forthcoming research for identifying ambulatory fatigue alone, although it will provide useful information on walking ability in conjunction with other fatigability tests.

4.4. Self-reported measures of fatigue and the association to gait parameters

As discussed in Chapter Three, gait dysfunction and disturbances are commonly reported in pwMS [Sacco et al., 2011]. Fatigue as experienced and fatigability components are known to impact a pwMS' gait and its characteristics, although the direct association between gait characteristics and parameters remain inconsistent [Sacco et al., 2011; Kalron, 2015; Morris et al., 2002; Schwartz et al., 1996]. Kalron [2015] investigated the relationship between definite parameters of gait and self-reported measures in pwMS. The author explored the exact impact of fatigue on gait by assessing spatiotemporal parameters compared to subjective reports of the MSWS-12 and MFIS. In moderately disabled pwMS, there was a moderate positive correlation between MSWS-12 and self-reported fatigue ($r = 0.54$), as well as a significant negative correlation between step and stride length ($r = -0.32$) [Kalron, 2015]. Although fatigue correlated with five out of 14 spatiotemporal parameters, all correlations were $r < 0.35$, which are considered weak associations. The authors identified fatigue and its association to self-reported walking capabilities (MSWS-12), but only weak to no associations to spatiotemporal parameters [Kalron, 2015]. Morris et al. [2002] found similar results with walking parameters whilst investigating morning to afternoon measurements of fatigue and fatigability. Although pwMS demonstrated reduced walking velocity, stride length, and produced twice the variability in gait performance compared to the control group, the ambulatory parameters remained similar in the morning and afternoon measurements [Morris et al., 2002]. The authors speculated that these results suggested ambulatory mechanisms regulating human locomotion are different from those regulating perceived fatigue.

In another study, there were significant findings from self-reported questionnaires and the discrepancies in walking velocity in ankle power generation, peak knee extensor torque[13] , and knee power absorption at different phases of the gait cycle [Huisinga et al., 2011]. The four out of 30 associations between gait mechanics and self-reported measures indicated a lack of correlation. However, this suggests alterations in joint torques are likely to change the energy expenditure during walking. This may indicate a relationship between gait mechanics and fatigue, although the associations were limited. The authors further discussed the use of self-reported questionnaires in motor function performance and fatigability, and recommended these should not be used in isolation as indicators of motor disability [Huisinga et al., 2011].

In Sacco et al.'s [2011] study, significant negative correlations were found between the physical sub-score of the Wurzburg Fatigue Inventory for pwMS, and both cadence ($r = -0.44$) and stride length ($r = -0.5$). The authors also noted a significant improvement after a three-week rehabilitation programme, where individuals were able to actively engage in a degree of

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[13] Torque is a rotational force that can cause an object to rotate about an axis.

exercise without increasing their levels of fatigue [Sacco et al., 2011]. Although gait parameters demonstrated a significantly lower gait velocity, cadence, and a shorter step and stride length compared to the control group, persistent worsening of fatigue through exercise and physical rehabilitation was not expected [Smith et al., 2006]. The authors concluded that the negative correlation between fatigue and gait impairments may indicate a negative impact on rehabilitation outcome [Sacco et al., 2011].

The difference between limbs in terms of stance, single support, and step time has also been investigated in relation to fatigue [Kalron, 2015]. In the study, Kalron discovered an increase in variance in the parameters by an estimated 10%, and demonstrated gait asymmetry and its association with lower balance levels. The author suggested the exacerbation of fatigue as experienced could be due to the fear of loss of balance, which impacted upon stress levels and mental state in pwMS. Nonetheless, this is only a hypothesis and needs further research to assess indicators of fatigue triggers. In contrast, Alvarenga-Filho et al. [2014] have concluded that subjective outlooks of fatigue occur independently to neurological impairment and disability, such as walking function and ability.

4.4.1. Modified Fatigue Impact Scale and Multiple Sclerosis Walking Scale-12, and the congruence with gait parameters

The relationship between MFIS and MSWS-12 seems consistent in the literature, with numerous studies indicating a stronger association between MSWS-12 and MFIS compared to all other objective measures of walking [Kalron, 2015; Dalgas et al., 2018; Learmonth et al., 2013; Nogueira et al., 2013]. Kalron [2015] found the subjective ratings of fatigue in the MSWS-12 explained 30% of the variance in fatigue. A moderate correlation of 0.54 was determined, whilst it was not possible to establish significance in of the most spatiotemporal parameters [Kalron, 2015]. In a study by Dalgas et al. [2018], reported experiences of walking in MSWS-12 explained 24 to 40% variance of general and physical fatigue, respectively.

The most significant finding was drawn from a study by Learmonth et al. [2013]. The authors collected data from 86 pwMS, and found a strong correlation between descriptions of self-reported physical, cognitive and psychosocial fatigue, and self-reported walking disability was ($r = 0.76$). These findings may be explained by the MSWS-12 questionnaire that compiles diverse elements of walking, including areas of effort and concentration, in relation to walking ability. Consequently, stronger associations of self-reported fatigue in all areas of fatigue are increasingly likely to occur [Dalgas et al., 2018].

4.4.2. Real time patterns of fatigue and the congruence to gait parameters

Heine et al. [2016] explored the association between real-time patterns of fatigue and self-reported fatigue questionnaires. Although both measures are self-reported measures of fatigue, real-time assessment has the advantage of recall bias, and better reflects fatigue as experienced and daily fluctuations [Kim et al., 2010; Stone et al., 2005]. It can be seen as more valuable in individuals experiencing cognitive dysfunction, like pwMS [Kim et al., 2010; Stone et al., 2005]. The real-time patterns were assessed using SMS automated messages four times throughout the day, asking pwMS to rate their fatigue from 0 (no fatigue) to 10 (severe fatigue). Alongside this, three questionnaires were used at baseline (checklist individual strength (CIS), FSS, and MFIS). The authors found a poor association between fatigue questionnaires and real-time scores, with only 6% variance [Heine et al., 2016]. The authors suggested that the model of real-time scores may provide a better description of individual variations for daily patterns in MS fatigue, as it holds no limitation to a bias of reflectivity. It could, however, highlight that daily time points of fatigue lack convergent validity in comparison to fatigue questionnaires, and may not be a valid measure. In addition, measuring a single time point may not sufficiently measure fatigue and encompass its multifaceted nature. On the contrary, conventional fatigue measures could not accurately assess the day-to-day fatigue experience. Overall, although there was a poor association between results in real-time fatigue scores and the conventional fatigue questionnaires used. Sleepiness was found to be an important confounder between the two, indicating the importance of severity of sleepiness for perceived fatigue in MS [Heine et al., 2016].

Overall, there are limited spatiotemporal associations with self-reported fatigue that pwMS experience. The literature on the relationship between gait characteristics and fatigue remains somewhat controversial. Descriptions of self-reported physical, cognitive, and psychosocial factors of fatigue and self-reported walking ability are more consistent and convey a stronger relationship. However, both are reported by pwMS themselves as a form of a subjective outlook. Therefore, this only offers one outlook of fatigue: the individual's outlook. Universally, pwMS describe fatigue as feeling worse as the day progresses, with levels of fatigue considerably higher in the afternoon. However, Morris et al. [2002] found no significant difference in physiological parameters of fatigability.

4.5. Limitations in previous studies

Discrepancies in the literature regarding the comparison and relationship between fatigue as described and physiological measures of fatigue may be due to the differences in tests of the performance of fatigability and subjective assessment [Dalgas et al., 2018]. A direct comparison of studies is not applicable to all studies, as measurements assess different aspects of fatigue that can determine different results. Additionally, consideration of the experimental design could also impact and influence results in relation to the dependent and independent variables, the experimental setup, and protocol [Dalgas et al., 2018]. As discussed previously, pwMS are more likely to fatigue as the day progresses, therefore the time of day the experiments are performed should be considered as an impacting factor.

Dalgas et al. [2018] reported conflicting thoughts on the dependent variable in ambulatory fatigue studies and whether walking or fatigue is the dependent variable. The independent variable is a variable that is changed or controlled to explore the direct effect on the dependent variable. Therefore, is important to determine both in studies. Although both variables could be dependent variables when investigating fatigue and gait, one could argue that the dependent variable is fatigue in the majority of studies, due to fatigue being under investigation and continuously monitored for change.

Other factors, such as small sample sizes and the cross-sectional nature of most studies. do not allow for the analysis of fatigue behaviour over a long time period, which ultimately does not help determine cause and effect. Lastly, the phenotypes of MS and a lack of clarification may influence results, as studies have shown individuals with progressive MS are more likely to experience fatigue [Razazian et al., 2014].

4.6. Conclusion

Overall, there are weak to moderate correlations between short and longer walking tests, descriptions of fatigue, and walking measures. The literature does indicate a degree of correspondence between descriptions of fatigue and walking capacity, however, it is inconsistent [Dalgas et al., 2018; Loy et al., 2017].

It remains unclear in the literature whether fatigue directly affects walking or vice versa. Dalgas et al. [2018] found self-reported measures gave a limited explanation of the variance of results in walking capacity tests. Previous studies have indicated that fatigue is not a stable phenomenon, with limitations of perceived fatigue to rely on the accuracy of reflection and effectively reciting fatigue through the current questionnaires. Furthermore, physical fatigue and fatigability may not be the best tool to reflect physical fatigue alone, and other measurements should be used in conjunction with self-reported experiences to accurately determine the whole phenomenon of fatigue [Morris et al., 2002; Romani et al., 2004; Huisinga et al., 2011].

PwMS experience shared and universal features of fatigue. Nevertheless, fatigue needs to be understood as a whole phenomenon to establish the multiple facets pwMS experience and portray. Due to the inconsistencies in walking capacity tests and self-reported measures, the aim of this PhD research is to explore fatigue from an experiential view, that will enlighten the foundational components of fatigue and further direct the quantification of fatigue.

As stated in the introduction of this chapter, the literature provides only a partial view of fatigue. However, phenomenological exploration will allow individuals to reflect and effectively express their experiences of fatigue that self-reported measures may not fully encompass. By establishing the foundations of fatigue, the relationship between gait, fatigue, and fatigability may become more apparent and be determined. Fatigue cases, to establish all the facets of the symptom, will further increase current understanding of the relevance of objective biomarkers of fatigue in ambulation to fatigue as experienced.

Chapter Five: Rationale, research aims and questions

The purpose of this chapter is to offer a bridge and rationale between the context of what is already known about MS fatigue and the aims and objectives of this research. The gap in the literature is pinpointed, and the methodical reasoning for the study is presented, beginning with the rationale, subsequently followed by the research questions, aim and objectives.

5.1. Rationale

There is a lack of a unified definition of MS fatigue [Kluger et al., 2013]. Some previous researchers have differentiated the term fatigue (an experiential state that pwMS describe and feel) [Kluger et al., 2013; Loy et al., 2017; Mills & Young, 2008; Multiple Sclerosis Council for Clinical Practice Guidelines, 1998] from fatigability (objective measurements of performance decrement as fatigue is progressing) [Kluger et al., 2013; Loy et al., 2017; Leone et al., 2016; Severijns et al., 2017]. Fatigue has been investigated qualitatively and is described as an all-absorbing phenomenon, which is an important component in understanding the needs of pwMS and facilitating their health and QOL [Flensner et al., 2003]. The different states of fatigue have been explored within the literature, including the lived body and how it plays a significant part for pwMS who suffer from fatigue. However, the lived body and embodied experiences of both fatigue and fatigability are less well established in the literature.

From a physiological perspective, although there is a growing body of promising data for the measurement and monitoring of fatigue, biomarkers are insufficiently validated and lack consistency to serve as a gold standard [Shema-Shiratkzy et al., 2019]. Ambulatory fatigue has been identified in gait deterioration through various parameters (reduction in step length, cadence and ROM in lower extremity joints), however, findings lack consistency and significance [Psarakis et al., 2018; Shema-Shiratzky et al., 2019; Taborri et al., 2019]. A direct comparison between methods of fatigue detection and protocols continues to be problematic, as researchers use different approaches and methods of analysis to identify fatigue.

In this research, it was assumed that, as pwMS commonly tire with sustained physical exertion, changes to performance measured in physiological gait metrics are likely to decrease whilst performing the 6MW [Beatty et al., 2012; Phan-Ba et al., 2012]. Velocity is a versatile outcome measure that is easily administered, valid and reliable in detecting change [Middleton et al., 2015], and has been used to detect ambulatory fatigue in pwMS [Leone et al., 2016; Phan-Ba et al., 2012]. Nonetheless, it is not possible to use velocity alone to detect the characterisation of changes in velocity, and therefore to explain why changes in velocity have occurred. Wearable inertial sensors provide a more detailed measure and can be used to assess gait kinematics to detect specific gait characterisations. These parameters can be used to make precise measurements that can be interpreted for treatment and management interventions for ambulation and fatigue.

Angular velocity is a measure of the rate of change in velocity around a specific axis. It has been used within studies to assess changes in gait and coordination [Motta et al., 2016; Taborri et al., 2019]. However, limited research has been done to explore the changes in peak angular velocity (ω) at the thigh as well as the ankle and examine the characteristics of these changes through each consecutive minute of continuous, sustained walking [Crenshaw et al., 2006; Leone et al., 2015; McLoughlin et al., 2016]. Measurements of peak ω reflects the control of movement in the rate of change of flexion and extensions (mediolateral axis) at the thigh and ankle joints to assess movements of the lower extremity. Velocity and peak ω therefore allow the detection and characterisation of change. To incorporate a standardised measure (velocity) with a measure that will provide gait characterisation may aid in the understanding of future measurement and management of more effective walking in pwMS. To the best of the author's knowledge, no published studies include an estimation of lower limb kinematic changes in peak ω during each consecutive minute of the 6MW.

In this exploratory study, the nature of fatigue is identified as multifaceted, as single study approaches often lack the diversity necessary to understand fatigue as a whole [Mayoh & Onwuegbuzie, 2013]. To understand the congruence between fatigue, walking capacity and descriptions of fatigue, the aim of this research was to identify the similarities and differences between fatigue as experienced and ambulatory fatigue, drawing from rich phenomenological findings to develop raw experiential data. The use of a concurrent mixed method phenomenological research approach in this study mirrors the complexity of the phenomenon being studied, and also allows for confirmation and cross-validation of fatigue [Creswell, 2009]. Howe [1988] suggested that this approach presents great benefits in terms of cohesion and holistic discussion, which naturalised phenomenology researchers aim to do. Naturalised phenomenology researchers address human experiences in a pragmatic manner, and this approach provides an effective methodology of a first-third person counterpart[14]. Fatigue has been recognised in the literature as an intricate, complex, and highly "subjective" symptom

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[14] Both first and third persons that are equivalent to each other.

that is dependent on an individual's physical and mental capacity. By investigating the experiences of fatigue through phenomenology, this research will enable a rich foundation of understanding the phenomenon, and highlight the subjective aspects of conventional measurements of fatigue through sensor-derived measurements. "A mutual alignment from each discipline could provide third person accounts to illuminate previously unnoticed aspects of mental experience, and on the other hand, guiding the empirical questions, analysis and interpretation of the third person findings in light of the phenomenal invariants of the mental experience." [Berkovich-Ohana et al., 2020].

Fatigue needs to be understood from a foundational perspective, to critique classifications and grasp domains, and delineate the phenomenon. To achieve this, the lived experiences of fatigue will be explored to crucially delineate the phenomenon as experienced and to maximise the descriptive accounts of pwMS. Alongside this, velocity and peak ω will be explored to get a view of fatigue as experienced and physiological fatigue, from both perspectives.

5.2. Research questions

The central question:

1) Do gait parameters appropriately demonstrate fatigue or fatigability in pwMS, and does this correspond to any degree with fatigue as experienced by pwMS?

Phenomenological question:

2) What is the phenomenon and meaning of fatigue as experienced by pwMS?

Physiological question:

3) Do lower extremity body parts differ in physiological parameters during fatigability in the 6MW? More specifically, do peak angular velocity of the thigh and ankle vary, and do either indicate ambulatory fatigability?

5.3. Research aims & objectives

The overall aim was to deepen the understanding of MS fatigue and related phenomena, and to use this knowledge to facilitate the development of specific instruments and measurements used in research and clinical settings. A clear differentiation between the characteristics of fatigue as experienced and physiological fatigue could also assist the development of fatigue-tailored interventions in MS. In this project, two very different disciplines were drawn together to bridge physiological assessment with first person accounts, using naturalised phenomenology as a guide.

Taking a phenomenological oriented approach:

A) Explore and delineate the experience of fatigue in pwMS, and

B) Produce an essential description of fatigue as experienced by pwMS, that characterises unique variations and universal features of the experience.

Using physiological measures:

A) Evaluate fatigability changes in the 6MW by exploring gait parameters of the ankle and thigh using overground walking velocity and peak angular velocity,

B) Explore and examine measurements of fatigue compared to an individual's description of fatigue, and

C) Assess the usefulness of the methodological approach in this field.

Chapter Six: Methodology and methods

6.1. Methodology

Fatigue can manifest and affect pwMS in various manners, typically impacting one individual differently from the next. The multitude of the symptoms are often complex and difficult to specifically measure and manage via interventions, and fatigue has frequently been explored in a variety of disciplines. The nature of fatigue is multifaceted in pwMS, but research approaches in single studies often lack the necessary diversity to understand fatigue characteristics as a whole [Beckerman et al., 2020].

The usefulness of delineating phenomenological analyses with physiology and more conventional scientific approaches prove essential to gain a precise description of the explanandum. Researchers adopted a naturalised phenomenological approach aiming to identify and localise the relevant physiological correlates of a given phenomenon [Zahavi, 2010]. Researchers may utilise both sciences to gain insight and a mutual enlightenment from one another, concerning fatigue in pwMS [Gallagher & Meltzoff, 1996]. Phenomenological description may assist in unravelling the essential meaning of such physiological measurement; physiological parameters provide a degree of quantifiable measurement, which is assessed for usefulness in monitoring and tracking fatigue. To understand (a) how fatigue is manifested through ambulation and velocity, and (b) whether this corresponds to pwMS' perception of fatigue, it seems appropriate to use a naturalised phenomenological approach.

For this research, Varela's neurophenomenology [1996] was a key influential approach, guided by a study by Gallagher et al. [2015]. In the final chapter of his book *The Structure of Behaviour*, Merleau-Ponty discusses the problematic issues of Kantian transcendental philosophy, and suggests a redefinition of such to attend to the real world [Merleau-Ponty, 2006]. He states: "the ultimate task of phenomenology as philosophy of consciousness is to understand its relationship to non-phenomenology. What resists phenomenology within us – natural being, the 'barbarous' source Schelling spoke of – cannot remain outside phenomenology and should have its place within it." [Merleau-Ponty, 2006; Schmicking & Gallagher, 2010]. Rather than researching in a conventional manner of objectivism or in a qualitative aspect to gain subjectivism, Merleau-Ponty asks the reader to reconsider, and to search for a dimension that is beyond the lines of objectivism and subjectivism, to a more embodied holistic approach.

An embodied holistic approach is congruent with the challenges of understanding more deeply and further exploring the complexity of fatigue in MS. The procedure of the present research is outlined in Figure 6.1; this can be understood as a mixed methods approach, but within a neurophenomenological framework. An overview of the basic outline of an embodied holistic approach to investigating MS fatigue is also provided in this figure. The detailed naturalised phenomenological orientation is discussed in section 6.4. This pictorial representation provides an overview of how the specific methods were brought together within this research.

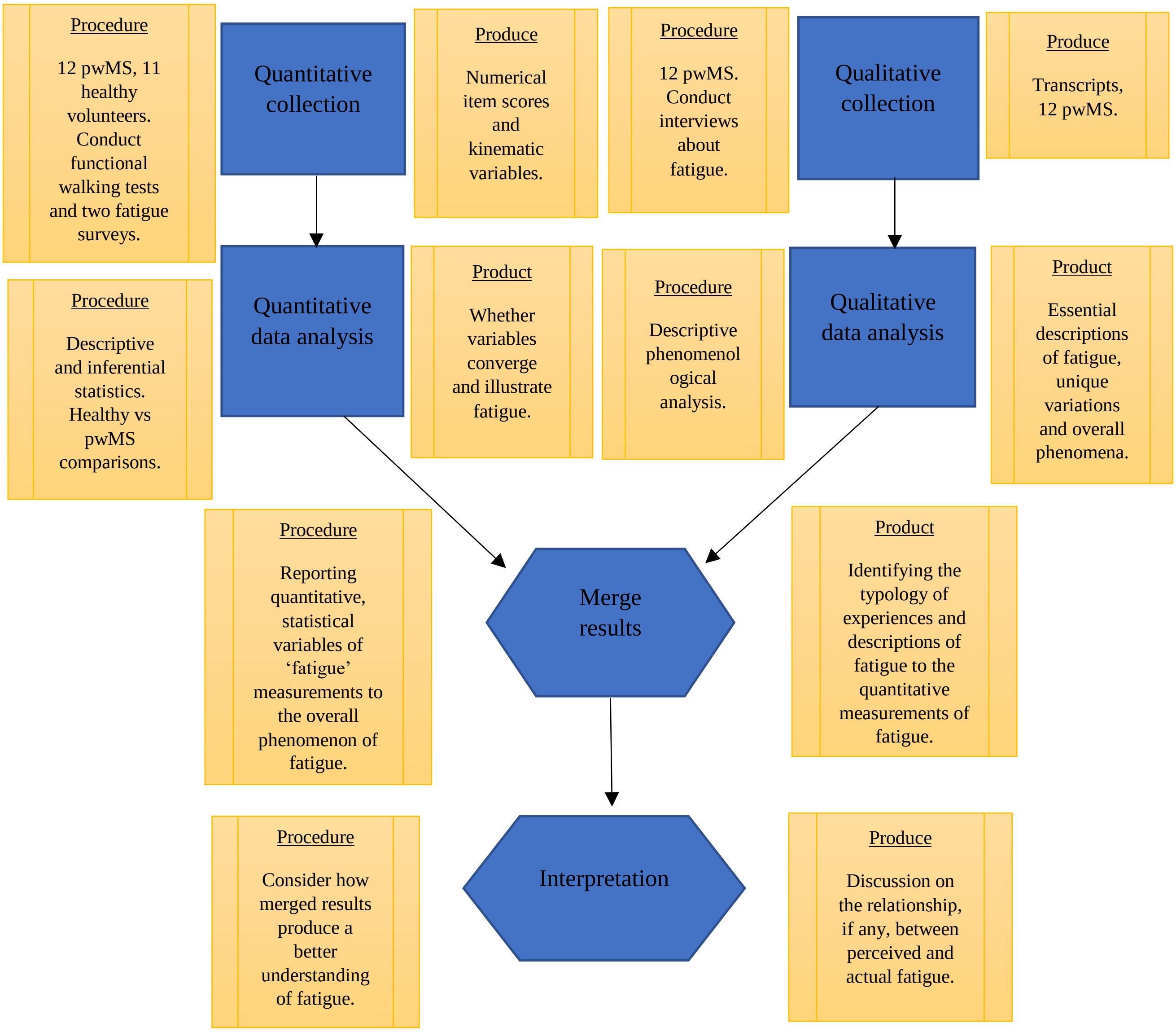

Figure 6.1.: Procedural diagram of the research.

In this chapter, neurophenomenology as an approach and the basic neurophenomenological concepts within cognitive science research are considered. A phenomenological rationale is offered, and the neurophenomenological stance likewise considered. This will be set within a context providing insight into the epistemological and ontological considerations of phenomenology and other scientific disciplines.

A discussion of pre-awareness and preunderstanding as key ideas within phenomenological research will be highlighted, alongside an account of the researcher’s preunderstanding of MS fatigue, and the steps taken within the approach to adopt a phenomenological attitude. This will be followed by a presentation of the background context and overarching influences upon the methodology, and a discussion of descriptive phenomenology and its historical touchstones. The umbrella term of “naturalised phenomenology” will be used to question if phenomenology can be naturalised and fully utilised within mixed methodology and more conventional scientific approaches. The chapter concludes with a detailed description of data collection, both physiological and phenomenological.

In Figure 6.1, the outline of the entire research project is illustrated, from data collection to the final discussion and interpretation of the results. As the design incorporated a convergent parallel approach, the physical tests were conducted on the same day as the phenomenological interviews. One short walking task was performed at baseline, followed by a 6MW to elicit fatigue then the short walking task was repeated before conducting the phenomenological interview. Physiological data included descriptive (stopwatch measurements) and inferential (sensor measurements) statistical analysis. Interview data included in-depth descriptive phenomenological data analysis. The convergence of results was explored in an embodied holistic approach, with both sets of data of equal status. Methods for data collection and analysis will be revisited more thoroughly in section 6.5.

6.1.1. Neurophenomenology

Neurophenomenology (NP) is a specific methodology integrating phenomenology with empirical data from a neuroscientific approach, under the umbrella methodology of naturalised phenomenology. In this approach, practitioners address the study of experience and consciousness in a pragmatic way to explore the embodied condition of the human mind [Bayne, 2004]. The methodology was developed by a neuroscientist, Varela, in the mid-1990s. He wanted to broaden and progress the study of consciousness by utilising different disciplines to explore the difficult remaining questions of consciousness [Varela, 1996]. Varela’s understanding of consciousness interrogated the question of “what do we mean by human experience?”, by attempting to understand the *structure* of experience [Varela et al., 1995]. He considered the transition of Descartes’ idea of a mind as a subjective consciousness to

Brentano's intentional mental state and Husserl's structure of intentionality. He guided the discussion to a more embodied experience, rather than the notion of consciousness as disembodied thought (namely "the brain in a vat"). This redefined the study of consciousness as the study of conscious lived experience [Valenzuela-Moguillansky et al. 2017].

Varela appreciated that most neuroscientific research uses psychophysiological methods that are unobtrusive and continuous, and can be beneficial as the results are seen as unbiased and objective. However, Dirican & Gokturk [2011] indicated these methods had limitations as indirect measurements of experience (such as blood flow or brain waves) can be difficult to interpret. Also, such methods can have weaknesses with temporal and spatial resolutions (for example, functional magnetic resonance imaging, or fMRI). Generally, it is impossible to fully interpret the results of conventional data analysis without evoking a description of the experience from the individual participant. Compared to traditional self-reported measurements of experience, phenomenological methods allow for a much richer description, giving an in-depth understanding of an individual's experience.

Although controversial, Varela's research aimed to develop a body of consciousness research that involved a central component of an experimental component of cognitive phenomena alongside typically neuroscientific measurements [Valenzuela-Moguillansky et al., 2017]. He challenged researchers to be open to phenomenological research and exploring the study of experience in a novel and multidimensional way; he attempted to "loosen the hold of both objectivism and subjectivism and encourage further communication between science and experience, experience and science" [Varela et al., 1995]. Many researchers have used this methodology in an attempt to broaden the cognitive sciences: examples include studying awe and wonder in outer space, pre-reflective experience of an epileptic seizure, and ongoing conscious state during a simple perceptual task [Bockelman et al., 2013, Petitmengin et al., 2007; Lutz 2007].

In a promising NP study, Petitmengin et al. [2007] investigated the anticipation of epileptic seizures in nine individuals, using neuroscientific measurements and phenomenological interviews. The authors encompassed a neurophenomenological framework, exploring whether neurophenomenology could guide and determine each methodology to reveal something new. Petitmengin et al. [2007] identified from previous studies that the measures used are difficult to interpret in terms of the correlation between behavioural measures and physiological measures. As such, they conducted two sets of interviews with each participant, to illicit rich descriptions of previous seizure experiences. As in previous literature on this phenomenon, less than five minutes prior to seizure onset, electroencephalogram readings indicated a decrease in synchronisation among neural populations surrounding the epileptic focus in the brain [Le Van Quyen et al., 2001]. However, verbal reports described a state of fragility several hours before the seizure onset, suggesting a subjective state of experience considerably earlier than objective readings. This research indicates that the cognitive response does not correspond to the cerebral activity recorded, suggesting that awareness of the pre-reflective experience is central to further understand seizures and pre-seizure experience [Le Van Quyen et al., 2001]. Additionally, this highlights how lived experiences can enrich neurological analysis, which draws a deeper relationship between the lifeworlds.

Philosophical considerations of epistemology and ontology have important distinctions which the researcher should be aware of and consider throughout the research process [Bahari, 2010]. There is a requirement to draw connections between the assumptions researchers hold about reality and the way they go about developing knowledge. To conduct research effectively, a researcher must consider their philosophical assumptions (see section 6.3.). Briefly put, epistemology concerns the nature of knowledge and the way we set about obtaining knowledge; within research this includes the knowledge claims a researcher considers and makes to conduct their research [Bahari, 2010]. Epistemological assumptions can be regarded as a question of what is deemed acceptable in a discipline [Bahari, 2010]. Ontology is the study of being, concerning “what is”, therefore what constitutes reality [Scotland, 2012]. Saunders et al. [2007] state that ontology concerns the nature of social phenomena as entities, what they consist of, and what entities operate within them. Both epistemological and ontological assumptions will guide the researcher in employing methods that fit accordingly to the research questions and assumptions considered.

Characteristically, in a reductionistic science, practitioners could have an objectivist ontological outlook with a positivist epistemological approach, where statistical techniques and variables are explored to illicit findings with a degree of precision and predictability. The research is conducted by reducing phenomena to variables to investigate whether the provided description of the phenomena (hypothesis) is proven or not. However, following Gallagher et al. [2015], I attempted to steer away from complete reductionism and defend a non-reductionist position. By doing so, I made these initial assumptions:

> (1) A non-reductionist view is that we simply cannot understand systems of anything by reducing research to its most basic constituents within reason.

> (2) To hold such a complete explanation from these basic constituents is not possible even in principle for some systems.
>
> [Gallagher et al., 2015]

Theorists of neurophenomenology question if something can be studied that is subjective and first-person in a purely objective, third-person manner, without losing information in the process [Gallagher et al., 2015]. Gallagher et al. [2015] state phenomenologists argue that if the concept of the study involves experience, it would be unscientific to pretend to understand the phenomena strictly in just third-person. A neurophenomenologist aims to explore how precisely similar experiences correlate with neurological processes [Gallagher, 2003; Lutz et al., 2002; Varela 1996]. On the typically blurred overlap between aspects of fatigue, self and other, adopting a naturalised phenomenological approach could enable the researcher to provide a first-third person counterpart to the research of fatigue in MS.

6.2. Background context and overarching influence on methodology: Phenomenology

Strictly speaking phenomenology is the study of the phenomena. It is a complex and comprehensive philosophy, a scientific method that explores the lived experiences of individuals and one's consciousness and how one presents itself in the world [Giorgi et al., 2017]. It is a philosophical movement that began with Husserl, who attempted to establish philosophical and scientific knowledge of consciousness of the everydayness. Husserl believed nothing more could be achieved in relation to knowledge without pursuing a rigorous philosophical method to explore human experience [Giorgi, 2007]. According to Husserl, vigilant, rich descriptions of an individual's experiences help to develop our understanding of how appearances and everydayness present themselves, and what this means to us [Strle, 2016]. Phenomenological researchers are concerned with the "how" rather than the "what" of objects, exploring and enjoying the richness of everyday life [Zahavi, 2019]. Proponents of phenomenology have been considered as going beyond existing understanding and providing deeper and more meaningful productive insights [Colaizzi, 1978]. They focus on constructing a universal meaning of an experience and reaching a more profound understanding of the given phenomenon. Many researchers have used phenomenology to further understand "being", an individual's experience, condition and/or the environment/situation through the experiences of others [Finlay, 2011].

Adopting a phenomenological approach enables the exploration of every act of consciousness of every experience that individuals have. Each experience is intentional and associated with its intending object. The notion of intentionality applies to the theory of knowledge in philosophy: it is unlike the theory of human action, the purpose we have in mind when we act [Sokolowski, 1999]. In phenomenology, the intention of something means the conscious relationship we have to an object [Sokolowski, 1999]. To be conscious of something, or of an object, may seem trivial and obvious, but human consciousness and experience have been understood from different aspects by philosophers over the centuries.

Phenomenologically, intentionality can depend on the type of objects being intended; different interpretation from different objects are intended differently. Depending on the individual, a picture can be pictorially intended, whereas an object at work may be perceptually intended. Intentions can be influenced by past self or other experiences; the intending act of a potassium metal and water reaction in a laboratory has a different intending act to the intending object of an office chair. The types of intention to interpret something can be different and layered, depending on the object or “thing” being intended [Sokolowski, 1999].

Proponents of phenomenology attempt to understand these intentions of a given experience to help them understand human knowledge and the way we relate to the world we live in. Phenomenologists recognise the truth of a phenomena: the act of making a judgement is how we articulate the presentation of parts of the world [Sokolowski, 1999]. It is not just an arrangement of ideas in our minds like a Cartesian philosopher might believe. The relation between world and subjectivity is merely accidental, as the mind is essentially open and reality is manifestable to each individual. It is thought to be something we must encounter in order to believe it is real, whether that’s practical engagement or perceptual awareness [Zahavi, 2019].

Brentano, a German philosopher and psychologist, believed an individual can commonly and consciously question the reality of an object, but not the act of thinking [Zahavi, 2019]. Intentionality plays an important role in phenomenology and is seen as the characteristic of consciousness, whereby an individual’s understanding of reality is merely perspectival, depending on the world and environment they surround themselves with [Zahavi, 2019]. Brentano argues that to believe is a particular type of mental act, which is to intend or be about whatever is believed [Jacquette, 2004]. For Husserl, the notion of intentionality encouraged his thoughts, conceptualising how physical and mental phenomena arise in consciousness, and both of which form phenomena through appearances from mental intentions [Husserl &

Gibson, 1962]. Epistemological understanding of phenomenology lies in the intentional relationship of everyday lives, the lifeworlds.

To understand phenomenological research in more depth, two words from German philosophy, *erfahrung* and *erlebnis*, can be considered. Both words can be directly translated into experience, although *erfahrung* also means “gaining knowledge”, and is used in relation to a general experience, for example, “I have ten years’ experience as a farmer” [Gallagher, 2015]. It has the same roots as experiment, and it is commonly used to describe actively doing something to gain knowledge. However, *erlebnis* is typically used to describe an event, when you experience something, for example, “I thoroughly enjoyed the experience of the wedding”. The root *leben* means life, to live through an experience, hence the lived experience.

Phenomenologists meticulously explore the engagement involved in a type of experience, a lived experience, *erlebnis*. An experience is conveyed and experienced differently in each individual. For example, there are many experiences of a global pandemic dependent on individual circumstances, but there is commonality of living through the pandemic. Phenomenologists are primarily interested in the journey, description and interpretation of a given experience, not necessarily its logistics.

6.2.1. Descriptive & interpretative phenomenology: Some historical touchstones

Husserl’s goal was to establish secure philosophical and scientific knowledge of human experience, in which consciousness plays a significant role [Smith & Thomasson, 2011; Giorgi, 2007]. Husserl wrote *Logical Investigations* and *Ideas I* to investigate the critical question of “what do we know as persons?”, in an attempt to better understand the depth of consciousness in a more methodical way [Husserl & Findlay, 1970]. By closely studying the descriptions of given experiences, Husserl hoped to better understand human experience, how one sees the world or object, and one’s intention and awareness at hand. Later, this methodology was classified as descriptive phenomenology, capturing the essences of phenomena through a descriptive lens of their characteristics [Giorgi, 2008]. Husserl had begun to conduct descriptive accounts after steering away from mathematics by gaining interest in the systematic reflection of the structures of consciousness and the phenomenon with it [Giorgi, 2008]. Descriptive phenomenology was a theoretical movement developed by Amedeo Giorgi in the early 1970s that was heavily influenced by Husserl and the surrounding concept of reductionist tendencies.

Alongside Merleau-Ponty, Heidegger (a student of Husserl) probed deeper by exploring ontology, questioning the philosophical stance of “what does it mean to be” and “how do we know what we know”. Heidegger broke the long tradition of Western philosophical tradition and argued against Descartes concept of dualism, in which the mind and body are distinct. Heidegger viewed a *being* as one, the mind and the body, and believed consciousness is not separate from the external world [Hamilton & Hamilton, 2015; Tedie Moskowitz & Wrubel, 2005]. Challenging Cartesian dualism, Heidegger introduced the concept of *Dasein* in his work *Being and Time* [1927/2013]. Dasein refers to our mode of being, instead of being self-contained subjects. He believed Dasein is existence itself, suggesting self and world are not two beings, but they belong together in the single entity: Dasein [Finlay, 2011]. Dasein reflects the notion of a “living being”; one reveals who they are through their doings and way of being with worldly things, such as objects, projects, relationships, language, culture and history.

Heidegger recognised the inter-subjectivity of the world and how beings remain in connection with each other through everyday engagement in the common world. He thought it was impossible for people to exist without dependency on each other or the sharing of communal norms [Finlay, 2011]. Heidegger believed that a person cannot rid themselves of what they already know and think [Watson et al., 2008]. A single entity, Dasein, cannot disconnect themselves from their self or world, as humans integrate themselves into their world from day one. Arguably, Husserl’s notion of bracketing was based on the principle of not influencing others by one’s thoughts and actions, nor stating a clear segmentation of self and world. Instead, one should attempt to diminish these thoughts and actions so that the pure phenomenon of the experience can be found [Sorsa et al., 2015].

Research can be enriched in terms of the elements of the lifeworld and the world of living experience by conscious beings, which Husserl considered to be a pre-reflective world. The lifeworld is not something that should be divided into strict categories in a type of quasi-quantitative model. It is elements of experiences, activities, perceptions, and judgments of an individual, which create a world that only they see and perceive, their world. Merleau-Ponty [2013] believed “the person is in the world and only in the world they know themselves”.

The lifeworld is a pre-reflective world prior to the conscious representation of the world as we know it [Merleau-Ponty & Landes, 2013]. These elements of the lifeworld can all naturally overlap, with specific elements that cannot but be expected to show themselves. Ashworth [2003] named these fractions to dismiss the idea of these elements being independent parameters, rather than overlapping meanings. Ashworth argues that empirical research can be strengthened and enriched by an explicit lifeworld analysis, such as phenomenology. The lifeworld fractions consist of self, sociality, embodiment, temporality (with its events), spatiality (with its objects), project, discourse, and mood-as-atmosphere [Ashworth, 2015]. Exploring the lifeworld through this research will assist in the understanding and knowledge of what is understood by fatigue and what fatigue means to pwMS from more than one perspective. Understanding the lifeworld will enable the presupposition and preunderstanding within MS fatigue.

As a qualitative approach, phenomenology has become increasingly popular outside the philosophical world, with Giorgi's [2016] psychological phenomenological method, Van Manen's [1990] hermeneutic approach, Smith's [2009] interpretative phenomenological analysis (IPA) approach, and Dahlberg's [2008] reflective lifeworld approach. Researchers in all domains of phenomenological research are interested in the experience and understanding the meaning of a given phenomenon. However, the application and theoretical philosophy grounding the many adaptations of phenomenological philosophy differ depending on intentionality, bracketing and interpretation of the given experience, which opens opportunities to apply phenomenology in other disciplines of science.

Study of lived experiences involves an immediate consciousness of life events that can give meaning to an individual's perception of a given phenomenon [Giorgi, 1997]. Phenomenologists focus on human subjectivity and discovering the meaning of particular phenomenon. A phenomenological investigation, in this context, involves searching for the meaning of MS fatigue, to provide a foundation of understanding of what fatigue is like as experienced by pwMS themselves.

The most prevalent debate within phenomenology is the approach and use of a particular phenomenological methodology. Finlay [2008] identifies research as phenomenological when it involves a rich description of lived experience or lifeworld, by encompassing a phenomenological attitude in which the researcher partially refrains from judgements of the phenomenon being investigated. Descriptive phenomenologists stay close to what is given and aim to reveal essential, general meaning structures of a phenomenon by restricting themselves from appropriate intuitive validations [Finlay, 2008]. However, interpretive phenomenology engages in the world of language and social relationships, it is more focused on our being-in-the-world and constitutes interpretation as inevitable [Finlay, 2008].

Langridge highlights that in practice, there is no hard boundary between the descriptive and the interpretive [2008]. Interpretation, as in pointing out something, can be seen as different to interpreting and pointing out the meaning of something. Wertz [2005] argued that interpretation may be used to grasp parts within larger wholes, but if it remains descriptively grounded, it could be classified as descriptive phenomenology. Finlay [2008] highlights the division within phenomenology and reflects it as more of a continuum with no definitive classification. The continuum within research paradigms continues to be challenged and pushed by philosophical debate and novel methodologies. Naturalised phenomenology sits on this continuum within the phenomenological and positivist dimension, with proponents aiming to explore phenomena in a new light.

6.3. Preunderstanding and the phenomenological attitude

In phenomenological-oriented research, it is particularly important to be aware of our own preunderstandings and potential inherent bias in order to recognise prejudices in the interpretation of the phenomenon under investigation [Nyström & Dahlberg, 2001]. What follows is a discussion of what is meant by preunderstanding and its importance. By identifying such presuppositions, the researcher acknowledges their preunderstanding of the topic under study, as without it, researchers risk gathering results that reflect their own preunderstandings and something that already exists in their understanding. Research in all disciplines requires the acknowledgement of one’s presuppositions; researchers should remain open to aspects of the phenomenon and have an awareness of their stance to aid in not predetermining or interpreting the phenomenon throughout the research project.

Dahlberg et al. [2008] use the term “bridling”, which denotes not only restraining one’s preunderstanding, but also learning to not obtain an understanding too quickly or carelessly. It is used to maintain an open and respectful attitude that allows the given phenomenon to present itself. Following Husserl and working within a lifeworld orientation, it is suggested everyone is immersed in the natural attitude. The natural attitude is the everydayness in which we see and live in the world, where we presume ourselves independent from the things around us. Our natural attitude represents the predetermined basis of all experiences and in this research “a step back” from the natural attitude is required [Nyström & Dahlberg, 2001].

Gadamer [1975] also suggests the importance of the understanding and awareness of our presuppositions as otherwise it is impossible to confront the otherness of phenomenon in the process of one’s research. In order to do this, the researcher must leave the natural attitude and find the research attitude, adopting an approach that lets the world show itself to the researcher [Nyström & Dahlberg, 2001]. The term "horizon" was used by Gadamer to describe what is conceivable as well as one's maximum limit of understanding. It is this position, according to Gadamer, with which one can overcome presuppositions and expand the horizon of meaning [Gadamer, 1975].

In attempt to better understand preunderstanding, our interpretations of the "real world" are direct reflections from presuppositions in our internal world and pre-structures, not direct reflections of the "real world" itself [Gadamer, 1975]. Simply put, any interpretation of the world is not completely free from presupposition [Welch & Palmer, 1971]. All preunderstanding emerges from history or tradition (this encompasses culture, health beliefs, experience of healthcare and so forth) that the researcher is familiar with. The meaning of such prior contexts can affect the present questions and the way we project ourselves in understanding. Gadamer concisely stated this in *Truth and Method* as to "be aware of one's own bias, the text can present itself in all its otherness, and this asserts its own truth against one's own fore-meanings" [Gadamer, 1975]. Complementing each other, Husserl and Gadamer dealt with the complexity of withholding preunderstanding by both approaching it differently. Husserl used methodological reduction, termed bracketing, in an attempt to withhold all presuppositions, whilst Gadamer explained and annotated the preunderstanding of his research [Nystrom & Dahlberg, 2001]. There has been much contentious debate about this issue within the phenomenological research community, but research in any manner cannot be interpreted without historical derived conceptions [Finlay, 2008]. To better understand the structure of preunderstanding is to understand how we get our presuppositions [Nystrom & Dahlberg, 2001].

Tradition and culture themselves do not stand over our thinking of preunderstanding. Nevertheless, they are in the horizon within which one conducts their thinking. History or tradition cannot be fully objectifiable without an element of prior conception, which therefore implies the need for epistemology to deal with a phenomenon. Epistemology is an interaction of the self that encounters things, as well as the things encountered in a dialectical process [Nystrom & Dahlberg, 2001], thus epistemology is an important aspect of preunderstanding. According to Gadamer, interpretation of something or one are never fixed, as meaning is always there. An open attitude when confronted with new experiences will enable one to see the otherness of the phenomenon, according to Gadamer [1975]. He states "…a person who is called experienced has become so not only through experiences, but is also open to new experiences…the experienced person proves to be, someone who is radically undogmatic…is particularly well equipped to have new experiences and to learn from them" [Gadamer, 1975].

To understand how this can be applied to research, Husserl's theory of intentionality should be considered. Intentionality, according to Husserl, is one's intentional relationship with the things that make up one's daily life, and understanding the meaning of the things that one uses and sees arounds them that signify their world [Mcintyre & Smith, 1989]. Thus, intentionality also encompasses the filling in of partially accessible qualities or characteristics of an object which are not directly presented but lie within one's conscious. Husserl labelled these "apperceptions", that philosophers comprehend preunderstanding to be unavoidable without, and are part of being able to gain knowledge [Husserl, 1970]. Churchill & Wertz [2015] conveyed that an adequate conception of consciousness is fundamental for any research, which Husserl [1913/1962] put forward in his notion of intentionality.

To understand the importance of presupposition within phenomenology, the considerations of preunderstanding in other disciplines are of interest. In psychology, Piaget adopted the word "accommodation" to explain his theory on the dependency of biological and environmental factors when encountering a new situation [Piaget & Inhelder, 1973]. In the early phases of accommodation, a child is more likely to change its presuppositions regarding things it encounters. However, as adults, we are less likely to radically change our interpretations of the world, as we have relatively fixed cognitive structures.

In cognitive science, these structures are known as "schema" and they shape the way we experience everything we encounter. It is suggested that part of our preunderstanding is preconscious and pre-reflective, and being aware of these schemas makes us more self-aware of our understanding [Charon, 1989].

Another psychological theory is Klein's theory of "splitting" [Klein, 1975]. Splitting occurs when a small child creates a primitive psychological structure in order to begin understanding impression and expression. For example, such expressions from its mother are segregated into good or bad, so the foundations of their primitive defence system are split. If a researcher is dominated by splitting, the preunderstanding of adults could be a severe obstacle for the openness required to understand the lifeworld in all its complexity.

In social sciences, societal and cultural differences can develop different values and opinions dependent on who an individual interacts with, and where. Proponents of symbolic interactionism theory focus on the interaction between an individual and dynamic social activity where individuals are constantly experiencing interactive changes [Nystrom and Dahlberg, 2001]. According to theorists, an individual’s interpretation is directly affected by these societal and interactional changes, as it is a world that they can define. Moreover, history and culture affect what we see, understand and interpret in each experience or situation. According to Gadamer, in order to gain methodological consciousness, the researcher should learn to understand themselves and their position in history. Gadamer called this “history of effect”: if the researcher understands their judgements and prejudices, and avoids their own interpretations, they will be able to see the otherness of an experience whilst conducting research [Nystrom & Dahlberg, 2001]. This openness to their own bias will allow the researcher to perform the history of effect, but this does not mean absolute openness can be achieved. Therefore, openness should be the researcher’s self-awareness, in which the researcher can bracket or question to the best of their ability [Nystrom & Dahlberg, 2001].

An important aspect of descriptive phenomenology is the suspension of judgement and prior experience from the natural world, to focus purely on the experience and phenomenon being investigated. Although there is very much an ongoing debate about the logistics of what to bracket and how, it is claimed that by adopting a presuppositionless approach and bracketing prior experiences, a researcher can return to pure consciousness of the phenomena [Beech, 1999].

Building on Husserl, Giorgi et al. [2017] emphasises the importance of bracketing. He states that all-natural attitudes of daily life and common sense can cloud what is seen, and which can therefore affect potential research findings [Giorgi et al., 2017]. By doing so, the researcher can strive to minimise their ability to unconsciously bring assumptions about the topic or given experience into the research process [Hamill, 2010]. Giorgi [1985] highlights to what extent the phenomenological method itself can be bracketed. Giorgi [1985] suggests a general phenomenological approach whereby the researcher adopts imaginative variation of meaning and intuition of structures. By this, the researcher should explore all possible meanings before understanding the general structure of experience in the research, and attempt to embrace the meanings for the individual by appropriately bracketing and entering the individual’s lifeworld.

Husserl thought that by adopting a phenomenological attitude, researchers can focus on the appearance of phenomena, how things are, and how they matter to us [Giorgi et al., 2017]. The process of adopting this phenomenological attitude allows one to philosophically reflect and makes one aware of one’s involvements in their realm. This reduction should not be looked upon as an exclusion of reality, rather a suspension, to explore the true descriptions and experiences of the experiencer. The researcher aims to understand and reflect on their own experiences, to perform the phenomenological attitude and to not assume any commonality in experience, or interpret from a previous belief or research that will influence the participant and the study: “The phenomena of experience are before us, ready for our developing theory of consciousness” [Dahlstrom et al., 2016]. Researchers are not able to engage in pure reflection due to the nature of the aims and objectives of research. However, a pragmatic approach, which Giorgi argues is a modified scientific phenomenological reduction, can be applied to empirical research [Finlay, 2008]. Bracketing allows researchers to seek reality and for reality to be researched, instead of attempting to make reality vanish from view [Finlay, 2008].

6.3.1. My own preunderstanding

Drawing from Gallagher et al. [2015], proponents of NP take on an active/embodied approach and this is a specific form of embodied cognition from Varela and Merleau-Ponty [Varela et al., 2016]. This study allows for a pragmatic dimension to phenomenological reduction, by using naturalised phenomenology, in attempt to deconstruct the subject-object duality that is often used in research methods, and draw on a more embodied approach [Giannotta, 2017].

I have taken this stance in this research. The experience under investigation requires not only brain function, but also bodily responses in a physical, social, and cultural environment. A structure/object is not just a structure of being-in-the-world, it is a dynamic coupling between the brain-body-environment, and one cannot exist without the other [Gallagher, 2018]. Chemero [2009] discusses this whilst exploring the function of an object as not just the function of an object-in-general, but what the object offers in a particular situation. He further indicates the behaviour of the object cannot be reduced to differences in brain function alone without considering the details of the body and the world [Chemero, 2009].

Proponents of NP use phenomenological clusters that provide reportable categories and allow the participants to define their own experience on the basis of nothing other than their own experience. Unlike neuroscientific studies, the experiences are not predefined, and participants are not presumed to simply respond to specific stimuli [Gallagher et al., 2015]. According to Gallagher et al. [2015], a participant’s experience generates the data and categories, so nothing is predetermined, allowing more precise correlations between physiological data and experiential accounts. This type of integration allows the researcher to capture a fuller picture and avoid the imposition of external biases of assumptions of prior experience.

As an osteopath, I was familiar with fatigue in MS in a clinical setting and its basic clinical presentation. The notion of fatigue influencing bodily factors, such as motor weakness, increased difficulty with balance and sleeping, were aspects I was aware of. However, I was less familiar with the multidimensional nature and depth of fatigue. The depth of fatigue has on multiple factors involving cognitive impairments, and fatigue can impact behaviour and disrupt daily activities. Insight from the literature have assisted my understanding of the multifaceted presentation in physical and cognitive domains and the impact of psychosocial and existential factors fatigue has on pwMS.

To enhance credibility in the study, I engaged in continuous self-reflection to ensure I accurately illustrated the participants' experiences and remained close to the text. This process was guided by giving primacy to the participants understanding of fatigue and their experiences. I aimed to withhold preunderstanding (see section 6.3) from any clinical or academic presumptions, and maintain a critical stance of descriptive phenomenology so all interpretations were grounded within the data by staying close to the participants descriptions [Whittemore et al., 2001].

Ideas about MS fatigue and the various theories [Flensner et al., 2003; Krupp, 2010; Mezini & Soundy, 2019] were suspended. For example, fatigue has been theorised in different manners and in most of the literature, fatigue is defined in narrow functional ways. One approach to suspend preunderstandings was that interviews that were open and allowed participants to describe things in their own words. Another way was to use research questions that concerned the meaning and experiential nature of fatigue. This also meant having a sense of caution about the way in which fatigue had previously been defined through various professional and clinical perspectives. Additionally, by following Gallagher et al. [2015], I strived to avoid judgement and self-analysis and helped the participants "accomplish the suspension, redirection, and receptive openness…to allow the participants to describe all experiences". I used probing questions about the experience being described, and the descriptions were unravelled only from the experiences themselves. This aided in the avoidance of assumption about MS fatigue.

According to Nystrom et al. [2001], preunderstanding can never be fully grasped. Nevertheless, reflection and re-reflection can assist one's understanding and preunderstanding. To be aware of one's own bias means one must be open to the historicity of human understanding [Nystrom & Dahlberg, 2001]. In this way, phenomenology has developed my self-reflective process and understanding for the possible factors that could influence an individual's perception, understanding and judgement. Descriptive phenomenology allowed me as the researcher to directly discover and analyse fatigue as a phenomenon, with the aim of developing a description of the lived experiences of pwMS.

6.3.2. Phenomenological rationale

Merleau-Ponty [1963] highlighted that the strong correspondence between contents of experience and neural processes is itself a fact of experience. Neural processes are a type of experience that drive coordinated movement, attention, perception, reasoning, and intelligent behaviour from learning and memory. These therefore cannot be taken as a foundation of the reality of the experience.

Merleau-Ponty described “the flesh” as what is both seen and seeing, touched and touching, felt and feeling. However, this cannot be reduced to a pure seeing subject or a thing seen. It is an experience, and the brain, a perception and the perceived body come together to this term, the flesh, which brings potential to make room for the concept of science and nature [Bitbol & Petitmengin, 2017]. As Merleau-Ponty suggests, nature is not completely independent from the perceiver in an experience [Gallagher, 2018]. Even though phenomenologists are typically opposed to objectivism (positivism), Heidegger and Merleau-Ponty both argue for an internal relation between the mind and world, where the two are inseparable from one another [Zahavi, 2019]. Merleau-Ponty considers “the world is inseparable from the subject, but from a subject who is nothing but a project of the world; and the subject is inseparable from the world but from a world that it itself projects” [Merleau-Ponty & Landes, 2013].

This guides us to the concept of Merleau-Ponty’s notion of motor intentionality, where something is not an objective thing in the environment but can show up only in relation to the perceivers body or skill, therefore including the perceiver in the definition [Gallagher, 2018]. There is a dynamic coupling between the brain-body environment, as the function of an object is never purely the function of an object in general. The behaviour cannot be reduced to differences in brain alone, without the detail of the body in the world too [Gallagher, 2018].

The Varelian stance is neuro-materialist and anti-metaphysical orientation of the original enactive approach [Giannotta, 2017]. Bitbol [2012] discusses the orientation as a dissolution rather than a solution to NP that has existential and methodological components. Varela could easily reject NP not as an idealism or dualism, as he rather set immersion in a multidimensional practice of phenomenological and scientific inquiry [Bitbol, 2012]. Hence, Gallagher thought of NP as a case of scientific pluralism, where it not only leads to epistemic abundance, but also a way of coping with several issues. It is not possible to predict the course of scientific development, therefore the idea of bringing about a single all-encompassing theory would be done with great difficulty, as different sciences have different values and motives [Vörös et al., 2016]. According to Varela, it is absurd that we try to capture a theory of the objective world from one out of many of the multitudes of our situated standpoints [Varela, 1996]. The only acceptable approach is to widen the field of attention in philosophy again, by considering the whole span of human life, with a modification on the reflection and awareness of one's present situation and escape towards theoretical ideals [Varela, 1996]. The so-called "hardness" of the hard problem in NP narrows down to the concept of changing our perception of science itself, and the process and rigidity of practical training [Bitbol, 2012]. These can be softened in two ways. Firstly, through the acceptance of renewed and broadened idea of science, opening and reframing the problem of the origin of consciousness by dissolving an appropriate existential and epistemological stance rather than looking upon it in its original setting. The second way these can be softened is thorough training the seriousness of one's mind to the phenomenological attitude and exploration of experience [Varela, 1996].

According to the neuro-materialist dissolution, traditional scientists advocate a focus on the object of the study (mostly neurophysiological processes) so that an explanation of the conscious experience is given when there is a display of correlation between an object and some first-person accounts [Bitbol, 2012]. An increasingly accurate correlation between neurophysiological processes and first-person accounts should be within the framework as an explanation of consciousness in neurophysiology [Bitbol, 2012]. However, it does not consider that chance determines whether or not this is a two-way correlation. There is a tendency to be so absorbed in the intentional stance and its natural object that the lived experience in the background is mistaken for one of its objects [Bitbol, 2012].

In this research, the philosophical differences between phenomenology and physiology are acknowledged, but it is more important to understand the research question relating to the "how" and "what" of the specific topic under investigation. Cherryholmes [1992] reported the stance pragmatists take on research, stating that they need to stop asking questions about reality and the laws of nature, and focus directly on real life research problems themselves. In this study, a pragmatic approach is used, which incorporates a worldview arising from actions and situations rather than antecedent conditions [Morgan, 2007]. Although there is discussion on the philosophical assumptions of the research, pragmatists are more focussed on methods and the research problem, using all approaches available to understand that problem [Creswell, 2014]. The diversity of methodologies and understandings of fatigue and its multifaceted presentations are a suitable fit a pragmatic approach.

6.4. Naturalised phenomenology

Neurophenomenology, as stated previously, is an interdisciplinary method of researching within neuroscience and phenomenology [Roy et al., 1999]. It was conceptualised by integrating disciplines to formulate an approach that fits all disciplinary backgrounds in terms of philosophical underpinnings and conventional generalisations. Neurophenomenology lies within a naturalised phenomenology approach.

To “naturalise” is an umbrella term in scientific academia, comprised of different claims and concepts formalised and integrated into an explanatory framework [Roy et al., 1999]. Although naturalised phenomenology is in its infancy, it is a progressive methodology which has the potential to bridge different disciplines and move research in a new direction. This approach is intended to encompass phenomenology with reductionistic sciences, to enhance the accounts of experience, and to offer insights from explanatory data that will aid understanding and potentially guide this data to new directions [Dahlstrom et al., 2016]. As such, this approach is relevant and potentially very useful to study experiences such as fatigue in MS, which manifests external physical symptoms but is also a phenomenon that is lived through and experienced in the everyday by people with MS, with everyday impacts. Naturalised phenomenology has been developed similarly to other concurrent mixed methodologies, where each discipline (for example physiological measurement and peoples’ accounts of the experience) has equal methodological status. The hope is that different domains can interact over time to become increasingly coherent with one another and “co-evolve” [Dahlstrom et al., 2016].

Scientists from a variety of disciplines adoptt different approaches to investigate experiential states, depending on the research topic being investigated. However, with each approach, reducing variables to focus on these specific states can only be viewed from their specific, direct approach. Typically, conventional cognitive science research has persistently ignored the so-called phenomenological dimension by dismissing the pure subjectivity: “…by disregarding this dimension, by disregarding subjectivity and the first-person perspective, cognitive science is also disregarding a crucial aspect of the mental phenomena.” [Zahavi, 2004]. Gaining rich insights into the accounts of phenomena may reveal data not previously exposed in science. For example, phenomenology has been considered to play a significant role in experimental design that Gallagher [2010] calls "front loading phenomenology". This design has been used to gain phenomenological insights to aid in the development of a research design for empirical experiments. Its sequential approach and resulting phenomenological data allows researcher to gain insights, ideas or clarifications of a research project that will then assist in the guidance of the experimental framework for the study.

The task for reductive science is to reduce the phenomena to the most elementary parts to understand a given hypothesis; for something to count as natural, a reduction to some level must be done [Gallagher, 2018]. The idea of naturalised phenomenology continues to be debated, with some philosophers favouring it, and others heavily questioning its value. Although it is beyond the scope of this research to attempt to resolve these complex issues, it could be argued that some philosophers miss an important concept about naturalisation that Gallagher [2018] points to. Gallagher directs us to Merleau-Ponty's and Varela's interpretations and notions of embodiment. To argue his point, Gallagher uses Pollard's argument as opposition to discuss embodiment and his analysis of body schema. Pollard interprets Varela's concept of Merleau-Ponty's embodiment as having a double sense, as it involves both the body as context, and the experiential body as lived of cognitive mechanisms [Varela et al., 2016]. Varela et al. [2016] considers cognitive mechanisms to be grounded in the biological body: "…By using the term embodied we mean to highlight two points: first that cognition depends upon the kinds of experience that come from having a body with various sensorimotor capacities, and second, that these individual sensorimotor capacities are themselves embedded in a more encompassing biological, psychological and cultural context".

Taking all this into consideration, Pollard [2014] claims this rejects epistemological dualism and the idea that human subjectivity can be reduced to cognitive mechanisms that belong to nature as science. The concern is not over the perception of the "perceiver-individual" world, but the common principles of an explanation between sensory and motor systems guided in a perceiver-individual world [Pollard, 2014]. Furthermore, Gallagher's description of the "body schema" was seen as reductionist, by associating motor systems and neglecting the holistic approach of body schema according to Pollard [2014]. Pollard thought the plural term body schemas referred to a collection of motor systems, instead of perceiving it as a dynamical structure that tends to involve the whole body in its relation to the environment [Gallagher et al., 2006]. Gallagher argued that Pollard and many who oppose naturalising phenomenology miss the deeper philosophical significance of naturalisation and the different concept of nature that Merleau-Ponty claimed as a truth of naturalism [Gallagher, 2018]. To naturalise something directly depends on what one means by nature. Pollard may be correct in his interpretation that naturalised phenomenology as de-transcendentalised, but Gallagher [2003] suggests that phenomenology and cognitive sciences should develop a fuller and more holistic view of the cognitive life, the life of the mind and the embodied.

Mixed methods research (MMR) continues to be challenging yet promising opportunity in enhancing the way new information is studies and explored. The “paradigm wars” only became apparent in the past half- century, when philosophers reacted to the application of positivism in health and social sciences, arguing that there was a missing subjective dimension and interior aspect of research [Easterby-Smith et al., 2012]. When experiencing in the world, we receive information from physical events or objects, but the experience itself comes subjectivity, and we process and reflect on these events individually to gain understanding and compute the world around us. Without one another, a complete representation of the surroundings and phenomenon under study is arguably more difficult to understand. Proponents of MMR attempt to co-determine a given experience by trying to eliminate the limitations in both quantitative and qualitative methods, to offer richer insights that could complement each other (see Figure 6.1 for the study diagram) [Creswell, 2009; Gall et al., 2007]. McKim [2017] found MMR studies to have rigorous methods, a newer history, and provide a deeper meaning of phenomena than singular qualitative or quantitative methods alone. Although it continues to be challenging, MMR can provide methodological flexibility to produce abundant and comprehensive data.

According to Mayoh & Onwueguzie [2012], phenomenological research methods can be adapted and provide a good component in the emerging movement of MMR, but this has not yet been formally conceptualised. Even though there are ontological and epistemological differences between the paradigms, the authors argue that axiological and methodological parallels between phenomenological and quantitative methods. This allows for the combination of these methods within a single study, with a single overarching paradigmatic framework [Mayoh & Onwueguzie, 2012]. Axiology refers to the nature of ethics and what we value. It plays an important role in forming research questions and understanding the issues around a research topic [Biddle & Schafft, 2015]. Johnson & Onwueguzie [2004] recognise that people are embedded in a holistic network of beliefs and are ultimately affected by their beliefs and attitudes, being never completely value-free. However, as researchers, post-positivists attempt to remain as objective as possible, so as not to have any impact on the data being produced and minimising the influence these values, thereby increasing research validity. This attitude of recognising and reducing the role of the researcher is also performed in descriptive phenomenology and could arguably provide a justification for combining phenomenology with quantitative methods.

Husserlian phenomenology is a transcendental phenomenological approach with a particular method of *epoché*, or reduction, to draw descriptive and rich insights from only the individual's experience, without influence or bias from external factors. Husserl stated that epoché and reduction could be seen as philosophical reflections to liberate us from our natural dogmatism and make us realise our own consciousness [Zahavi, 2019a]. Proponents of naturalised phenomenology attempt to explore such phenomena from a more pragmatic approach, with a shift in the way of obtaining knowledge, yet certain methodological considerations should be determined. Methodologically, Bockelman et al. [2013] points out the concerns with neurophenomenology and suggests areas of improvements to advance the interdisciplinary approach. The explanatory gap is the unbridgeable gap between physiological processes and human experiences from a first-person account. According to Zahavi [2004], the most promising approach to shortening the explanatory gap between third- and first-person research is Husserlian phenomenology.

Husserlian phenomenologists offer refined accounts of consciousness and a better understanding of the relation between objective processes and their phenomena. Subjectivity was always central to Husserl and he dedicated much of his time to exploring the structures of experience, time-consciousness, body- and self-awareness, and intentionality [Zahavi, 2004]. To use this approach of phenomenology with third-person measurements, Zahavi emphasises the naturalisation of such should be heavily considered in order to avoid any kind of ontological dualism. Nevertheless, Husserl himself was known to be avid anti-naturalist, emphasising this in his long essay in 1911 where he calls naturalism a fundamentally flawed philosophy [Husserl, 1987]. He argued that naturalistic reduction of ideality leads to scepticism and this was one of his major arguments in his fight against psychologism in his book, *Logical Investigations* [Husserl, 1984, 1987; Zahavi, 2004]. Husserl also expressed that philosophy cannot be defined in mathematics and any limitation of mathematical procedure is unfruitful and wrong [Husserl, 1976, 1984].

However, the empirical subject and the transcendental subject are not two different subjects, but rather two different ways of conceiving one and the same subject. The empirical subject is being aware of oneself as an object in the world, and the transcendental subject is being aware of oneself as a subject in the world. Which, by observation, raises the question: how one can begin to naturalise such? Zahavi suggested [2004] one way is to distinguish two different phenomenological approaches to consciousness. Husserl occasionally refers to transcendental phenomenology and phenomenological psychology. These are both used to explore consciousness, but through different approaches. According to Husserl, phenomenological psychology is used to investigate intentional consciousness in a non-reductive manner. It is consequently a form of descriptive and intentional psychology which takes the first-person perspective seriously, but remains within the natural attitude [Zahavi, 2004]. Nonetheless, true transcendental phenomenologists are interested in the dimension of subjectivity and have a much more philosophical approach. Thus, to facilitate naturalising phenomenology is to use phenomenological psychology and ignore the transcendental dimension. However, this throws into question whether this is phenomenology. Ultimately, it is a philosophy, but the concept of phenomenology between applied and transcendental is mutually agreed as a method of taking the first-person seriously and by getting closer to the things themselves.

In his thesis, Kiverstein [2005] explores naturalism and phenomenology in an attempt to close the explanatory gap between the two, and argues there is room for ontology subjects of experience in naturalism. As discussed, phenomenologists believe the world we perceive is shaped by our ways of observing and interacting with it, a worldview that is focused on subjectivity, which we each see through our own lens. This view is debated to defend the argument against naturalism, as Kiverstein states this view shapes our reality, as it is our reality. This therefore supports the idea that the conscious mind has a place in a naturalistic attitude. He claims that creating room for subjective facts is vital for attempting to close the explanatory gap, which opens the possibility for naturalised phenomenology.

In addition to this argument, one of Husserl’s aims with descriptive phenomenology was to understand objectivity through subjectivity [Gadamer, 2004]. Mayoh & Onwueguzie [2012] contested this as an opening in the potential philosophical gateway to phenomenology and the more deductive methods of research. Although descriptive phenomenology is concerned with the interpretation of experience, the acceptance of the objective in Husserl’s approach could provide a level of understanding between phenomenological methods operating with more deductive scientific methods [Mayoh & Onwueguzie, 2012].

Zahavi [2019] explores the concept of epoché and reduction, and its place within phenomenology and applied phenomenology. It has long been debated how the phenomenological method should be characterised from different methods of descriptive, interpretive, hermeneutic, IPA, and empirical phenomenological psychology (EPP), all of which adopt a phenomenological approach. However, only half of these apply epoché and reduction to their methods.

The core of phenomenology as a philosophy is to step back and explore the nature of the knowledge being studied, questioning the overall usefulness and effectiveness of reduction within phenomenology [Zahavi, 2019]. From a Husserlian position, the first step in traditional psychology is to employ epoché to acquire detailed descriptions of the subject/s being explored [Husserl, 1970]. As Mayoh & Onwueguzie [2012] would later agree, Husserl stated that in all sciences, specific themes or variables are bracketed, to enable focus on the research topic at hand, but the method, theory and reasoning behind this reduction can differ [Husserl, 1970]. Nevertheless, without bracketing these specific beliefs and attitudes as suggested by Husserlian phenomenologists, a researcher can use previous knowledge and literature to support and aid them in their research, arguing this is likely to increase understanding of the phenomenon being explored. Phenomenological analysis is used to explore a phenomenon, whether an object or subject. However, to naturalise phenomenology, it can be questioned whether the distinction between the two disciplines be reduced and integrated [Zahavi, 2019].

According to Kirchhoff & Hutto [2016], establishing correspondence between subjective experience and neuro-physiological processes does not explain how lived experiences occur. However, without assuming the distinction between subjective experiences and neurophysiological processes, proponents of NP aim to explore the distinct differences between objective and subjective poles of experience. Here, the focus is on establishing correspondence between both poles of a given experience that relies on introspective accounts. Taking this into consideration, NP addresses the hard problem of consciousness by dissolving it [Bitbol, 2012].

According to Gallagher et al. [2015], the NP methodology could be seen as closely related to integrative pluralism [Mitchell, 2004]. The idea is that not all natural phenomena can be fully explained by a single theory, therefore having multiple explanations involving factors at various levels and scales (such as neuroscientific measurement, psychological and phenomenological approaches) all contribute to an integrative explanation [McGivern, 2008]. Looking at a broader context of the term pluralism in society, this entails multiple people, groups or entities sharing political power. From an epistemological stance, integrative pluralists take the stance that there is not one consistent means of approaching truths about the world, but many. Thus, considering fatigue as a symptom that presents in multiple manners, it could be argued that this needs to be conceptualised and addressed in a multidimensional manner to comprehend the whole phenomenon and its intersubjectivity.

In summary, naturalised phenomenology is a novice methodology, in which the concerns with the laws of nature are considered, but more importantly there is a focus on the research topic under investigation. Although there is confusion about the principles and implementation of NP, Gallagher and Zahavi touch on the boundaries and distinction of NP, and how it could benefit science and researchers studying human experience:

> "The phenomenological interest in the first-person perspective is not primarily motivated by the relatively trivial insight that we need to include the first-person perspective if we wish to understand mental phenomena. Rather, the phenomenologists focus on the first-person perspective is as much motivated by an attempt to understand the nature of objectivity, as by interest in the subjectivity of consciousness*".*
>
> [Gallagher & Zahavi, 2012].

6.4.1. Further methodological considerations

Phenomenological data cannot be reduced to the use of mathematics or statistics: the problem lies in knowing the meaning and value of the knowledge. The epistemology that lets the method rule a whole research project, forcing the researcher to control their phenomena to suit the method and leave out such meanings that do not fit a certain method or model [Dahlberg & Dahlberg, 2020]. The common natural attitude fits the scientific rule to only measure what is measurable and fit the phenomenon in focus. Research needs a methodology and epistemology that is capable of creating research that answers the existential question and allows for multifaceted designs of data generation and analysis [Gallagher & Zahavi, 2012; Zahavi, 2019b].

Since the introduction of neurophenomenology over 20 years ago, there has been vast improvement and progress in the theoretical basis of first-person methods, with many researchers attempting to conduct neurophenomenological studies and recognising the importance of the experiential dimension. However, attention needs to be paid to the challenges of first-person methodologies and how presuppositions should be bracketed. Additionally, NP researchers need to consider the framework between first- and third-person accounts, and the relationship between the two. This guides thinking in the design of experimental paradigms in order to respect the tools and requirements of first-person methodology.

The preunderstanding, the process of thought and understanding, and the evolution of thought, are systematic historical processes that have, over time, led to various interpretations of NP. Gallagher [2018] briefly questions the alternatives to scientific reductionism by potentially rethinking nature, as Merleau-Ponty [1968] envisioned a dynamic, multidimensional approach, that a singular discipline alone should not get the final say because “existence is never just one thing” [Gallagher, 2018]. The key questions to consider are which elements do we allow change and which identity do we want to keep within NP, for NP to encompass richer research but also develop a methodology that succumbs to a level of ontological and epistemological understanding? Zahavi [2019] provocatively suggests that healthcare professionals that wish to draw on phenomenology for research should not look to it as a non-rigorous method, but an open-minded attitude and theoretical framework that can be used in conjunction with other methods.

Referring back to Figure 6.1, the primary purpose of this research is to describe fatigue from first- and third-person perspectives. Improving the understanding of what fatigue means to individuals with MS is of interest, as is exploring if the individual’s physical fatigue as measured with sensors relate to the fatigue that is experienced.

6.5. Methods

6.5.1. Study design & ethics

A cross-sectional mixed methods study (naturalised phenomenological study) with a convergent parallel design was conducted to enable the use, analysis, and interpretation of qualitative and quantitative data. Observational data were collected exploring gait and coordination, and perspectives of pwMS’ experiences of fatigue were collected through a phenomenological interview.

The experimental procedure was approved by the tier two university ethics committee (University of Brighton). Each participant was fully informed about the nature of the research study and gave written consent.

6.5.2. Participants, recruitment, sites, and interviews

Twelve pwMS and eleven age-matched healthy individuals participated in the study (63 ± 7.59 and 57 ± 10.1 years old, respectively). The research was conducted at two sites: 1) the University of Brighton, Health Sciences department, and 2) MS Sussex Centre, West Sussex. The inclusion criteria were that participants were over 18 years old and could walk 100m unaided. For pwMS, there were further inclusion criteria of a definite diagnosis of MS, and a score between 1 to 5.5 on the self-administered Expanded Disability Status Scale (EDSS-S). There were no restrictions on the type of MS. Orthopaedic conditions in the trunk or lower extremity that affected gait, or the inability to complete the assessment physically due to any other chronic illnesses, excluded participants from the study.

Recruitment was conducted through purposive sampling at the Eastbourne MS Society and the MS Sussex Centre. The researcher attended events such as coffee mornings and talks to promote the study, but also general days of attending the MS Sussex Centre with information at hand if people expressed interest. For the healthy cohort, participants were recruited through the University of Brighton and the University of the Third Age (U3A). Word of mouth was used through the staff at in university’s health sciences department, and an informal talk was given to U3A at a community hall in Eastbourne. The study was described in poster-form, displayed in both the Eastbourne MS Society’s and the MS Sussex Centre's newsletters. If participants showed interest, a participant information sheet was given via email or in person. As expected, recruitment was slow; it was challenging to engage the interest of pwMS as the research was an investigation of fatigue, its exacerbation, and experiences of fatigue.

The assessment days were conducted between the two sites, depending on the preferences of individual participants. The interviews were conducted immediately after the physical assessment, in a separate and private room. These were conducted in a conversational manner, focusing on the experiences of fatigue. The interviews were recorded on a Dictaphone, which was placed in between the researcher and participant to receive the clearest recording possible.

I (the researcher) began the interview by asking the pwMS for a concrete description of their lived experiences: “Can you discuss with me your lived experiences about MS fatigue in as much detail as possible? You may start by reflecting on the assessment you have just completed.” The interviews and analysis process were guided by Giorgi’s descriptive methodology [2009], entailing an open-ended interview with appropriate probing and clarification when needed.

The length of interviews ranged from 20 to 50 minutes, depending on the participant's articulation, description, previous experiences of fatigue, and willingness to share. The content of the interviews was focused on the pure, essential description of fatigue and common daily life situations. Some of the participants who experienced fatigue most of the time, had difficulty relating and describing one particular experience. In situations like this, the researcher asked the participants to reflect on a typical day. Following the interviews, all interview data was securely loaded onto the researcher's university computer, which was password protected. The data were then transcribed by a professional transcription service in preparation for data analysis.

6.6. Procedure for assessment day (see Appendices 3(i) and 3 (ii) for full protocol)

Each participant completed a demographic form, the EDSS-S, and two questionnaires to assess the participant’s fatigue and disability (MFIS and MSWS-12) before the assessment and interview began. These forms took approximately 20 minutes to complete. Each participant was given a study ID pseudonym (M088, M089 and so forth). Subsequently, five safe, non-invasive sensors were placed on each participant in the following locations:

- Left and right ankle on the lateral aspect 2cm above the lateral malleolus
- Left and right thigh on the lateral aspect with the most distal part of the sensor 5cm above the superior border of the patella
- The body of the sternum

Figure 6.2A.: X-io NGIMU sensor.

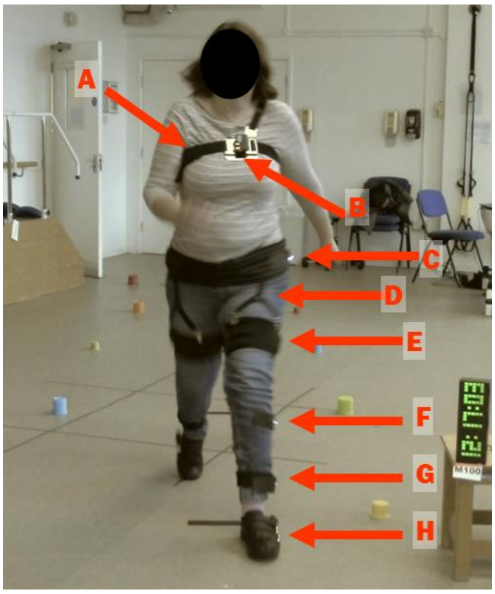

Figure 6.2B.: Frontal view of a pwMS walking. A: Harness, B: Sternum sensor, C: Sensor & light at hip, D: Thigh Fasteners, E: Thigh sensor, F: Fibula head (light only), G: Ankle sensor & light, H: Shoe sensor.

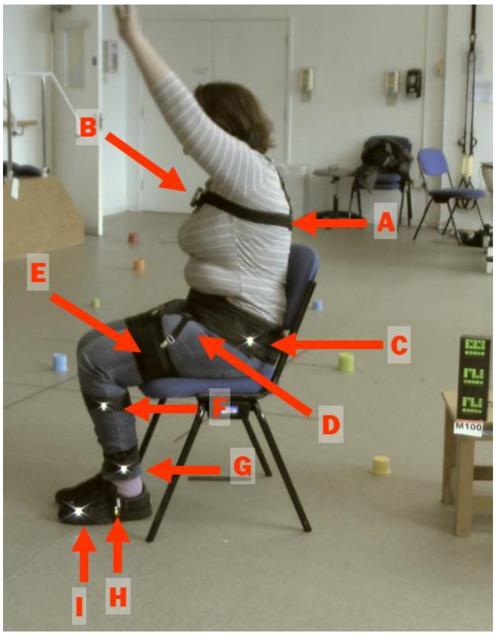

Figure 6.2C.: Lateral view of a pwMS seated. A: Harness, B: Sternum sensor, C: Sensor & light at hip, D: Thigh Fasteners, E: Thigh sensor, F: Fibula head (light only), G: Ankle sensor & light, H: Shoe sensor, I: Toe light.

The sensors (see Figure 6.2A) were orientated with the positive x-axis pointing superiorly (proximally). Sensors were placed on the lateral surfaces of limbs to avoid interference with walking, and over clothing, fitted with Velcro elastic straps, with an elasticated harness placed around the ribs and left shoulder to secure the sternum sensor. All participants wore standardised running shoes (Lonsdale), fitted to the correct size.

A repeated outcome measure was used by conducting baseline measures of a short walking test, the T25FW. A 6MW was performed to elicit fatigue, and then the measurement from the baseline period was repeated immediately after the 6MW. The walking assessment lasted approximately 12 minutes. After completion of the walking tasks, the sensors were removed (approximately three minutes to remove) and after a short rest (5-10 minutes), the phenomenological interview took place. The entire procedure for a single participant lasted approximately 90 minutes.

6.6.1. The self-reported questionnaires

The EDSS-S was used to assess the eight functional systems to evaluate and monitor the disability of pwMS, as graded from 0 (no disability) to 9 (bedridden). The questionnaire consists of 18 statements based on the original EDSS, but were assessed by the patient rather than the physician [Bowen et al., 2001]. Bowen et al. [2001] developed the EDSS-S to create a more accessible, cost and time-effective measure for researchers to use. It demonstrates acceptable reliability and validity when compared to the physician administrated EDSS, with an 84% agreement and scores within one point of each other in more than 70% of cases [Bowen et al., 2001]. It is worth noting, individuals using the EDSS-S usually score higher than the physician administrated EDSS [Bowen et al., 2001].

The modified version of the FIS (the MFIS) consists of a self-administered 21-item questionnaire that encompasses physical, cognitive, and psychosocial aspects of fatigue derived from interviews concerning how fatigue impacts pwMS [Fisk et al., 1994].

The MSWS-12 is a self-reported measure of an individual’s walking ability, consisting of 12 questions. It is a reliable and valid patient-based measure of the impact of MS on walking [Hobart et al., 2003].

6.6.2. Independent variables

Two walking tests were conducted: the T25FW and the 6MW.

6.6.2.1. Six-minute walk (6MW)

The 6MW is commonly used to assess ambulatory capacity during six minutes of walking and has been identified as a valid, reliable, and reproducible test of endurance ambulation performance in pwMS [Goldman et al., 2008]. The 6MW lasts long enough to elicit steady-state aerobic metabolism and it is sensitive to mobility disability, walking impairment and fatigue [Goldman et al., 2008; Motl et al., 2012; Savci et al., 2005]. The assessment was conducted according to Goldman et al. [2008] with a walkway modification due to facility limitations (a 25ft walkway, unlike American Thoracic Society [ATS] guidelines of 100ft). Participants were instructed to walk as fast but as safely as possible back and forth on the 25ft walkway, to cover as much ground as possible. The walkway was measured and then marked using a manual measuring tape. Stopwatch measurements started on the word “go” and ended on the six-minute mark. Participants were informed of the time after each minute and were instructed to stop exactly where they were at the six-minute mark.

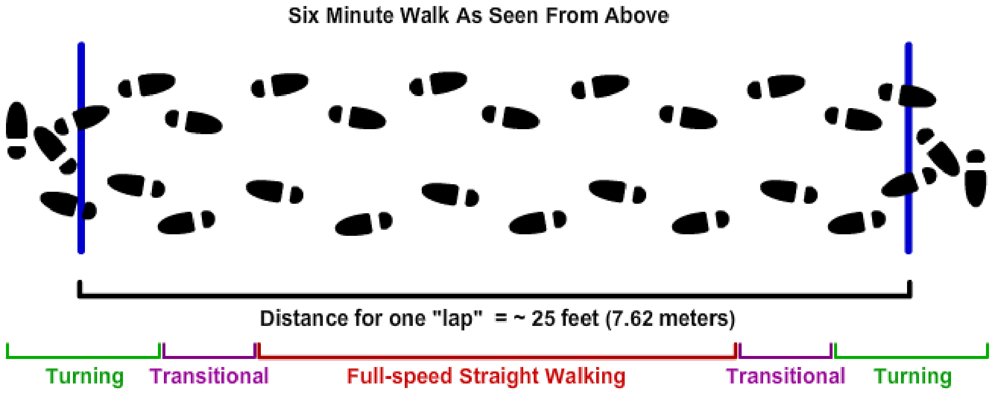

Figure 6.3.: 25ft walkway aerial view.

6.6.3. Dependent variables

Wearable inertial sensors (NGIMU, X-io sensors, Bristol) with three dimensions each of accelerometry, gyroscopy, and magnetometry, were used for gait assessment [Madgwick, 2010]. These sensors were factory-calibrated with each x-NGIMU node sampled at 100Hz. All sensors were factory-calibrated for gravitational acceleration (accelerometers) and angular velocity (gyroscopes) and incorporated an onboard algorithm for the estimation of heading and quaternions. Data acquisition was synchronised by the recording of individual sensor signals via Wi-Fi according to the standardised software from the manufacturer. Data from the sensors were aligned with other measurements and video recordings and all synchronised to the same clock. Directions used for the sensors (namely pitch, roll, and yaw) are shown in Figure 6.4. Kinematic parameters of the thigh and ankle were calculated to identify velocity, peak angular velocity, and inter-step interval during the 6MW. Stopwatch measurements of time for all walking tests (seconds) and total distance walked (feet) for 6MW were recorded. Lastly, phenomenological interviews were conducted to gain an in-depth understanding of the participants’ experience of MS-related fatigue in their everydayness. As part of the phenomenological process, open-ended questions were used to assist reflection for the participant.

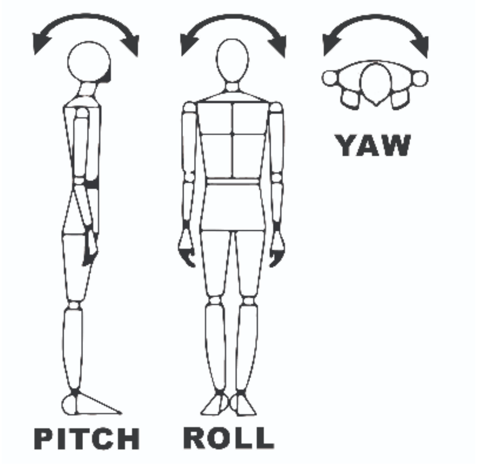

Figure 6.4.: The approximate directions of pitch, roll, and yaw as described in this research. Pitch rotation around the medio-lateral axis, roll rotation around the dorso-ventral axis, and yaw rotation around vertical (superior-inferior) axis (credit to C. Westling, from Witchel et al., 2018).

6.6.4. The process of phenomenological analysis

Phenomenology refers to a human-scientific approach whereby one does concrete analyses of meanings of specific experiences by using steps consistent with Husserl’s philosophical phenomenological vision [Giorgi, 1997]. The qualitative data was collected by interviewing participants on their experiences of fatigue. The researcher aimed to keep the participant's attention focused on the experiential aspects of the research, to maximise the descriptive accounts and reduce certain beliefs and external influencing factors. Phenomenological analytic procedures were used in this research, following the step-by-step data analysis of Giorgi et al. (derived from Husserl) as a guide. Descriptive phenomenology gave me structure and acted as “training wheels” to attend to the phenomenon. Following Giorgi’s descriptive method allowed me to be faithful to the phenomenological orientation. The step-by-step analysis is as follows:

1) The first step is to read through the written descriptions provided by the participants all the way to the end. In order to do a proper analysis, one has to know how the described lived experience ends.

2) While the everyday natural attitude is sufficient for the first step, the rest of the analysis requires that the researcher assumes the attitude of the phenomenological (or scientific) reduction. This means that the objects that emerge within the description are

> taken to be phenomena or simply objects that present themselves to the consciousness of the experiencer but the notion that such objects really exist in the way that they present themselves is not acknowledged.
>
> 3) Now, since descriptions can be lengthy they have to be broken into parts so that proper analyses of the descriptions can be done. Since phenomenological analyses are concerned with the discrimination of meanings the separation of the parts of a unified description is based upon meanings, and each part is called a meaning unit and it is determined by a careful rereading of the description with the intention to distinguish parts from a phenomenological perspective.
>
> 4) Once the meaning units are determined, the task of the next step is to transform the meanings contained in the description in phenomenologically sensitive ways. Thus, the attitude to achieve this task requires one to not only be in the attitude of the phenomenological (scientific) reduction but also that one be sensitive to the meaning of what is being expressed.
>
> 5) The last step is to get the general structure of the experience. This is done by reviewing all of the transformations written in the second column in order to determine the essential ones. [Giorgi et al., 2017]

Aspects of the lifeworld will be considered throughout the stages, especially in analysis: (1) selfhood, (2) sociality, (3) embodiment, (4) temporality, (5) spatiality, (6) project, and (7) discourse [Ashworth, 2016].

After exploring the essential features and overarching phenomena in pwMS' interviews and experiences of fatigue, data analysis of sensor data were conducted. Ankle and thigh kinematic representative graphs were constructed to identify key features of the gait cycle, to enable data analysis of gait parameters.

6.6.5. Kinematic identifications of the ankle and thigh

Before describing the data analysis and statistics, representative data of raw sensor data (pitch gyroscope Z) in a pwMS and healthy control at the ankle and thigh will be presented. This illustrates how each phase of the gait cycle was identified and used in this study.

6.6.5.1. Ankle kinematics identification graphs

Pitch gyroscope data from the ankle sensors were used to determine the duration and rate of movement of the ankle and knee joint during the 6MW. Figures 6.5A and 6.5B show pitch (gyroscope Z) of the right ankle in a pwMS and a healthy control. Identification of the peaks and transients include the start point, maximal toe flexion, toe-off, peak angular velocity, heel strike, and endpoint to calculate duration and peak angular velocity.

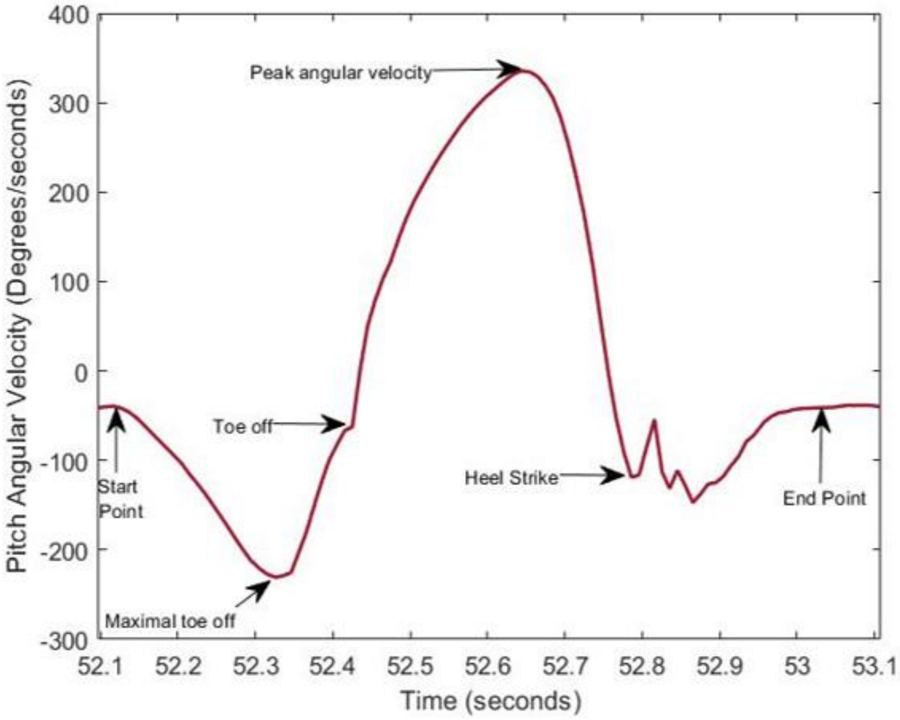

Figure 6.5A.: Representative trace of a pwMS (M092) right ankle peak identification of one gait cycle.

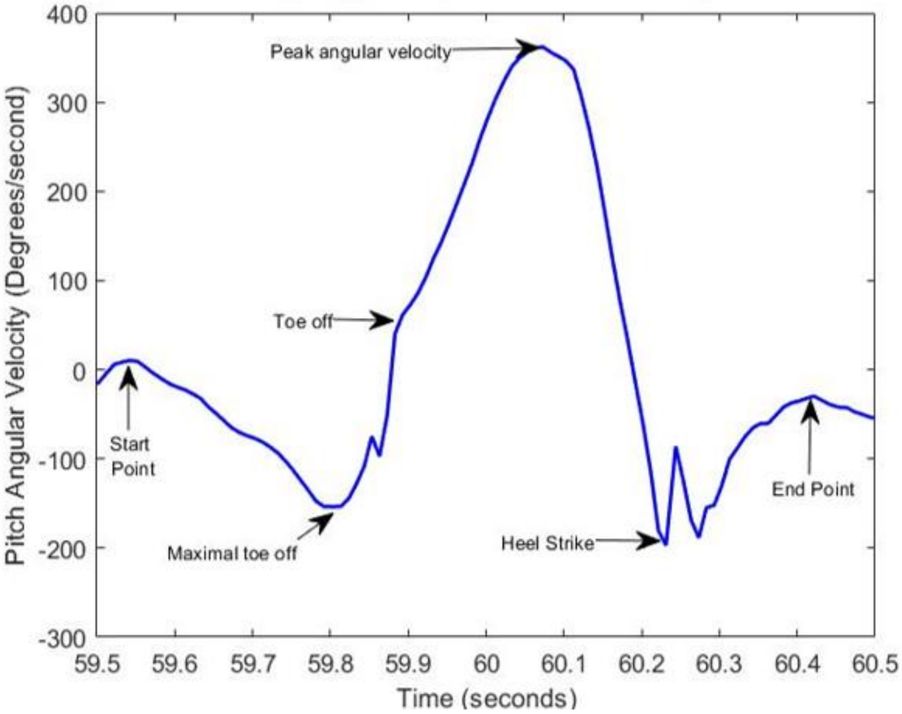

Figure 6.5B.: Representative trace of a healthy control (M099) right ankle peak identification of one gait cycle.

The start point represents the beginning of the gait cycle, foot flat, the ankle rocker allows momentum as the body weight moves from the heel to the forefoot. Plantarflexion increases as the heel rises to prepare for propulsion. Maximal toe-off was detected at the peak negative angular velocity as the weight is transferred to the forefoot. Toe-off was identified as a brief deceleration before maximal peak angular velocity where maximal toe flexion occurs. Mid-swing is representative of the peak angular velocity and was identified as the maximal peak of each gait cycle. Heel strike was identified as the initial negative transient after maximal peak angular velocity where the heel first makes contact. The endpoint marks the end of the gait cycle of the ankle, where the foot returns to foot flat.

6.6.5.2. Thigh kinematics identification graphs

Figures 6.6A and 6.6B represent pitch gyroscope data of the thigh in a pwMS and healthy control that were used to identify the relevant peaks and transients, to detect stages of the gait cycle. The following gait identifications were derived from gyroscope (pitch) data: start point, start flex, flexpeak1, toe-off, flexpeak2, terminal swing, heel strike, braking, knee lock, extendpeak1, end extend, and endpoint. Start flex, zero flex, terminal swing, braking, and end extend were used as an approximation and used to determine each stage of the gait cycle for the 6MW.

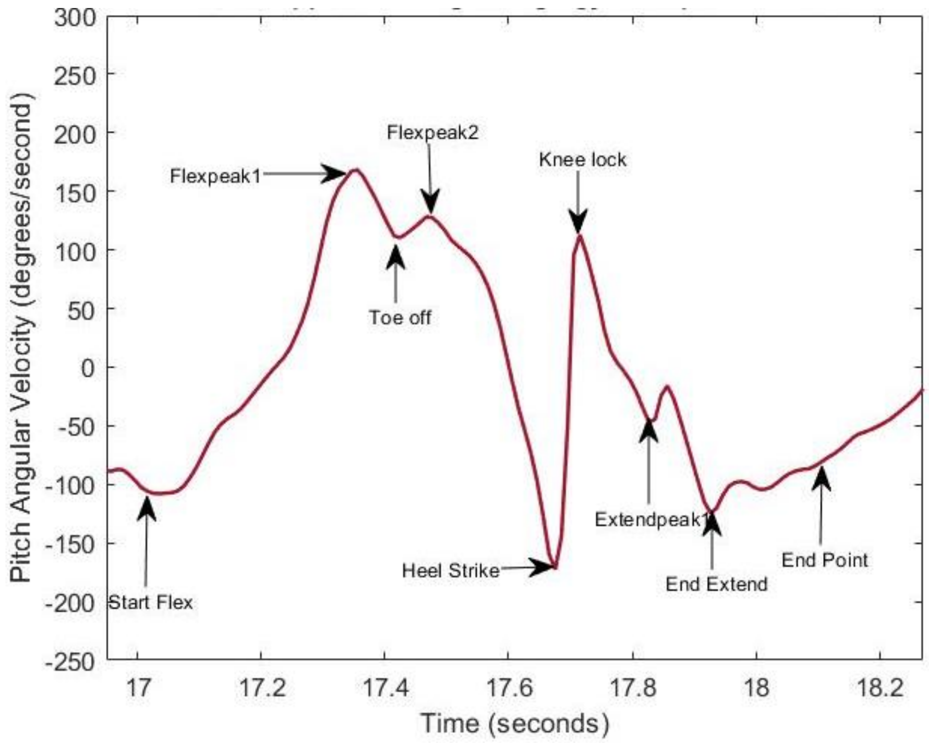

Figure 6.6A.: Representative trace of a pwMS (M089) right thigh peak identification of one gait cycle.

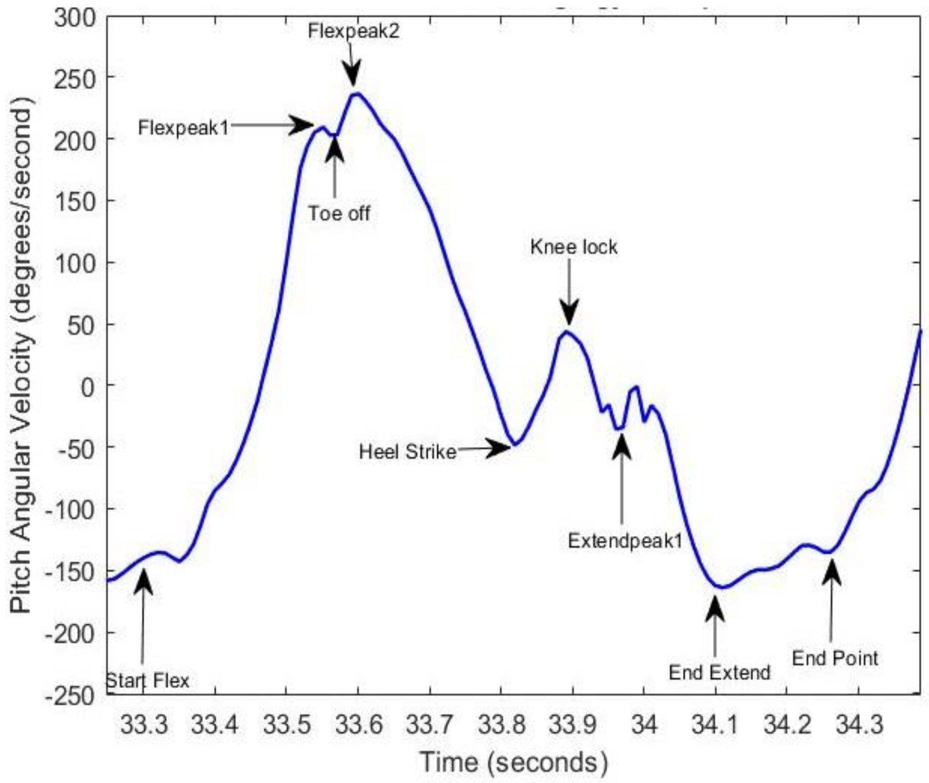

Figure 6.6B.: Representative trace of a healthy control (M102) right thigh peak identification of one gait cycle.

6.6.6. Sensor data analysis

Analysis of waveforms was conducted in MATLAB (Natick, Massachusetts, USA) with peak detection algorithms based on a low pass filter of the signal. Data was imported and the appropriate channel was selected. Purpose made scripts were used to perform data analysis to calculate peak ω and inter-step interval throughout the 6MW using the DTW. The steps were recognised via pattern recognition (DTW) that fits repeating data from the participant (the query) to a pre-established template [Barth et al., 2015]. The DTW can be used to fit a query that may vary in time or speed to the standardised template [Myers & Rabiner, 1981]This was used to mark out points of interest where the steps and heel strikes were in this research. The ω signals of pitch at the ankle and thigh (gyroscope z-axis) were fitted to a template pattern that is representative of taking one step (one gait cycle) during walking. There were two templates for the ankle and thigh that were both linearly scaled (including the query signal) from -1 to 1, where zero values were maintained. A template overlay of the DTW is shown in Figure 6.7.

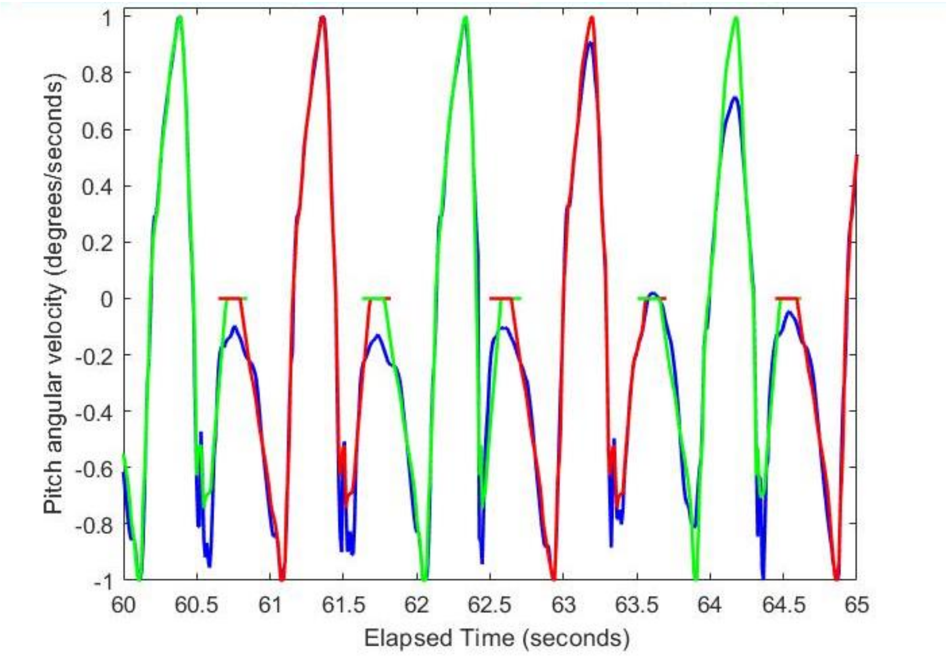

Figure 6.7.: Representative trace of DTW overlay (identical templates in green and red) of M100 right ankle onto pwMS data for the ankle gyroscope Z axis (blue trace). This graph shows five seconds of the 6MW. Where no blue is visible (i.e. under the red and green templates), the fit of the query signal to the template is nearly perfect, showing that the automated pattern recognition of DTW can recognise individual steps extraordinarily accurately, despite the variation in timing and angular velocity between steps

Performance decrement during the 6MW was objectively quantified by focusing exclusively on the time periods where the participant was walking straight. This required accurate elimination of data during turning. Turn detection (TD) was performed by analysing magnetometry signals at the sternum in order to identify and remove each turn before further gait analysis. TD was measured by the change of local magnetic field measured in both horizontal magnetometry Y (dorsoventral) and Z (mediolateral) axes. The detection of square-like waves (see Chapter Nine on TD, section 9.3.2.2.) was calculated using an algorithm that forms a histogram to identify the bimodal pattern of the magnet signals; the two modes are the forward and backward laps of the participant. The difference between each sample value from the two modes determined the initial estimate of direction. The algorithm consensus value for each sample used a four-second window to determine whether the median of instantaneous measures was forward or backward. The change in direction was stabilised by a pair of Boolean values that toggled at either the start or end of the turn. The TD data was then removed to investigate the peak ω of the thigh and ankle of the dominant and weak leg. This was compared to the average of both legs of healthy participants.

A Microsoft Excel spreadsheet was developed for each 6MW performed and each phase of the gait cycle (as shown in sections 6.6.5.1 and 6.6.5.2) was organised into columns that were separated into sheets of accelerometer magnitude values, gyroscope magnitude values, elapsed time, inter-step interval at heel-strike, and turn times. To calculate kinematic characteristics at the ankle and thigh, the gyroscope magnitude was calculated from gyroscope X, Y, and Z signals to represent more accurate data of overall motion that would not be influenced by small eccentricities of individual sensor placement on the body. The following equation was applied:

$$\sqrt{(Gyro\ X^2 + Gyro\ Y^2 + Gyro\ Z^2)}$$

Average peak ω for each minute was calculated by assembling every step's maximum peak swing (from DTW) and, based on the elapsed time values for the steps, removing ω values associated with the turns that had been identified by magnetometry signals. The peak ω values were then sorted into each minute of the 6MW. The dominant and weak legs were both calculated and assorted accordingly.

To measure the decline in peak ω from the first to all the other minutes of the 6MW (as a reflection of fatigue as performance decrement) to compare how far the peak ω deviates from minute one, the average of peak ω values from minutes two to six were subtracted from the first minute. This calculated how far the peak ω deviates from minute one by identifying the degrees per second change in ω. The mean value of each minute was then determined and plotted. Additionally, calculations were made in an attempt to identify changes in gait and fatigability by repeated baseline measurements (T25FW), and the first and last minute of measurements of the 6MW (distance covered and peak angular velocity of the thigh and ankle). The parameters were then subtracted from one another (the last measurement subtracted from first) to produce a composite measure of fatigability.

6.6.7. Statistics

The normality of the data was confirmed by visual inspection of histograms, followed by Shapiro-Wilk and Kolmogorov-Smirnov tests. Data acquired from the stopwatch measurements and the sensors were not consistently normally distributed. MATLAB was used for inferential statistical tests to assess the significance and the strength of association between variables. Parametric tests used were analysis of variance (ANOVA) and unpaired t-tests. Non-parametric tests included Kruskal-Wallis ANOVA, Wilcoxon sign rank and Mann-Whitney U tests. To investigate the minute-to-minute change within the 6MW, the mean value of each peak ω from pwMS to healthy control from minutes two to six were subtracted from minute one. To calculate the correlation between descriptive statistics and the composite measures of fatigue, Spearman's correlation coefficient was used.

Chapter Seven: Phenomenological findings and discussion of fatigue in MS

In this chapter, a rich description of an individual's experiences of fatigue is presented. These are divided into four constituent parts: the familiar body falling away, sweeping sudden fatigue towards stasis, cloudiness of consciousness, and managing the everydayness. A biographical summary of each pwMS is given, to portray and characterise each phenomenological journey of fatigue. Through the phenomenological discussion, fatigue is highlighted as experiences through lifeworld insights and relational experience. The embodied experience and aspects of selfhood are recognised as significantly important to pwMS in this phenomenological study.

7.1. The constituents: Familiar body "falling away"

Fatigue was experienced as an extremely unpredictable journey, with a common emphasis on a specific part of the body "falling away". There was an adjustment away from bodily familiarity as a background context, where bodily and psychological actions were altered with little choice. The challenges faced were many, as bodily actions noticeably changed through, for example, an increase in leg dragging, coordination and balance impairment, reduced lower limb strength and heaviness, and increased choking and slurred speech. Participants often described a sense of "losing control" over their body as a whole-body phenomenon, and occasionally referred to it as almost unresponsive. Descriptions included "treading treacle", and M090 described climbing a flight of stairs using a comparison to climb her Everest. Another participant reported the everyday difficulty of movement and mentioned the transition of sitting to standing needing substantial energy and the occasional use of assistance with a stroller. When severely fatigued, any form of small movement was considered a great deal of effort, such as the motion of lifting an arm reported as not even possible due to complete exhaustion. Visual markings on shoes were emphasised as a useful indicator of ambulatory fatigue and impairment, as one participant suffered from severe leg dragging from fatigue when first diagnosed.

Often fatigue brought the need for a forced exertion. For example, it would make M089 grit her teeth in an attempt to get up from a chair. She described her right leg as "mushy" because of the numbed sensation and lack of control. Fatigue was sometimes referred to as a trigger. M084 would experience physical numbness from the chest down when fatigued, which affected the sensation in her legs and feet, almost a half body in a sensation of numbness. The continuous bodily sensation alterations were described in various ways as penetrating sensations, such as “broken glass” and “pebbles under her knees”. The feeling of the body slowing down, halting function, and not permitting full ability to perform daily activities added an element of overwhelming frustration to most individuals. The disruption experienced and often consequent lack of understanding by others caused exasperation for most, partly due to the invisibility of fatigue to others.

The dilemmas inherent in changes to the sense of their embodiment lay within the domain of a kind of denial, and called for new effortful learning by participants to acknowledge their fatigue. The notion of acceptance and acknowledgment was typically part of the process of coming to terms with their existence with MS. Some participants stressed the importance of fatigue acceptance and a kind of letting be, as this process had an impact and knock-on effect on the management of fatigue,

> …that’s the card you’ve been dealt, get on with it, accept it, that’s what you’ve gotta do. (M094)

Some participants reported improvements in the relationship between MS and fatigue, once the transition to some kind of acceptance took place. M094 expressed this in a resolute way, such determination and motivation to continue living “as normally as I know” how, by exercising, socialising with family, and going on holiday. Even on a day defined as a “non-starter day” or “MS day”, some participants needed a sense of accomplishment within their day, thereby forcing themselves to undertake activities, even if it was as little as walking for a short period of time.

An inner monologue was mentioned as a motivational strategy, for example for M094 to continue walking (during the 6MW assessment): “I’m getting tired now, right shut down, don’t think about the time, just concentrate and keep going”. The inner battle with self was described often. Some participants wanted to achieve a task whilst fatigued so that in the end they believed they had not given in to fatigue; a sense of not being beaten by fatigue was important. M097 made sure to do certain desired activities, although believed that listening to her body was the best strategy for coping with her fatigue. Otherwise, fatigue would affect her later on and more significantly:

> But I think you have to make yourself do things but at the end of the day you have to listen to your body and when your body says you've had enough, you've got to sit down. It's no good trying to fight it because it just makes you feel worse. (M097)

The everyday unknown nature of the body was changed, and the body's existence became apparent and visible. When embodied perception had shifted, a feeling of "going off course" was experienced. Therefore, embodied changes created hesitation on many levels and included aspects of everydayness such as simple walking and stepping:

> …just to make sure, second guess yourself in thinking, second guess yourself in walking, stepping, running, I wouldn't attempt, but I'd probably be okay about it, I ride a bike and I feel fine riding a bike, I feel safe to do that, if I'm gonna be doing that kind of exercise, running I, although I go to a gym, um, I wouldn't risk running on the running machine. (M105)

However, the sense of hesitancy was very deep and sometimes even required a heightened sense of awareness, as M105 described for example how he "second guesses" his foot placement for walking and stepping in a painstaking way. Participants also tended to be aware of body image and how others portrayed them. Fatigue for a few participants would penetrate through physical actions and leave outward signs, such as the swaying of the torso and scuffing of the feet, which was quite often visible to others. M084 reported that her partner would get agitated about her posture and general stance when she was fatigued, referring to it as "you've got your Quasimodo on again". However, she saw this as support, by regularly monitoring her walking to inform her when she might need walking aid and direct help.

Spatial awareness was heightened for M084, with symptoms needing physical support unless confident in the surrounding environment. In the event of falling, M084's equilibrium had to be restored in both her cognitive and bodily state. This was taxing, and she felt ensnared by this. It caused self-imposed constraints for ease due to an unreliable body and effort. Until M084 felt ready, she was unable to walk again: "I've got to get my headspace right before I can get my body space right". Time is required in order to restore herself and regain equilibrium. Physical aid from other people would not help her, as the act of being helped up by others would immediately cause the inability to stand on her feet.

Through these novel and sometimes subtle changes, a participants' body implies fatigue within the lifeworld, but with sensations that caused a sense of uncontrollability, or where the body sporadically decreased in usual bodily function, especially in the lower extremities as through common daily activities such as walking was reported to be of much more difficulty.

7.2. The constituents: Sweeping sudden fatigue towards stasis

Participants described a specific facet of extreme fatigue that assailed them and took control over bodily and self-function. M090 experienced crippling fatigue characterised as “treading treacle”. This was the inability to move any limbs, which physically hurt due to the overwhelming wave that created a sensation of severe heaviness in her legs, which caused her to feel “as if she was walking through sand”. One of her first memories of this paralysing fatigue experience was at her workplace, where she excused herself from a meeting so she could crawl and lie under a desk in the closest room “for a minute’s peace”. The cumbersome severe bodily sensation led her to a decision to go immediately to the hospital wheelchair-bound, as the fatigue was too debilitating to ignore, so debilitating it took her one hour to walk 50m to the bus stop.

This all-encompassing kind of fatigue “hit” another participant, M105, in the lower extremity as his legs literally gave way, without any prior warning:

> …it’s like I fell down a hole, that’s how I felt. I walked through the hallway, felt fine, took me jacket off, put it round me, to hang it up, walked through into my kitchen and then I was on the floor. (M105)

There was no notion of trying to stop himself from falling as the incident happened too fast for him to be aware of it. He interpreted his legs giving way as an instant reaction, “they just literally stopped working”. He had no recollection of falling, apart from the motion of falling forwards. No preconception or awareness of embodiment was afforded to him before his body took this action and therefore, confusion was a common emotion experienced for him post-incident as he attempted to grasp an understanding of what and why it had happened:

> …confused as to why it happened, not confused as to where I was, or who I am or… I just was thinking, what happened there? It’s like I fell down a hole, that’s how I felt. (M105)

In a different way, sudden fatigue with stasis was like being drained of all movement or energy. For example, M093 recounted the distinct experience of fatigue related to her flight to America. The process of a nine-hour flight, going through passport control, and queuing for luggage heavily impacted her state of function, as she was bedbound for two consecutive days on the arrival at the start of her holiday. The inability to move any part of her body as her limbs felt unwieldy, the smallest movement of sitting up was not feasible as she felt depleted, “absolutely exhausted” and drained of any energy,

> … I went to America when I got off the flight, we were going through passport control and I felt really terrible. I felt I just had to lay down, I just had to lay down, I couldn’t even function, I couldn’t do anything. We planned, there was twelve of us, we planned we were gonna go to Magic Kingdom and everything, I couldn’t do it, I couldn’t go out. (M093)

This impacted her planned activities as she was unable to function to any level of her normality, resorting to resting and lying down for two days.

A common characteristic described by participants was the experience of reduction in bodily control. M097 described the overwhelming nature of fatigue that caused her “hands to uncontrollably shake”. This increased difficulty to do daily tasks, like putting earrings in or walk a short distance, with legs described “as heavy as lead”. Outdoor world factors affected individuals’ fatigue. One participant mentioned the summer heat exacerbated his fatigue, rapidly by taking his breath away:

> …just takes the oxygen and your breath away and you feel you can’t breathe. You get very tired very quickly. (M094)

Although some participants expressed enjoyment from sunshine, the increase in temperature affected the way some participants were able to live with and function with their coordination, such as leg sensation and general movement.

Once the wave of fatigue experienced collapsed, an element of stasis and a sensation of motionless was characterised in pwMS. Some participants described the bodily inability to move due to fatigue, and kept their body as still as possible, with lying on the floor as a coping strategy until the peak of fatigue had passed. Most participants needed all their senses to be reduced or dampened down momentarily and senses had to be rested to revitalise: “I have to shut my eyes, lie down in silence” (M092). The need for a calm and restful surrounding gave participants no choice but to rest, sit down and recharge. This aftereffect required a rest period as the body is known to be tired. The physical action of “putting my feet up” was part of the recovery process for M105. Participants used analogies to explain the kind of resource deficit or depletion experienced in fatigue:

> …it's like having a reservoir, and when it's empty, it's empty. If I keep trying to go then I get pay back later on, it's usually worse. (M096)

For some participants, the resting period was exceedingly long. For example, M090 was bedbound for several months and completely restricted, with a complete loss of sense and sight, but this was temporary and reversible over a long time period. The statement "I mean I just did nothing, I just was in bed" creates a sense of darkness as time became static for her, "…all I wanted to do was just lie there and sleep it off" (M090). During these months, simple life necessities, such as going to the toilet, were made extremely difficult.

At its extremes, fatigue can be all-engrossing for pwMS, and sometimes fatigue caused temporary debilitation to most senses. It was often described as a wave of heaviness that was experienced as intractable and only able to be controlled by participants through understanding their own individual limit.

7.2.1. Body and self

Remarkably, M097 expressed the feeling of the body being separate from self altogether. She also described her body speaking to her in her internal voice, "…it's aching, stop moving, sit down and relax", speaking to self to encourage body function and reconnection. Some participants experienced a feeling of body detachment, as they experienced no control over their legs, almost as if "an alien had taken over control".

Some participants had to relearn how to walk, and the jerky and unnatural movement of the lower limb extremity movement created a sense of disconnection from the whole embodied self:

> …having been a keen mountaineer for all my life, but not a mountain walker I describe myself as, I had to learn to walk again, weird, really weird. I mean the first ones clearly it was because my legs, my leg muscles weren't working properly um because my, my main disability and it's only a mild one, the spasticity, and so my, cos whenever I walk, even now, I, I feel whether it's obvious or not, I mean the move, the movement is totally jerky all the time, every time I walk, it's jerky… I have to do is relax, and just sort of stick them out and hope they land in the right place, well that, that's how I learnt to walk again. (M083)

Without fully comprehending the reasoning behind this, she then went on to say:

> …but somehow the whole system seems to work together, and I don't, I don't understand how it works. (M083)

A disassociation of the whole was only succumbed by time. A sense of control and adjustment was achieved through preparation to compose oneself into their correct state of self to then feel ready to function within their body. Another participant's natural movement that once was taken for granted was now more difficult, as the natural unconscious movement no longer worked effectively. Concerning the prompts to consciously think of each phase of her leg movement whilst walking, cogitate her leg placement and movement:

> I know, I always have to prepare myself where I'm going to go and have to use a stick. Because any unevenness, and I'm, I forget to think of my feet, and I'm, I'm gone. (M089)

And the taxing concept of initiating body movement for each step as individuals felt the need to advise their body, especially lower extremity on when and how to move:

> …your brain tells your foot or your you know, you, you learnt how, you know, when you're sort of, how you stretch and how far you have to go to get that glass. But I probably think it's already there, then I'll do this. It's likely that with, with, with the leg, my, you learn to walk and then you don't think about walking anymore do you? While I have to actually um err relearn you know, every time I'm walking I have to think of my feet. (M089)

M084 occasionally remarked on the state of body and reversibility as her legs occasionally struggled to hold her body in a certain position, therefore demanding herself to rest and sit on the floor. The demanding notion of continuously instructing her legs to walk would exacerbate her bodily fatigue, causing no choice but to rest and restore herself. This made multitasking increasingly difficult, even for those who felt they were able to multitask prior to diagnosis:

> I could never do window shopping you know. Where you either walk along and have a look at a window, can't. I have to stop and look at the window and then carry on. No, no because um as soon as my head is turned. My, my balance and everything goes out… (M089)

This change of identity gave a tone of embarrassment as one participant felt out of control and useless in front of her work colleagues when discussing her ill-health retirement. With the disengagement of her body, she described her body as "useless" as she hadn't gotten properly dressed in months and was portraying an image she did not necessarily want to convey to colleagues. Her sense of agency was weakened, and she expressed little control over her bodily image. Her selfhood was altered and revealed to colleagues in a non-typical way. Both her sense of ownership and agency felt lost as she explained the concept of change by going into retirement, as well as her sense of self and external image to others.

Another change in body imagery, M105 expressed the unconscious swaying of the torso was conveyed to surrounding people not as MS or a health condition, but a man who was inebriated. Regarding the interaction of mobility of the self and body, M092 explained that exercise kept her perceptively strong, even if after some exercise classes she felt exhausted bodily. She felt the importance of exercising the whole self:

> …unless I keep myself well physically, I'm not gonna keep myself well mentally…so the two together are so important. (M096)

Overall, an element of body disengagement as a dislodge from the self and a dislocation from the body makes individuals hyper-aware of the feeling of instructing their body to move. The communication between self and body was exceptionally frustrating as the ability to multitask was gone. M084 found that the act of walking and window shopping at the same time was impossible: the ability to concentrate on the act of walking and observing the shops was not possible. Also, if M105 found himself organising multiple things in his head at once (in an attempt to prioritise), he would get fatigued and this would cause blurred vision. The act of multitasking caused an almost overwhelming feeling of inefficiency.

7.3. The constituents: Cloudiness of consciousness

As well as bodily implications, many participants described an overbearing sensation of "a cloudy conscious" affecting the ability to process thoughts or make clear decisions on any functional level they felt was normal for them. This was often described as "brain fog", "fuzzy head", "mind fog", and "muzzy headed", and would make pwMS feel a sensation that they had been "switched off".

A range of cloudiness was described depending on the individual, the day, and the cause of impact. For example, M084 explained the draining feeling of processing information all the time and had become familiar with, and knew well, its impact on and delay to her thought process. She describes how fatigue predominantly influenced her state of mind and consequently impacted her sense of being whole. There was an underlying intrinsic awareness of her symptoms as a whole phenomenon. Here, her “equilibrium” needed to be restored in order to function, and this was a demand that had to be lived with:

> I’ve got to get my headspace right before I can get my body space right. (M084)

The self-imposed constraints used in order to manage an unreliable body required her to constantly readjust “herself” and “her body”. This process of vigilance that was an ever-present demand made her tired and frustrated as she “felt like she was attempting to escape from it constantly”. Similarly, M105 referred to “a time delay for cogitation”; tasks such as completing a form and reading a book would trigger his inability to understand and think clearly. He expressed how this was also linked to a semi-reliance on medication, to help cope with the lower extremity symptoms, but he did not exceed a high dose of medication, as he experienced it as affecting his thought process, creating “brain fog”.

The time of the day was reported as burdensome for pwMS: mid to late afternoon was described as a time of significant dips in energy levels. M092 coped through a kind of discipline, refusing to make any important decisions at this time of day because she would often “experience a blur and fogginess in judgment”. The inability to fully comprehend something, big or small, often caused what she described as “emotional fatigue”, a heightened frustration that led to more fatigue. The conscious act of delaying a decision until the next day because of her clouded judgment could cause a lot of frustration because, before her diagnosis, she was good at multitasking. However, she naturally wanted to avoid making “silly mistakes”, so preferred to wait and manage tasks with sequenced rest periods placed throughout the day.

A sense of frustration resonated throughout the participants’ descriptions, as forgetfulness and the ability to do more taxing tasks would cause confusion, disorganisation, and annoyance. M092 explained that one thought could manifest into bigger thoughts and spiral into “the worms in my brain”. This created psychological fatigue as her brain decided it “wants to play mind games” and causes her difficulty in sleeping.

M104 described an experience with therapeutic flaxseed oil and continually forgetting to take it. He acknowledged the importance of placing the flaxseed oil within sight as a visual prompt, otherwise he would repeatedly fail to take it. The distraction of other everydayness, such as making dinner, brushing teeth, or having a glass of wine, would distract him from taking the oil, which often led to frustration: “you know that drives me mad”. To better manage his time, he had a diary with lists and reminders of personal and professional events, although even with such a diary, he could still be forgetful.

This “emotional fatigue” was exacerbated by the uncoordinated ability to do a task pwMS wanted to do. A curb in the activity left some individuals frustrated which had a knock-on effect of weariness. M097 expressed that alongside concentration, emotions were tiring, and would struggle with tasks involving fine motor movement such as sewing. Such demands on concentration would lead to a level of frustration and anxiety, and the continuous concentration could sometimes trigger fatigue or emotional fatigue.

Triggers for “brain fog” often included a level of physical exertion, such as from standing up for long periods of time, an exercise class, or exerting oneself too much by general physical activity. There were some variations in triggers, but over-stimulation would commonly and typically be the cause of “brain fog”. Thought processes and verbal ability was often heavily disrupted as “brain fog” occurred. Without condensed concentration, a deep and sudden sense of disruption could be experienced, such as M096 with choking, slurred speech, and watery eyes.

Social events, such as Christmas, could be tiring. M096 described an event with 13 people in the same room. There were increasing noise levels, and she was unable to concentrate on any conversation. She stated that finding a quiet room to rest alleviated her fatigue before she could go back to socialising. Her fatigue was described in peaks and troughs, with physical exertion exacerbating her state of mind the most. Another participant described her experience of a highly social situation with external noises that caused her to “glaze over” at a stage in the evening. Multiple conversations and surrounding external noises caused bombardment and the feeling of being overwhelmed. This restricted her ability to listen or engage in conversation because she became increasingly weary and interpersonally “shut down”:

> …we're with people at a dinner table or in a restaurant or anything, I then get to the stage where I actually, what's the word I am looking for? I glaze over… And I just don't listen to what anybody's saying. Because I feel, the voices and the noise I think I just want to ... and I just switch off basically. (M097)

Overall, fatigue impacted many aspects of everyday life and gave most participants a feeling of haziness, with dramatic impacts on sustained attention, memory, speed, and flexibility of information processing whilst fatigued.

7.4. The constituents: Managing the everydayness

One of the most telling matters of discussion was the everydayness of fatigue, the initial fluctuation of lifestyle, and the management of such. The unpredictable course of fatigue created a level of anticipation with all notions of everydayness that had a diverse span, from work administration to foot placement and being conscious of walking; M105 reported he quite often would “second guess myself”.

The management and meaning of time were more planned, as everyday activities were increasingly more difficult than before diagnosis. An intrinsic analysis of individual temporality and how it can affect the temporal and conscious horizons of their everydayness. Cleaning the house was scheduled and divided into two sessions, with a fitted rest period in between to prevent severe fatigue setting in. Not only chores, but leisure activities such as walking, would be thought out and planned. Sitting down and appropriate breaks were often organised so pwMS could split their time accordingly, to make sure they could carry on with their day. M092 expressed the importance of routine, as planning was vital for her to do everything she intended to do. Time management for tasks was performed with arranged comfort periods placed throughout the day otherwise “silly mistakes” were made:

> … it’s kind of like, right okay I need to go to the supermarket this morning, so then I know that once I’ve got back from the supermarket, I need to have, there’s a time, and I can sit down, to, yeah, if I was coming into the centre to do an exercise class, I need to know that I’ve got half an hour to sit down, have a cup of tea… Prepare and move on to the next thing, but that’s an unconscious thing almost, it’s, that’s just my life and I’m not working now, so I have the flexibility to be able to do that. (M092)

Socially, she still enjoyed going out with friends on the weekend and having a glass of wine, but the following day she would not be functional and described as a “complete wipeout” due to complete energy depletion. If M104 had planned a social night with friends, he would pre-plan work the following day and book the morning off to manage his fatigue so it wouldn’t impact him later. M105 used the analogy of managing his fatigue:

> …it’s like a tank of energy, once the energy has ran out, fatigue will hit. (M105)

Day trips or activities were uncommon for pwMS, as they were unable to manage the whole day out unless they carefully planned very little for the following day. Scheduling in exercise followed by rest breaks was a pattern M094 was inclined to follow, as he would walk most days, followed by sleeping on the sofa for 30 minutes. Monitoring fatigue and understanding the amount of energy they have was crucial for all pwMS, every aspect of their everydayness was taken into consideration and involved planning to tailor around their fatigue. Most participants' thought processes were altered to adapt to their fatigue when people suggest different activities, "how am I going to manage that, when am I going to rest?". Fatigue greatly impacted their lives, "my whole life is a compromise", as it has closed participant' horizons.

Other lifestyle adaptations involved dietary, work, and exercise changes. A handful of participants were on, or had tried, the Overcoming MS Diet[15] (OMS) to help manage their fatigue but also generally their MS. According to M105, the diet theory is based on the body's cellular structure; since we eat a lot of processed food and dairy, the autoimmune system thinks the cells are not correct and starts attacking them. Therefore, going on a vegan diet, with the addition of fish, supposedly changes the cellular structure in the body, which may stop the autoimmune system from attacking itself. The diet reportedly takes three to five years to show a difference, so most participants had not noticed much of a difference yet, although they felt hopeful.

Participants who were still working all had to adopt techniques to manage accordingly. M104 learnt to do tasks systematically, one task at a time, otherwise he was more likely to forget something and not do the task correctly. Additionally, he would quite often take timed naps in the office to manage his fatigue and quieten his mind.

M094 and M096 still worked part-time, but could work from home, and expressed gratitude for the ability to still work and for the workplace to understand their situation. Although M093 no longer worked, she coped with her fatigue better. Before she left work, she remembered trying to find reasons to rest her eyes or ways to relax for a short period of time,

> I can remember even being at work, thinking, sitting at my desk thinking, oh I just need to go up to the loo, just go up to the loo and sit on the loo for sort of ten minutes, because I used to think, I just need to close my eyes, I feel so tired. (M093)

She found subtle ways to try and manage her fatigue as well as trying to hide it from colleagues to protect herself.

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[15] OMS was developed by Professor George Jelinek. It is a plant-based wholefood diet with the addition of seafood. Professor Jelinek recommends cutting out all saturated fat, processed foods, eggs, dairy and meats.

Generally, exercise was thought to benefit pwMS, as most participants suggested the positive feeling physical activity gave them. Although participants were aware and cautious of their fatigue, most of them purposely performed and implemented a level of physical activity daily or up to four times a week into their routine. M096 believed she became stronger after exercising at the gym, as she found going about her daily activities easier if she felt physically fit:

> …going to the gym, and as I get stronger then obviously erm, I find things easier but then I was going to the gym in the summer and we went on holiday on the canal boat and I really noticed how much easier I found it getting on and off the boat and stuff… (M096)

Another participant conveyed resolute determination in attempting to do some form of physical activity daily, even if it was a short walk around the block, as he thought that exercise keep his MS at bay.

The type of activity was touched upon as an important component whilst exercising, as participants did not want to feel unsafe, unbalanced, or partake in an activity they feel would exacerbate their fatigue. Activities such as group MS classes, walking, or cycling were a few that participants enjoyed doing. Participants put boundaries in place so that they did not over-exert themselves. There was a level of fear and anxiety of exacerbating their fatigue, therefore not overexerting became a priority:

> …all the things that you want to do with children, are quite restricted. You know because my husband will say well we're going up the downs, we're going sledging. I can't go. Because it is just uneven and I get unbalanced and it's just not safe for me to do that sort of thing. So those sort of things that were every day occurrences I could do with my children, I can't do with my grandchildren. (M097)

M104 knew bodily exertion exacerbated his fatigue and had learnt over time what his body could manage. A strategy at night to withhold his fatigue was to clear his mind and write down his thoughts if he was unable to sleep. He deliberately did not read the time, as knowing the time would burden him and he would become aware of when he had to get up, consequently affecting his sleep.

Fatigue tended to affect participants differently in terms of severity and the type of activity or task they sought. After accepting and learning their fatigue exacerbations, participants tended to adopt different coping mechanisms to situations when fatigue was triggered. M096 felt she had learnt to manage it well. If she was in a supermarket and felt fatigued, she would become static, stand completely still, and wait for her husband to find her. If she was in the supermarket for more than 30 minutes, she would feel overstimulated and confused and as a result, would “cut out”.

Other coping mechanisms involved an aspect of escapism. M105 taught himself mindfulness in attempt to get away from the feeling and calm his mind down, whilst M104 felt the motion of physically putting his feet up and lifting the weight off his feet relaxed him:

> …you know when you get home from a hard day, and you just wanna sit down and you go ahh, and now for me, it’s that ahh, put, put me feet up and you think ahh that’s better. (M105)

Some participants were obliged to use assistance – such as walking sticks, wheelchairs, and priority boarding – whilst traveling as without, they would experience extreme fatigue described as sweeping sudden fatigue.

A less visible coping strategy involved compromise. M105 sold concert tickets to one of his favourite bands in order to avoid a situation where fatigue could be exacerbated and trigger his legs to give way and collapse. The concept and process of the evening he described as a worry, walking to the venue, standing tickets, and then drinking would increase the likelihood of fatigue.

Some participants wanted to comfort other pwMS and attempt to lift the spirits of others to bring a sense of togetherness. M094 enjoyed the feeling of his own presence to be heard, by interacting and gladdening other pwMS around him in the MS centre:

> I think I like sitting here sometimes, someone comes in a bit down, I will talk to em, cos I think I can lift them here… you could see, he lifted up for me, I dunno if I’m, cos it’s a bloke or I had a different attitude, I’ve got, the girls are very good, but they haven’t got charisma to talk to people like that. (M094)

Most participants felt a good sense of support from people who fully understood the condition, hence enjoyed utilising the local MS society or centre, as this surrounded them with like-minded people. For exercise purposes, a few participants stressed the importance of this understanding and felt the gym classes and instructor at the MS centre was specifically tailored for their needs, knowing the limits and therefore benefiting them the most.

The reliance on others was an aspect all participants experienced and shared. A level of dependency in a multitude of everydayness allowed participants to continue partaking in daily activities, from food shopping to social events such as watching football. As stated above, M096 felt better management of her fatigue through her significant other's assistance. She relied on him for support when her fatigue peaked, as she would wait for him to find her in the supermarket if she became overstimulated. M104 described an experience of his reliance on a friend's support to help him walk out of the football stadium. Fatigue projected bodily by causing his proprioception to drop. making him sway uncontrollably. He reflected that the image of him swaying would be similar to someone who has had "too much to drink", as the fatigued swaying could be accompanied by slurred speech.

Leaning on others was not always a welcomed gesture. M097 explained that it was necessary to learn to rely on others to cope with her everydayness better, but sometimes aimed to do what she could for herself, to not feel purposeless:

> I just have to be prepared for everything I want to do and if I think I can't do it, because my husband is always saying don't do that, I can do that. But sometimes you feel that you've got to do something. (M097)

A sense of purpose resonated in participants: the reality of no longer being able to work full-time or at all, alongside the inability to do certain social, bodily, or cognitive activities from before diagnosis created a certain loss of identity. Since 2015, M090 had not been working and therefore made time for other activities she enjoyed, such as gardening and walking. However, she felt she didn't have a sense of purpose anymore, due to losing her career which she occupied a lot of her time with:

> I don't know, when you lose your career, you know what you've done forever it's quite hard. I mean I do enjoy doing different things, but, erm, I don't feel I have a sense of purpose anymore. (M090)

Most participants felt there was a lack of understanding and clear differentiation from MS-related fatigue to tiredness expressed in the general population. There was some difficulty to describe fatigue, as it is so dissimilar to general tiredness that the general population may experience. The fatigue sensations participants experienced were reported to be unlike other experiences; it was not a symptom you can ignore or "push through". Its sporadic and erratic behaviour gave participants the feeling that nothing could be achieved, with only the desire to rest. The nature of fatigue could differ from day to day, and cause frustration and anxiety because of the uncertainty of the timing, duration, and severity. Managing the everydayness often had to be strategic and require a level of adaptation in order to cope with all otherworldly aspects.

7.5. Overarching description of the phenomenon

Fatigue was dubious and unpredictable; it was experienced as a comprehensive and global phenomenon. A range of sensations concerning severity and symptomology were reported in participants, as fatigue presented novel and unpredictable bodily function. There was a kind of certainty in the unknowing nature of fatigue and how it presented itself through the body, sometimes subtle, however apparent and visible to pwMS.

Bodily sensations “from the inside” were gauged differently to how the body was conveyed to the outside world to others. The invisibility of fatigue sometimes created an illusion of a fit body to others. Only sudden fatigue, dramatically infiltrating through the body, could be seen by others. The heaviness of fatigue was evident and all-absorbing as it caused temporary debilitation to most senses. Some participants experienced complete unresponsiveness in bodily function, with the ever-growing feeling of need for calm. Over-stimulation through bodily exertion or perceptive overload exacerbated fatigue levels, as a sweeping sudden reactional fatigue was commonly described. The immediate impending feeling of fatigue created nothing but a desire to rest, to withdraw, to stop, with the inability to accomplish anything and desire to do nothing, at its extreme to lie down anywhere.

Fatigue centralised embodiment with the feeling of restriction, heaviness, and impairment. Familiar tasks and actions were increasingly more difficult to perform. The disengagement of the whole embodied self was expressed as a disconnect – the communication between taken for granted bodily “systems” felt unconnected and often dislocated. This particular kind of disconnection created a natural movement to become unnatural, as everyday activities such as walking required vigilance, and necessarily become monitored and demanding of concentration and physical effort. The acceptance and feeling of fatigue after unintentionally altering body imagery was a process that often led to the familiar body falling away. Body identity shifted into being-in-the-world only as they knew now. This bodily change directly impacted sociality and emotional well-being.

Cloudiness diminished individuals’ overall thought processes and decision making, as fatigue created a time delay. The inability to process thoughts occasionally raised emotional fatigue, where heightened frustration caused more exhaustion. Fatigue formed a delicate awareness and novel anxiety within every situation participants found themselves in, even through the everydayness of their lives. Managing the everydayness had to be strategic for all participants. After acceptance, there was a process of adapting and understanding their fatigue. This understanding led to coping mechanisms, where organisation and preparation for each day was vital.

The journey of fatigue waivered and travelled in peaks and troughs, as fatigue ranged from “feeling energised to feeling depleted and feeling stasis”. There was a sort of continuum of a sensation of fatigue as it changed over time, a scale of the subtle fatigue infiltrating the everydayness but also the extremity of being completely taken over by fatigue. Here, it overpowered both bodily, and what participants called mental or psychological, function. Fatigue is an all-engrossing phenomenon that takes captive unconscious facets of emotion, bodily and perceptive aspects of an individual’s everydayness, and causes deep disruption to daily rhythm.

7.6. Biographical summary of each participant

7.6.1. M083

Before diagnosis, he experienced pre-bodily awareness, as symptoms of leg dysfunction and numbness caused his legs to stop functioning after only 30 minutes of walking, which he was aware was not a long duration for him. As the symptoms continued, after 18 months he saw a neurologist. However, surprisingly the test results came back negative, even though he was conscious something wasn’t right. Determined to get his leg function to normal capacity, he decided to attend a gym in attempt to regain his stride. Still detecting an unnatural bodily issue, which he described “as though an alien has taken over your legs, and it’s not very clever at walking, completely out of control”, he visited a podiatrist. This resulted in a second referral and the diagnosis of his MS. A sense of relief was conveyed as the symptoms he was experiencing became understood.

As he was diagnosed with progressive MS, he expressed a sense of urgency in attempt to take control by exercising a lot, because he was not prescribed any medication. He had always been aware of the body detachment he experienced, where he would lose control over his lower extremity and believed his legs to have a mind of their own. Even though he was a keen mountaineer, he found his body had to restructure and relearn to walk. The experience of jerkiness and spasticity were often encountered, and at the time of interview, he still had to consciously instruct his legs to walk. He regained control of bodily functions by performing rehabilitation exercises that he believed improved his balance and coordination. Although aware he was most likely weaker, he functionally felt better within himself than he did five years ago.

Peripheral aspects such as the common cold would provoke his fatigue and cause any level of exercise to not be possible. He described fatigue as very much situational: the summer heatwave exacerbated his fatigue, which affected the EDSS-S he had to complete prior to the assessment. In the assistance of improved embodiment, physiotherapists and the use of walking sticks drastically improved his ability to walk. Without a walking stick, “a mile can feel like a marathon”. He expressed a continuous incentive was a concern, as motivation to be productive could be problematic. A schedule with regimented rest periods helped prevent this lack of motivation and energy, otherwise his writing and thought processes would be affected. Inner self-motivation could be difficult, but discussing it with others could often make him feel more energised. A change in himself as his reaction to stress and change caused him to panic and be unable to think straight.

The nature of fatigue is always unexpected, which he distinguished from other chronic conditions. However, over time he established a clearer understanding of self and his body, to better manage his fatigue by exercising.

7.6.2. M084

At the time of diagnosis 27 years ago, she was a mother of two young children, managing a multitude of issues involving her recently deceased father, her new diagnosis, the inability to work, and bringing up two young children. Forced to take early retirement due to poor working conditions, she felt additional financial stress as her income was halved, causing economic consequences by moving to a new house and her husband taking on a new job.

Her fatigue instigated embodiment implications as she felt novel but continuous sensations that impacted her from her chest down to her feet, with descriptions of the “feeling of walking on broken glass” and “pebbles under her knees”. The bodily fluctuations created awareness of temperament and mood fluctuations. This awareness continued with bodily spatial awareness and the lack of control she felt over her body when fatigued. She expressed a conscious control of her body by instructing body parts she felt were not reliable.

An element of body dominance as sociality was affected, she found herself becoming more isolated due to her fatigue. She consistently focused on her body and movement, with the need to continuously clarify this to others, which she found exhausting, directly impacting her social life. A raised awareness of the lack of bodily control caused a constant need for physical aid in ambulation, unless she felt confident or familiar with the surrounding environment. If she did fall, the term “my equilibrium must be restored” was verbalised. The readjustment of her self and being must be done before she felt her body was readjusted for her to move again. This constant adjustment was taxing as she felt ensnared and constrained by her fatigue.

An element of escapism was expressed as her body felt unreliable. Due to this distrust of her body, there was increased concern over ambulation and actively going out. However, she received support from others, such as her husband and his knowing of her fatigue. He regularly monitored her walking, indicating when walking aid was needed. Fatigue was known as a “brain game” to her. She stated the continuous sensation of processing thoughts and information caused frustration and ultimately exacerbated her fatigue: “the cogs are constantly whirring”. Overall, M084 felt significant novel bodily sensations that affected not only bodily movement and ambulation, but also had social consequences with family and friends. The reduced ability to perform daily activities due to fatigue caused economic consequences, heightened anxiety, and psychological weariness.

7.6.3. M089

M089 once worked at a hospital, but was retired at the time of interview. She felt her everydayness was increasingly difficult, including activities such as cleaning, walking, and exercising. Due to this, daily preplanning was performed so she could maintain and control her energy and fatigue levels. Environmental aspects such as heat would affect her bodily function in terms of coordination, leg sensation, and movement. The impact of heat would make her legs feel like lead, with simple activities such as walking to be of more difficulty.

She was awareness of conflicting bodily movement with any physical exertion prior to diagnosis. Forcing herself to exercise would agitate her fatigue and would make her grit her teeth in discomfort. The sensation of heaviness in her legs as a physical feeling of gravitational pull made her legs to feel like they were dragging. She described her right leg as feeling “mushy” due to the lack of motor control and the feeling of unpredictability. There was a sense of relearning to walk when fatigued, as every movement that was once taken for granted was now a conscious movement. Engaging in all movement created a reduced sense of control, where multitasking would be impossible.

Her spatial awareness had reduced and she described being “clumsier”. She felt she never walked in a straight line as her balance was very much affected. Without a level of support, walking could be unnerving due to uneven ground or unfamiliar environments. As a result, her husband made sure to clear items away to reduce tripping or falling. She expressed a feeling of gratitude towards her partner as he understood her condition and cared for her appropriately. Her perception and judgment had altered, she ws now more very much aware of prior involuntary movements, and embodiment centralised her fatigue experience.

7.6.4. M090

She experiences her first MS symptom in 1996, whilst she was pregnant with her son. After diagnosis later that year, she did not experience symptoms until 2002, when she encountered her first relapse. Several stressful aspects contributed towards her first relapse, as she separated from her husband and was experiencing additional stress at work. Despite radical coping strategies, she continued to work until she physically couldn’t due to the crippling fatigue, resulting in a hospital visit where she was wheelchair-bound.

Embodiment aspects began to impact her significantly, as she experienced severe pins-and-needles in her scalp, and she cut off her hair for a sense of relief. She described the altered sensation of whole-body movement difficulty as “treading treacle”, where extreme levels of fatigue would be so overwhelming it would cause physical pain. This relapse caused her to be bedbound, with a temporary loss of sense and sight. A sense of darkness was described as time became still for her. The complete lack of energy and utter exhaustion made even lifting her hand up exhausting. After months of no work, work colleagues visited her to recommend an ill-health retirement. She felt her own self-identity had changed in how family and work colleagues saw her. A tone of embarrassment was expressed as she felt useless. She was prescribed anti-depressive medication to cope with the process, adaptation, and decisions she had to make from secondary effects of the illness, as she stated she did very little the following two years.

Adapting lifestyle and dietary changes, she was able to take up a job as a social worker until she experienced another two relapses. She felt all her relapses were precipitated by the stress of her personal relationship with her husband, including financial disputes and disagreements. She emphasised fatigue as a whole-body phenomenon. The invisibility of it made it difficult to explain, and for others to accepts and understand. Fatigue was not something to “push through”, as this led to worsening fatigue. She questioned her self-identity as she felt little sense of purpose due to no active occupation. She admitted spending an estimated 50% of her time in bed, only actively getting up for Italian classes and helping a lady who is bedbound.

7.6.5. M091

M091 highlighted embodied projection of fatigue through his lower extremity, described almost as a pain, that is often accompanied by numbness and a burning sensation. He was aware that after a specific duration of exercise (20 minutes), the feeling of fatigue in his legs was triggered. He was only consciously aware of his legs as a bodily implication of fatigue by movement, and he often sat down in attempt to rest them. The general loss of strength in his legs became a lot more significant due to previous enjoyment of long walks and cycling that needed lower extremity endurance and strength. The feeling of exhaustion was often experienced at the end of the day and occasionally did not feel revitalised after a night’s sleep. He expressed that the continuous cycle of non-refreshed sleep would create a feeling of continuous fatigue, where bodily projections of leg cramps would occur at night. The unsettling feeling of exhaustion after sleep could leave him with little willpower to get up for the day. His perception of sleep was reportedly better at the time of the interview, although he expressed uncertainty as to whether routine or diet improved this. Subjectively he felt his management of fatigue was significantly better than during his first relapse, which he experienced seven years ago. However, he was unsure whether modifiable lifestyle contributions, such as dietary changes, helped with this or not.

There were certain elements of his MS that he had to adapt due to fatigue, although he aimed for normality in life, as he expressed determination to continue like before his diagnosis. Spatial concerns with stairs, pavements, and uneven surfaces made him more conscious and therefore more cautious of his surroundings. He found spatial comfort by exercising on a treadmill instead of rough terrain like a national park or beach. He felt an increase in confidence whilst walking on the treadmill due to the surrounding environment but also a sense of control over time spent walking and the stable surface of the treadmill.

Determined to continuously perform exercises for the mind and body, he believed he had a strong mindset, although fatigue could create difficulty concentrating occasionally. Self and sociality required more organisation than before diagnosis. He expressed an enjoyment in going to the cinema with his unlimited card, due to the lighting and temperature of the room. The feeling of relaxation came from the spatial and temporal aspects of the cinema environment. The additional physical support of a stick was used for balance, but he only used this in a crowded environment, and it was used as more of a precaution than anything else. He was unwaveringly determined for fatigue to not take away his independence.

7.6.6. M092

She first encountered symptoms shortly after the birth of her son. Later that year, she was diagnosed, and felt a sense of relief as the uncertainty and inability to cope with a new-born was answered by her diagnosis. Overwhelming fatigue was the first symptom she experienced, and this was consistent throughout her MS. The severity of fatigue could sometimes make her feel ill, leaving her no choice but to rest, sit down, and recharge. The process of complete rest required her to put her legs up and head down, which she described as a “complete power down”, in order to recharge.

The invisibility of fatigue could make it difficult to manage. Due to the lack of projection for others to understand, she felt it is not something people can clearly perceive. She emphasised the differentiation between fatigue and tiredness in the general population with a sense of frustration because she felt people did not fully understand MS fatigue. She distinguished MS fatigue from the desire to sleep, describing fatigue as a whole-body phenomenon, in which the body is almost unresponsive, specifically the lower extremity, with noticeable reduced strength and limb heaviness.

The hot weather could exacerbate and trigger this overwhelming fatigue, even simple movements such as walking down a few steps can be a considerable effort. In the late afternoon she would get a “cognitive blur and fog”, which affected her thought process and decision making. Due to this, she did not make any major decisions in the afternoon, normally waiting until the next day. The inability of not understanding something, big or small, could often cause what she described as “emotional fatigue”. Unable to cope with not understanding or making “silly mistakes” cause frustration, as prior diagnosis she was good at multitasking. However, at the time of the interview, she had to consider time management for all tasks, making sure there were rest periods throughout the day. Time management was of great importance to her, knowing when and where to use her energy wisely was something she had to adjust to and learn to do.

She enjoyed participating in activities at her local MS centre, as classes are tailored for each individual and their needs. It was a safe place, a comforting nature of surrounding space. She often felt a sense of accomplishment with one exercise class, as her fitness instructor pushed her to the limits of what she could do. Although bodily energy was depleted and typically exhausted after exercise, she felt exercising kept her mind strong, therefore pushed herself to exercise, as she emphasised the importance of it. In other, less familiar surroundings, she expressed a heightened sense of anxiety, as the uncertainty of bodily movement and foot placement could potentially increase her likelihood of tripping. She was more aware of her walking in less familiar environments.

In relation to otherness, she experienced support from others at the centre, from the fitness instructor but also other pwMS. There was pressure to socialise with family at specific events, like Christmas, where she didn't want her MS to get the better of her, but this usually exacerbated her fatigue. Her appearance to others mattered as she didn't like to be selfish in situations and let people down. She had a sense of being pulled in multiple different directions to please everyone, with the tendency to not consider herself.

When she was fatigued, it disturbed her sleeping patterns. Her thoughts fired off and triggered other thoughts and worries which spiralled into what she described as "the worms in my brain". This caused perceptive fatigue, which could generate exaggerated thoughts, where small problems could manifest into bigger problems. Fatigue was sporadic in nature and could differ from day to day. Some days, her energy levels remained considerably low throughout the day and she felt there wasn't a lot she could do about it. Other days, there was a multitude of things, activities, or thoughts that exacerbated her fatigue. She called these "MS days", as she found it difficult to describe in any other form.

M092 stopped working 11 years ago before it significantly impacted her quality of life. She felt relief after finishing work as she didn't have this pressure anymore. Embodiment was valuable to her, so bodily fatigue was stated as the most prominent and worst symptom, because it stopped her from doing what she wanted to do.

7.6.7. M093

She was in Las Vegas walking down the strip when she experienced her first bodily symptom of foot drop. Her foot drop was visible, as her husband questioned the problem and she was unable to lift her left foot. Returning from the trip, she was sent to a physiotherapist, then a neurologist, where she was diagnosed in 2012. Unknowingly, her body was portraying differently to her friends as she wanted to sit down more with social activities. However, at the time of the interview, she recognised it was fatigue, although she was unaware of this at the time. Before diagnosis, she described the unknowing experience of fatigue at work, strategising ways to increase her rest breaks by sitting on the toilet for longer so she could rest her eyes, in attempt to elongate resting without visual change to her peers. At the time of the interview, she recognised other associated symptoms prior to diagnosis, with incidences of foot drop and double vision.

M093 didn't suffer from fatigue on a daily basis, although she could recall memories of overwhelming fatigue. A specific experience was flying to America, and how the process of going through passport control, queuing up, and flying for nine hours affected herself and her body. It impacted her ability to move any part of her body, and the smallest movement felt like the biggest exertion, with extreme limb heaviness and the feeling of complete exhaustion.

She expressed a belief that MS presents differently for each individual. The most prominent feature for her was displayed bodily through her left leg dragging. She had an increased awareness of her leg, as she believed she was more prone to tripping/falling. Heaviness in her leg was aggravating, but not painful. External influences of heat typically did not affect her, conversely, she enjoys the heat. She incorporated adaptive ways to enjoy the sunshine by sitting in the shade and using the air-conditioning unit. She had no sleep disruptions from her MS but believed a morning routine and schedule helped with this.

7.6.8. M094

M094 admitted the denial of his diagnosis for approximately ten years. Following a relapse after Christmas three to four years ago, he came to the realisation he had been ignoring his MS. He believed he had a much better relationship with his MS once he had addressed and accepted it. Motivated to keep himself active, he considered that not addressing and avoiding MS can worsen it by "going down the plughole".

No particular activities seemed to trigger his fatigue, but if he had a busy day, he allowed himself to accept his reduced energy levels. The hot weather affected him bodily. He described fatigue as instantly hitting him as it physically took his breath away with a rapid wave of tiredness. Fatigue could occasionally be experienced without an apparent reason at the beginning of his day, which he described as a "non-starter day". Even on a non-starter day, he needed a sense of accomplishment, therefore still aimed to walk around the block. He tried to look for positivity in any given situation by being determined not to let fatigue get the better of him, "I always try and be the glasses are full".

He knew fatigue was commonly expressed in the MS community and he himself experienced it. However, the notion of “pushing through it” is articulated as he normally felt better after a gym session. He listened to his body and used time accordingly by allocating an hour of his time to rest if he became drowsy.

He was still working when he got diagnosed, but had to begin working from home as the increased likelihood of injury at work could have led to complications for the company. He expressed gratitude towards work understanding his condition and allowing him to continue working from home. He could work 3-4 hours a day, and it gave him an interest and something to do, feeling a sense of purpose through his work. He felt involved by continuing to socialise and partake in family activities, a sense of appreciation that his family cared and looked after him at these events. He expressed a feeling of joy as he recounted his Normandy trip and the ability to cycle (on a three-wheeled bike) up to 80 miles throughout the duration of his trip. He sometimes experienced coordination and balance impairments standing from sitting, therefore occasionally used a stroller for assistance. Unbalanced bodily actions when fatigued urged the need to sit down and rest. He believed bodily exercise preserved his health and kept his MS dormant, therefore consciously pushed himself to exercise as much as he could.

He stated that MS is a different experience for everyone, therefore, pwMS must try everything to know what best works for them. He raised concerns knowing an individual who used to be highly active but at the time of the interview was wheelchair-bound because of MS, all in the time frame of two years. However, he enjoyed lifting the spirits of people who suffered from chronic conditions, bringing a real sense of togetherness as he considered having the ability to do so.

7.6.9. M096

M096 acknowledged fatigue was present early in her diagnosis and remained present throughout her MS. Throughout a typical day, she experienced fatigue but it expressed more dominance in the afternoon. However, working with her fatigue, she adopted a routine to incorporate a rest period at this time. Other adaptations she made included travelling with assistance, as without she would feel body implications for several consecutive days after, describing it as a “complete wipe out”. Body implications were described as feeling weak, emphasising muscle weakness, with the need to sleep to recuperate. Predominantly, her thought processes and communication were heavily disrupted by fatigue as “brain fog” settled in. Her thought processes and communication could become slurred as it took her longer to make sense of things. Without focusing on her body, little concentration could trigger choking and watery eyes. Remembrance of choking on bottled water when fatigued made her conscientiously perform throat exercises to manage her choking. A significant issue with fatigue was the uncertainty of temporality, as it was irregular and sudden.

Exercise helped her fatigue management, with the feeling of increasing strength after the gym as certain activities came easier to her. However, she struggled to do day trips without extensive planning, unlike before diagnosis. At the height of her fatigue, fatigue dominanted and the slightest movement could feel exhausting: “the stairs turn into a mountain to climb”. Her fatigue was described in peaks and troughs, with body exertion exacerbating her perceptive abilities more so, yet having a routine helped with this. She reiterated that without planning, her fatigue could not be managed efficiently, and she had to manage her routine around fatigue otherwise her energy levels dropped.

Her social life was affected by situational events. Noisy environments affected her ability to concentrate which resulted in increasing levels of fatigue. As a result, she managed her fatigue by resting in a quiet room for up to a half-hour. Any form of overstimulation could cause complete energy depletion as she felt disconnected from the outside world. An element of frustration came with this as she disliked informing others of her inability to do or not do something. Her present self and self-awareness gave her the ability to manage experiences and situations accordingly. If overstimulation occurred, she felt she just “cuts out” and often became confused. She felt that fatigue “closed her horizons a lot” by compromising and pre-planning every aspect of her life.

7.6.10. M097

She felt exhausted pre-diagnosis working full-time with multiple aspects of her life exacerbating her fatigue. Although her first symptom was not fatigue, embodiment was dominant as right foot drop and leg dragging was prominent and caused the inability to physically lift or move her leg. Although better at the time of the interview, she thought her right leg continued to be problematic, due to the visible markings on her shoes. A sudden wave of fatigue that she described as a “fuzzy head” could cause a draining feeling in her lower extremity and she experienced the sensation of swaying and unbalance. Whether she encountered swaying or not, the feeling of going off course was often experienced with fatigue, which induced an element of anxiety about falling. She had a tendency to avoid stations or environments that would cause her to fall. Activities performed prior to her diagnosis were no longer an option for her. Spatial factors heavily influenced the feeling of uncertainty and inability to do activities as uneven ground induced a fear of falling. She did make herself do specific activities like walking, but believed listening to her body is the best strategy for coping with fatigue specifically otherwise she will “hit the wall”. The sensation of hitting the wall filled her with the inability to do anything, regardless of the surrounding environment. Peak levels of fatigue affected her body control, as her body physically shook from fatigue. This restricted what she was able to do, but she felt organisation of every life aspect was necessary to manage her fatigue. She emphasised the necessity of preparation as she wanted to do what she could for herself and not always lean on others. Nevertheless, she knew she had to rely on others because of her MS.

Highly social situations with multiple external noises could cause her to “glaze over” at a stage of the evening, unable to listen or engage in conversation because she would “switch off” and become very weary. Talking in a room with lots of people could be overwhelming and she could feel bombarded. She used to be very sociable, but with MS it could be difficult and exhausting to meet friends, as she thought people did not understand, because it was not clear. This overwhelming fatigue encouraged a need to “get away from it all” and rest in peace by quietening her senses to feel rested. Reducing all senses created a coping mechanism for her, the need for calm and space, and cutting off from the world momentarily assisted in the recovery of overwhelming fatigue. Becoming static in movement and thought was part of her resting protocol and recovery from fatigue.

Fatigue had a tendency to spike in the afternoon, with sporadic bursts of energy in the morning. This spike caused her to nap every afternoon. She labelled this “downtime”, where she would fall asleep in a reclining chair, clearly stating the difference between this and lying down in bed at night to sleep. She stated a necessity for rhythm and routine to her daily activities, otherwise fatigue would heavily impact her. Bodily gestures voiced their desire to her when she needed to rest, “it’s aching, stop moving, sit down and relax”. The silent nature of the body was changed, becoming visible and present. Emotions and increased levels of concentration could be tiring. The ability to perform fine motor movements like sewing could be increasingly difficult, and it took longer to complete such activities. This could cause frustration and anxiety about performing certain activities. Fatigue was part of her everydayness and was incorporated into her daily life, which she managed as best as possible.

7.6.11. M104

M104 was a manual labour worker who significantly recognised the increasing difficulty to carry cement bags at work, highlighting that his body felt weaker and somewhat unfamiliar. Fatigue was a global phenomenon for him, projecting all over his body with the description, “it is all over me”. The act of running would cause breathing to be harder. He felt a bodily imbalance, with the left leg weaker which could lead to it “catching” or “scuffing”. The first recognition of this was prior to his diagnosis. Whilst working out, he would trip over an increasing amount, without understanding why. However, at the time of the interview, he was receiving physical assistance from functional electrical stimulation (FES) which helped with this problem.

He identified the marker effect of his MS with muscle wastage and noticeable reduced muscle strength. The extreme, overpowering sensation of fatigue disabled the ability to function in any mannerism. This forced him to rest by sitting down and switching off in every aspect. During this time period, he struggled to do any bodily actions, but he had learnt over time what his body could manage. When experiencing fatigue, he would relax and rest his body. He taught him mindfulness in attempt to “get away from it all”. A strategy for coping at work involved taking a nap for 15-20 minutes that tended to “calm the mind down”.

To help manage his time effectively, he used a diary with a list of reminders of personal and professional events, although even with such a diary, he could still be forgetful. He expressed that confusion, disorganisation, and forgetfulness could frustrate him. His level of concentration could fluctuate, which affected his memory and ability to multitask. He learnt to do tasks systematically, otherwise his forgetfulness would have a knock-on effect. With the need to pre-plan for such social events by prearranging work the following day, he learnt to not exert himself as sleep helped him recuperate. Without extra sleep and rest, he would be less alert and have a “fuzzy head” which would affect his productivity.

The journey of his diagnosis began whilst experiencing adhesive capsulitis and was experiencing constant pins-and-needles in his fingers. After a collection of nerve conduction tests, the doctor suspected it was ulnar nerve irritation, but later discovered it was MS after a magnetic resonance imaging (MRI) scan was performed. He expressed confusion as to why his diagnosis wasn’t detected sooner, as he had experienced symptoms for a long time. However, he acknowledged that typically Caucasian people were more much likely to get it. He adapted his food intake and nutrition with OMS diet. The diet consists of a vegan diet with the addition of fish, but it supposedly takes three to five years to show a difference, hence no change had been noticed at the time of the interview, but he was determined to continue with it.

The everydayness of fatigue would come into effect after work, when he would struggle to do everyday tasks, such as making dinner and brushing his teeth. Prior to reading about fatigue, his perception of fatigue impact was only physical, but after noticing his coordination and thought process changes, he began to understand how fatigue impacted him more holistically in other unexpected aspects. Without being conscious of MS at the time, it still affected his body's ability before diagnosis. Whilst skiing, he was unable to lift his left leg as well, which caused him to tighten his bindings which eventually caused a complete calf rupture.

Overall, physical exertion was a known trigger for fatigue, especially after a taxing day at work that impacted his perception and ability to do mental tasks. He understood his body and MS more so at the time of the interview, therefore believing he managed his fatigue better.

7.6.12. M105

When diagnosed in 2018, he did not detect fatigue as a noticeable first symptom, although it was one of the most prominent at the time of the interview. Administration work was noticeably more taxing, as completion took longer, but also because he "second-guesses" himself that he had done the work correctly. The meaning of time created an element of doubt as his work productivity lessened. He experienced a bodily reaction of unexpected and sudden leg dysfunction that caused him to fall as both legs gave way. There was no preconception or awareness of this embodied change that indicated this action, nor any pre-bodily signs. Confusion was a common emotion after the incident, as he attempted to understand why it had happened. He experienced a lack of sensation in his feet with shoes on, but also in his hips and thighs when he was fatigued. Fatigue was displaced through the lower extremity as the legs tightened and pulsated, but he was semi-reliant on medication to help him cope with his lower extremity symptoms. He did not exceed a high dose of medication as he felt it affected his thought process and created "brain fog".

The visual symptoms of fatigue were exacerbated depending on activity. Reading less than a chapter of a book would trigger a blurred vision, as did the act of organising multiple things at once in his head. The term "mind fog" was used as thought processes and understanding became unclear from everyday cognitive tasks such as filling in forms. The mind fog was always associated with a time delay. He always allowed time for any activity as the need for calm didn't exacerbate his fatigue. He believed in a "tank of energy", managing and reserving his energy day-to-day helped him cope with fatigue. Relaxing his body by sitting down and putting his feet up was a coping strategy. Preparation was essential to help him with the day ahead when fatigue kicked in immediately after waking up.

He had to reconsider his social life as he had to rely on friends to stop him from over swaying and falling over when watching football matches. He experienced a sense of otherness as his friends assisted him when his proprioception was poor. He was aware of his image and body identity when swaying, as it may have been misinterpreted as someone who was intoxicated. He compromised on social activities like concerts and gigs because of the risk of his legs collapsing. The situation would affect his whole social activity due to the worry of the uncertainty of his unpredictable body reactions. Other peripheral factors such as temperature impacted him, but the cold influenced his fatigue more so than heat, as he felt his body tighten up using energy to keep warm.

He encountered hesitation on components of everydayness such as walking and stepping as he experienced a heightened sense of awareness by “second-guessing” his foot placement, work, and most everyday tasks. However, occasionally his conception of his MS felt skewed because aside from his fatigue, the lack of symptoms could lead him to temporarily forget his MS.

7.7. Lifeworld insight of fatigue in pwMS: Phenomenological discussion

The lifeworld is a fundamental concept that Husserl considered as pre-reflective; it focusses on what we perceive, rather than how we perceive it. Husserl argued by distinguishing the essences from a given experience, it might highlight the qualities of specific phenomenon and its distinctiveness [Brooks, 2015]. The following two sections focus on two aspects of the lifeworld analysis that this study specifically drew attention to.

7.7.1. Embodied experience

Within phenomenology, the analysis of the body as we live it can be experienced through body schema and body image. In his article on embodied experience, Gallagher [2006] proposed the position that “phenomenology understands intentionality as a form of being-in-the-world and recognises the importance of embodied action for shaping perception and an interpretational framework is different from purely functional or syntactic interpretations of empirical data”. Body image is a perceptual, conceptual, and emotional attitude towards one’s own body. It can be influenced by a set of beliefs or attitudes and affected by cultural and interpersonal factors [Ziemke et al., 2007]. Body schema can be seen as a sensory-motor system of preconscious and sub-personal processes that involve movement to operate in an automated way [Ziemke et al., 2007]. It involves processes to function without reflective or perceptive awareness and can shape the intentional experience and behaviour of an individual [Ziemke et al., 2007].

The distinction between the two is subtle, but it can be useful to understand the intricate dynamics of bodily movement and experience. Denny-Brown et al. [1952] reported a study in which a female subject's body schema was present, but her body image was partially absent following a stroke. Physically, her gait was normal with no noticeable motor weakness. However, she excluded the left side of her body: she failed to dress her left side, comb the left side of her hair, or recognise when her left slipper came off her left foot. She suffered from a neurologically caused defect in perception related to the left side [Denny-Brown et al., 1952].

In this research, a few participants felt their body as separate from their self and body schema. Although aware of this body alteration/s, their body image reflected fatigue in mannerisms out of their control. The sub-personal motor system processes were occasionally unnatural and neglected as a sense of body detachment as described. The preconscious action of walking, which was once taken for granted, was no longer part of their subconscious body schema, as the jerky and unnatural movement led them to believe they had to relearn to walk again. The conscious prompting of putting one leg in front of another and initiating all bodily movement easily became taxing as there was an element of body detachment. The dissociation between self and body as the cognitive instruction of movement felt the only option to be able to move and walk. One participant felt no preconception or awareness of embodiment with fatigue and his torso swaying, and there was no recognition without others vocalising it. His body image portrayed bodily dysfunction without his consciously being aware of this dysfunction, although he felt fatigued in himself.

Merleau-Ponty conceptualised perception as an embodied experience, which does not consist of one object having effects upon another. He posited that perception occurs in-the-world rather than in the mind [Merleau-Ponty, 1968]. His phenomenological principle was that the subject and object are correlated in an inseparable way, an incarnate subject [Moran, 2010]. As explained by Moran [2010], Merleau-Ponty argued that "consciousness is transcendence through and through". To consciously see is the action of vision and sight is achieved by the thing seen [Merleau-Ponty, 1968; Moran, 2010]. Merleau-Ponty discussed the flesh of the body and the flesh of the world to indicate the body is more than an object, and that which mediates the world to experiencing subject [Merleau-Ponty, 1968].

In this research, fatigue is identified as a symptom that can potentially always be present, and present undertones of body schema or/and body imagery that sometimes, but not always, penetrate through the body and become visible to others. It has been described as expressing itself in tangible aspects that encompass an embodied experience, occasionally succumbing to an overwhelming aspect of fatigue.

The rendered static aspect of sweeping stasis fatigue can be related to well-being and Heidegger's concept of *existentiale*. According to Heidegger in *Being and Time*, well-being is understood as having access to all existential and behavioural possibilities that include spatiality, temporality, intersubjectivity, embodiment, and mood [Heidegger, 1962]. Without one of these possibilities, well-being can be affected, and an individual's lifeworld can be shifted. Toombs [1993] highlights several ill-health descriptions where the restoration of well-being is focused on facilitating these possibilities to the best of the individual's ability. In this research, individuals have expressed the missing dimension of all *existentiale* possibilities through the experience of sudden fatigue; the well-being is affected bodily, socially, spatially, and temporally.

Fatigue almost holds and cuts off the possibility to these possibilities as it causes a sense of isolation and restriction in individuals [Galvin & Todres, 2018]. The dynamic relationship between the body and the world in pwMS and fatigue can be explored by the notion of the lived body [Merleau-Ponty, 1963]. The body is more than an objective, physiological body. It is the centre of all systems coordinates, which Toombs refers to as the vehicle of seeing [Toombs, 1993]. However, MS fatigue can be seen to disrupt the centre of systems as the orientation and bodily intentions can change unintentionally. The reduction in bodily control with daily tasks of lifting up an arm and putting earrings in was described as difficult due to the overwhelming bodily dysfunction as bodily capacities change. The embodied experience of overwhelming fatigue was felt as crippling fatigue in the lower extremity. Extreme heaviness in the legs caused the inability to function and was so severe, it could cause physical pain. One participant described crawling under a desk to allow for temporary peace whilst fatigue took over their body and self.

With *existentiale* dysfunction, routine experiences can feel effortful, with the surrounding world appearing different. The incapacity of temporarily being-in-the-world with the lived body can be referred to as existential fatigue, with the limitation of bodily, emotional, and social aspects [Toombs, 2001]. Body identity was articulated and altered as an individual's bodily projection changed through the limitation of existential fatigue. The temporary inability to think, act, or process any incoming information caused a few participants to be unable to walk, with functions such as lifting an arm up to be problematic. Toombs [2001] expressed her personal experiences of body identity as her disability progressed to wheelchair usage. A sense of diminishment and a feeling of shame was expressed as she felt her students would think less of her now that she was unable to stand on her own two feet [Toombs, 2001]. The relationship between emotional well-being and bodily being is typically expressed as an element of a change in body identity, whether it is temporary or permanent. Where there was a shift and change in temporal experiencing, temporality is sought but also not sought for fatigued participants. The need for intrinsic temporality was sought whilst restoring and regaining strength from fatigue. Participants wanted the time to themselves in circumstances caused by fatigue that involved falling, exerting themselves for too long either by movement or cognitive activity. The meaning of time shifted: it often took longer to partake in and perform most activities, which gave participants a sense of slowing down which was expressed as difficult to accept.

Toombs [1993] recognised the difference in semantics once she accepted her wheelchair as an integral part of the body: “using” rather than “being in” a wheelchair. A few participants verbalised the acceptance of fatigue being part of their everydayness. The notion of acceptance was stressed as important, as the acceptance allowed individuals to transition into their present living body and begin to learn and adapt to fatigue being part of them. The identity and selfhood of the once familiar body changed, and the process of acceptance allowed for improved fatigue management therefore improved fatigue levels. Schüssler [1992] concluded that individuals who did not accept their illness or consider it uncontrollable tend to use emotional coping strategies which are reported to be less effective for coping.

Eatough & Shaw [2019] explored the experiences of an individual living with Parkinson’s through a lifeworld perspective. The individual described her relationship to the disease as having an evil twin, creating opposition for her in her daily life because her body, responsiveness, and sense of self continuously changed [Eatough & Shaw, 2019]. The embodied self could be lifted by proactively dancing, so the individual felt her Parkinson’s faded out of awareness and gained what Sartre would call “passed-over-in-silence” [Sartre, 1956]. A few participants described an embodied self in relation to the lack of control over the body, as if someone else was in control: “you know this sort of, they sometimes say it’s as though an alien has taken over your legs, and it, the alien is not very clever at walking, completely out of control". They described a feeling of body detachment, almost having to relearn to walk again, and a disconnection of bodily movement, the act of bodily movement, and the self. The body felt separate from the self altogether, with one participant feeling the need to talk to her body to encourage reconnection of system coordinates so they could function as a whole. The evil twin might be the individual's perception and explanation for the complex relationship between her changing body and changes in sense of self [Eatough & Shaw, 2019]. The authors suggest the interpretation of this evil twin metaphor to serve a purpose for the individual to acknowledge the limitations Parkinson's brought and acting as a motivation to face her Parkinson's. Similarly, participants referred to "an alien taking over your legs" with the acknowledgment of an episode of fatigue and the unpredictable and uncontrollable actions fatigue has on the body. This may suggest the recognition of limitations and the complex nature of the symptom.

In summary, fatigue is sporadic in its nature and severity, but the effect of bodily function and the embodied experience tends to be a process of comprehension and acceptance that can unfold in multiple layers depending on the individual. More importantly, embodiment and bodily function are of great value to pwMS. Fatigue is seen as a barrier on many levels. Nevertheless, basic physical function allows the ability to do daily tasks and activities, and this ultimately creates a sense of independence for pwMS (see Chapter Ten for more on the discussion of embodied experience).

7.7.2. Relational experience: Selfhood

Social situations with excessive external noise would create a cognitive haze and a state of disengagement and would cause the inability to concentrate on any conversation. A feeling of bombardment would cause increased weariness and decreased interpersonal abilities. This lack of engagement was due to increased levels of fatigue and was expressed as overwhelming, and participants would often feel exhausted. Overstimulation of any form would give a sense of disconnection to the world as energy levels diminished. The feeling of guilt and being perceived as lazy when unable to continue to meet a social commitment is frequently discussed within the literature and within this research [Turpin et al., 2018; Knaster et al., 2011; Tabuteau-Harrison et al., 2016]. The interplay between fatigue and communication would become more apparent, similarly to Blaney & Lowe-Strong [2009] who found others would incorrectly perceive pwMS as being drunk or lost whilst experiencing fatigue in a social situation. Flensner et al. [2003] found the increasing severity of fatigue would cause the lack of feeling in control. Yorkston et al. [2001] reported that fatigue limited the opportunities for communication participation as it dictated pwMS' lives. This minimised social interaction and fulfilment was a barrier that impeded cognitive abilities in a work or social setting [Yorkston et al., 2001]. This disruption to communication and sociality would cause the rising need for a quiet surrounding, to rest all senses. This was a shared coping mechanism that often included quiet rooms, napping, or being by oneself until individuals felt a level of replenishment to interact again [Yorkston et al., 2001].

A feeling of isolation was conveyed, as body dysfunction from fatigue affected sociality through the constant need to inform others, which commonly heightened anxiety and psychological exhaustion. Researchers found the loss of ability in the presence of others made them more likely to stay indoors and choose to become more isolated [Flensner et al., 2003]. The dimension of invisibility to others made individuals' daily living harder for others to understand [Stuifbergen & Rogers, 1997]. Apprehension of future events can exacerbate an individual's fatigue and fear of experiencing fatigue. A limited understanding from non-MS individuals of the difference between MS fatigue and tiredness was repeatedly expressed. Although Eilertsen et al. [2013] explored fatigue in post-stroke patients, the authors found that individuals actively avoided certain social situations, as these were a significant stressor and would typically provoke increased stress, which increased the likelihood of experiencing fatigue. Frustration was a mutual feeling articulated in all studies, as fatigue can significantly impact pwMS and their identity in given situations [Eilertsen et al., 2013; Flensner et al., 2003; Stuifbergen & Rogers, 1997].

Barker et al. [2019] explored the experience of identity and identity change in pwMS. Concealing the disease was often described at the early stages of the disease, as individuals had the desire to maintain their pre-diagnosis identity and preserve their sense of self to maintain high levels of self-esteem [Barker et al., 2019]. The effects of increasing symptoms led individuals to re-evaluate their sense of self as they began to discover MS was an integral part of them [Barker et al., 2019]. Concealment was conveyed within the present research, as a few participants expressed the need the "push through" and ignore aspects of their MS. This type of suppression has been reported to cause latter effects to emotional and overall well-being, as fatigue is a symptom that cannot be ignored [Schüssler, 1992]. The denial of acceptance often saw increased experiences of fatigue as the confusion of identity and selfhood was not adapting to the new, changing body.

Social interaction and support were sought from partners and family members for finances, physical assistance, and emotional support, but this could be reflected in both a positive and negative light in pwMS [Barker et al., 2019; Miller, 1997]. Although pwMS agreed social support decreased levels of anxiety and encouraged emotional well-being, some participants felt people treated them in a condescending manner that would cause upset and a negative social interaction [Miller, 1997]. Some participants' sense of agency ran through their significant other, the feeling of managing their fatigue was conducted by both of them, and executing daily tasks could be seen as a co-dependency. Activities including food shopping would be done together, with the significant other fully understanding their partner's limits. A sense of reliance on others was found regarding everyday activities of social, bodily, and intellectual states of being.

In this research, participants described that they felt bodily and social reliance on significant others, friends and family. One participant felt visible, physical reliance on friends at events, such as watching football matches, where fatigue triggered bodily dysfunction. His friends had to physically hold him up as his body identity shifted into the outsider interpretation of someone being intoxicated. Another participant described reliance on her significant other in daily activities such as food shopping. When her cognitive ability was affected by fatigue whilst shopping in a supermarket, her coping strategy was to stand still and wait for her husband to find her. Overstimulation of any sense could exacerbate her fatigue and cause an instant reliance on her husband. Her capacity to feel in control of all elements of her life was reduced by fatigue alone. Fatigue can infiltrate what an individual allows into their mind, and it can toy with emotions, intellect, and bodily states that impacts a pwMS' sense of agency. There is a continuous fluctuation of diminished individual control and agency. The inability to undertake a broad range of both physical and cognitive activities was described as a sense of disembodiment, as participants no longer felt they had full access to their body in a way that they previously felt before diagnosis.

Flensner et al. [2003] found pwMS' personal abilities, activities, and the surrounding environment was restricted whilst fatigued, as they typically had to rely on others to accomplish something. This reliance was used as part of coping with fatigue, but it wasn't always seen as positive. Some individuals expressed comfort incorporating close family as an extended arm for assistance, but others felt embarrassment, shame, or did not have help as an option [Flensner et al., 2003]. Social identity theorists [Tajfel et al., 1979] suggest that depending on how people see themselves in the social situation they are in, they can have multiple identities. According to Barker et al. [2019], pwMS can have multiple identities, highlighting a pattern of recognising MS and choosing to either adapt it into their social identity or compartmentalise it. Identity appeared to be directly linked to coping strategies; if any participant had a degree of support and strategies to manage numerous fatigue-related scenarios, they were more likely to feel a level of control over their fatigue. Nonetheless, without support and strategies, an individual's agency is disturbed and as a result, their sense of identity is altered. Fatigue impacts pwMS through the reduced ability to work, and activities of social, bodily or cognitive ability changed some participants' identity. Unlike in the study by Barker et al. [2019], multiple identities were not observed in the present research. However, there was a clear distinction between participants' old and new identities, from before and after their diagnosis, and the impact fatigue had on all constructs of their life. The new identity had to overcome, manage and understand fatigue before the new identity was accepted. Some participants reported the acceptance of fatigue and identity took up to a decade. The new identity came with challenges of body imagery, sociality, temporality and sense of agency as discussed in this chapter.

In summary, selfhood was affected by the new identity participants had to establish and accept. Socially, there was a universal reduction in social interaction. Participants were faced with a tone of embarrassment as changes to bodily movement, function and cognitive ability were shown to others. A continuous, changing body caused a mixture of emotions in how others would act and view them. The annoyance of reliance and dependency was quickly discovered in different aspects of their lives, which ultimately altered their sense of agency and identity.

Fatigue infiltrates an individual's lifeworld with embodiment and selfhood emphases at the centre of the continuum of experiences. Fatigue is unique and depends on the individual. It is a complex phenomenon that is believed to be misunderstood and undermined by others. This leads to elements of emotional states that have been revealed within this research as another possible trigger of fatigue. Descriptive phenomenology is a powerful research approach for exploring challenging problems such as MS fatigue. This approach has enabled the understanding of a complex phenomenon and improved the awareness of fatigue and its multiple facets. Phenomenology has revealed the experiential view, from a first-person perspective, through the lived experiences of pwMS. It has drawn out the essences of fatigue, that further probes interest to explore fatigue from a third-person perspective, and to examine any confluence between the two. In the chapter nine, fatigue is explored via a different approach, in attempt to identify and characterise ambulatory fatigue. Exploring fatigue from a physiological perspective will enable understanding of the differences and similarities in fatigue as experienced to physiological fatigue, which will be discussed in Chapter Ten. In the following chapter the method of turn detection (TD) in three signals of inertial wearable sensors were explored. A method of TD was used to effectively remove the turns to explore gait parameters during the 6MW, and was necessary for analysis of fatigue to be successfully investigated.

Chapter Eight: Automated methods for turn detection with the use of gyroscopy, magnetometry and accelerometry signals

In this chapter, the use of gyroscope, magnetometer, and accelerometer signals for 180-degree TD are explored, and the explicit comparison of each is investigated. Three algorithms were applied to a group of MS participants and an older healthy control group the 6MW, with sensors located at the sternum and ankle. This method of analysis was required to effectively investigate gait parameters and fatigue within the 6MW; the turns need to be removed in order to compare gait characterisations at maximum speed during the straight walkways. TD and characterisation are important in the identification of ambulatory analysis, so that researchers can reliably identify these characterisations in different gait populations and explore the behaviour and patterns in turning. However, for this research, TD was important for the identification and elimination of turns so ambulatory analysis could be successfully executed. The aim for this chapter was to identify and remove turns by an automated algorithm directly from raw sensor signals; automated algorithms for TD would be time efficient and, even though some automated algorithms exist [El Gohary et al., 2014], researchers in this discipline would benefit from optimising how automated recognition works. Exploring different automated TD methods help identify each methods strengths and weaknesses, and identify the methods that suit different populations and gaits most effectively.

It should be noted that ambulatory fatigue could potentially influence TD characterisation and could be of interest in future research. In this study, the gait characteristics in ambulatory fatigue were of interest, therefore, only changes to walking were explored. The walking experiments were conducted on a 25ft walkway where participants would typically turn at least 30 times during a 6MW. Consequently, to explore fatigability in gait, these turns had to be eliminated to focus on gait parameters for a "steady-state" walking along a straight path.

This chapter is divided into three parts. The first part comprises an investigation and comparison of three methods of TD and characterisation using gryoscopy, magnetometry and accelerometry, with signals located at the sternum during the 6MW in an older healthy population. The second part, consideration is made whether signals at the ankle can successfully identify TD and characterisation, compared to the sternum in gyroscopy and magnetometry signals. Lastly, in the third part, signals in individuals with gait abnormalities (namely pwMS) are explored, and there is a comparison of all three methods located at the sternum. Magnetometry and accelerometry-based TD were tested against the gyroscope method of El Gohary et al. [2014] (ground truth). The accuracy of each method of TD was also tested for each sensor location and explored in pwMS who demonstrate gait abnormalities. The areas of signals and algorithms that could not be applied are highlighted, and the reasoning and significance of this is discussed.

8.1. Abstract

TD during ambulation based on raw magnetometry indoors may be subject to idiosyncratic magnetic fields associated with interference, and its consistency has not been described in the literature. Ambulatory participants from healthy and MS cohorts wearing NGIMU sensors (X-io, Bristol) with nine channels of data (accelerometry, gyroscopy and magnetometry) affixed to the sternum and ankle performed a six-minute walk that included 180-degree turns. Magnetometry and accelerometry-based TD was tested against the gyroscope method of El Gohary et al. [2014] (ground truth). Recognition by magnetometry on the sternum was 99.85% accurate. The correlation between TD based on the magnetometry signal from the sternum versus the ankle was fair (92.98%), whereas the correlation between TD based on vertical gyroscopy signals from the sternum versus the ankle was excellent (99.85%). TD based on the vertical accelerometry signal was 89.11% accurate. In a small cohort of pwMS, the correlation between TD of gyroscopy and magnetometry signals at the sternum was also accurate (98.66%), but the correlation of accelerometry and gyroscopy was poor (24.94%). These findings indicate that magnetometry signals located at the sternum can be used for 180-degree TD in an older healthy and multiple sclerosis cohort.

8.2. Introduction to TD

TD and its characterisation are important in the assessment of gait and coordination in a variety of populations. In a clinical setting, gait kinetics and kinematics are conducted through clinical motor tasks such as TUG and longer walking tests such as the 6MW, both of which entail 180-degree turns. Ambulatory turning is an omnipresent task that occurs in daily activities and living. It requires complex gait changes and multi-limb coordination for safe ambulation and functional independence [Jørgensen et al., 2002]. Wearable sensors have become a powerful tool to perform gait analysis, in particular the assessment of turning to gather insight on motor control [Bertoli et al., 2017]. To investigate and identify TD, IMUs can involve the use of gyroscopy, magnetometry or accelerometry signals, which measure and record specific acceleration (including gravitational attitude), angular velocities and local magnetic forces [Bastiaansen et al., 2020].

In previous studies, researchers have measured TD using these signals with the most widely used method by El Gohary et al. [2014]. El Gohary et al. [2014] used gyroscope signals located on the trunk to detect the peaks of the vertical component of the angular velocity. This algorithm has been applied and used in the study of numerous populations that display different gait characterisations [Bertoli et al., 2016, 2017, 2018). Bertoli et al. [2016] tested four methods for TD in two one-minute walking tasks applied to a variety of gait conditions of older healthy people, stroke survivors, people with Parkinson's, and people with chorea. The test methods included three gyroscope methods and one magnetometry method [El-Gohary et al., 2014; Fleury et al., 2007; Nguyen et al., 2015; Novak et al., 2014]. Interestingly, the test methods in the older healthy population and people with Parkinson's all detected the correct amount of turns. The method used by Fleurys et al. [2007] obtained excellent results and demonstrated no extra or missed turns using magnetometry signals in the lower trunk from detecting local magnetic field changes. Magnetometry signals have been used for TD since 2015 with Oberndorfer et al. [2015], but the methodology has never been explained.

Bertoli et al. [2018] further explored TD and characterisation in older healthy adults and people with Parkinson's disease using gyroscope signals at the ankle. They investigated the usefulness of a common method for detecting 180-degree turns from the lower back sensor and adapted it to measure the usefulness of the ankle sensor [Bertoli et al., 2018]. On average, both groups had an onset of detected turn delay of 130ms and 160ms in comparison to the sensor located on the lumbar spine. Although dependent on the walking speed, the turn duration applied to the ankle was on average 300ms shorter for both groups [Bertoli et al., 2018]. Corroborating findings from Novak et al. [2014], their results consistently produced worse onset detection with respect to the lumbar located methods for both the IMU and stereo-photogrammetric systems.

The act of turning requires a coupling between anticipatory postural adjustments and scaling of walking, making it a challenging motor task [Nutt et al., 2011]. The ability to turn safely is important for functional independence, and previous research has highlighted that individuals with a degree of movement disability display abnormal turning characteristics, even if the ability to walk straight is unaffected [Horak et al. 1992; Salarian et al., 2009; King et al., 2012]. Turning and turn identification can become more difficult in people with increased gait variability, such as with pwMS [Motl et al., 2017]. TD in different gait characterisations are essential to identify an adaptive algorithm by considering all gait characteristics of all populations, but also to identify the similarities and differences in turning characteristics.

An explicit comparison between all methods of gyroscopy, magnetometry, and accelerometry is needed within the literature. Although for the magnetometry signals the recognition and middle of turn have been established, the characterisation and duration of turns has yet to be described. Magnetometry signals for this study were imperfect square waves that are described in the methods and discussion sections above (sections 8.3 and 8.5, respectively). The turns are detected by the change in strength in the local magnetic field that we can identify in part of the algorithm (see Figure 8.1). Figure 8.2 illustrates the detection of square waves, of which the participant walking along the 25ft walkway and the changing of direction to turn that is forward and backward signal that crosses zero. M104 displayed clear turning and walking throughout the 6MW, which is demonstrated in Figure 8.2. These two figures show promise for TD using magnetometry signals and, would be a revealing signal for TD methods. Thus, the comparison of different signals would further explore the usefulness and accuracy of different TD methods.

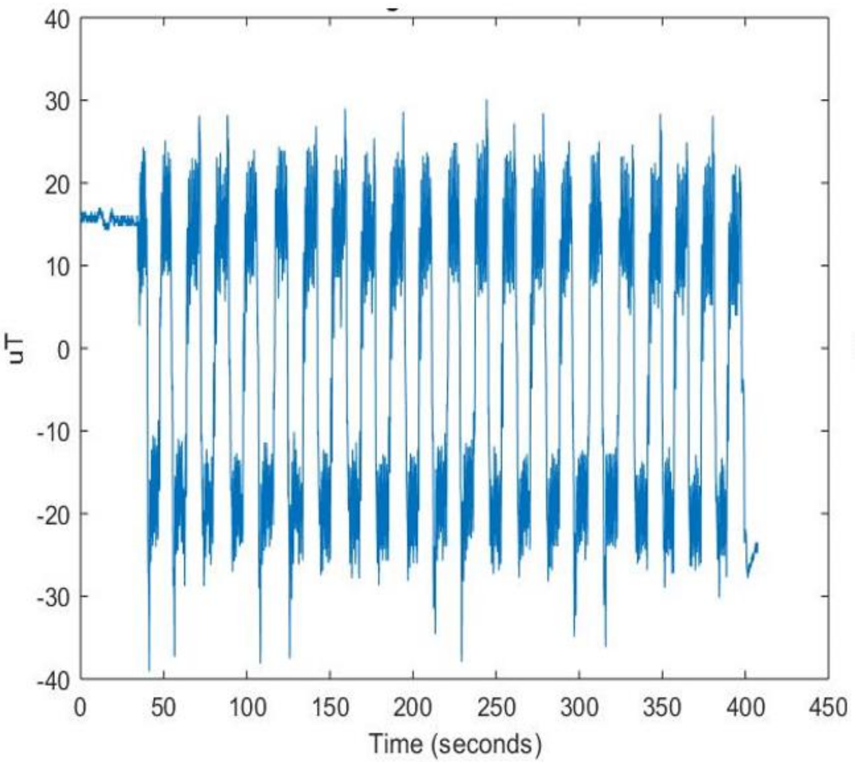

Figure 8.1.: Representative trace of Sternum magnetometry (anterior-posterior axis, Z) M104 6MW.

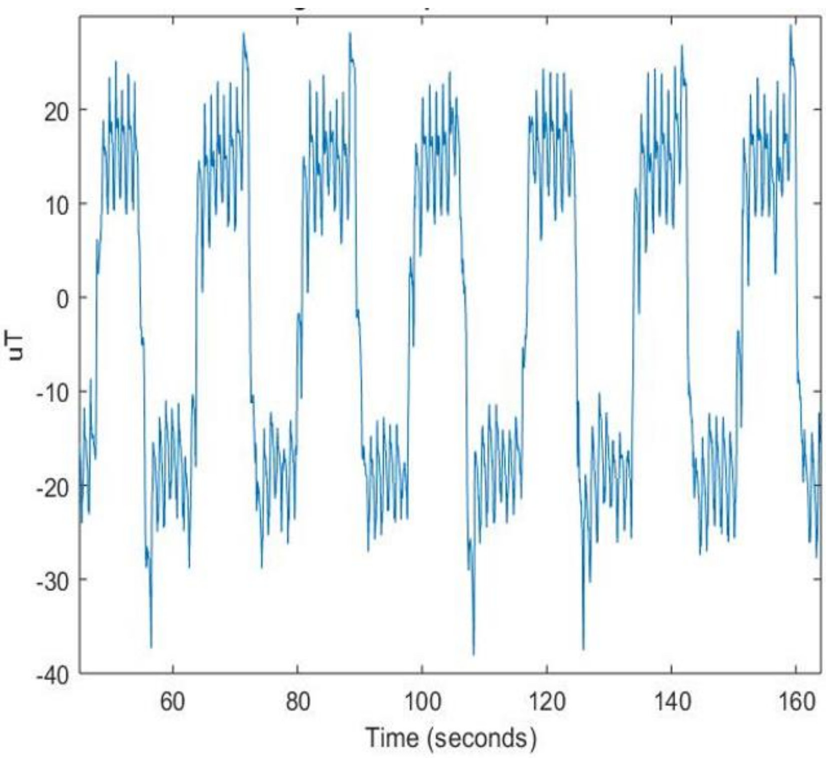

Figure 8.2.: Representative trace of Sternum magnetometry (anterior posterior axis, Z) M104, 100 second snippet.

Furthermore, the use of magnetometry signals located on peripheral extremities, such as the ankle, has not been successfully explored. The comparison of these methods is needed to identify the accuracy of each algorithm and highlight the usefulness and importance of detecting the start, middle, and end of turn. One main difference in this study was the placement of the sensor. Typically, singular sensors are placed on the lower lumbar spine, or the wrist and ankle in previous studies [El-Gohary et al., 2014; Mancini et al., 2017; Pearson et al., 2013]. In this study, the sternum (and the ankle) were used; it is one of the most stable placements as it is least affected by movements during swing phase. The sternum is less likely to have extra movements that will confound TD. In order to verify the accuracy of the TD methods used, the centre of the turn, and the duration of the turn was calculated.

This study was divided into three parts. In the first section, three methods of TD and characterisation using gyroscopy, magnetometry and accelerometry with signals located at the sternum during the 6MW in an older healthy population were investigated and compared. In the second section, it was considered if signals at the ankle could successfully identify TD and characterisation compared to the sternum in gyroscopy and magnetometry signals. Lastly, in the third section, the signals in individuals with gait abnormalities (namely pwMS) were explored, and all three methods located at the sternum were compared.

8.3. Methods

8.3.1. Experimental design

Twelve pwMS and eleven older healthy participants (63 ± 7.59 and 57 ± 10.1 years old, respectively) were recruited. The study was conducted at two sites: 1) the University of Brighton, Health Sciences Department, Eastbourne, and 2) the MS Sussex Centre, West Sussex. To be eligible for the study, participants had to be over 18 years old and be able to walk 100m unaided. For pwMS, they had to have a definite diagnosis of MS and an EDSS-S score between 1 and 5.5 (average and SD, 5.13 ± 0.61). There were no restrictions on the type of MS diagnosed. Any limitations to orthopaedic conditions in the trunk or lower extremity that affected gait, or the inability to complete the assessment physically due to any other chronic illnesses, were exclusion criteria for this study. The experimental procedure was approved by the tier two university ethics committee (University of Brighton). Each participant was fully informed about the nature of the experiment and provided written consent.

NGIMU wearable sensors (X-io, Bristol, UK) were used, with three dimensions each of accelerometry, gyroscopy and magnetometry. Data was recorded at 100Hz. All sensors were factory-calibrated for gravitational acceleration (accelerometers) and angular velocity (gyroscopes) and incorporate an onboard algorithm for the estimation of heading and quaternions. Data acquisition was synchronised by the recording of individual sensor signals via Wi-Fi according to the standardised software from the manufacturer. Subsequently, four sensors were safely and non-invasively affixed onto each participant on the ankle, thigh and sternum. The left and right ankle sensors were placed on the lateral aspect 2cm above the lateral malleolus, and the torso sensor was placed on the body of the sternum. The sensors were orientated with the x-axis pointing superiorly (proximally), placed over clothing and fitted with Velcro elastic straps, with an elasticated harness placed around the ribs and left shoulder to secure the sternum sensor. All participants wore standardised running shoes (Lonsdale), fitted with the correct shoe size.

The 6MW was performed and conducted according to Goldman et al. [2008], with a walkway modification due to facility limitations (25ft walkway, unlike the ATS guidelines of 100ft). Participants were instructed to walk back and forth along a 25ft walkway continuously for six minutes, performing a U-turn at each end of the walkway. Each participant was instructed to walk at a comfortable speed but to cover as much ground as possible. The turn direction was not imposed, although participants were asked to start the first step with their right leg.

Stopwatch measurements started on the word “go” and ended on the six-minute mark. Participants were informed of the time after each minute and were instructed to stop exactly where they were at the six-minute mark. The total number of turns were observed and recorded during the 6MW.

8.3.2. Methods of turn detection and characterisation

Turns were detected and characterised using three methods of gyroscopy, magnetometry, and accelerometry from the sternum and ankle signals. Interference of signals caused bleed between data channels in some participants and methods. However, the following characterisations were used to detect turns in MATLAB R2018b.

8.3.2.1. Gyroscope turn detection and characterisation

Following El Gohary et al. [2014], the algorithm takes advantage of accelerometry measurement to correct any baseline drift from integration of angular velocity from gravity [El-Gohary & McNames, 2012]. X-io sensors, like the Opal sensors used by El Gohary et al. [2014], provide orientation estimates, q, in quaternion form that transform body frame sensor measurement, w^b, into inertial frame, w^i, using the following equation:

$$w^i = q \times w^b \times q^{-1}$$

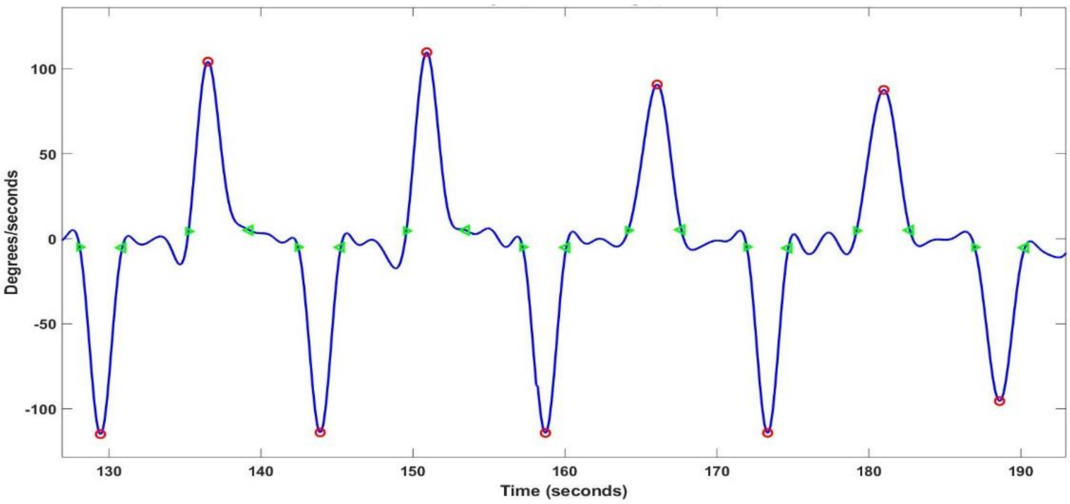

Figure 8.3.: Representative trace of Gyroscope (X) turn detection M095 (sternum)signal of a participant alternating between clockwise and anti-clockwise turns ("figure of 8" pattern). The red circles indicate automated detection of the middle of the turn, the green triangles indicate automated detection of the beginning and end of the turn.

By using the transformed rotational rate, w^i, the angular velocity of pitch was extracted from both sensors and filtered with a low pass 1.5Hz filter to remove the high frequency components. Turns were detected from the peaks recorded from yaw signals of the angular velocity. For each local maximum of the filtered $w^{i}_{z,}$ (a turn) 5 degrees per second was assumed from the start and end of each turn. A 15 degrees per second threshold crossing was set for each peak where the filtered w^{i}_{z} exceeds 15 degrees per second. It is highly unusual for a human to make a U-turn in less than 0.5 seconds and more than 10 seconds, therefore, turns were merged if participants turned in the same direction separated by less than 0.5 seconds. Then turns lasting for more than 10 seconds and less than 0.5 seconds were discarded. Lastly, the net turn angle was calculated by integrating vertical angular velocity (equation shown below) overturn duration, discarding results less than 45 degrees.

$$\theta_z = \int w_z^i$$

8.3.2.2. Magnetometry turn detection and characterisation

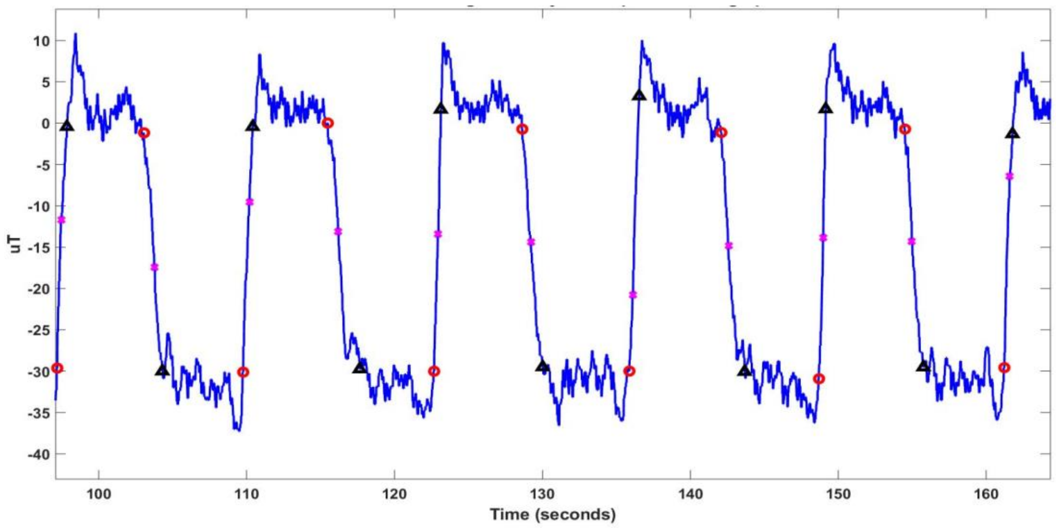

Figure 8.4.: Representative trace of Magnetometry (Z) turn detection M100 (sternum) during a 6minute walk. Turns are sudden changes in magnetic signal (nearly vertical lines) while walking on a straight pathway is represented by a more stable signal (jagged horizontal lines). The magenta circles indicate the middle of the turn, red circles show the beginning of the turn and black triangles indicate the end of the turn.

TD was measured by the change of local magnetic field measured in both horizontal magnetometry y and z axes. To identify turning using the change in the raw (unfiltered) local magnetic field, the two statistical modes of the bimodal field strength (see Figure 8.4) were associated with walking in opposite directions, and the turn was the rapid continuous transition between modes. The detection of square-like waves was calculated by an algorithm that formed a histogram to identify the bimodal pattern of the magnet signals; the two modes are the forward and backward laps of the individual. The difference of each sample value from the two modes determined the initial estimate of direction. The algorithm consensus value for each sample used a four-second window to determine whether the median of instantaneous measures was forward or backward. The change in direction was stabilised by a pair of Boolean values that toggled at either the start or the end of the turn. Different thresholds were used for the upward and downward transitions to prevent variations in the raw signal from prematurely triggering turn identification.

8.3.2.3. Accelerometer turn detection and characterisation

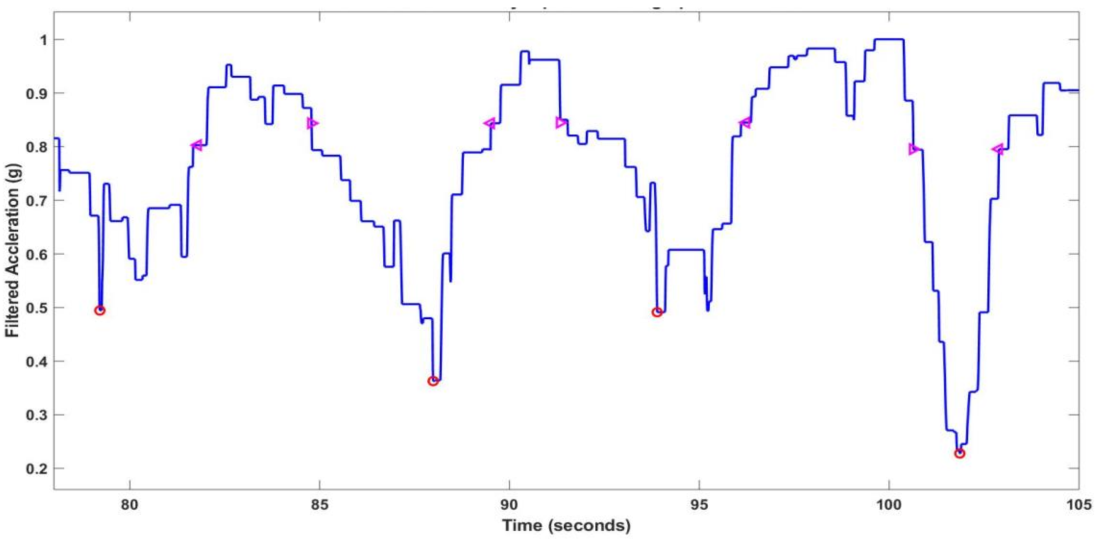

Figure 8.5.: Representative graph of Accelerometer (X) turn detection M095 (sternum). The red circles indicate the middle of the turn, the magenta triangles indicate the beginning and end of the turn.

Accelerometry signals were used in the x-axis to detect regions of reduced vertical variability as a participant slowed down during the step cycle. Acceleration of the sensor is the rate at which the sensor changes it velocity. The concept of the accelerometry algorithm is to detect the deacceleration of an individual (as humans slow down to turn); plainly this method will detect false positives in walkers who slow down or stop in the middle of walking on the straight pathway. The method depends on the principle that the action of turning reverses the forward momentum of an individual; therefore, as an individual brakes, the vertical variability (bouncing up and down whilst walking) of acceleration decreases. The algorithm created a window of 50 samples (0.5 seconds) that was applied for the range filter to allow at least half the duration of one step. At each sample, a range signal was calculated as the range of the window from the difference in the highest and lowest values. Turns were identified as the local minima from the range signal. A percentage threshold was used and set at 80% to recognise the start and end of the turn. This allowed 80% of the change in variability to full speed to be accepted as the turn. A sudden decrease in a range signal in the vertical component would then detect a turn.

All turn outputs for all methods of the sternum and ankle were then extracted into Microsoft Excel spreadsheets. A purpose-made script for matching turns was applied to best match the middle/peak of each turn for each method and comparison under investigation. This reduced and filtered out simple errors of misaligned matching turns. Matching turn data was calculated by matching the timed middle/peak of the turn of each method. The matching turns were then saved in Microsoft Excel spreadsheets for analysis.

8.3.3. Data analysis

The first and last turn was discarded from each method and comparison because the initial standing position of the participants was sometimes not stable. As the El Gohary et al. [2014] method is the most widely recognised and used method for the detection of turns in wearable sensors, this method was used as a key comparator to magnetometry and accelerometery. The sensor located on the sternum was used as the key comparator when investigating gyroscopy and magnetometry signals in the ankle. To compare methods and the location of the sensors, the duration of turn, peak of turn, and number of turns detected were calculated. The mean, mean absolute difference, and standard deviation were then calculated. The mean absolute difference was calculated as it addresses and identifies the non-negative value between each method comparison. The commission and omission error percentage rates were calculated for each comparison. The commission error percentage rate calculates the number of turns identified in the comparative method that are missing in the "gold standard" method (the El Gohary method, or the sensor positioned at the sternum). The omission error percentage rate calculates the number of turns identified in the "gold standard" method (El Gohary method, or the sensor positioned at the sternum) that are missing in the comparative method. Each table demonstrates two side-by-side comparisons between three methods. Bland-Altman analyses and plots were used to illustrate the comparison of methods using the timed peak turn points of each method/location of a sensor.

8.4. Results

The descriptive statistics of the mean duration of turn, mean absolute difference timed peak turn, mean absolute difference duration of turn, commission and omission error rates of turns are shown in Tables 8.1, 8.2 and 8.3. The timed peak turn of each method and comparisons are presented in the Bland-Altman plots provided in Figures 8.6 to 8.11.

8.4.1. Comparison of magnetometry and accelerometry signals to gyroscopy signals in the sternum

In the first section of this study, TD of magnetometry and accelerometry methods were compared to gyroscopy signals used by El Gohary et al. [2014] in older healthy participants. Magnetometry had a smaller mean absolute difference in timed peak turn and duration of turn (0.21 ± 0.28 and 0.71 ± 0.92, mean ± SD, respectively) in comparison to accelerometry signals (0.54 ± 0.71 and 0.98 ± 1.25, respectively; see Table 8.1). The commission and omission error rates of number of turns detected in El Gohary versus magnetometry were considerably less when compared to El Gohary versus accelerometry. The lowest percentage was calculated at less than 1% in magnetometry signals, at 0.15% in commission error rates, whereas the highest percentage was calculated at 10.89% in accelerometry. Accelerometry signals calculated a longer duration of turn time to both gyroscopy and magnetometry signals.

Table 8.1.: Healthy group sternum IMU of El Gohary compared to Magnetometry and Accelerometry signals. The table compares the mean absolute difference timed peak turn (the centre point of turn), and mean absolute difference of duration of turn (the beginning to the end of the turn) of the El Gohary method compared to the magnetometry, and then the accelerometry method to El Gohary method at the sternum. In the third row, the mean duration of turns (in seconds) for each individual method is displayed. The commission error rate in the second column calculates the number of turns identified with magnetometry that are missing in the El Gohary method (as a percentage). The omission error rate calculates the number of El Gohary turns identified that missing in the magnetometry method (as a percentage). In the third column the commission error rate calculates the number of turns identified with accelerometry that are missing in the El Gohary method (as a percentage). The omission error rate calculates the number of turns identified with the El Gohary method that are missing in the accelerometry method (as a percentage).

	Sternum		**Sternum**	
Healthy	**El Gohary**	**Magnetometry**	**El Gohary**	**Accelerometry**
Mean absolute difference timed peak turn (seconds ± SD)	**0.21 ± 0.28**		**0.54 ± 0.71**	
Mean absolute difference duration of turn (seconds ± SD)	**0.71 ± 0.92**		**0.98 ± 1.25**	
Mean duration of turn (seconds ± SD)	**2.68 ± 0.47**	**2.49 ± 0.96**	**2.68 ± 0.47**	**3.13 ± 1.28**
Commission error rate of turns detected (%) (range)	**0.15 (0-1.69)**		**10.89 (0-59.10)**	
Omission error rate of turns detected (%) (range)	**1.06 (0-3.33)**		**1.82 (0-4.16)**	

Figures 8.6 and 8.7 show two Bland-Altman plots of the timing of the peak turn of older healthy participants of the El Gohary versus magnetometry method, and El Gohary versus accelerometry method located at the sternum. The Y-axes of the all the Bland-Altman plots demonstrates the interval of agreement and indicates the difference between the two measurements. As illustrated in Figure 8.6, there was a high correlation between the two methods for timed peak turn, and the output values demonstrated an equal and random distribution. All output values lie within the interval of agreement indicating agreement in identifying the centre of the turn between gryoscopy and magnetometry signals at the sternum. Similarly, Figure 8.7 shows a high correlation between accelerometry and El Gohary timed peak turn detections, but there are output values below the confidence interval line, indicating that not all outputs lie within the 95% confidence interval. Both Bland-Altman plots show a mean and estimated bias as zero or close to zero. This indicates that both methods systematically produce similar results to gyroscopy signals with sensors located at the sternum. The two plots illustrate small limits of agreement; Figure 8.7 of El-Gohoary versus accelerometry shows a limit of agreement smaller than 1 and -1 seconds indicating the bias is small. However, both comparisons show the methods are essentially equivalent.

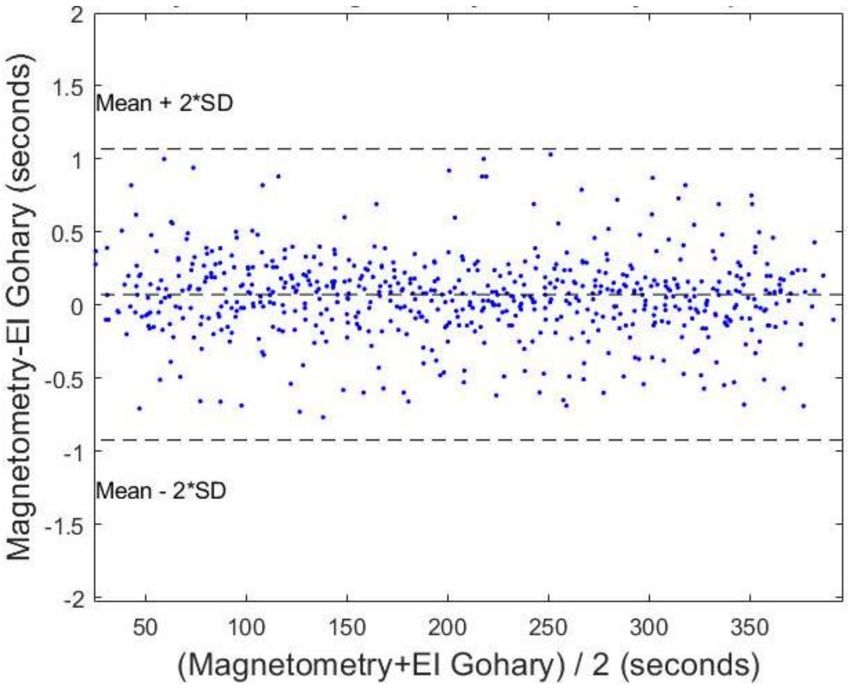

Figure 8.6.: Timing of the peak turn using our sternum magnetometry method vs. the method of El Gohary during healthy walking.

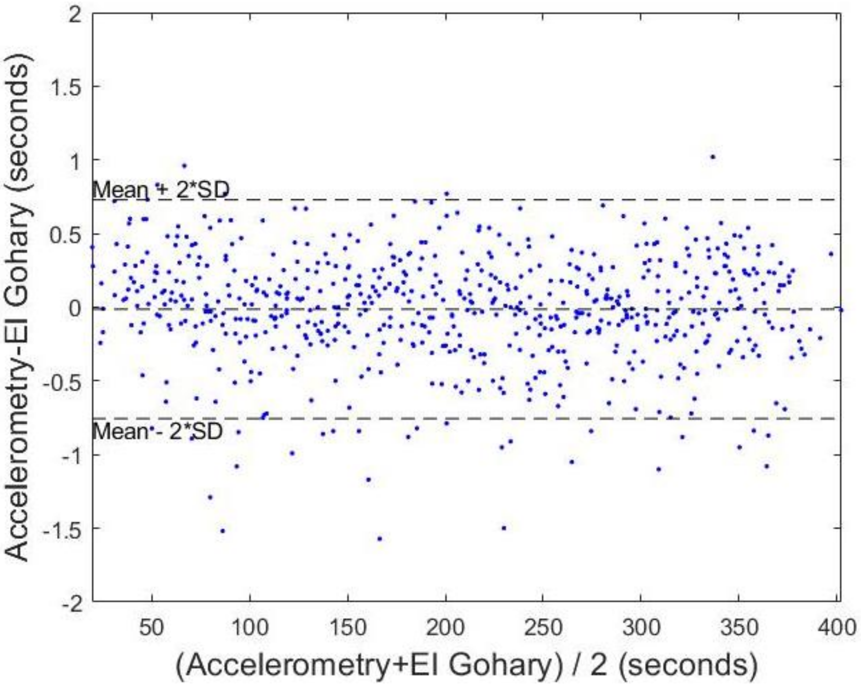

Figure 8.7.: Timing of the peak turn using our sternum accelerometry method vs. the method of El Gohary during healthy walking.

8.4.2. Comparison of sensor location at the sternum to ankle in gyroscopy and magnetometry signals

Subsequently, following up from section one and identifying El Gohary and magnetometry calculated lower error rates, the differences in the two methods in relation to the location of the sensor was explored. In the second section, the sternum and ankle signals of gyroscopy and magnetometry were explored, determining the calculations already stated above. Magnetometry failed to detect any turns in four participants in the ankle, therefore these participants were discarded from this section of analysis. Both gyroscope signals calculated low commission and omission error rates of 0.15% and 0.61%, respectively. The mean absolute difference in timed peak turn in gyroscope signals in the sternum and ankle calculated a smaller difference than the magnetometry signals by 0.25 seconds (see Table 8.2).

Table 8.2.: Sternum & ankle IMU of El Gohary and magnetometry signals. The table compares the mean absolute difference timed peak turn (the centre point of turn), and mean absolute difference of duration of turn (the beginning to the end of the turn) of the sensor positioned at the Sternum, compared to the sensor positioned at the ankle, in both the El Gohary method and magnetometry method. In the third row, the mean duration of turns (in seconds) for each individual method is displayed. The commission error rate in the second column calculates the number of turns identified at the ankle that are missing at the sternum in the El Gohary method (as a percentage). The omission error rate calculates the number of turns identified in the sternum sensor that missing in the ankle sensor, in the El Gohary method (as a percentage). In the third column the commission error rate calculates the number of turns identified at the ankle sensor that are missing from the sternum sensor, in the magnetometry method (as a percentage). The omission error rate calculates the number of turns identified at the sternum sensor that are missing from the ankle sensor, in the magnetometry method (as a percentage).

Sternum vs. ankle	**El Gohary**		**Magnetometry**	
Healthy	**Sternum**	**Ankle**	**Sternum**	**Ankle**
Mean absolute difference timed peak turn (seconds ± SD)	**0.25 ± 0.66**		**0.83 ± 1.13**	
Mean absolute difference duration of turn (seconds ± SD)	**0.20 ± 0.32**		**1.49 ± 1.76**	
Mean duration of turn (seconds ± SD)	**2.68 ± 0.47**	**2.62 ± 0.55**	**2.88 ± 1.01**	**2.31 ± 1.19**
Commission error rate of turns detected (%) (range)	**0.15 (0-1.69)**		**7.02 (0-24.29)**	
Omission error rate of turns detected (%) (range)	**0.61 (0-3.39)**		**33.17 (0-87.72)**	

As displayed in table 8.2., there was a notable difference in the two side by side comparisons between the sternum and the ankle sensors in the El Gohary and Magnetometry methods in the mean absolute difference timed peak turn, and duration of turn. Gyroscope sternum and ankle signals calculated a 0.20 second mean absolute difference, whereas magnetometry methods calculated a 1.49 second mean absolute difference between the sternum and the ankle signals. This demonstrates a smaller difference between the sternum and the ankle with the El Gohary method compared to the magnetometry method (which the commission and omission rates demonstrate). The difference TD initiation and completion using the gyroscope was not so strongly affected by changing the placement from the torso to the ankle, whereas changing the sensor placement had a much more extreme effect upon the magnetometry method of TD. The percentage omission error rate of turns detected in magnetometry was 33.17%, with a range of 87.22%; thus, in some cases using magnetometry to detect turns from an ankle sensor resulted in many failures to detect turns (compared to the more reliable detection occurring on the torso sensor).

Figures 8.8 and 8.9 show two Bland-Altman plots of the timed peak turn located at the sternum in gyroscopy and magnetometry signals. Figure 8.8 shows a narrow limit of agreement that indicate the two methods of sternum versus ankle El Gohary TD have a smaller difference at identifying the centre of the turn, and are essentially equivalent. Figure 8.9 indicates a slight positive bias in output values. The limits of agreement are wider than gyroscope signals which indicate bigger differences in output values in the sternum and ankle, and could suggest ambiguous results. The outlier output values located from -2 to -3 are from one participant (M088).

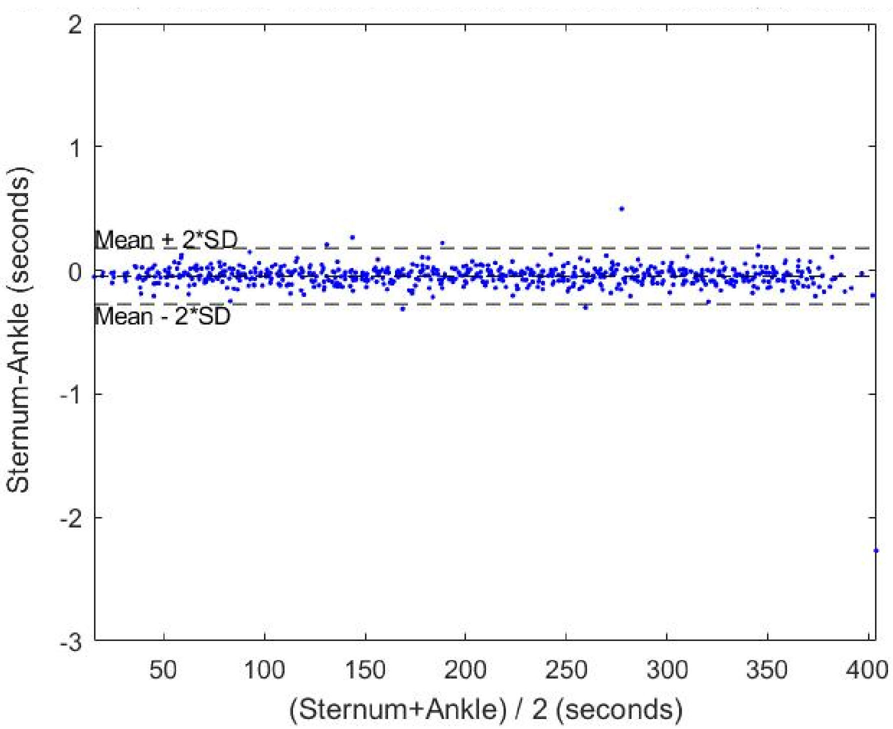

Figure 8.8.: Timing of the peak turn sternum versus ankle using the method of El Gohary for healthy walking.

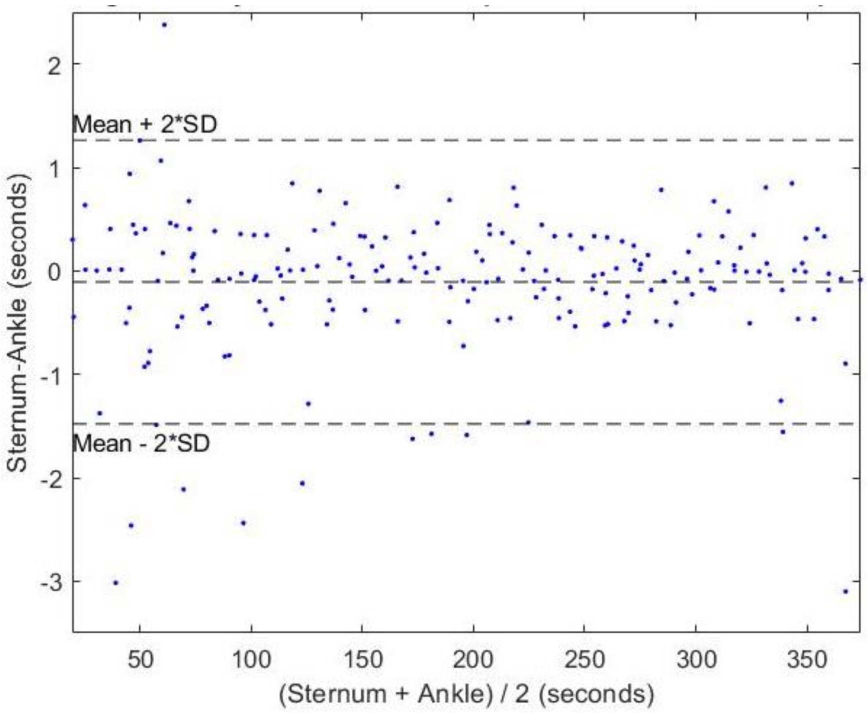

Figure 8.9.: Timing of the peak turn sternum versus ankle using the magnetometry method for healthy walking.

8.4.3. Comparison of magnetometry and accelerometry signals to gyroscopy signals in pwMS

In the final part of this study, TD in pwMS with all three methods with signals from the sternum was explored. Gyroscope signals were compared to magnetometry and accelerometry signals to identify the success of TD in people with gait abnormalities. In the magnetometry, the mean absolute difference in duration of turn was sustainably shorter and had a smaller standard deviation (1.11 ± 1.38 seconds) compared to accelerometry (2.09 ± 9.59 seconds). The timed peak turn was slightly earlier in accelerometry (0.28 ± 0.37 seconds) to magnetometry of (0.33 ± 0.41 seconds). Magnetometry commission and omission rates of turns detected were both 1.36%, but accelerometry calculated more variability commission error rates with 75.06%. The omission rates were considerably less at 1.56%. Thus, accelerometry based TD in this population was as expected unreliable, with potentially high rates of extra turns detected as well as high variability in the turn start and end points, when compared to magnetometry.

Table 8.3.: PwMS sternum IMU of El Gohary compared to magnetometry and accelerometry. The table compares the mean absolute difference timed peak turn (the centre point of turn), and mean absolute difference of duration of turn (the beginning to the end of the turn) of the El Gohary method compared to the magnetometry, and then the accelerometry method to El Gohary method at the sternum. In the third row, the mean duration of turns (in seconds) for each individual method is displayed. The commission error rate in the second column calculates the number of turns identified with magnetometry that are missing in the El Gohary method (as a percentage). The omission error rate calculates the number of El Gohary turns identified that missing in the magnetometry method (as a percentage). In the third column the commission error rate calculates the number of turns identified with accelerometry that are missing in the El Gohary method (as a percentage). The omission error rate calculates the number of turns identified with the El Gohary method that are missing in the accelerometry method (as a percentage).

Three methods	**Sternum**		**Sternum**	
PwMS	**El Gohary**	**Magnetometry**	**El Gohary**	**Accelerometry**
Mean absolute difference timed peak turn (seconds ± SD)	**0.33 ± 0.41**		**0.28 ± 0.37**	
Mean absolute difference duration of turn (seconds ± SD)	**1.11 ± 1.38**		**2.09 ± 9.59**	
Mean duration of turn (seconds ± SD)	**3.53 ± 0.65**	**3.01 ± 1.35**	**3.59 ± 0.70**	**3.70 ± 9.55**
Commission error rate of turns detected (%) (range)	**1.34 (0-26.32)**		**75.06 (12.5-281.25)**	
Omission error rate of turns detected (%) (range)	**1.34 (0-26.32)**		**1.56 (0-10.53)**	

Figure 8.10 shows variability consistently across the Bland-Altman plot indicating a high correlation between El Gohary and magnetometry methods, where the two methods are essentially equivalent. The limits of agreement are narrow (however, not nearly as narrow as figure 8.8), with an estimated bias falling just below zero that shows the bias is small and both methods produce similar results. Figure 8.11 displays a mean, estimated bias of zero, indicating accelerometry signals produce similar timed peak turn results to gyroscopy signals. However, the output values are more variable ranging from 2 to - 4. The limits of agreement are wider than in Figure 8.10, which suggests more ambiguous results and a larger difference in output values in accelerometry signals.

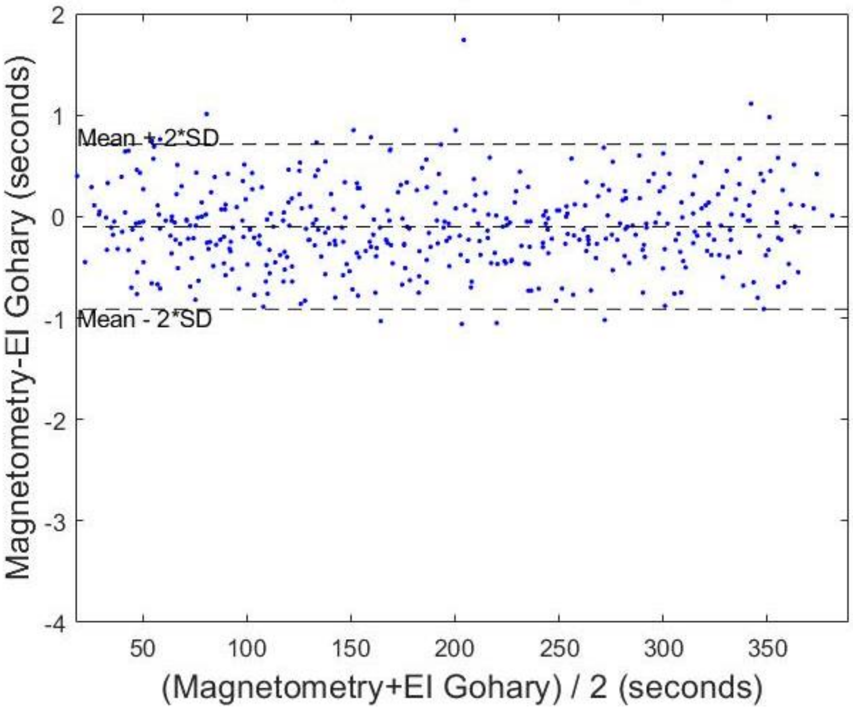

Figure 8.10.: Timing of the peak turn using the method of El Gohary versus magnetometry from the sternum for walking in MS participants.

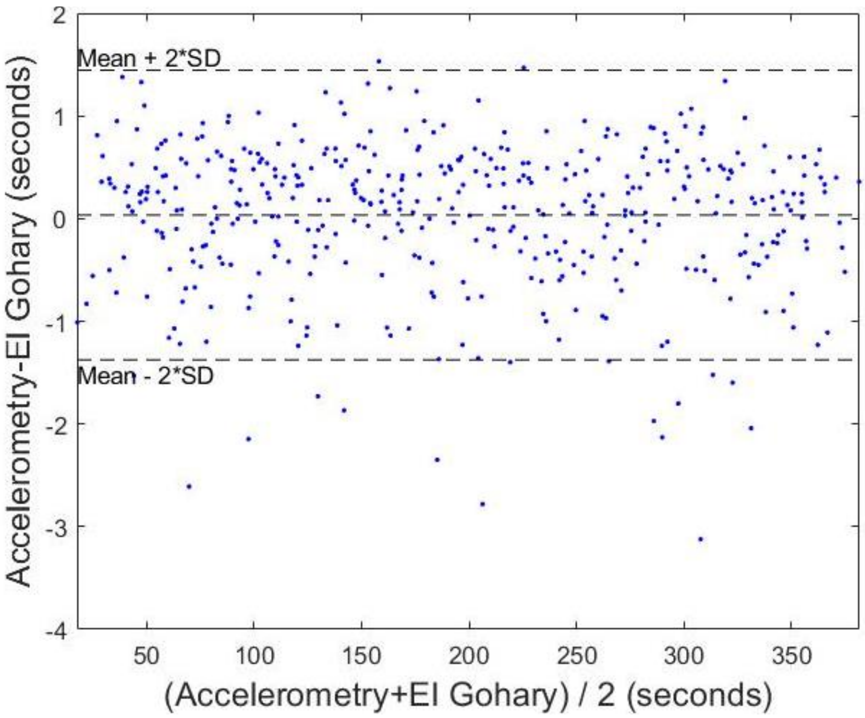

Figure 8.11.: Timing of the peak turn using the method of El Gohary versus accelerometry from the sternum for walking in MS participants.

8.5. Discussion

In this study, the use of TD methods using three different signals in a small cohort of older healthy and more challenging MS participants was investigated. It was divided into three sections to explore the success of identifying and characterising turns in gyroscopy (El Gohary), magnetometry, and accelerometry signals located at the sternum, ankle and in pwMS. To the best of the authors' knowledge, the characterisation of TD in magnetometry and the explicit comparison of three signals has not previously been described in the literature. It was demonstrated that magnetometry with respect to the location of the sternum can provide good recognition at detecting the middle/peak of the turn compared to gyroscopy signals, with a commission error rate of 0.15% and 1.34% in the older healthy and MS group, respectively. The El Gohary method applied to the ankle had a detection rate of 99.85%, with a mean absolute difference time in the duration of the turn of 0.20 seconds compared to ground truth. This value calculated a smaller duration of turn time difference than magnetometry signals located at the sternum.

As expected, there were extra turns detected by the accelerometry method, but the extent of this excess was much larger than expected in the healthy walkers. There was a 10.89% commission error rate in accelerometry signals at the sternum in TD in the older healthy group. Accelerometry demonstrated increased variability in TD and identified more (false) turns than the ground truth in most participants. One potential explanation for this in both groups, but particularly in the MS group, may be due to the methodological approach of identifying smaller vertical variability during the step cycle, which may detect any time period of slowing down. The mean age of both the older healthy and MS group was 57 ± 10.1 and 63 ± 7.59, respectively. Age and reduced velocity of gait should be considered within this algorithm, as gait speed is an important measure and clinical marker in older people and is impacted with age [Busch et al., 2015]. Additionally, pwMS typically have a reduced walking velocity, smaller step time, and cadence than the general population [Motl et al., 2012]. Gait abnormalities and inconsistencies are much more likely to occur in pwMS, especially throughout the duration of the 6MW. Because continuous walking may become increasingly difficult and pwMS may fatigue, they are more likely to intermittently slow down their walk before reaching the turning point.

Our data show that magnetometry can be a useful TD method when the sensor is placed on the torso, but when the sensor is placed on the ankle, our direct TD calculation method for magnetometry was almost worthless. Quantifying turns in magnetometry with respect to the ankle IMU demonstrated highly variable results with a range of 24.29% and 87.72% in commission and omission error rates, respectively. Alternatively, the experiments were performed in three different geographic locations where magnetometry interferences could have disrupted the sensor magnetometry signals. Signals located at the ankle may have resulted from interference of other IMUs on the body, or noise from other electrical objects in the surroundings that may affect the local magnetic field. Bleed in the ankle between the different X, Y and Z channels is more likely to occur due to the anatomical positioning and movement in the ankle in comparison to the upper torso or sternum. Thus, we would predict that TD using magnetometry from an ankle-based sensor would be difficult to achieve accurately unless a substantially more sophisticated calculation was employed, such as AI.

In contrast, magnetometry signals compared to El Gohary signals at the sternum demonstrated fewer variable results with a range of 0.15% and 1.06% in commission and omission error rates, respectively. This indicates a small range and error rate between the two. Additionally, the Bland-Altman graphs show a narrow limit of agreement (on the Y-axis) with all output values inside the limit of agreement. This further supports the usefulness of magnetometry signals for TD at the sternum. However, Bland-Altman graphs are only used to explore the limits of agreement between two methods, it does not confirm whether a method is acceptable or not.

Magnetometry works by identifying the strength of the magnetic field in relation to its magnetic north. It can be used to detect the centre point of the turn in 180-degree turn by identifying the sudden change in signal to the opposing direction. However, the detection of turns of more or less than 180-degrees may be more difficult to identify due to the angle of the turn. The detection of a 45-degree turn would provide a much weaker change of direction in relation to the strength of change in the magnetic field, therefore, much harder to identify the peak turn in an algorithm. Furthermore, although magnetometry identifies the peak of the turn accurately, it seems less reliable at the sternum at detecting the duration of the turn due to the inability to calculate the angle of the turn which would help indicate the start and end of the turn.

8.5.1. Limitations

One limitation of this study is its small sample sizes, which may limit the generalisability of findings. TD methods were only applied to two populations, and not to other populations of different gait characterisations. Purposive sampling was used to match age and similar demographics between the two groups, therefore other features were not accounted for and may have affected the results. Although magnetometry signals remain highly useful for the detection of strength and change of the local magnetic field of a given location, accurate and clear readings may be more difficult to obtain indoors. This is due to the presence of magnetic field anomalies as other metal or magnetic objects or other electrical devices may affect the magnetic field and interfere with results [Li et al., 2012].

Given the results of magnetometry TD at the sternum, developing magnetometry signals located at other parts of the torso or head could potentially provide a useful method of TD for 180-degree turns for researchers without the use of a sternum sensor. Previously, trialling gyroscopy algorithms on peripheral extremities modified the angular velocity threshold and other factors such as the timing of turns, the range of merging turns, and the minimum turn angle [Bertoli et al., 2018]. To apply magnetometry TD on peripheral extremities, sophisticated algorithms and forms of pattern recognition will have to be considered.

The suggestion of sensor fusion for TD should be considered. Sensor fusion combines signals to create a single measurement system to provide a more complete picture of the phenomenon under investigation [Ligorio et al., 2016] Invariably, such fusion involves estimation and inaccuracy. Combining signals of gyroscope and magnetometry for TD could potentially provide smaller error rates and complement each other to strengthen the characterisations of TD. For 180-degree TD, gyroscope signals could additionally add to magnetometry by calculating the turn angle. The turn angle would assist in detecting the start and end of the turn, whereas the detection of change in the magnetic field would indicate the middle of the turn.

The use of sensor fusion has been described in many disciplines. Li et al. [2009] investigated the incidence of falls using accelerometry and gyroscopy. The sensors were attached to the chest and thigh to measure inclinometry of the trunk and thigh gravity where the thresholds differentiated between intentional and unintentional transitions [Li et al., 2009]. In addition, wearable and ambient sensors have been used to monitor human activity [McIlwraith et al., 2010]. The sensor fused algorithm combined video frames with accelerometry and angular velocity to determine the likelihood of a posture and detect any pattern in posture [McIlwraith et al., 2010]. Although sensor fusion algorithms can be difficult to assess, the extent each sensor influences the algorithm, therefore, the development of benchmarking methods and calculating the effect of each signal has on the overall performance and algorithm, is of importance [Ligorio et al., 2016].

8.5.2. Unexpected observations

Although magnetometry signals show promise for automated TD, the magnetometry algorithm was unable to detect turns in all participants. The raw data of M086, M099, M100, and M101 of magnetometry signals located in the ankle are displayed in Figures 8.12 to 8.15, showing signals that failed to detect turns using the algorithm.

Interestingly, participants M099, M100, and M101 were all tested in the same room, with an increased likelihood of a similar layout concerning the conduction and direction of the walkway. It is possible that the local magnetic field was disrupted by interference of other anomalies in the room, and this impacted the magnetometry readings. Alternatively, the magnetometry of each axis only detects the magnetic field parallel to the signal that is travelling in that direction; therefore, if the sensor does not cross that signal, it will not detect any signal.

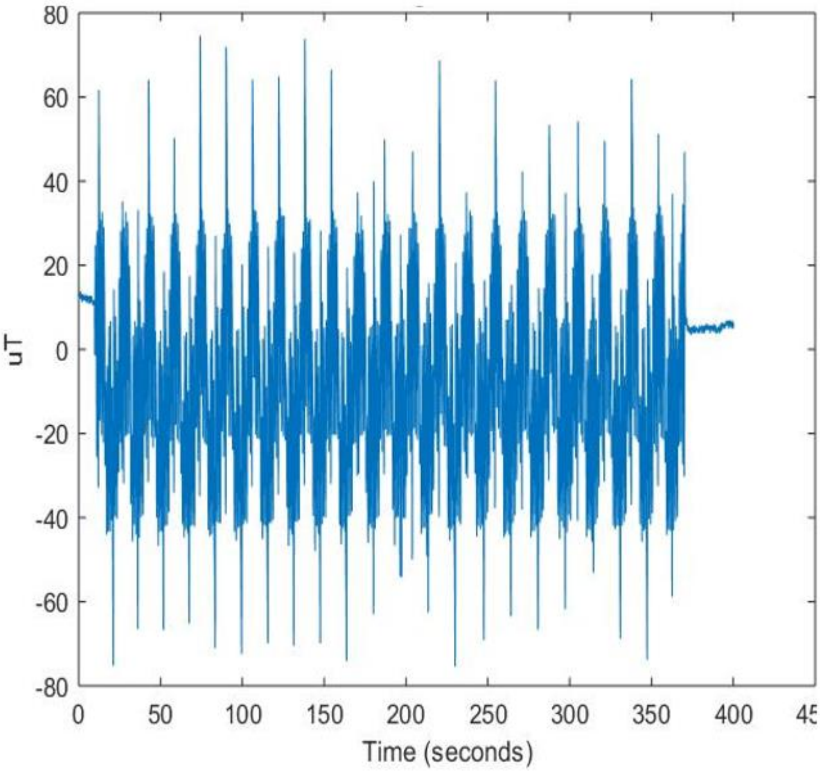

Figure 8.12A.: Representative trace of Ankle M086 Magnetometry (mediolateral axis, Y)   6MW.

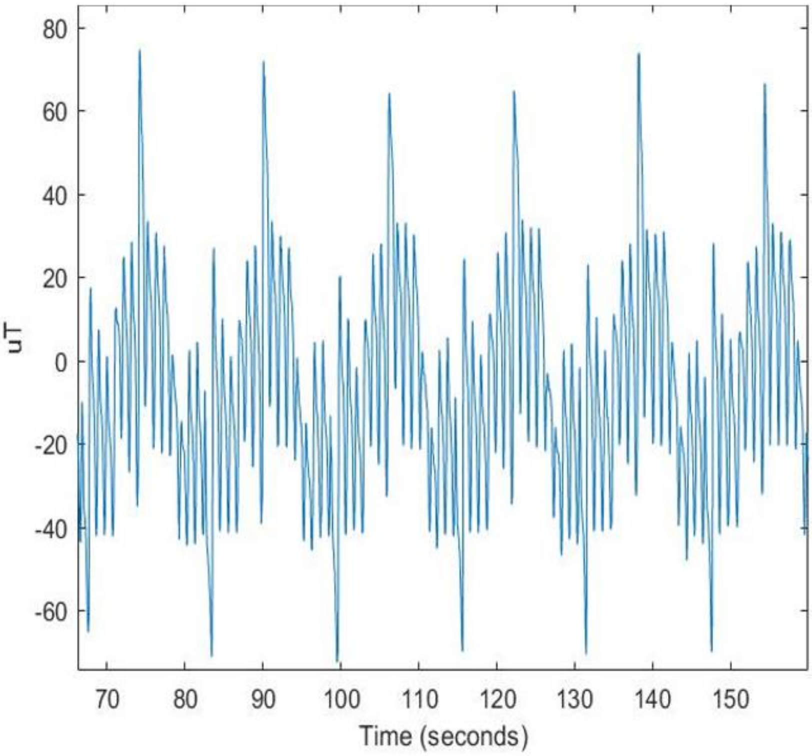

Figure 8.12B.: Representative trace of Ankle M086 magnetometry (mediolateral axis, Y) snippet of 6MW.

M099 z-axis (Figures 8.14A and 8.14B) shows imperfect square waves only in the positive axis; therefore, a magnetic field is detected, but irregularity of the signals occurred. One possibility is the ankle z-axis was perpendicular to the room's magnetic field; therefore, only part of the field that was parallel to the signal’s axis was logged. If the z-axis was facing perpendicular to the magnetic field, when the participant turns, there was a moment when the ankle turns straight into the magnetic field, but returns at or close to zero when the ankle is perpendicular to the magnetic field again.

M100 z-axis (Figures 8.13A and 8.13B) displays similar interference to M099. However, the participant was turning to face the room's magnetic fields opposite pole while turning at the end of the walkway. If the z-axis of the ankle was perpendicular to the room's magnetic field, the participant’s turn at the end of the walkway would only register the magnetic field when it was parallel. This would cause disruption and lack of turn detection.

Likewise, M086 (Figure 8.12A and 8.12B) y-axis was suspected to only be parallel to the magnetic field during turning on the walkway. There was a poor separation between the peaks and troughs of the square waves, and this was not helped by the fact the variation of walking at the end was noisy (a lot of bouncing up and down). Hence, there are no clear square waves to detect a 180-degree turn or change of turn.

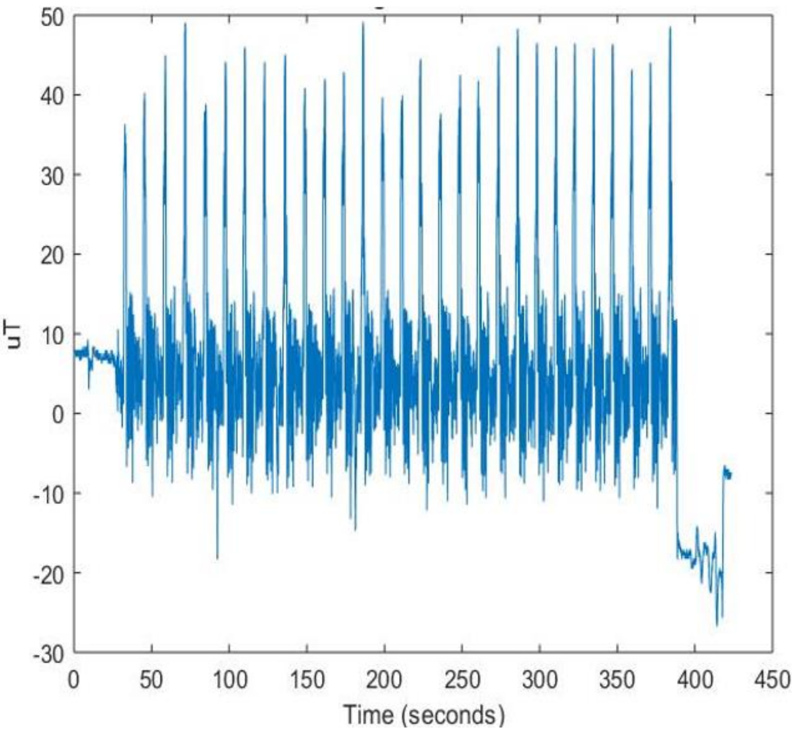

Figure 8.13A.: Representative trace of Ankle M100 magnetometry (anterior posterior axis, Z) 6MW.

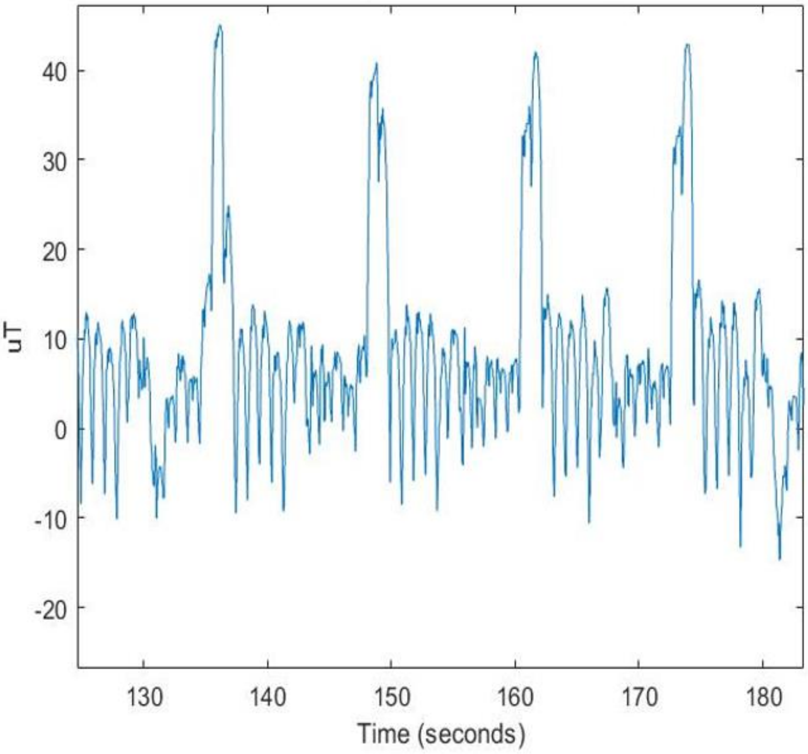

Figure 8.13B.: Representative trace of Ankle M100 magnetometry (anterior posterior axis, Z) snippet of 6MW.

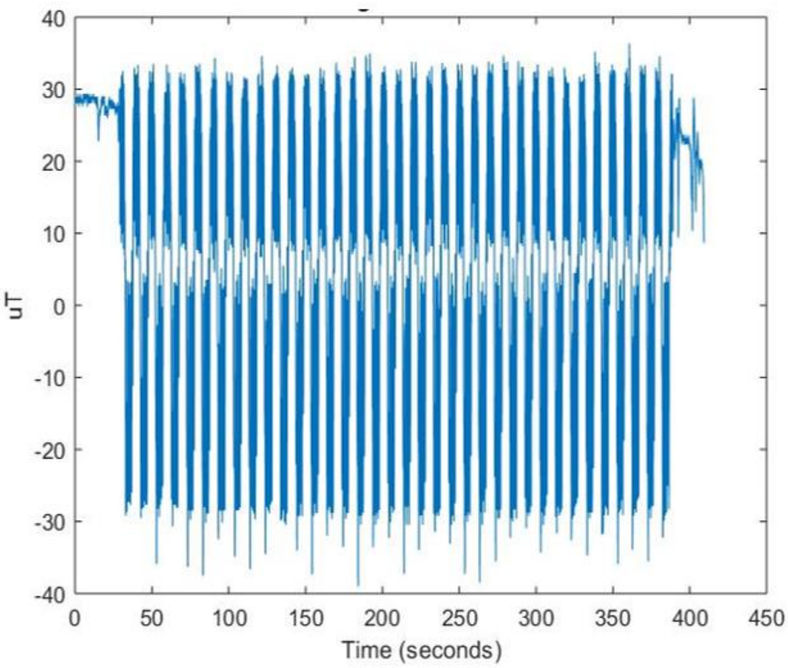

Figure 8.14A.: Representative trace of Ankle M099 magnetometry (anterior posterior axis, Z) 6MW.

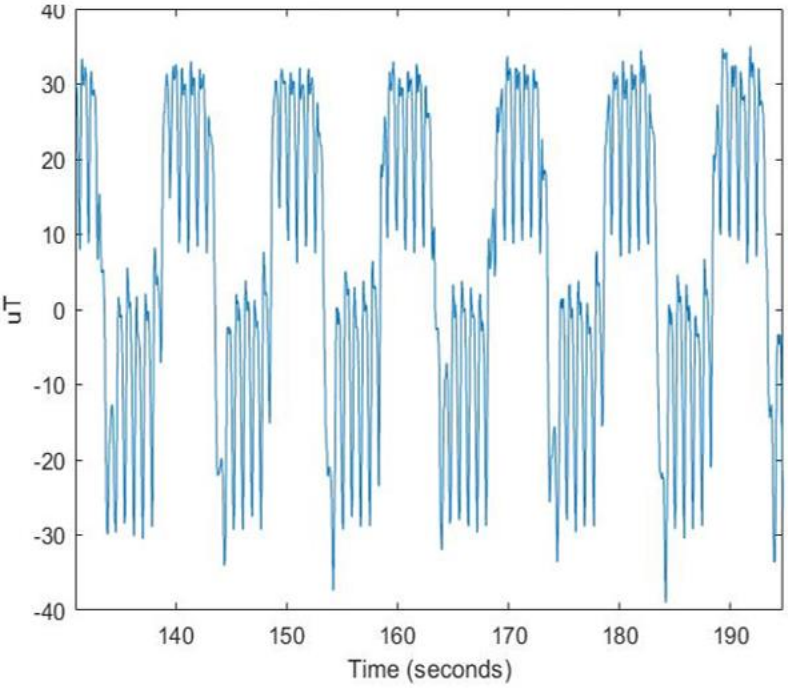

Figure 8.14B.: Representative trace of Ankle M099 magnetometry (anterior posterior axis, Z) snippet of 6MW.

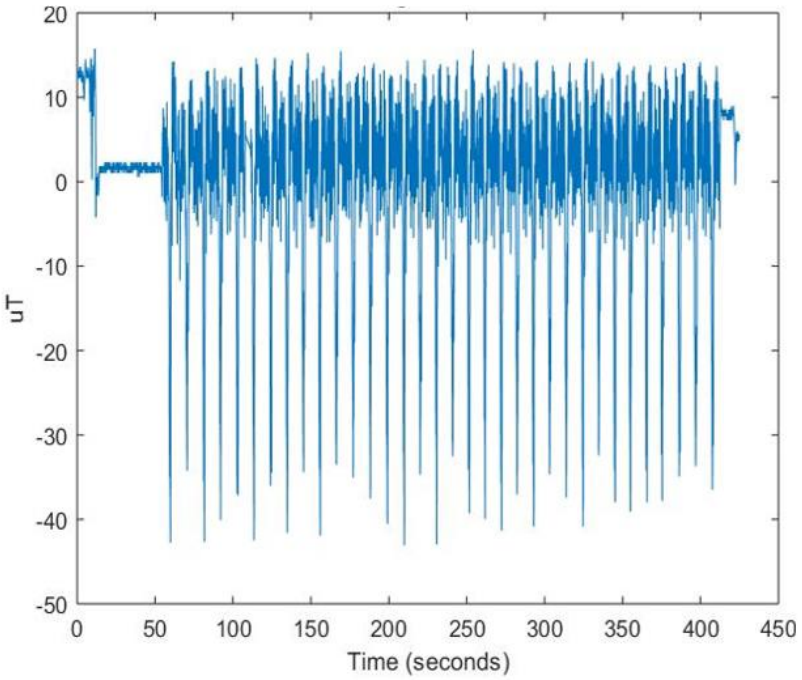

Figure 8.15A.: Representative trace of Ankle M101 magnetometry (anterior posterior axis,Z) 6MW.

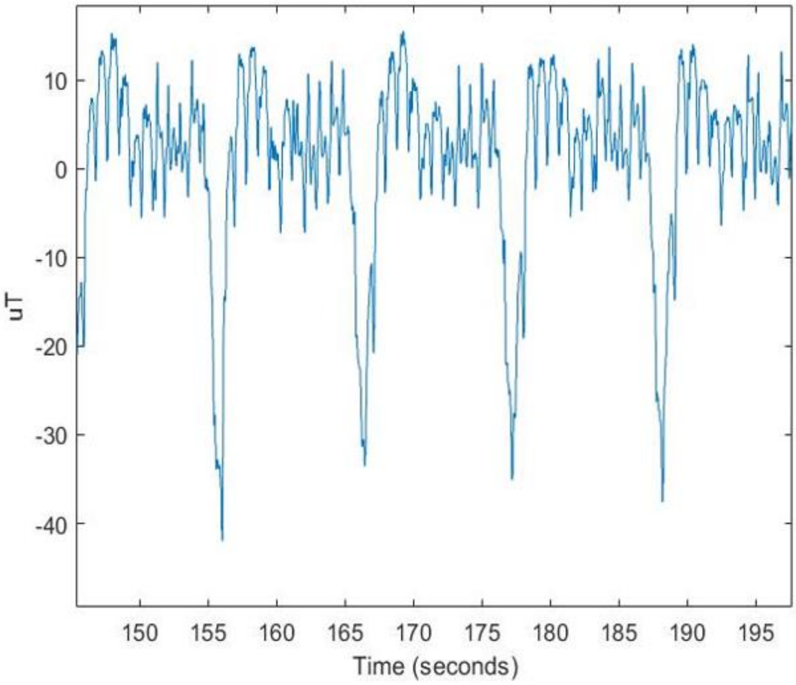

Figure 8.15B.: Representative trace of Ankle M101 Magnetometry (anterior posterior axis, Z) snippet of 6MW.

Lastly, although M101 (Figures 8.15A and 8.15B) z-axis signal had identified peaks and troughs of the square wave, there were incursions that disrupted the signal during the walkway.

One possibility is the positioning of the sensor: if the sensor was facing slightly vertical, the magnetic field could have dropped to zero with every step during the walkway (it seems similar to M086 but with more variation during the walkway).

Overall, even though TD was not 100% successful in magnetometry signal algorithm, they provide a useful tool for identifying a change of direction in wearable sensors and should be further explored to develop the detection of turns in wearable sensors. As highlighted, the limitation of magnetometry in these sensors is the exposure to nearby magnetised objects that affect and disrupt the signals. The presence of electrical devices and batteries could contribute to this interference. To mitigate these disruptions, alterations to filtering and thresholds might be useful, as might be the inclusion of pattern recognition.

8.5.3. Magnetometry turn detection methodology future suggestions

The algorithm for magnetometry TD uses two different thresholds to prevent small variations in the signals from creating false turns. These thresholds ultimately identify the forward and backward laps on an individual by windowing the samples of the data and applying an appropriate toggle to the sample at the beginning and end of the 180-degree turn. Although this accurately detects a 180-degree turn at the sternum, it creates an issue with precision and detection in the ankle. To increase this detection and allow a single central threshold for using magnetometry signals for TD, applying a filter to the raw data may help. Currently, the algorithm uses raw data to detect the changes in direction, but if a filter was applied, the imperfect square waves would smooth the signal. A smoother signal would produce cleaner graphs and identify peaks and troughs easier, which would ultimately smooth the corners of the square waves off. This filtering could then be used with a single threshold in the middle, between the modes of the square wave that could potentially detect the middle of the turn easier. Alternatively, the end of each turn (one end of a straight line on a magnetometry graph) could be used to recalculate the middle of the turn more accurately. The upper and lower signals of the square waves are used to identify the two local modes of the raw data, if the centre between these two modes could be detected, it would precisely calculate the middle of the turn.

These suggestions may assist in the accuracy of TD in magnetometry signals, although they are only considerations for future research and have not been applied to this study.

8.5.4. Additional considerations

Chapter nine establishes gait characteristics throughout the 6MW may change in pwMS due to fatigue or other neurological impairments that impact gait. Changes in gait characteristics could make the detections of turns in pwMS more difficult. The sensor signals and pattern could change through changing gait characteristics, which could affect the algorithms for TD. This could make the results inconsistent and more variable and should be considered with TD in populations of variable gaits.

In relation to the sensors, the use of gyroscope signals is advantageous in comparison to accelerometers, as gyroscopes are less likely to be influenced by gravity. Therefore, they are less likely to be influenced by sensor placement [Greene et al., 2010]. For magnetometry signals, potential magnetic interference of a sensor closer to the floor is more likely. The magnetic field is known to be nonuniform in indoor environments, typically with stronger disturbances closer to the floor [de Vries et al., 2009].

8.6. Conclusion

This research provides new insights into methods of TD with the use of three different signals and suggests magnetometry signals located at the sternum can be used for 180-degree TD in healthy and MS populations. The use of an NGIMU sensor located at the sternum has proven to be accurate for TD using El Gohary and magnetometry methods, and should be considered for future research. The El Gohary method at the sternum and ankle, as displayed by the Bland-Altman graphs, demonstrate a high correlation and almost equivalence in TD; it highlights the El Gohary method performs superiorly compared to the other methods, especially in relation to the position of the sensor. The limitations of this study are recognised, and it is suggested that future research is needed to develop magnetometry signals to be incorporated with gyroscopy signals in a variety of populations for multiple locations on the body.

The following chapter attempts to establish fatigability in gait parameters during the 6MW; grasping fatigue from an alternative perspective, physiologically, it may enable and further our understanding as fatigue as a whole.

Chapter Nine: Ambulatory motor fatigue results

As discussed in section 5.1., velocity is a versatile and reliable measure to detect fatigability changes in pwMS, however, it is unable to detect the characterisation and explain why the changes in velocity occur. Angular velocity (ω) can detect the rate of change in velocity of a certain axis, and is able to detect a change in gait characterisation. The predominant focus in this section of the research was to explore gait kinematics in ambulatory fatigue by investigating the changes in velocity and peak ω at the ankle and thigh in pwMS. Peak ω has not be used to study changes in the lower extremity for each consecutive minute of the 6MW [Crenshaw et al., 2006; Leone et al., 2015; Mcloughin et al., 2016]. Velocity and peak ω may provide a deeper understanding to the effect of fatigue on walking for future measurement and management. As mentioned in Chapter Three, gait deterioration for fatigability has been studied in relation to spatial and temporal parameters of stride time and length, step time and length, and durations of stance and swing phase and ROMs [Leone et al., 2016; Psarakis et al., 2018; Shema-Shiratzky et al., 2019; Taborri et al., 2019]. However, there are only weak to moderate findings in the attempt to search for biomarkers for motor fatigue in pwMS. Taborri et al. [2019] found consecutive ROM decrements in pwMS in the lower extremity at the ankle, knee, and hip in minutes two, three, and five of the 6MW. The authors confirmed a change in gait patterns and demonstrated pwMS continuously reduced in gait performance in comparison to healthy participants [Taborri et al., 2019]. These gait pattern changes may cause pwMS to spend double the amount of energy walking and they are more likely to reduce walking velocity through sustained, continuous walking, concerning distance covered and time to complete a task [Comber et al., 2017].

Consequently, in this research, the change in sensor-derived peak ω in pitch (in the near sagittal plane, z-axis) was investigated, and the continuous pattern whilst executing the 6MW in the thigh and ankle joints was explored. A reduction in peak ω throughout the 6MW in both the ankle and the thigh was expected. To measure the change in peak ω, the mean peak ω was calculated, then subtracted from the first minute of the 6MW to determine the deviation throughout each minute of the 6MW. Understanding the peak ω of the thigh and ankle will allow the interpretation of how the lower limb extremity performs during fatigability. The direct relationship of the ankle and thigh peak ω throughout the 6MW is yet to be established in the literature, with limited existing research on measurements specifically at the thigh. Hence, the rate of change in pitch (z-axis, for laterally mounted sensors) during peak swing phase throughout 6MW might provide a useful biomarker for gait fatigability. The dominant and weak leg identified in this research were described by participants themselves.

There were variable results with inconsistencies in the dataset, similar to previous observations by Oberndorfer et al. [2015], presented at European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS). Although Oberndorfer et al. [2015] found indications of ambulatory fatigue in increasing stride time and decreasing cadence in some pwMS, the results were not universal and variable between participants. In the rest of this chapter, it is concluded that the 6MW with the use of wearable sensors does not consistently (in all participants) elicit measurable ambulatory fatigue in pwMS. Although the results of this research generally agree with those in the study by Oberndorfer et al. [2015], the 6MW did influence some pwMS and their gait, but not universally. One possible explanation for the inconsistent results is confounding factors, such as the level of disability and ambulatory ability, because pwMS who have a mild disability are more likely to be unaffected by the 6MW. This experimental limitation may be relevant for both analysis and the design of future research. One reason in attempt to quantify ambulatory fatigue was the hope to provide clarify on how to measure fatigue, as “subjective” fatigue may not provide an accurate measure for fatigue as a whole. Unfortunately, we were unable to quantify ambulatory fatigue in this chapter. Following this, in chapter ten (section 10.1), the “gold standard” of subjective measurement (MFIS), fatigability and sensor fatigability measures were explored in order to examine any correlation between the different measures. This was conducted before the further exploration of phenomenological and physiological reflections. Unfortunately, little correlation was found between “subjective” and “objective measures in section 10.1., however the recruitment inclusion criterion was only measured by disability (EDSS-S 1-5.5), not specifically fatigue. PwMS in this study did state they experience fatigue, however, there was no established measure for the recruitment process. Nevertheless, chapter ten further discusses this, and begins to draw on the continuum of fatigue.

9.1. Participant demographics

The two test groups were older pwMS and older healthy controls. PwMS were recruited from a local MS charity centre (MS Sussex Centre) and a local MS society (Eastbourne MS Society). Older healthy individuals were recruited from the University of Brighton and the local U3A (Eastbourne). The baseline measurements are displayed in Table 9.1. Group values are reported as mean ± standard deviation with a Mann-Whitney U test used to compare between groups and a Wilcoxon signed-rank test to compare paired data within the MS group. A Kruskal-Wallis test was used to compare minutes of the 6MW in both populations. Age, height, and weight were not significantly different between groups. An EDSS-S average score of 5.13 indicated some degree of self-reported mobility impairment and disability.

Table 9.1.: Participant demographics

	PwMS	**Healthy controls**	
Participants (n)	12	11	
Gender (M/F)	5/7	4/7	
Disease type (RRMS/PPMS/SPMS)	8/3/1	-	
	Mean ± SD	**Mean ± SD**	**P-value**
Age (years) (range)	63 ± 7.59 (49-77)	57 ± 10.1 (45-78)	0.109
Height (cm)	171.5 ± 11.24	166.31 ± 9.53	0.254
Weight (kg)	69.91 ± 15.50	69.96 ± 10.28	0.878
EDSS-S (points)	5.13 ± 0.61	-	

9.2. Exploration of gait deterioration

The slope patterns shown in Figures 9.1, 9.2 and 9.3 demonstrate selective sensor measurements of the peak swing values at region of interest (ROI)s in the dominant thigh of three pwMS and one healthy participant throughout the 6MW. Each triangle in the graphs below represent one step, where, the peak swing value is the maximum thigh rotation of a participant's gait in one gait cycle. The slow drift toward zero represents what one would expect if fatigability was causing a decrease in the thigh's physical movement during the swing stage of the stride. Normally, due to the positioning of the sensors, values are positive on the right thigh and negative on the left thigh; however, right thigh values were multiplied by negative one for a clearer comparison of swing values. These patterns were not universal, but indicate participants with MS (not all) slowed down their gait as the task continued (especially towards the end).

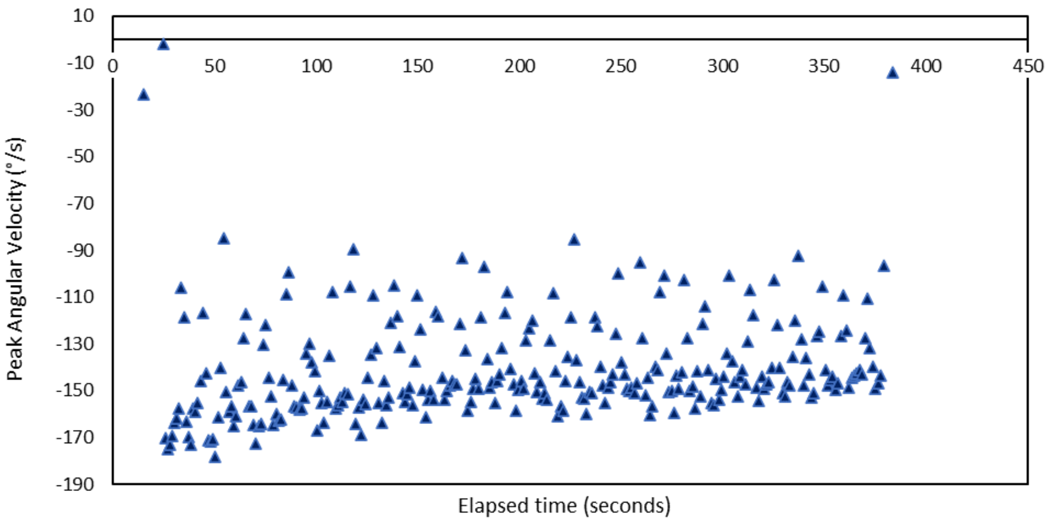

Figure 9.1.: Selective trace of M097 (MS) peak swing values of ROIs thigh dominant (left) during the 6MW. The values at t = 20, 25, and 380 seconds are missed turns, confirmed by video observation.

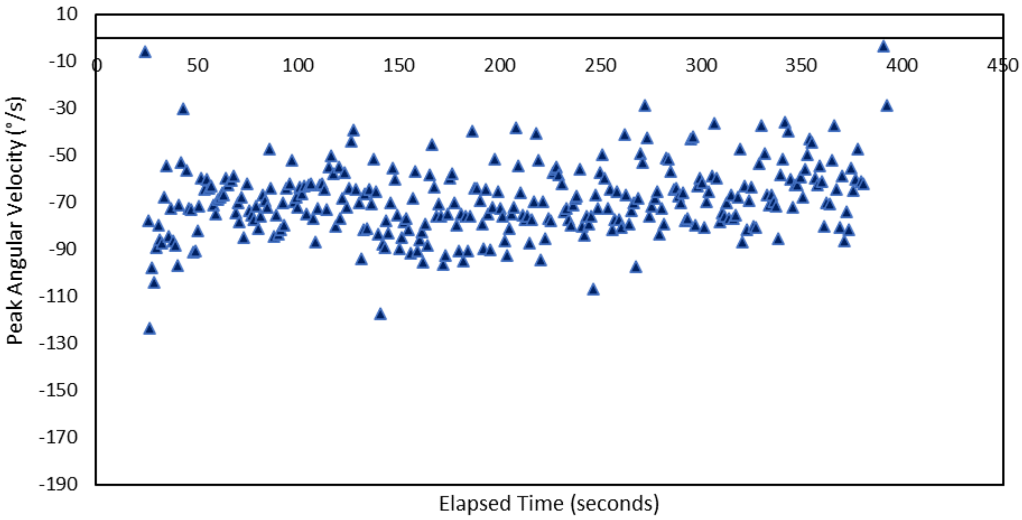

Figure 9.2.: Selective trace of M092 (MS) peak swing values of ROIs thigh dominant (right) during the 6MW. The values at t=25 and 390 are missed turns, confirmed by video observation. The values for the right thigh were multiplied by negative one for the ROIs.

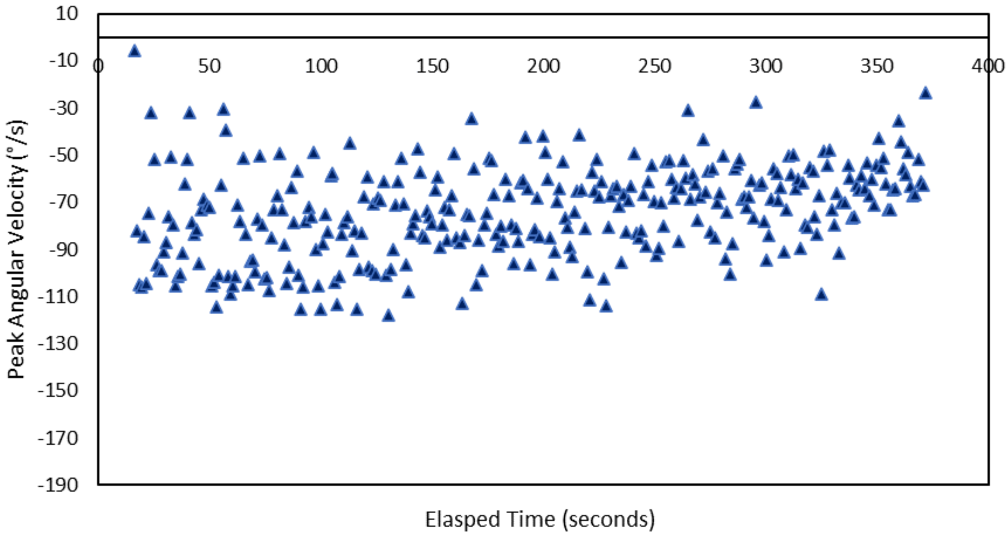

Figure 9.3.: Selective trace of M096 (MS) peak swing values of ROIs thigh dominant (right) during the 6MW. The value at t= 20 is a missed turn, confirmed by video observation. The values for the right thigh were multiplied by negative one for the ROIs.

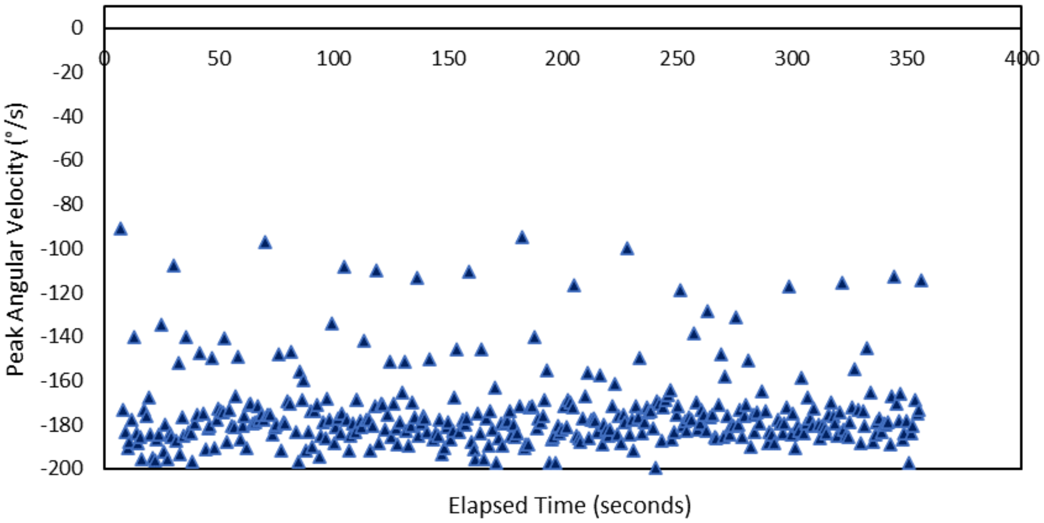

Figure 9.4.: Selective trace of M085 (healthy) peak swing values at ROIs of left thigh during the 6MW.

The MS participants shown here had EDSS-S walking scores ranging from 4.5 to 5.5, suggesting a degree of ambulatory impairment. To compare, a selective trace of an older healthy participant (M085) peak swing values at ROIs in the left thigh is shown in Figure 9.4. The values show no distinct decrease or reduction throughout the 6MW.

To explore the peak swing values further, the pitch peak ω (gyroscope Z) is used to calculate the rate of change in ω in flexion and extension during the swing phase over the duration of 6MW that might provide a useful biomarker for gait fatigability.

9.3. Gait kinematics of the thigh and ankle in pwMS

9.3.1. Peak angular velocity in pwMS

The ω represents the rate of angular velocity at which an object rotates around a specific point or axis in a given time period. When mounted on the lower extremity, ω reflects the speed of rapid displacement during swing, and on the thigh inverted values of ω reflect the reverse rotation during stance. Here, it is used to specifically investigate the peak swing value of the ω of each gait cycle and the rate of change in the ankle and thigh throughout the 6MW.

Figure 9.5 is a representative trace of raw gyroscope Z (pitch) data on a T25FW before the 6MW. It shows the peak ω of both an MS and a healthy participant, detecting the maximum value of ω during the T25FW.

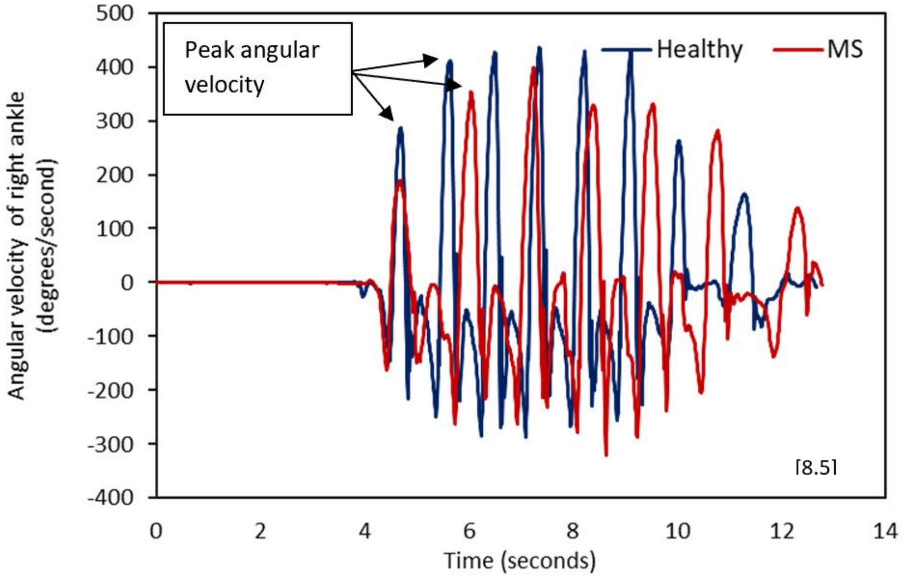

Figure 9.5.: Representative trace of raw gyroscope Z (pitch) data T25FW (pre-6MW) of a healthy (M085) and MS (M084) participant. The red trace shows an MS participant, the blue line a healthy participant. The peak angular velocity is indicated with arrows.

Monitoring gait during the 6MW provides an opportunity to investigate changes that occur through sustained, continuous walking. In previous studies, each one-minute segment has been used to detect the change in performance during the 6MW [Burschka et al., 2012; Goldman et al., 2008]; therefore, peak ω measures of each minute throughout the 6MW may potentially provide new insight into gait fatigability parameters. Due to the conflicting results in this research, in the following section, the range and variable data within peak ω measures is illustrated. Walking velocity and patient-reported outcome measures are then discussed.

9.3.2. Variable peak angular velocity results in pwMS

In this research, the change in peak ω throughout the execution of 6MW was investigated, and a reduction and decrease in peak ω was expected. The changes in the ankle were expected to reduce before the thigh in peak ω values (Taborri et al. [2019] observed ROM decrement in the second minute in the ankle, but only the last minute in the hip). As mentioned previously, some researchers believe the 2MW is sufficient for clinical measurement of fatigue in pwMS; however, based on repeated observation of 6MW trials, gait deterioration can appear beyond two minutes, and is associated, to a degree, with subjectively reported walking difficulty [Engelhard et al., 2016]. Due to this, it is expected that minute one to three could represent a diminution in psychological motivation. Of the MS participants, 54.5% had significant reductions in peak ω from minute one to three in their weak ankle, but only 9.1% exhibited continuous, consecutive decrements after minute three. The dominant ankle only showed a significant reduction from minutes one to three in 18.2% of MS participants, with no continuous decrease in peak ω in any participants for the rest of the task. In Figure 9.6, an MS participant's peak ω in the weak ankle is shown, with decrease during the entire execution of the 6MW; this is the fatigability pattern we sought but only rarely found in our participants.

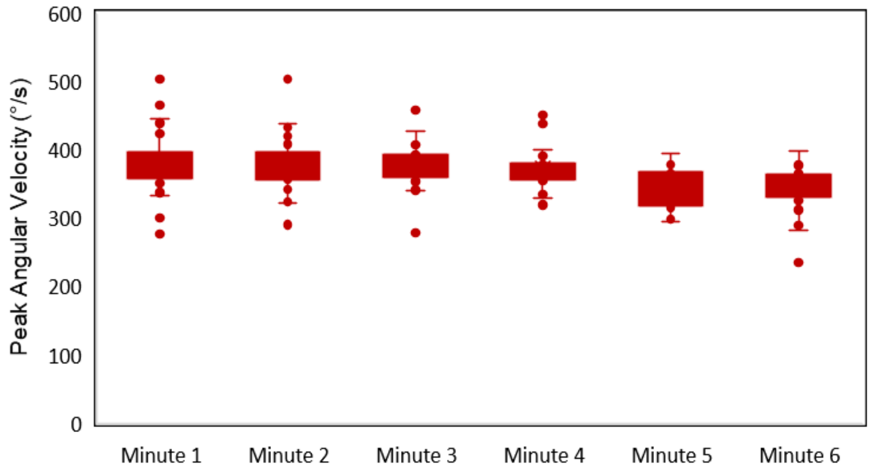

*Figure 9.6.: Representative participant (MS) M092 "weak" **ankle** pitch peak angular velocity during the 6MW. Minimum, first quartile, median, third quartil ınd maximum values for peak angular velocity values from minute 1 to minute 6. The red dots outside of the box plot and range bar indicate outliers.*

For the thigh, 27.3% of MS participants significantly and consistently reduced in peak ω in the weak thigh from minute one to three in the 6MW, yet no participants consistently and continuously reduced after minute three of the 6MW. A significant decrease from minutes one to three was also observed in the dominant thigh of 27.3% of peak ω with no MS participants significantly decreasing after minute three. Although not significant, 18.2% of MS participants did gradually decrease in peak ω from minutes two to the end of the walking task. In Figure 9.7, an MS participant's peak ω in weak thigh reduction (not significantly) throughout the 6MW task is shown.

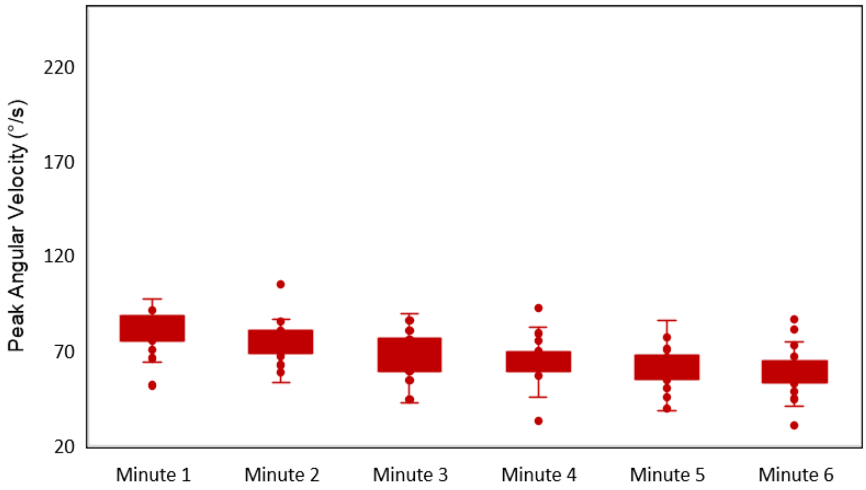

Figure 9.7.: Representative participant (MS) M097 "weak" ***thigh*** *pitch peak angular velocity during the 6MW. Minimum, first quartile, median, third quartile and maximum values for peak angular velocity values from minute 1 to minute 6. The red dots outside of the box plot and range bar indicate outliers.*

However, as indicated, not all MS participants demonstrated a decrement in peak ω during the 6MW. In Figure 9.8, a gradual but continuous increase in peak ω is shown from minute one to five, with only a decrease in the last minute of the walking task in the "weak" thigh. In Figure 9.9, the first two minutes of walking is illustrated, showing a decrease in peak ω, followed by an increase in peak ω from minutes four to six. A wide range of peak ω values in both plots are observed, but more outliers in M089 weak thigh are identified. Both representative graphs highlight the variation of peak ω in MS participants throughout each minute of the 6MW.

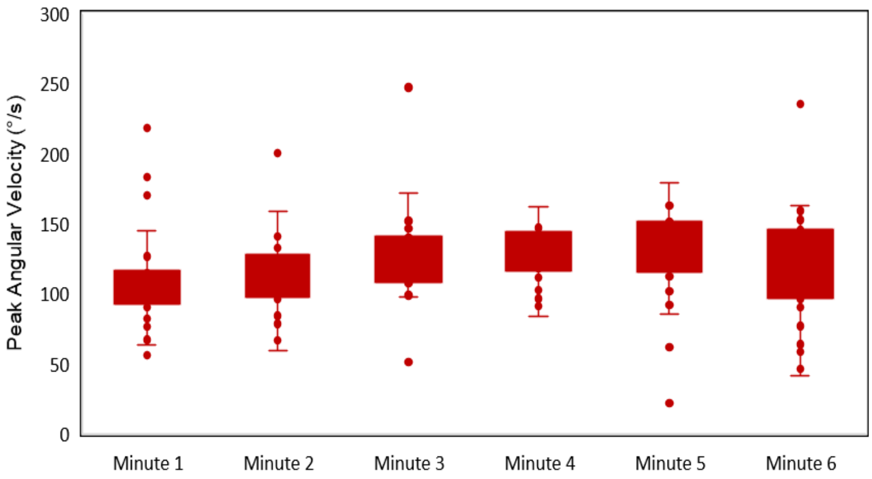

Figure 9.8.: Representative participant (MS) M089 "weak" ***thigh*** *pitch peak angular velocity during the 6MW. Minimum, first quartile, median, third quartile and maximum values for peak angular velocity values from minute 1 to minute 6. The red dots outside of the box plot and range bar indicate outliers.*

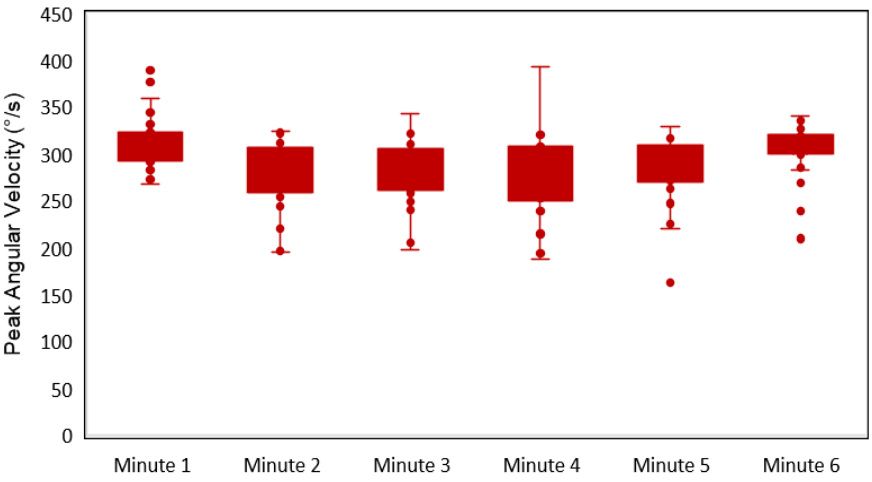

Figure 9.9.: Representative participant (MS) M104 "weak" ***ankle*** *pitch peak angular velocity during the 6MW. Minimum, first quartile, median, third quartile and maximum values for peak angular velocity values from minute 1 to minute 6. The red dots outside of the box plot and range bar indicate outliers.*

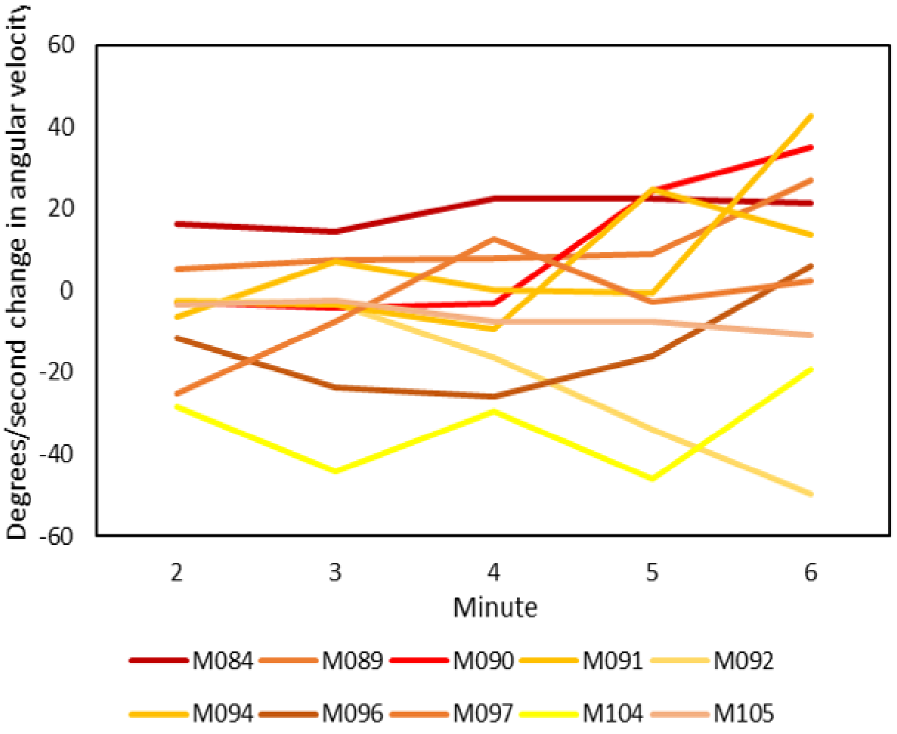

Figure 9.10.: Peak angular velocity change (from baseline during minute one) of MS participants in dominant ankle for each consecutive minute compared to the first minute of the 6MW.

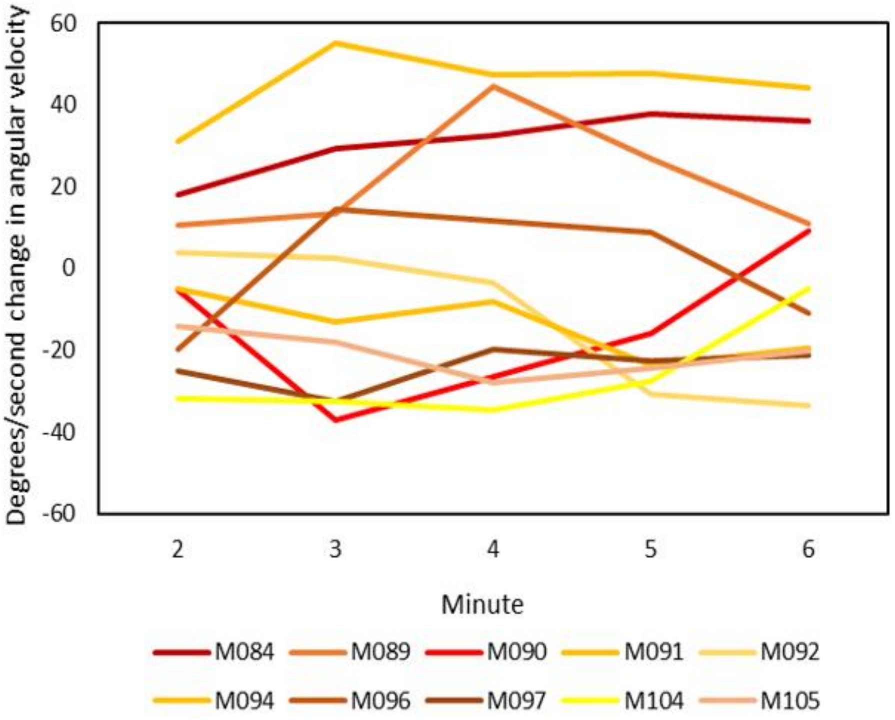

Figure 9.11.: Peak angular velocity change of MS participants in weak ankle for each consecutive minute compared to the first minute of the 6MW.

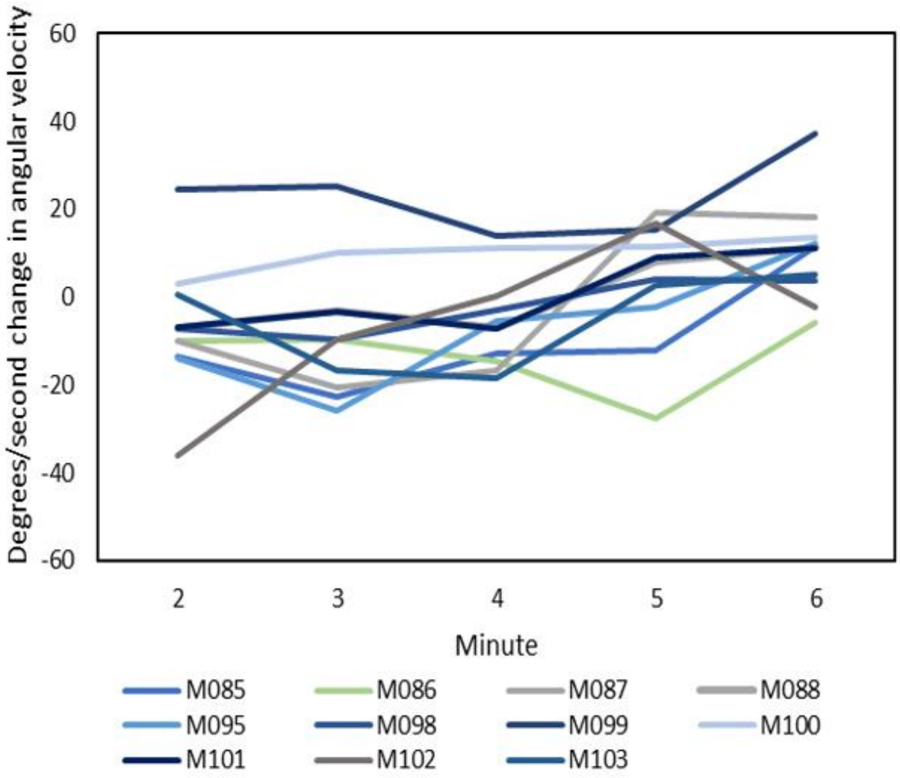

Figure 9.12.: Peak angular velocity change of healthy participants in the right ankle for each consecutive minute compared to the first minute of the 6MW.

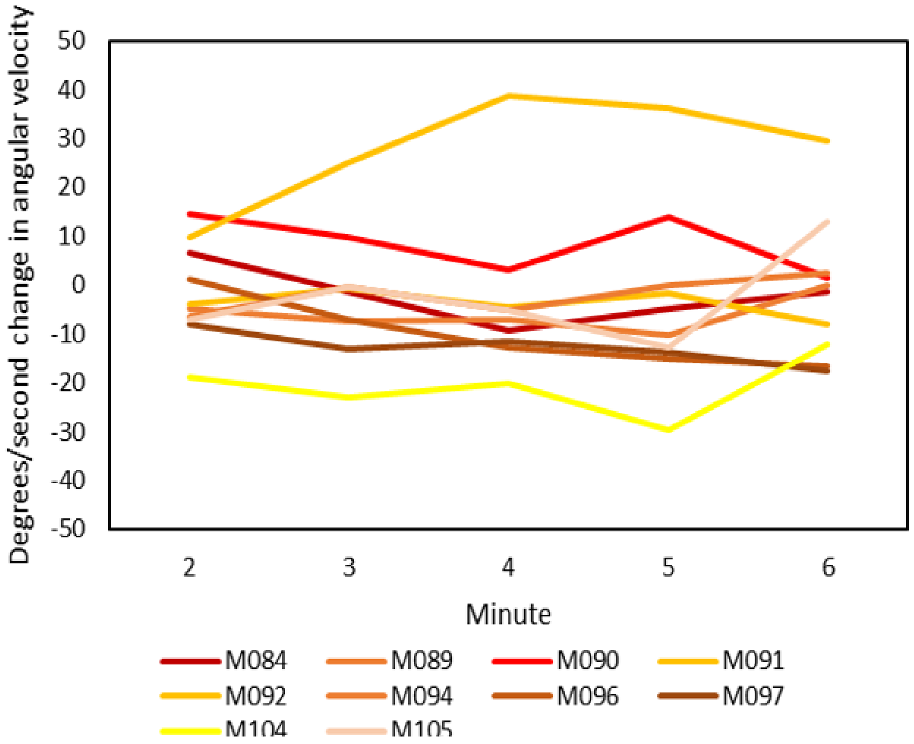

Figure 9.13.: Peak angular velocity change of MS participants in dominant thigh for each consecutive minute compared to the first minute of the 6MW.

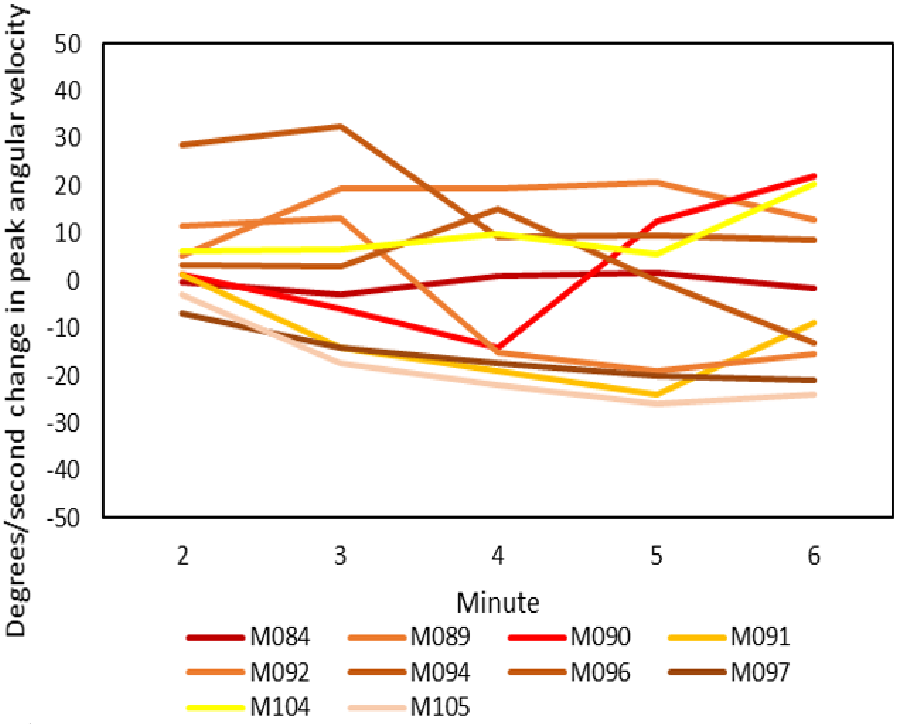

Figure 9.14.: Peak angular velocity change of MS participants in weak thigh for each consecutive minute compared to the first minute of the 6MW.

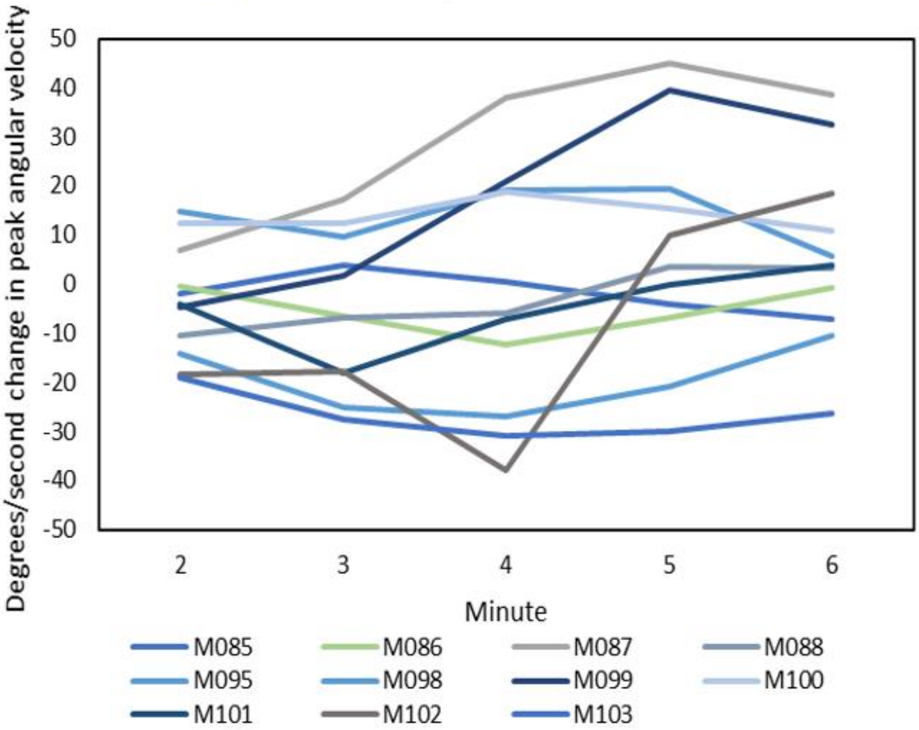

Figure 9.15.: Peak angular velocity of healthy participants in the right thigh for each consecutive minute compared to the first minute of the 6MW.

Although inconsistent, the results indicated a larger proportion of MS participants significantly decreased in peak ω at the ankle from minute one to minute three (54.5%) in comparison to the thigh (27.3%), suggesting the ankle peak ω is more likely to decrease before the thigh in pwMS. In Figures 9.10 to 9.15, minute-by-minute changes of mean peak ω in both the ankle and thigh is shown for both populations, by identifying the degrees per second change in angular velocity for each consecutive minute compared to the first minute of the 6MW. This illustrates the deviation of each minute in comparison to minute one in each participant.

The line graphs show no consistent change in peak ω in relation to an increase or decrease in a pattern of velocity throughout the execution of the 6MW. Figures 9.10 and 9.11 illustrate that in only two MS participants were there decreases in the change of degrees per second of mean peak ω at minutes three to six in the dominant and weak ankle compared to minute one. Similarly, two MS participants increased in the change of mean peak ω at minutes three to six, with one participant increasing from minute four to six in the dominant ankle. Four MS participants demonstrated a sharp increase in the dominant ankle in the mean peak ω in the last minute in comparison to minute one. However, this could have been from end of task effect where psychological motivation and pattern strategy could have been affected [Leone et al., 2016]. Figure 9.12 illustrates the healthy participant group in the right ankle, where five participants increased in mean peak angular velocity from minute three to six. No healthy participants continuously decreased in mean peak ω, but one participant did decrease from minute one to five, then increased in the last minute.

In MS participants, the dominant thigh only decreased in mean peak ω in one participant from minute three to six, with another participant decreasing from minute four to six. However, five participants did decrease in the last minute of the 6MW in mean peak ω with only two participants increasing in the last minute. MS participants’ weak thigh reduced in mean peak angular velocity from minute two to six in two participants compared to minute one. One participant did decrease continuously from minute two to five until an increase in the fifth minute. Three participants decreased in the last minute of the 6MW in mean peak ω, whereas three participants similarly increased in the last minute. To compare, four healthy participants in the right thigh increased in minutes two to five in mean peak ω, but one participant did decrease from minute three to six. Interestingly, six MS participants did decrease in mean peak ω from minute two to three in the dominant thigh, with five decreasing in the weak thigh. Other changes fluctuated in value and no consistent pattern in all mean peak ω line graphs was observed. The range of mean peak ω values were wider in MS participants compared to healthy participants in the ankle, but were narrower in the thigh in comparison to healthy participants. The data indicates that there were variable results in the pattern of peak ω throughout the 6MW and that the changes in peak ω were inconsistent.

9.4. Overall ambulatory results

Overall, in healthy controls when comparing their walking using the T25FW task before ("pre") and after ("post") the 6MW, stopwatch measurements reduced in time (from 4.22 ± 0.63 to 4.19 ± 0.75 seconds), thus, their walking speeds increased after the nominally fatiguing task of the 6MW. By contrast, MS participants after the nominally fatiguing 6MW increased in duration and reduced in velocity (from 5.77 ± 1.39 to 5.83 ± 1.69); in this sense, pwMS did seem to exhibit some modest fatigability on average. Notably, not all MS participants increased in duration in the T25FW, with some reducing in duration (see Figure 9.17). As expected, due to their disability pwMS were significantly slower than healthy controls in both T25FW-pre ($p < 0.001$) and T25FW-post ($p < 0.01$). Also consistent with the disability of pwMS, on average, MS participants walked a shorter distance during the 6MW, suggesting a slower velocity compared to healthy controls (975.9 ± 184.74 and 1474.77 ± 238.98 respectively; $p < 0.01$; see Figure 9.18). There was no significant difference within the MS group in the T25FW pre- or post- 6MW ($p = 0.831$), or distance covered from minute one and minute six of the 6MW ($p = 0.242$). In patient-reported outcomes measures (MSWS-12 and MFIS) significantly more subjective fatigue was reported in MS participants compared to healthy controls in all sub-scores and measures (see Table 9.2.).

*Table 9.2.: Results and gait kinematics of the ankle and thigh in MS participants and older healthy participants. Both the dominant and weak leg were compared to the healthy group, *indicates p < 0.05.*

Patient-reported outcome measures	**PwMS (mean ± SD)**	**Healthy (mean ± SD)**	**p-value**
MSWS-12 (points)	36.92 ± 5.19	14.18 ± 5.78	< 0.001*
MFIS total (points)	42.42 ± 19.29	12 ± 11.72	0.001*
MFIS physical (points)	19.25 ± 9.96	6 ± 6.26	0.003*
MFIS cognitive (points)	19.83 ± 7.69	4.82 ± 6.21	0.0004*
MFIS psychosocial (points)	3.33 ± 2.27	1.12 ± 1.72	0.018*
Stopwatch measurements			
T25FW-pre (seconds)	5.77 ± 1.39	4.22 ± 0.63	<0.001*
T25FW-post (seconds)	5.83 ± 1.69	4.19 ± 0.75	<0.001*

6MW (feet)	975.9 ± 184.74	1474.77 ± 238.98	<0.001*
	Pre/Minute 1	**Post/Minute 6**	
Average pwMS T25FW-pre vs. -post (seconds)	5.77 ± 1.47	5.85 ± 1.77	0.831
Average pwMS 6MW minute 1 vs. minute 6, distance covered (feet)	170.45 ± 35.25	166.36 ± 37.15	0.242
	PwMS (mean ± SD)	**PwMS (mean ± SD)**	**Healthy (mean ± SD)**
6MW	**Dominant leg**	**Weak leg**	**(average of both legs)**
Ankle total maximum peak angular velocity (degrees/second)	350.37 ± 85.72*	359.87 ± 93.91*	447.17 ± 63.88
Thigh total maximum peak velocity (degrees/second)	145.53 ± 54.09*	121.43 ± 57.44*	194.64 ± 72.68

Overall, pitch gyroscope signals calculated a reduced peak ω in MS participants in both the dominant (350.37 ± 85.72 degrees per second) and weak leg (359.87 ± 93.91 degrees per second) in comparison to healthy controls at the ankle (447.17 ± 63.88 degrees per second; $p < 0.01$). Similarly, the total peak ω at the thigh was lower in the 6MW compared to the healthy group (194.64 ± 72.68) in both the dominant (145.5 3 ±54.09) and weak thigh (121.43 ± 57.44; $p < 0.01$). However, as shown throughout each minute of the 6MW in peak ω, gait deterioration and fatigability were not clearly demonstrated or consistently elicited objective measurable fatigue.

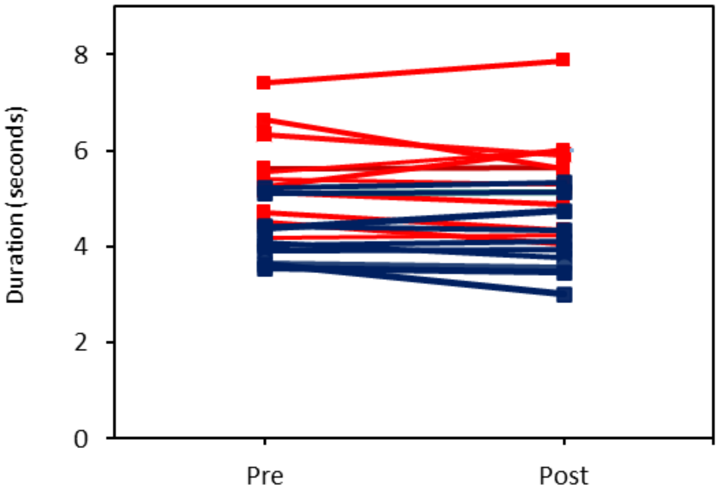

Figure 9.16.: Healthy control (blue) vs. MS participant (red) T25FW pre- & post-6MW.

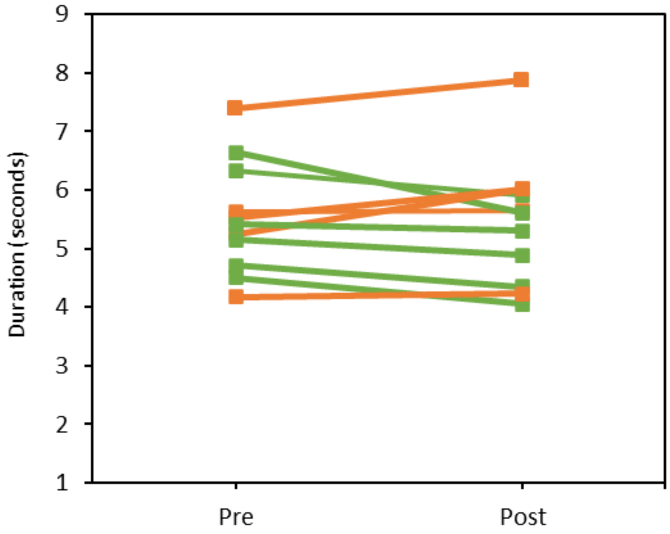

Figure 9.17.: MS participants T25FW pre- & post-6MW. Green indicates a decrease in duration, orange indicates an increase in duration.

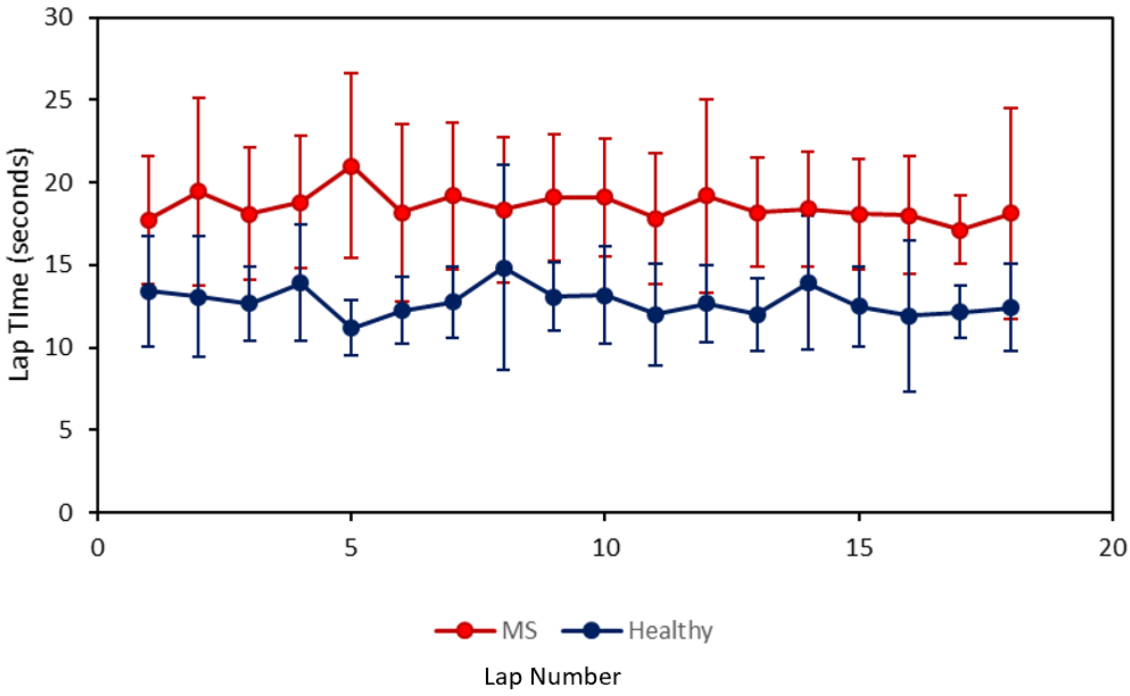

Figure 9.18.: 6MW duration healthy control vs. MS participant.

Overall, there was no distinct and significant difference in how MS participants' pitch peak ω responded to fatigue within the 6MW. Additionally, there was no significant difference in walking velocity of repeated baseline T25FW measurements and distance covered from minute one to minute six. In relation to the deviation of mean peak ω from minute one, the most noticeable change was the decrease in mean peak ω from minute two to three in the dominant thigh in MS participants. However, universally there was no congruous pattern in mean peak ω in the ankle and thigh in MS participants, which the line graphs demonstrate.

The lack of detection and change in these measurements and peak ω in the thigh and ankle could have been for several reasons. Firstly, the hypothesis could have been incorrect, and fatigue does not impact and weaken the lower extremity or lead to objective changes in gait fatigability. However, the likelihood of this is low as established by previous studies with a reduction in walking velocity, spatial and temporal parameters, and ROM decrements in the lower extremity [Leone et al., 2016; Shema-Shiratzky et al., 2019; Taborri et al., 2019]. Leone et al. [2016] found changes and a decrease in the distance walked throughout the 6MW, demonstrating that more than one third of pwMS displayed walking-related motor fatigue. Taborri et al. [2019] observed significant effects of walking-related motor fatigue by the continuous decrease in ROM in the ankle, hip, and thigh. Lastly, Shema-Shiratzky et al. [2019] found a variety of gait parameters to demonstrate gait deterioration through sustained, continuous walking. The changes in gait performance and velocity of the lower extremity are prevalent in previous studies, therefore the likelihood of pitch ω to not be impacted in the lower extremity from continuous sustained walking from fatigue seems unlikely.

Alternatively, the wrong experiment could have been conducted in relation to the variability of results. The 6MW was performed to elicit ambulatory fatigue, as in previous studies researchers have successfully used the assessment for performance ambulatory fatigue in pwMS [Engelhard et al., 2016; Leone et al., 2016; Qureshi et al., 2016; Shema-Shiratzky et al., 2019; Taborri et al., 2019]. There is a possibility that the 6MW did not exacerbate walking-related fatigue and was therefore insufficient to cause fatigability. However, in this study the 6MW did influence a very small number of pwMS in relation to walking velocity pre- and post-6MW and dominant thigh peak ω within minutes two to three, and the last minute of the 6MW, although not significantly or universally.

It is likely that level of disability affects the level of fatigue. Mildly disabled pwMS are less likely to be affected by the 6MW as their ambulatory ability is more likely to be less impaired. Shema-Shiratzky et al. [2019] found gait performance in lower cadence, step regularity, stride regularity, and poorer stride time variability to only be significant for moderately disabled individuals and suggested the effect of gait is dependent on the degree of disability. The authors found that pwMS with a moderate disability also report having a worsened walking ability and a higher burden of physical and psychosocial fatigue [Shema-Shiratzky et al., 2019]. Additionally, in their 2018 pilot study, van der Linden et al. found that moderately disabled pwMS had a significantly reduced cadence between their first and last 10 gait cycles during the 6MW. Moderately disabled pwMS therefore might be more affected by the 6MW and show fatigability more significantly than mildly disabled pwMS. Even though in previous studies researchers have elicited fatigue through the execution of the 6MW, an even longer walking assessment may demonstrate walking-related fatigability in mildly disabled pwMS.

Shahrbanian et al. [2018] found MS-related disability and fatigue to be the main predictor for pain presence. It was suggested that the common aetiology of CNS and nerve fibre damage could be associated with the impact of disability, pain, and fatigue levels [Lublin & Reingold, 1996; Shahrbanian et al., 2018]. Hence, the more severe the disability in pwMS, the higher the fatigability. On the contrary, fatigability may only affect moderately disabled individuals, with only fatigue impacting those mildly disabled. However, this has not been established in the literature and leads to fundamental questions about fatigue that remain unanswered. The lack of definition and terminology can constrain the progress and development of interventions, but this will be discussed in Chapter Ten.

Lastly, the sample size was small. It is possible that not enough participants were tested in order to detect an effect. This can limit the interpretation of results as it more commonly leads to higher variability, which ultimately affects the reliability and can cause bias. In this study, the average level of disability was an EDSS-S score of 5.13. In line with Bowen et al. [2008], the EDSS-S can be interpreted as a whole point higher than the physician-administered EDSS. Following this guidance, the average level of disability drops to the mildly disabled category in most studies. PwMS at this level are typically able to walk without any aid and are self-sufficient. It could be argued that this skews the results in this study and fatigue and fatigability in moderately disabled individuals was not explored. Additionally, this degree of disability could be another reason why significant fatigability was not found in this cohort of pwMS.

Interestingly, although overall the results conflicted, parameters of the thigh in this study demonstrated a degree of gait deterioration in the last minute of the 6MW in mean peak ω values in comparison to the first minute in MS participants. In the majority of previous studies, researchers have predominantly focused on parameters of the ankle, due to the significance of foot and ankle issues in relation to muscular, neurological, and mechanical dysfunction in pwMS [Rusu et al., 2014]. However, observations of the thigh are less common, but may provide useful due to the importance of mechanical movement during a gait cycle and the knee/thigh experiencing two phases of flexion and extension in each gait cycle [Perry, 1992].

To conclude, most participants in this study did not experience fatigue through ambulatory measurements. The degree of disability, the type of gait parameters, or sample size could have impacted and contributed to the variable results. It is suggested that the degree of disability is contributes to the change in gait fatigability. However, future research should investigate this in relation to different levels of disability, the duration of walking, and the assessment of peak ω through each minute. If mild and moderately disabled pwMS were categorised effectively, a composite of velocity and ω measurements could indicate whether the association between disability and fatigability occurs. Clarification of such could help shape future interventions for fatigue within MS and assist in the recognition and understanding of fatigability. Furthermore, distinct biomarkers of fatigability could be investigated through parameters of the thigh that could provide and help stratify heterogenous MS fatigue groups that could assist clinical practice in the monitoring of effects of intervention and prognosis.

Subsequently, the next chapter attempts to discuss and explore both phenomenological and physiological analyses in this study. It explores the phenomenon in hope to find a richer and fuller meaning of fatigue. It draws upon each dataset and attempt to navigate the understanding of fatigue.

Chapter Ten: Integrating ambulatory results and phenomenological findings

Naturalised phenomenology is a novice methodology, proponents of which attempt to encompass first- and third-person accounts to develop and improve our understanding of human science and experience [Gallagher, 2015; Reinerman-Jones et al., 2013; Varela et al., 1991]. The aim and basis of naturalised phenomenology offers a potentially insightful opportunity to 'try out' this methodological approach within the present research that was timely. It seemed appropriate to approach MS fatigue more deeply, as MS-related fatigue is often a symptom that is addressed as either subjective and/or objective phenomenon. From a positivist, reductionist perspective, MS fatigue has a subjective cast that invites a more objective description, so a mixed methods approach provides an opportunity for hypothesis generation [Glaser, 1965] and following a thread [O'Cathain et al., 2010]. Nevertheless, concerns about the principles and the challenges of implementing naturalised phenomenological studies remain.

The notion of embodiment interpreted by Merleau-Ponty and followed specifically by Varela et al. [2016] has been attempted by Gallagher [2006], ‘‘In regard to embodiment, I want to explore to what extent and in what way an awareness of my body enters into the content of my conscious experience? ... Does intentional action, for example, involve an explicit or implicit awareness of the body?... To what extent, and in what ways, are consciousness and cognitive (noetic or mental) processes, which include experiences related to perception, memory, imagination, belief, judgment, and so forth, shaped by the fact that they are embodied?’’. The term “embodied” can be influenced by the type of experiences that arise from the bodily experience, but these experiences are also embedded within a physiological and psychological context [Wilkes et al., 2017]. Gallagher [2006] considers “dynamic processes or structures” should be considered not only on a neurological level, but also a phenomenological level.

Fatigue has often been divided into a form of dualism in MS fatigue research. An underlying division between “subjective” and “objective fatigue” has left an incomplete and partial view of the phenomenon and it is arguably more difficult to understand. Kirchhoff & Hutto [2016] argued that the association between subjective experience and objective measures does not explain how lived experiences occur. However, proponents of NP do attempt to establish any confluence or even congruence that can be ascertained between the subjective characteristics of the experience and objective measures of physiological parameters, which will allow a more complete picture of the phenomenon under investigation.

In this research, the development of a richer and fuller meaning of MS fatigue was attempted. The employed methodology was one attempt to integrate diverse research accounts from both first- and third-person accounts. It was used to explore a) the usefulness of the integration, and b) offer an attempt to develop insight into the dynamic complexity of fatigue and the complexity between the human mind and bodily behaviour in experiences of all sorts [Bockelman et al., 2013]. In the present chapter, congruences that may or may not be possible between phenomenological and physiological findings are reflected upon.

The overarching aim of this research was to explore and delineate fatigability measures and fatigue as experienced. Fatigability was explored through ambulation in attempt to facilitate measurement by monitoring pwMS (compared to older healthy individuals) with continuous, sustained walking. Subsequently, experiences of fatigue were explored through phenomenological interviews and analysis. The two sets of data were reviewed to assist in the tailoring of fatigue interventions in MS. To further establish this, any confluence between gait characteristics recorded and the qualities of subjective experience which was described by participants were monitored and reported.

The process, undertaken in part in a discovery-oriented and reflective mode, included a simple correlation of patient-reported outcome measures and objective measures of fatigue, followed by a summary and reflection on the phenomenological findings, seeking patterns, similarities, and contrasts to physiological data. The aim of the process was to discover if one set of data could assist understandings of the other, to establish a deeper and greater meaning of fatigue and at the same time fundamentally reflect on all findings. The cases themselves (see section 10.2) indicate contradictory findings that the majority of MS research notoriously produces. The cases demonstrate variability in the congruence between fatigue as experienced to physiological fatigue. However, a naturalised phenomenology approach does merit reflection upon the understanding of fatigue and its many facets, including kinds of fatigues (physical-related fatigue, intellectual-related fatigue, emotional-related fatigue, and so forth) as emerged from the research.

10.1. Patient-reported outcome measures compared to objectives measures of fatigability

Firstly, calculations were made to identify fatigability by repeated baseline measurements (T25FW) and the first and last minute of measurements of the 6MW (distance covered and peak angular velocity [ω] of the thigh and ankle). The parameters were then subtracted from one another (the last measurement subtracted from the first) to make a composite measure of objective fatigability. This was then compared to patient-reported outcome measures by determining the correlation coefficient. As expected, Table 10.1 demonstrated a high correlation between all self-reported questionnaires of MFIS total, MFIS physical, and MSWS-12; note that MFIS specific quantifies fatigue, whereas the MSWS-12 quantifies disability, with only one MSWS-12 item relating to fatigue ("In the past 2 weeks, how much has your MS limited how far you are able to walk?").

Our cross-discipline analysis findings demonstrate that there were moderate negative significant associations between measures of the MSWS-12 and peak ω in the dominant ankle (Figure 10.3) and dominant thigh (Figure 10.2). This suggests the more disabled pwMS perceive themselves to be, the lower the metric of effort and pace (peak ω) in their dominant ankle and thigh become. In addition to this, the peak ω of the dominant thigh was significantly negatively correlated to MFIS total (Figure 10.1). The negative correlation demonstrates that the higher the self-reported disability/fatigue scores (MSWS-12 and MFIS total) correlates with lower the peak ω in the dominant ankle (only MSWS-12) and thigh (a metric of effort and walking pace), as expected. Unexpectedly, the results suggest the higher the self-reported MSWS-12 disability score, the more MS participants increased in velocity performing the T25FW-post. This indicates MS participants increased in walking velocity performing the T25FW-post (a nominal measure of fatigability) as perceived walking disability (MSWS-12) also increased; the implication is that increased subjective disability is associated with an objective learning effect on walking performance rather than a fatigability effect (Figure 10.4). These two results contradict each other, as subjective disability correlates with diminished effort, but subjective disability inversely correlates with objective fatigability.

As expected, the subjective measures of MSWS-12 and MFIS total and physical showed a stronger relationship than all objective measures of fatigue. The most obviously explanation may be due to the MSWS-12 questionnaire including certain aspects of walking ability, such as concentration and mental efforts that can be heavily associated with subjective fatigue

[Dalgas et al., 2018]. As mentioned later on in this chapter (section 10.3.2.), more complex walking tasks, such as the dual task paradigm (walking and talking tasks) may further assist our understanding of the confluence between fatigue and fatigability.

Weak negative correlations also were found in previous studies between self-reported measures (MFIS total and physical) to objective measures in the 6MW in terms of distance covered [Dalgas et al., 2018; Hebert & Corboy, 2013]. There are a few possibilities and different interpretations of these results. Firstly, the small sample size and a learning effect could have heavily impacted these results and should be interpreted with caution. The small sample size and Spearman's correlation coefficient could lead to a small cluster of points being randomly distributed and affect the precision of this order. This could have influenced both significant correlations in T25FW and peak ω findings (see scatter plots in Figures 10.1 - 10.4).

The small sample size should be taken into consideration, as typically the larger the sample size, the more reliable the correlation and reflection on the overall population. This study involved a small number of participants, which may have limited the precision of association. To extrapolate statistical analysis results to the overall population, a sample size of under 30 is arguably too small to ensure sufficient power. Hence, the correlations should be interpreted with caution. Self-reported fatigue questionnaires may be significantly negatively moderately correlated with either peak ω or walking velocity, but a larger sample size would help to clarify this.

*Table 10.1.: Spearman's rank correlation coefficient of the relationship between patient-reported measures and objective measures of fatigue, * indicates $p < 0.05$. Green font = strong correlation, magenta font = moderate correlation. The subjective measure in column two (MFIS total) suggest perceived fatigue in physical, cognitive and psychosocial aspects. The subjective measure in column three (MFIS physical) suggests perceived fatigue in physical aspects only. The subjective measure in column four (MSWS-12) suggests perceived disability. The objective measures in column five (T25FW post minus pre in seconds) and six (6MW, minute six minus minute one in feet) suggest possible fatigability. The objective measures in columns seven (minute six minus minute one in dominant ankle peak ω), eight (minute six minus minute one in weak ankle peak ω), nine (minute six minus minute one in dominant thigh peak ω), and ten (minute six minus minute one in weak thigh peak ω) suggest the amount of strength.*

	MFIS total	**MFIS physical**	**MSWS-12**	**T25FW post-pre**	**Min6-Min1**	**Min6-Min1 peak ω ankle**	**Min6-Min1 peak ω ankle**	**Min6-Min1 peak ω thigh**	**Min6-Min1 peak ω thigh**
						Dominant	**Weak**	**Dominant**	**Weak**
MFIS total	-	0.982*	0.737*	-0.109	-0.011	-0.328	-0.305	-0.615*	-0.187
MFIS physical	0.982*	-	0.727*	-0.151	0.025	-0.297	-0.283	-0.566	-0.151
MSWS-12	0.737*	0.727*	-	-0.479	-0.071	-0.644*	-0.416	-0.630*	-0.288

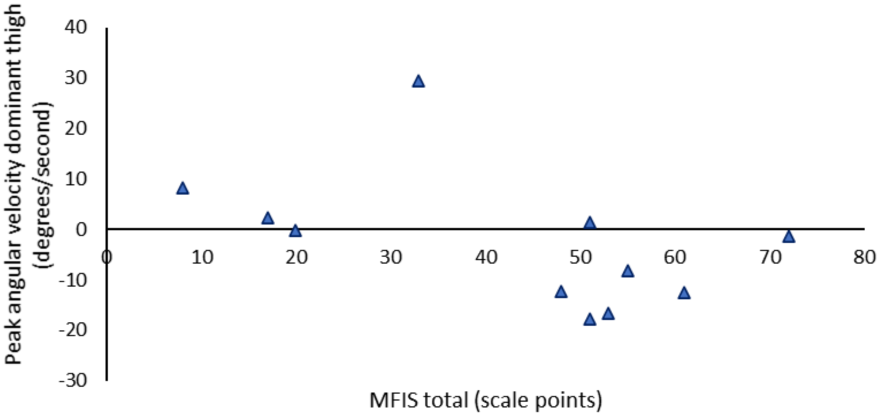

Figure 10.1.: Scatter plot of average peak angular velocity (degrees/second) in the dominant thigh (Minute 6 – Minute 1) plotted against MFIS total (points). Spearman's rank correlation coefficient = - 0.615, demonstrating a negative correlation between the two.

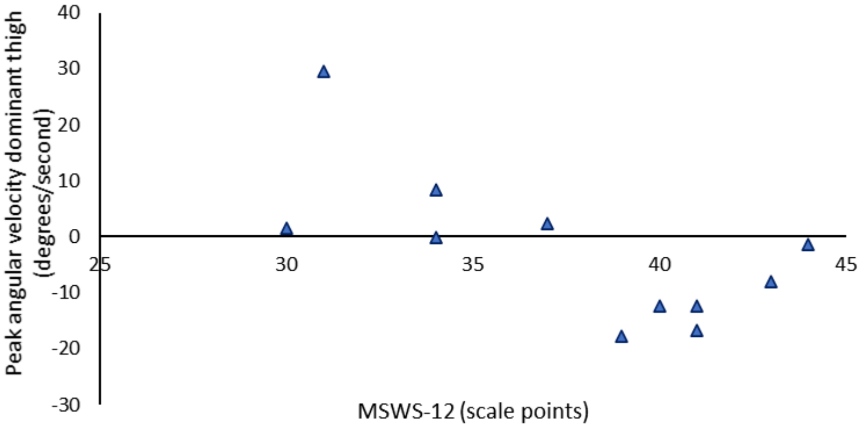

Figure 10.2.: Scatter plot of average peak angular velocity (degrees/second) in the dominant thigh (Minute 6- Minute 1) plotted against MSWS-12 (points). Spearman's rank correlation coefficient = - 0.630, demonstrating a negative correlation between the two.

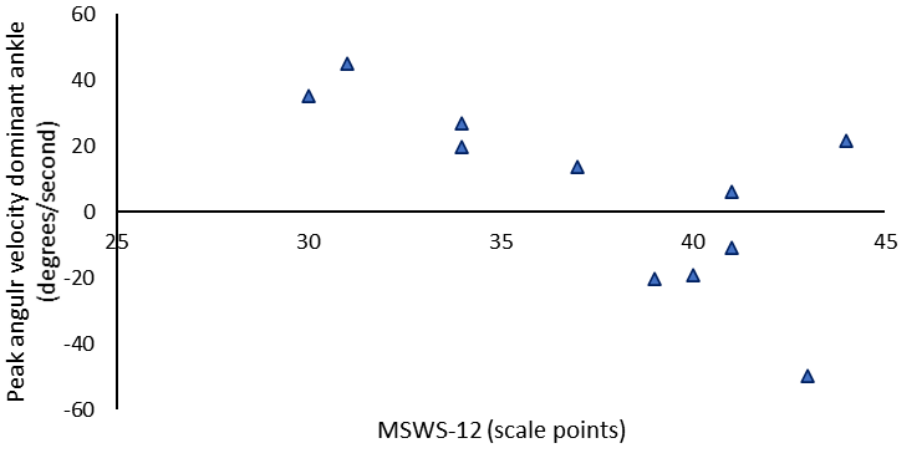

Figure 10.3.: Scatter plot of average peak angular velocity (degrees/second) in the dominant ankle (Minute 6 – Minute 1) plotted against MSWS-12 (points). Spearman's rank correlation coefficient= - 0.644, demonstrating a negative correlation between the two.

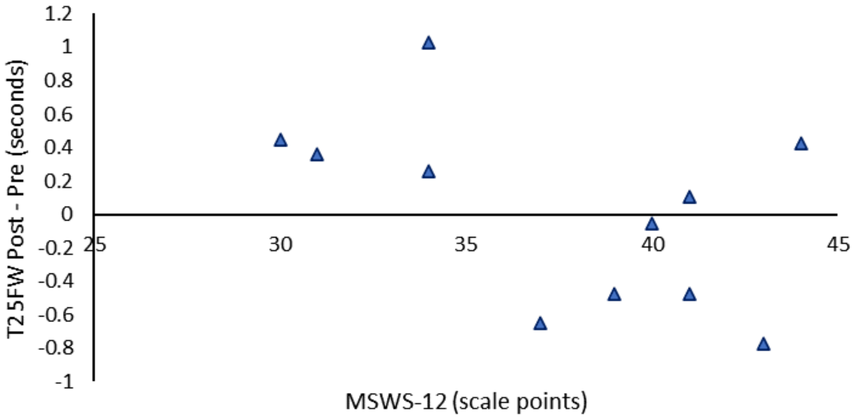

Figure 10.4.: Scatter plot of average T25FW (PostT25FW - PreT25FW) (seconds) plotted against MSWS-12 (points). Spearman's rank correlation coefficient = - 0.479, demonstrating a negative correlation between the two.

Another possibility is that the T25FW and MSWS-12 correlations could be due to the experimental design of the study. The T25FW-post could have been performed too late after the 6MW; therefore, individuals may have rested, and as a result, were no longer fatigued. This interpretation would imply the velocity values of post minus pre T25FW to be either random or due to uncontrolled conditions. Uncontrolled conditions in this experiment may have influenced participants' walking (learning effect, time of day, level of disability, or the experimental setup). Participants may have become familiar with the T25FW test or the walkway after the 6MW and, as a result, increased in walking velocity.

Another potential explanation for the inconsistent data could be the timing of the assessments, as they were not all performed at the same time of day. It has been suggested in the literature that fatigue worsens throughout the course of the day [Iriarte et al., 2000]. As stated later in section 10.4.1., the timings of the experiments were not all conducted at the same time due to the room availability. With this in mind, participants may have performed differently and possibly experienced more fatigue if all participation had been in the afternoon. The timing f completing the questionnaires may have also affected the results. Goldman et al. [2008] asked their participants to complete the MFIS in-between several 6MW tasks; hence, the participants may have felt more fatigue impact as they had just finished walking for six minutes. This shows real time sensations of fatigue compared to completing the questionnaire from memory at the beginning of the experiment (like in this study).

Taken together this data suggests that 'objective' fatigue may be somewhat related to 'subjective' fatigue but confounding factors may overlay and contribute also. The data may usefully point towards an objective biomarker of fatigability, but this was unclear and inconsistent within the data.

Even though the results suggest moderate correlations to peak ω and self-reported fatigue, the results follow previous studies and interpret inconsistencies and, only weak to moderate correlations in subjective reports of fatigue to physiological measurement [Dalgas et al., 2018; Engelhard et al., 2016; Goldman et al., 2008; Huisinga et al., 2011]. This is unsurprising, reflecting the complexity and difficulty of accurately assessing fatigue in MS, which has been problematic in research for many years. Table 10.1 highlights the incomplete and inconsistent representation of fatigue within the literature.

This leads one to question the methodological approach of previous studies on how to better understand fatigue as a whole and to grasp the suitability of current measurement. Phenomenological insights allow for the exploration of the nature of the experience, to reveal its depth and detail, and gives opportunity to reflect on all aspects of an individual's fatigue alongside and the current measurements of velocity and peak ω. Although the findings yielded important and interesting insights, the current literature only provides insight into a partial view of fatigue. Fatigue has been operationalised and attempts have been made to be break it down into characteristics that have not insightfully grasped the whole view of fatigue. Naturalised phenomenologists claim to reveal insights about the interaction between the subjectivity and objectivity of a phenomenon, and therefore, this methodological approach is aimed at facilitating the exploration of any potential congruence between the phenomenological descriptions and physiological measurements of fatigue. However, it allowed for investigation of individuals' experiences at different stages of their fatigue that may have been displayed in the physical assessment.

10.2. Fatigued as experienced and physiological fatigue in individual cases

To show the variability of parameters of fatigue, in the following section, the range of composite findings from a selection of participants is demonstrated. The measures of velocity and peak ω were selected from the first and last minute of the 6MW in an attempt to highlight pwMS walking without and then with fatigue.

From a phenomenological perspective, all participants described varying degrees and impacts of fatigue. Over half of the participants reported physical fatigue as their primary fatigue concern and the majority of participants stated physical fatigue overall affected their everydayness and ability to perform tasks, inhibiting ambulation and basic movement. The overlap of exertion that causes fatigue was commonly stated to influence both bodily and cognitive ability. Not surprisingly, fatigue was rarely described as solely impacting one aspect of functioning, although there was a commonality of physical exertion exacerbating fatigue irrespective of the type of fatigue individuals experienced.

The cases below are comprised of a phenomenological description of an individual's fatigue and experiences within the everydayness, and aspects of the physiological assessment itself. Parameters of ambulatory fatigue, including changes to walking velocity and peak ω, are also demonstrated and discussed. The purpose of this section is to illustrate the variability of physiological results in relation to experiences of fatigue, and suggest the co-existence of both sets of data interpreted as a whole, and explore if or how they can draw conclusions from each other.

10.2.1. Phenomenological fatigue and objective parameters with some potential confluence indicating fatigability

The following three cases display a degree of experienced perceived fatigue and physiological fatigue that could indicate objective biomarkers of fatigability and experiences of fatigue interacting with one another. The purpose of this exercise is to illuminate findings of fatigue that may have not previously been explored. The physiological findings in this section demonstrate participants slowing down in walking in two measures of velocity and peak ω. The peak ω shows reduced speed and movement in the thigh and ankle from the first of the last minute of the 6MW. Their walking speed also reduced in the T25FW and last minute of the 6MW. This, alongside the experiences of fatigue, could signify fatigability.

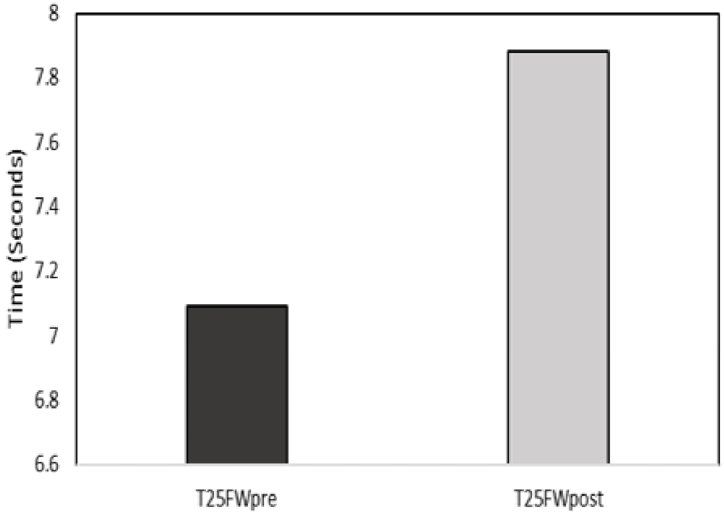

Figure 10.5.: M097 Timing (seconds) of the T25FW before and after performing the 6MW

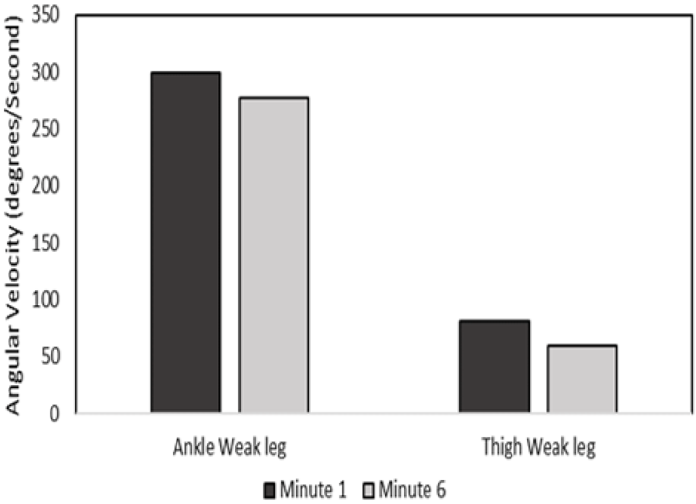

Figure 10.6.: M097 peak angular velocity of the "weak" leg in the thigh and ankle.

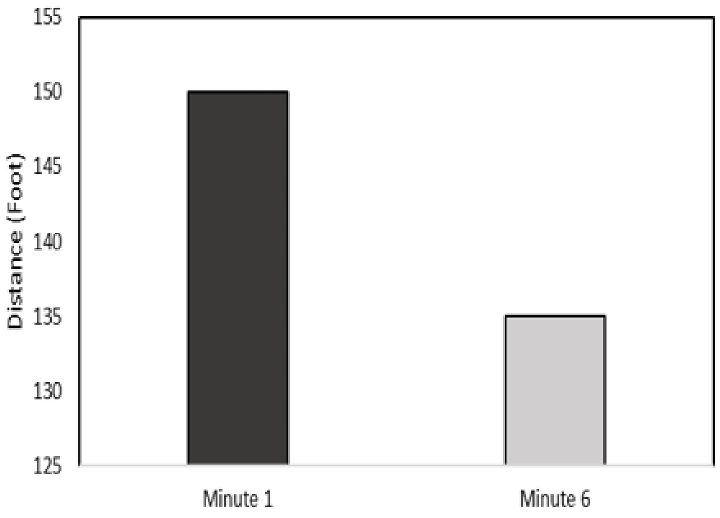

Figure 10.7.: M097 Distance covered (feet) in minute one and minute six of the 6MW

M097:

The baseline measure of at T25FW in 7.1 s suggests an ambulatory patient with a very high level of disability. The peak ω (pitch) decreased in both the thigh and ankle from minute six to minute one in the 6MW. This indicates a reduced rate of change in peak ω (i.e. walking effort) in that axis that could be influenced by her lower extremity perceived descriptions of fatigue. Pitch (z-axis) movement from the sensor in this study mirrored anterior-posterior movement that reflects flexion and extension of the thigh and ankle. Therefore, the decrease in peak ω and sensations of wearying legs coincided with each other to potentially indicate fatigue. The reduced velocity and peak ω indicates the participant walking slower in the last minute of the 6MW, and as a result, this may reflect fatigability.

M097 described a high degree of fatigue that fluctuated throughout the day, predominantly exacerbated by physical exertion. She differentiated tiredness from fatigue by the sporadic timing and heaviness encountered with fatigue. The sensation of ‘hitting the wall’ filled her with the inability to do anything, regardless of the surrounding environment: “Your body's just telling you not to do anything you know and if I get really fatigued, I start to shake.” Peak levels of fatigue could affect her body control, as her body could physically shake from fatigue. This restricted what she could do. A sudden wave of fatigue that she described as a “fuzzy head” could cause a draining feeling in her lower extremity and she would experience the sensation of swaying and unbalance.

Additionally, the feeling of being "muzzy headed" towards the end of the 6MW was expressed as she began to feel fatigued, get backache, and experienced double vision. Walking velocity reduced in the T25FW and the last minute of the 6MW. The duration of completing the T25FW increased from 7.09 to 7.88 seconds (slowing by 0.354 feet/s), and the participant walked 15ft less in the last minute of the 6MW. The extreme symptoms of fatigue that she experienced during the end of the task are reflected in her diminished walking performance; if anything, her walking performance decrement seems small compared to her induced symptoms.

An element of fatigue changed over time for her, as she encompassed fatigue as part of her everydayness at the time of the study. She embraced a certain rhythm to her daily patterns of fatigue to cope and manage herself accordingly. Overall, the participant stressed that she recognised fatigue as a major part of her MS. This may indicate a direct congruence between the two: the feelings of fatigue, and fatigue infiltrated through bodily movement, may potentially exacerbate one another. In this clearly disabled yet ambulatory participant who regularly experiences fatigue, observations of performance decrement were established that reflects the fatigued state she described during the interview; in fact, it was surprising that her unequivocal symptoms did not result in greater performance decrement.

M092:

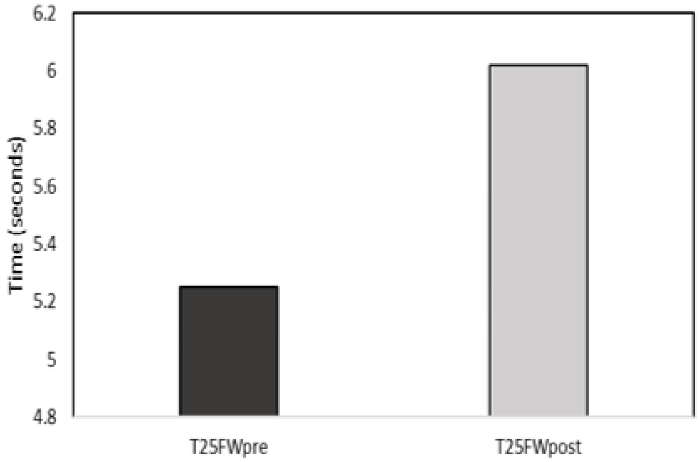

Figure 10.8.: M092 Timing (seconds) of the T25FW before and after performing the 6MW.

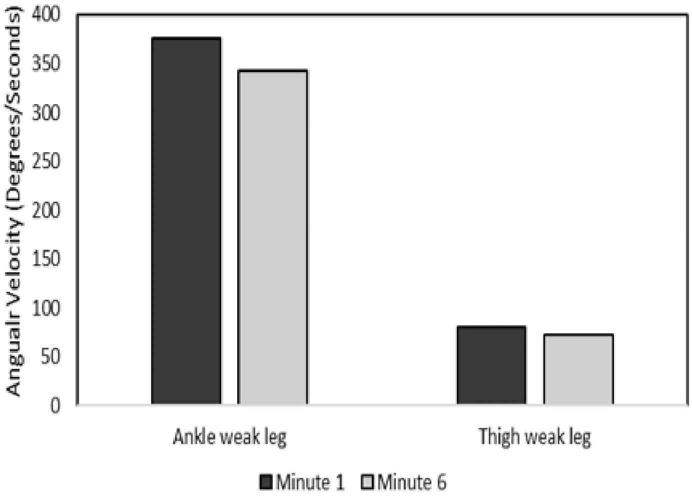

Figure 10.9.: M092 Peak angular velocity of the "weak" leg in the thigh and ankle.

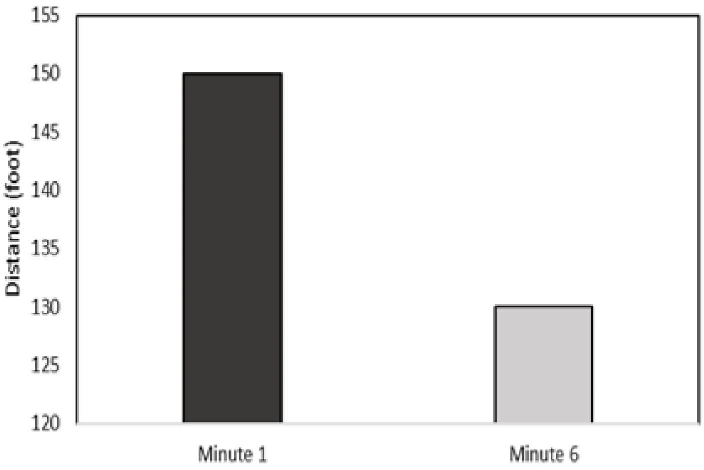

Figure 10.10.: M092 Distance covered (feet) in minute one and minute six of the 6MW.

M092 reported days where her energy levels would remain considerably low throughout the day and she felt there wasn't a lot she could do about it. She called these "MS days", as she found it difficult to describe them in any other form apart from the unpredictability of it. On other days, fatigue could be elicited by a multitude of things, activities, or thoughts that exacerbate her fatigue.

Fatigue was a whole-body phenomenon for her. The body was almost unresponsive, specifically the lower extremity, with noticeably reduced strength and limb heaviness. After the assessment, she felt fatigued in her lower extremity with the sensation of heaviness in her legs. The peak ω (pitch) decreased in both the thigh and ankle from minute six to minute one in the 6MW. The modestly reduced rate of change in peak ω in that axis could indicate her feeling of reduced strength and limb heaviness reported during the interview. The anterior-posterior movement that quantifies flexion and extension of the thigh and ankle declined in peak ω that determines a slower rate of change and movement at both the thigh and ankle that match her self-judgment of lower extremity limb heaviness. Figures 10.8 and 10.10 display a unequivocal reduction in walking velocity, with an increase of 0.77 seconds in the T25FW after performing the 6MW, and a drop of 20ft from minute one to six of the 6MW. All the physiological measures indicate the participant's walk slowing down, which could have been caused by fatigue.

M092 emphasised temporal aspects and fatigue affected her more so in the late afternoon (3pm starting), which she described as a "cognitive blur and fog". This accumulation of "silly mistakes" and not understanding something caused heightened frustration and "emotional fatigue", causing her to avoid making important decisions at this time of day. Time management was a priority for her to be able to perform and complete tasks with given rest periods placed throughout the day, although she felt her “whole life is a compromise.”

The severity of fatigue could project into illness if not managed efficiently. This leads to no other option but to rest, sit down and recharge. Preserving bodily energy was valuable to her, with bodily fatigue stated as the most prominent and worst affected as it hindered her from doing what she wanted to do. There seemed to be a juxtaposition between the two for M092: experiences of fatigue were described and demonstrated through intellectual and bodily impacts. Fatigue was experienced as a whole-body phenomenon and may have been quantifiable in changes of velocity and peak ω. In this PwMS, who is only subtly disabled (baseline T25FW = 5.2 s) but who describes fatigue as a central element of her experience of MS, her movements (ω) showed modest fatigability, but her overall walking performance (post minus pre T25FW and also min 6 minus Min 1 6MW distance) showed striking fatigability. This may suggest a psychological or motivational effect that was successfully elicited by our nominally fatigue-eliciting task (6MW).

M094:

M094 believed fatigue was commonly expressed in the MS community as a mutual feeling of tiredness, and he himself experienced it, but typically attempted to push through. He reported fatigue as unexplainable and occasionally could be experienced with no apparent reason at the beginning of his day, which he labelled a “non-starter day”. Coordination and balance could become impaired with fatigue. He described his inner monologue during the 6MW to motivate himself to continue walking, “I’m getting tired now, right shut down, don’t think about the time, just concentrate and keep going.”

Figure 10.11 shows M094 took over nine seconds to complete the T25FW even before the 6MW, with an increase of 0.77 seconds after the 6MW (slowing by 0.213 feet/s). This suggests his extraordinary disability (despite remaining fully ambulatory) without fatigue, modest walking performance decrement during the 6MW, and may demonstrate his psychological determination to push through the assessments. The walking velocity in minute six of the 6MW also reduced, but only by 5ft (5%). Additionally, there was a reduced rate of change in peak ω in both the thigh and ankle. This suggests fatigue did affect his walking ability.

He believed exercise benefitted him, so pushed himself to do as much as he could, even if it was just a short walk around the block. The hot weather dramatically affected him and exacerbated fatigue as it physically took his breath away, “just takes the oxygen and your breath away and you feel you can’t breathe. You get very tired very quickly*”*. He reported no other particular activities as triggering his fatigue, although he had a routine if drowsiness set in, by allocating an hour of his time to rest his body and simply do nothing. He believed acceptance of his MS helped him accommodate and ‘have a better relationship with it’. This may give insight into the intertwining relationship of fatigue in more than one aspect; the domains of fatigue were described through physical exertion that caused an inability to walk efficiently as his lower extremity was affected. Nevertheless, his mentality regarding his determination and acceptance permitted him to continue walking, even if he felt or experienced fatigue.

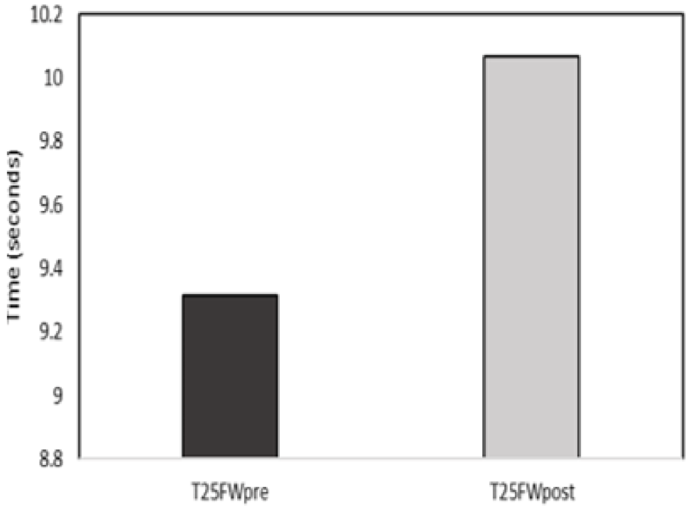

Figure 10.11.: M094 Timing (seconds) of the T25FW before and after performing the 6MW.

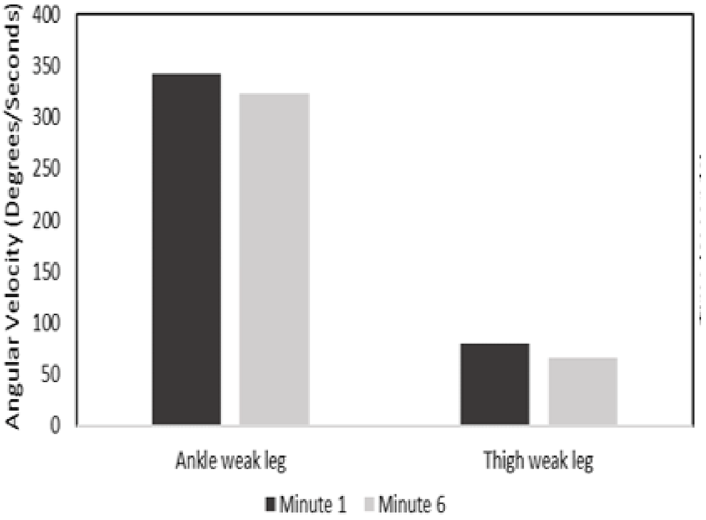

Figure 10.12.: M094 Peak angular velocity of the “weak” leg in the thigh and ankle.

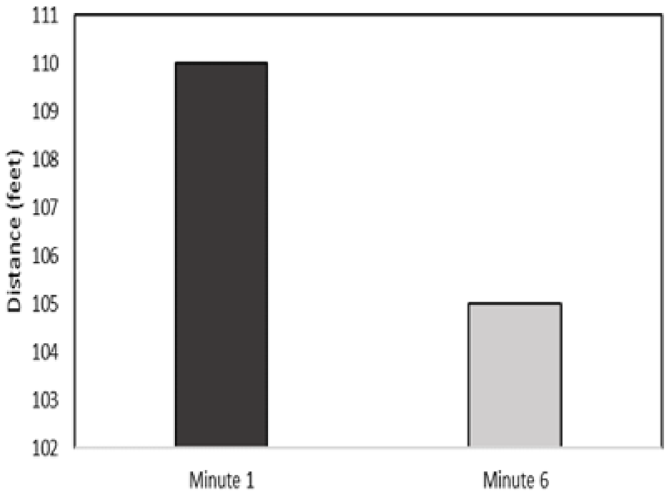

Figure 10.13.: M094 Distance covered (feet) in minute one and minute six of the 6MW.

All three participants suggested fatigability in all composite measures and phenomenological descriptions. Measures of velocity and peak ω indicate a degree of fatigue as their walking slowed down. However, results were not consistent across all participants. Fatigue was described as a *whole-body* phenomenon which suggests parallels between fatigue that participants experienced and felt, and physiological changes of fatigue that could be quantified.

A juxtaposition suggests fatigue and fatigability may be modestly but inconsistently related. The value of exploring these findings to search for the relationship between the two may assist in understanding the grey area of interwoven elements of fatigue as individuals feel and the fatigability that researchers can observe and quantify. There is some limitation to identifying the so-called relationship between the two, as reductionistic perspectives would argue that the experience remains difficult to quantify. However, this suggests the potential of congruence by exploring fatigue at its very foundation, of what pwMS experience themselves and what they describe, what they feel fatigue is.

10.2.2. Phenomenological fatigue and objective markers not indicating fatigability

Through the next two cases, a phenomenological description of fatigue as experienced is demonstrated. However, this fails to reveal physiological fatigability using the same composite measures as the previous cases. These incongruent results probe further questioning of the association between fatigue and fatigability and offer material for further reflection.

M089:

M089 described a physical gravitational pull that affects her legs with any degree of strenuous exercise. She characterised her legs as heavy, "feeling mushy", the gravitational pull creating a feeling of dragging her legs around due to her feeling a lack of motor control. Her body felt unpredictable and uncontrollable with fatigue, a very slight incline in gradient would cause her to struggle to walk. She described her "legs feeling like lead" as she felt a dragging sensation that often caused great effort to walk normally. She expressed she must "relearn walking every time" because she had to consider each phase of the gait cycle whilst walking. Natural movements that once were taken for granted were now more difficult for her, the natural unconscious motion of walking had disappeared.

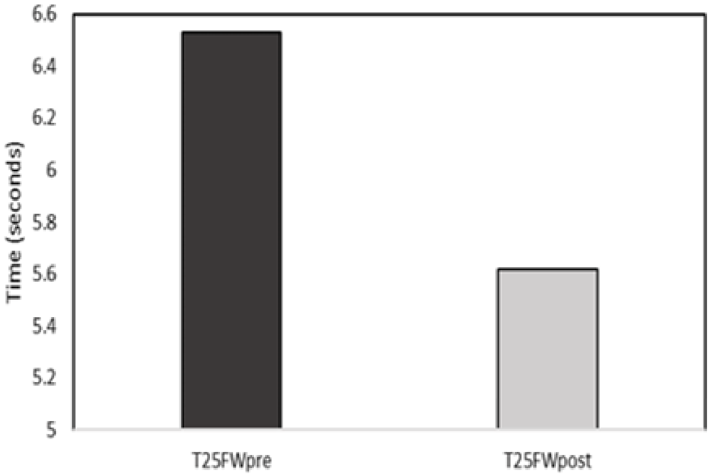

Figure 10.14.: M089 Timing (seconds) of the T25FW before and after performing the 6MW.

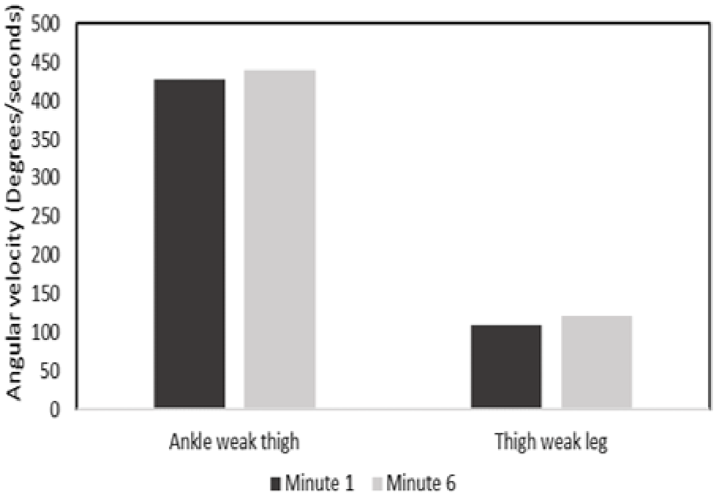

Figure 10.15.: M089 Peak angular velocity of the "weak" leg in the thigh and ankle.

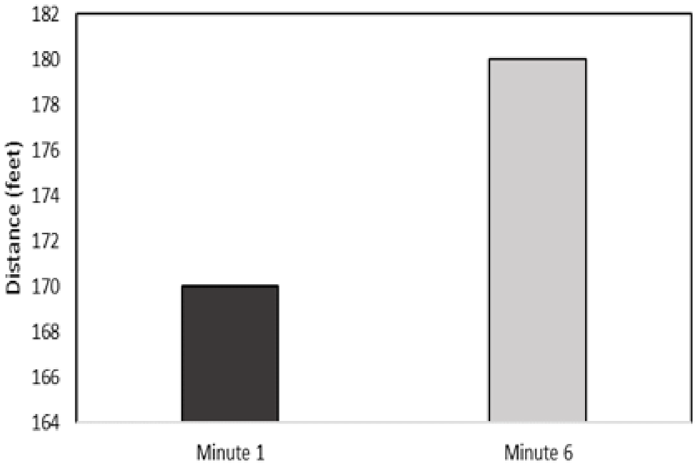

Figure 10.16.: M089 Distance covered (feet) in minute one and minute six of the 6MW.

She felt her coordination was not as efficient towards the end of the 6MW task as she felt increasingly unstable walking. However, she conveyed no significant fatigue where she felt unable to complete the assessment. To oppose this, the participant's T25FW increased in velocity by 0.588 feet/s (0.915 seconds over 25 feet); she also walked an extra 10ft further (6%) in the last minute of the 6MW compared to the first. Additionally, both the thigh and ankle peak ω increased in the rate of change in the last minute of the 6MW compared to the first. The change in peak ω suggests an increase in rotational velocity at the thigh and ankle of the flexion/extension axis movement. This increase could be a learning or motivational effect or a sense of determination that led her to walk faster, which would fit with her statement that she has to "relearn walking every time". However, it also could be interpreted as M089 not experiencing fatigability.

M090:

The altered sensation of whole-body movement difficulty was described as “treading treacle”, where extreme levels of fatigue would be so overwhelming, they could cause physical pain. She also emphasised fatigue was a *whole-body* phenomenon, “it’s not tiredness, it’s like treading treacle, you know you can hardly move your limbs”. Her complete lack of energy and utter exhaustion impacted her body, with considerable effort to even lift her hand. When fatigued, she felt it was an effort to walk in comparison to normal. The severity of her physical embodiment implications of the pins-and-needles impacted her cognition as well as physically.

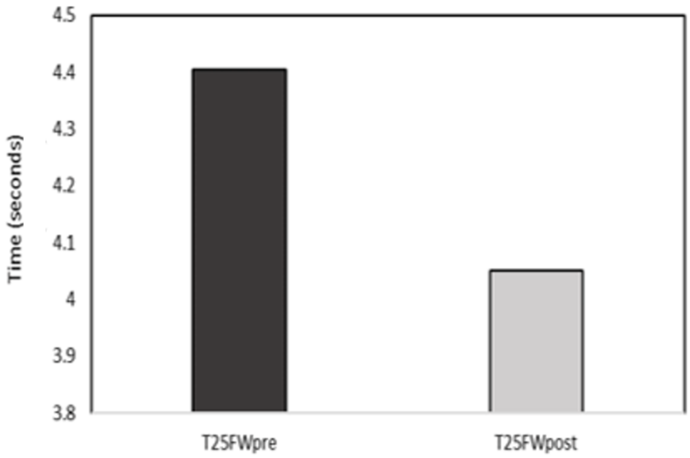

Figure 10.17.: M090 Timing (seconds) of the T25FW pre and post performing the 6MW.

She reported that MS fatigue was not something you could ignore and push through. Her recognition of MS fatigue was the feeling of persistent fatigue, with or without sleep or rest. Due to her experiences of crippling fatigue, only certain motives or activities got her out of bed. Despite this, physical measures of velocity and ω did not indicate a level of fatigue. The T25FW decreased in time, M090 increased in T25FW velocity after the 6MW by 0.49 feet/s (from 4.40 to 4.05 seconds). She also covered 5ft more (2%) in the last minute of the 6MW and both increased in peak ω in the thigh and ankle. Given that this PwMS showed almost no disability to begin with (pre T25FW = 4.40 s) and improved to the upper end of how well healthy people perform after experiencing the 6MW, it could be interpreted that our 6MW ambulatory task did not elicit any ambulatory fatigue, or that the participant experienced a learning effect on the walking tasks.

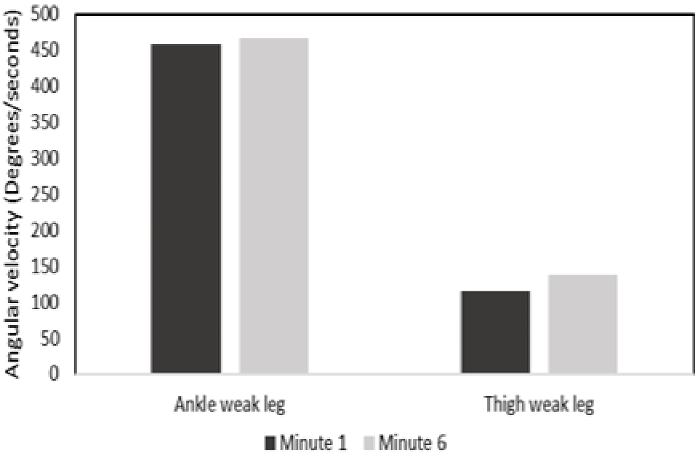

Figure 10.18.: M090 Peak angular velocity of the 'weak' leg in the thigh and ankle.

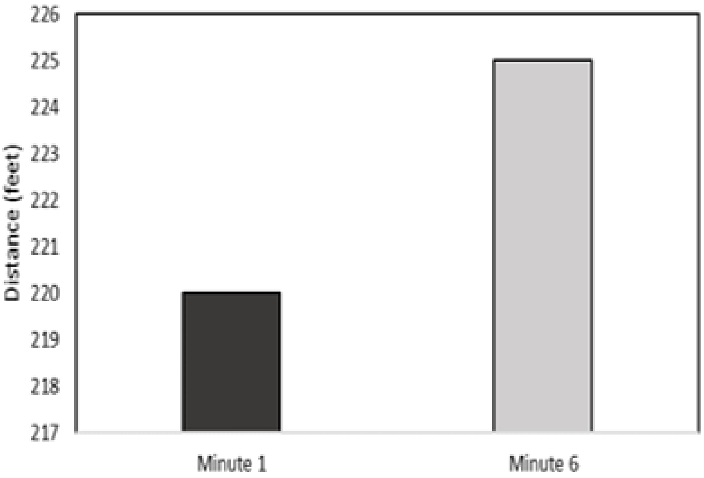

Figure 10.19.: M090 Distance covered (feet) in minute one and minute six of the 6MW.

Both M089 and M090 reported fatigue as a phenomenon that could be persistent and cause severe physical implications, including the feeling of increased ambulatory difficulty. Nevertheless, objective measures of velocity and peak ω failed to demonstrate this and displayed no fatigability. These cases both suggest that either we were unable to elicit fatigue in these PwMS using our methodology (6MW), or that fatigue as experienced does not relate to physiological fatigue, and they contradict each other. This could indicate that fatigue as experienced by individuals may be a separate entity physiologically to the objective measures of fatigue used in this study.

10.2.3. Phenomenological fatigue and mixed physiological parameters of fatigability

In the following two cases, phenomenological descriptions of fatigue and the mixed results of physiological fatigue measurement are demonstrated. These calculations primarily highlight the overall quantitative results of this research. The findings do indicate a degree of fatigability, but this is marginal and inconsistent.

M104:

For this PwMS who had only mild disability (and was still running his own company full time), prior to reading about fatigue, his perception of fatigue impact was only physical. However, after noticing his coordination and his thought process changing, he began to develop insight into how fatigue impacted him more holistically in other, unexpected aspects. Fatigue was a global phenomenon, it projected over his whole body, with the expression that "*fatigue is felt all of me*". The act of running would cause him to feel "absolutely drained" with exertion causing breathing to be more difficult.

The extreme, overpowering sensation of fatigue disabled his ability to function in any manner. He identified the marked effect of his MS with muscle wastage and reduced muscle strength, as well as with tripping and falling. Fatigue influenced him throughout his lower extremity; he was consciously aware of each part of his gait cycle and focused on his legs to decrease his likelihood of falling or scuffing his feet. He was aware he was scuffing his feet throughout the assessment. The peak ω was modestly reduced in the ankle during minute 6 compared to the first minute by 4.9 degrees per second. He also performed slower in the T25FW after the 6MW, from 4.09 to 4.23 seconds (both times plainly in the normal/healthy range). However, interestingly, the thigh peak ω increased by 20.6 degrees per second and there was no change in the distance covered from the first to last minute of the 6MW. as all the changes were small, and half implied improvement/learning while the other half implied performance decrement, it would be reasonable to suggest that in this PwMS that we did not elicit fatigability, and that the differences we observed were random variation.

He felt an impact of fatigue during the assessment, but reported it wouldn't affect him later that day. Physical exertion could lead to fatigue affecting his mental abilities, with the inability to think properly due to feeling too tired. He felt a bodily imbalance, with the left leg feeling weaker, as it would often catch or scuff. By listening to his body and the level of physical exertion, he managed his fatigue better than before and had learned over time what his body could manage.

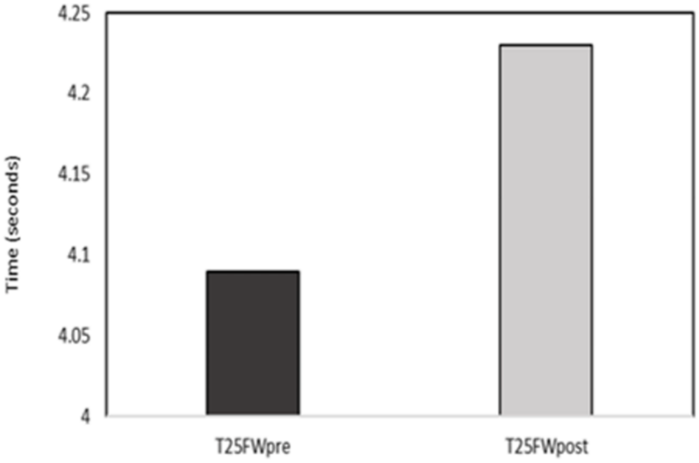

Figure 10.20.: M104 Timing (seconds) of the T25FW before and after performing the 6MW.

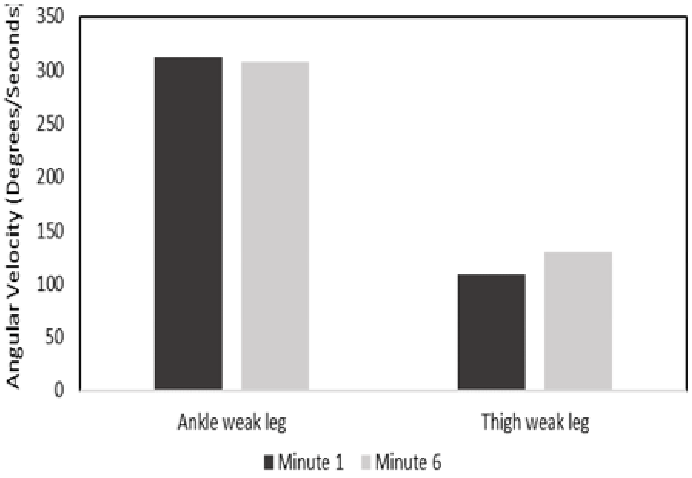

Figure 10.21.: M104 Peak angular velocity of the "weak" leg in the thigh and ankle.

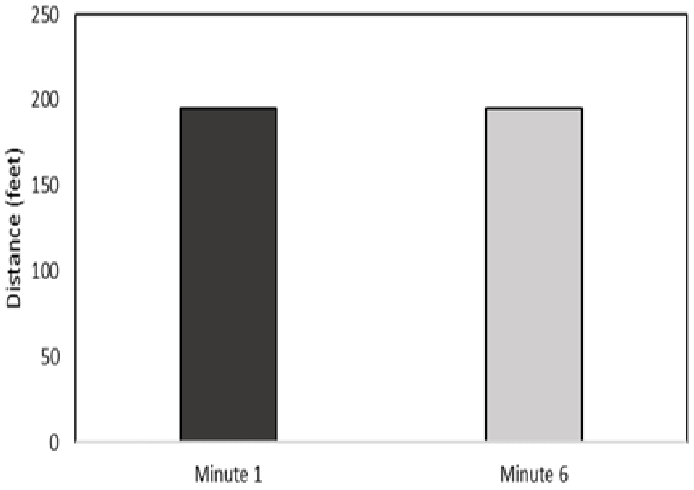

Figure 10.22.: M104 Distance covered (feet) in minute one and minute six of the 6MW.

M105:

M105 reported fatigue visually affecting him, through his slurred speech, blurry eyes, and a term he used, “brain fog”. The fog was associated with a time delay and disrupted his thought processes and understanding during everyday cognitive tasks, such as completing forms. Administrative work was more taxing as completion took longer, and he began “second-guessing*”* himself that the work he had done was done correctly.

He described his legs as if they had been running when fatigued, wanting to sit down as the muscles throughout the whole lower extremity tightened with the feeling of pulsation. He took gabapentin to help with these symptoms, as without it he would struggle and said the muscles would worsen, which impacted his fatigue levels. However, he felt taking a higher dose of gabapentin gave him more brain fog, therefore he halved his medication.

He reported that fatigue could make him physically sway: “You look like you’ve had a few the way you’re, the way you’re walking”. Fatigue specifically impacted his lower extremity and described it as “legs feel like lead”. He felt a bodily reaction to fatigue during the end of the 6MW assessment as tightening in the lower extremity occurred, which was portrayed through the distance covered in the last minute of the 6MW (decreasing by 6%), and both the thigh and ankle peak ω decreased. However, this was contradicted by the increase in velocity whilst performing the T25FW post 6MW, where he sped up by 0.12 seconds (speeding up by 0.104 feet/s). He reported that at initial diagnosis, he did not detect fatigue as a first noticeable phenomenon, but it became one of his main symptoms. In this PwMS who had borderline ambulatory disability but reported fatigue as part of his symptomology, the measurements made during the 6MW suggested modest fatigability, although his post minus pre T25FW performance suggested a learning effect. One possible explanation is that this PwMS did experience fatigability during the continuous 6MW but was able to recover between the end of the 6MW and the beginning of the second T25FW (a time period lasting 3 minutes 15 seconds).

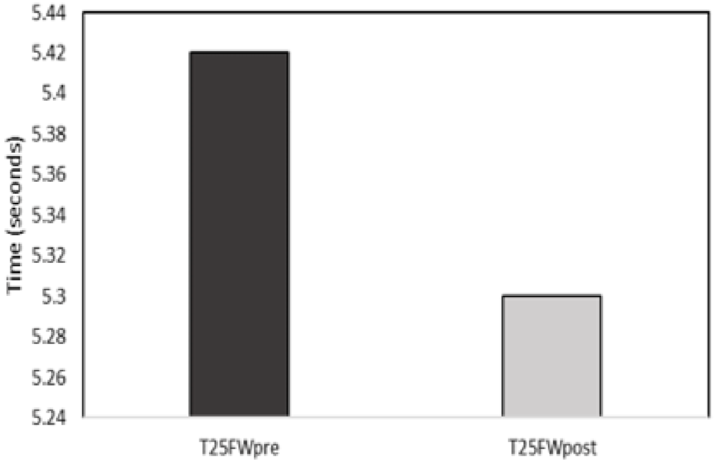

Figure 10.23.: M105 Timing (seconds) of the T25FW before and after performing the 6MW

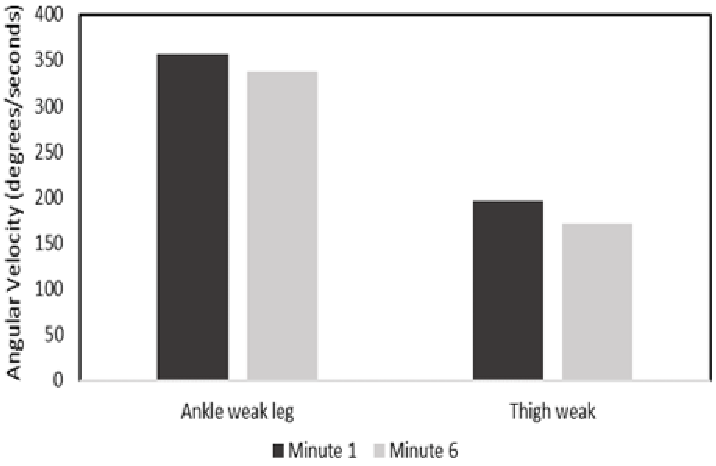

Figure 10.24.: M105 Peak angular velocity of the "weak" leg in the thigh and ankle.

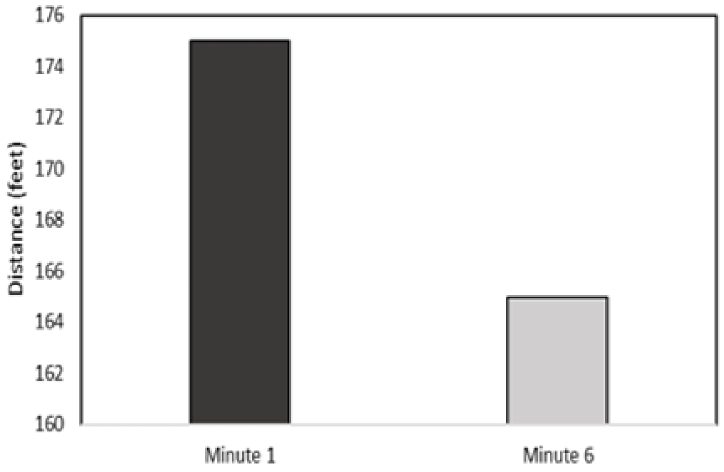

Figure 10.25.: M105 Distance covered (feet) in minute one and minute six of the 6MW

These two cases provide a mixture of composite measure results that did not universally display fatigability. M105 decreased in all composite measures that indicate fatigability, but increased in walking velocity after performing the 6MW in the T25FW. Whereas M104 decreased in walking velocity in the T25FW-post, but demonstrated no change in distance covered from minute one to minute six, and increased in peak ω in the weak thigh from the first to the last minute of the 6MW.

To summarise, the multiple indicators reflecting fatigability were identified in some MS participants, but they were not ubiquitous and failed to demonstrate a change in velocity and ω in all participants. The variety of physiological results was highlighted and discussed in Chapter Nine. However, in the following section, the similarities and differences in both sets of data are dismantled, and suggestions for future MS fatigue research are further discussed.

10.3. Lines of research

To confirm the physiological results of fatigability, the following boxed bullet points highlight the key findings.

- MS participants demonstrated only a 0.08 second difference slower in T25FW test after performing the 6MW.
- MS participants covered 4m distance less from the first to the last minute of the 6MW.
- There was no consistent change in MS participants in peak ω in relation to an increase or decrease in pattern throughout each minute of the 6MW at the thigh and ankle.
- The most promising parameter, although not consistent or universal, was the dominant thigh peak ω; five MS participants decreased in peak ω value in the last minute of the 6MW. Additionally, the mean dominant thigh peak ω values (minute six-minute one) was significantly negatively moderately correlated to self-reported questionnaires of the MFIS total and MSWS-12. This indicated that the lower the peak ω values, the higher the self-reported fatigue and walking ability.
- Compared to the older healthy group, MS participants significantly reduced in peak ω at the thigh and ankle.
- MS participants' walking velocity was significantly slower in the T25FW test in comparison to the older healthy group before and after performing the 6MW.

The findings described in Chapter Nine determine subtle but nonsignificant changes in walking velocity and peak ω in MS participants throughout the 6MW. The rate of change varied in each minute of the 6MW, with some MS participants beginning to reveal gait deterioration, and others not at all. However, to establish the significance of the parameters used, a larger cohort is needed where the fatigue status of each participant is carefully accounted for. The range of manifestations from the phenomenological findings does shed light on the granularity of physiological measurement. It begins to highlight that to objectively identify fatigue, a variety of measures may need to be incorporated, and even so, these measures might never be able to quantify the whole phenomenon of fatigue that is experienced by pwMS.

Nonetheless, this research begins to unveil the deep complexity of fatigue and touch upon the embodied experience and how this was prominent in MS participants. Fatigue impacted MS participants which unravelled multiple layers, dependent on the individual, the degree of disability, and the overall acceptance of their condition and fatigue as part of their everydayness. As stated previously in this chapter, the majority of MS participants reported physical fatigue as disrupting their ability to perform daily activities. However, physiological measurement demonstrated a mixture of results, with no easily identified data in terms of consistent gait change and deterioration throughout the execution of the 6MW.

Changes and a reduction in walking velocity in the T25FW did occur in 45.45% of the MS participants post-6MW. Similarly, the distance covered from the first to last minute of the 6MW did decrease in 54.55% of the MS participants. Although not significant, the changes and reduction in velocity do begin to show signs of fatigability in a few participants, and this perhaps sheds some light on the feeling of heaviness and impairment that was experienced by participants in this study shared from the phenomenological interviews. Fatigue was experienced and perceived through noticeable bodily actions in some MS participants and the taken for granted bodily action becoming disrupted. The noticeable change was often described by participants *as a sense of losing control over their body*. The feeling of the body slowing down by not permitting full ability of movement often added an element of sensing of the body even coming to a standstill.

Granting all this, the physiological results did not universally demonstrate these experiences. Some participants signified fatigue, but others did not. The inconsistencies may have been due to the composite measures not fully capturing fatigue and the 6MW not exacerbating fatigability. However, the type of tasks performed may have also not highlighted fatigue due to pwMS experiencing different domains of fatigue rather than physical fatigue and fatigability. Although the study involved pwMS who reported to experience fatigue, the inclusion criterion did not establish this; the inclusion criteria relied on the disability level (EDSS-S) and the participants agreeing on experiencing fatigue. Moreover, this could have impacted the results and levels of fatigability due to not taking into account who did and did not experience consistent fatigue. Through phenomenological findings, fatigue was discovered as a whole-body phenomenon which included cognitive, physical, and psychosocial stressors. It was described as impacting each individual with unique experiences and was unpredictable with timing and severity. Most MS participants agreed that physical exertion typically exacerbated the fatigue that they experienced, although it may not have aggravated fatigability in all pwMS.

Fatigue is repeatedly described as a concrete and subjective experience and conscious thoughts and mannerisms could impact how pwMS experience fatigue. For example, M090's physiological results indicated an increase in velocity and peak ω that portray a non-fatigued, even healthy individual walking. Nevertheless, it was prominent and overt from her interview that she was heavily affected by fatigue, to such an extent that it disrupted life as a whole. She went from a managerial role at work providing financial support and stability for her family, to the change with her diagnosis and fatigue implications, with little to no support from her husband or family. This emotional stressor of the increasing struggle to look after her son and marriage difficulties accumulated her fatigue. The change to her confidence in her body and her support network may have shifted her attitude and beliefs in what she had previously believed, and this caused a sense of uncertainty and unfamiliarity that made her feel her self-identity had changed. Episodic waves of fatigue were often triggered by emotional and interpersonal events that created what she described as “treading treacle and crippling fatigue”. Without the consideration that the task performed (6MW) did not effectively elicit fatigability, it could be interpreted that emotional pressures evoked her experiences of fatigue, not necessarily physical triggers. Fatigue was the most debilitating and prominent feature of her MS, and without it, her MS seemed almost transparent regarding locomotion and physical ability.

10.3.1. Experiential findings of the 6MW and reflection for clinical assessment

Most participants reported feeling only a slight degree of fatigue after performing the 6MW. Fatigue was projected mostly through bodily function, in particular, the lower extremity through the assessment. The feeling of heaviness was expressed as they felt less control of coordination and balance by “foot scuffing” and “leg dragging”. No sudden fatigue was experienced by participants, as described in Chapter Six. However, there was a sense of determination to complete the assessment for the majority of participants. There was an element of feeling safe: if a participant felt comfortable in the surroundings of the assessment by familiarity of the environment (familiar with the MS centre) or safe foot placement (as it was flat and even ground), they expressed less fatigue due to a sense of feeling secure. Additionally, there was no added emotional stress to exacerbate their fatigue, as participants expressed comprehension of the tasks being performed. This reduced anxious thoughts which ultimately lessened their perception of fatigue. Participants did express the growing desire to rest after the whole assessment was completed, by sitting down and relaxing.

A few participants did portray signs of fatigue whilst interviewing, M105 slurred his speech in the last ten minutes of the interview, as did M096. The ability to articulate description was sometimes affected as their train of thought was impaired towards the end of the interview, demonstrating that the effects of assessment just conducted were tiring for some. These insights only reflect basic phenomenological reflections of experience in fatigue. The lack of fatigue experienced throughout the assessment led to a limited description of which guided the reflections into other experiences of fatigue. Nevertheless, this assists the concept and development of drawing out a continuum of fatigue on the ranges of fatigue and fatigability that is expanded in Figure 10.26.

10.3.1.1. Value of phenomenological perspective

In phenomenological oriented reflections, the researcher is interested in the invariant self-organising structure of an experience. Similar to experimental designs being informed by specific theories, can experiments be informed by phenomenological insights? As phenomenological researchers grasp the essential characteristics of the context of an experience or event, phenomenology could provide a foundation for an experimental design to assist in the development and progression of standardised testing.

MS participants reportedly didn’t fatigue as expected with the 6MW and assessment. Traditional methods of research wouldn’t capture description from the participants themselves on the different aspects of how the experimental design influenced them. Through phenomenological reflection, detail of experimental design and practice could perhaps be tailored to investigate and gain further precision on measurement and management. Without understanding the experience, predictions and suggestions could be misinterpreted and phenomenological reflection could enable the researcher to gain a more global understanding of the phenomenon under investigation. The use of phenomenological insights into experimental science does not only add to experimental science, it could also be used to verify phenomenological findings and results from such experimental designs. As Rasmussen states:

> [...] one of the most important methods of investigation is that of phenomenological description, in other words, the description of what we experience... In order to gain knowledge about the experienced situation, we must hold ourselves to what is present in consciousness, must describe the phenomenological situation as we say. [Rasmussen, 1997].

10.3.2. Claims made on the basis of the findings and direction of study

In 1996, Varela [1996] claimed that the neurophenomenological programme shed new light on the explanatory gap that separated objective physical processes from lived experience. As a result of this, decades later growing research has evolved and developed NP in novel, different paths. In this research, a naturalised phenomenological study was conducted to investigate fatigue and the meaning of fatigue. Nonetheless, what was articulated? Fatigue has been studied from multiple aspects from objective measures of ambulatory, muscular, and physiological fatigue, to subjective viewpoints, predominantly focussing on patient-reported outcome measures. However, the domains of fatigue have often been broken down, only giving insight into a partial view of fatigue.

By understanding the whole view from a lived experience stance, the aim of this research was to grasp a foundational understanding of the whole of fatigue. This, in turn, provided the opportunity to explore an aspect of fatigability measures and to reflect on the similarities and differences of fatigue as experienced. The findings indicate that there are many phenomena of fatigue, and this research demonstrates a whole range of MS fatigue experiences from unconscious and conscious components of an individual's life.

As discussed in this chapter, this research begins to open up the complexities of fatigue and reflects what the data is beginning to point to. Fatigue was experienced by all participants; however, not all participants experienced fatigability. In light of this, the aim of this research project was to make meaning of this unexplained void, to structurally search for the essential characteristics of fatigue as a whole. The following claims were raised:

1) Ambulatory physiological measures do measure a small degree of fatigue. However, in line with published literature, this remains to be inconsistent [Engelhard et al., 2016; Goldman et al., 2008; Huisanga et al., 2011]. The physiological measures were focused on motor fatigue, more specifically ambulatory fatigue. Gait deterioration was expected to be shown in measures of walking velocity and peak ω during the 6MW. As highlighted in the previous section, fatigability was displayed through a reduction in velocity and peak ω in some MS participants, but not universally. In Chapter Nine, it was suggested that confounding factors, such as the degree of disability and ambulatory ability, may have impacted these results. Further development should focus on the association between disability level and ambulatory ability (walking velocity), and current parameters to improve objective markers of ambulatory fatigue in pwMS.

2) The phenomenological data provided insight into fatigue and its domains. It touched on the foundations of emotions, bodily, and perceptive aspects of individuals' everydayness that cause deep disruption to their daily rhythm. The feeling of an all-consuming and absorbing fatigue experience aligns with Flensner et al. [2003], who described fatigue as involving the whole of a human being. On the other hand, the notion of body reversibility and the lack of ability to consciously or unconsciously instruct bodily movement was not previously described in the literature. In accordance with Merleau-Ponty [1968], the subject and the object are inseparable from one another. Fatigue has been expressed as impacting both the subject and the object intangible aspects that often overlap (namely, physical body exertion to cause mental fatigue). However, a suggestion of the body feeling separate from self was described by participants in this study; their perception of their body reflected fatigue in mannerisms out of their control. The study shed light on fatigue and its heightened confluence with stigma. Participants described a shift to how they see, feel, and believe about themselves due to their experiences of fatigue compared to prior their MS diagnosis. This shift fluctuated and could affect how pwMS function and move. There was a desire for acceptance of fatigue, for stigma to diminish and not structure their daily lives. PwMS continuously expressed an inner battle of dignity, and to navigate how fatigue affects their occupation, hobbies, social life, and whether and how to tell people about their illness. To maintain dignity required time and acceptance of both MS and fatigue. Confidence, and the lack of, seemed to play a prominent part in their battle with dignity. The changes fatigue caused gave a shift to an individual's identity and were experienced as violation of dignity. Nevertheless, Spencer et al. [2019] found as pwMS gain experience of living with MS, their adaptations to social aspects may provide them to mitigate the impact of their stigma and restore their dignity. This phenomenological investigation broadens our awareness about what pwMS experience and live daily.
3) Although there was an overlap in the impact of fatigue within bodily or cognitive dimensions of experience, fatigability was only demonstrated in a small number of MS participants who did physically fatigue. These findings highlight the distinction between subjective measures of fatigue and fatigability. Fatigue was described as a feeling of an ever-present sense of lack of ability that all participants described to some degree. Fatigability was described as a prolonged exertion that caused overstimulation of either cognitive or bodily exhaustion. In their 2018 study, Shahrbanian et al. [2018] reported that fatigue contributed to pain presence, further suggesting the association of common aetiology due to simultaneous damage of nerve fibres across different parts of the CNS

[Lublin & Reingold, 1996]. In this PhD study, little association between the two was established, and variety in the response in levels of exertion, disability, and quality of life to fatigue in pwMS was found. Although the 6MW was not successful in eliciting fatigability in all participants, the PwMS all described a “non-starter day” or “MS day”, which often described similarities to fatigue of complete and all engrossing exhaustion.

4) From phenomenological insight, it became apparent that to evoke fatigability, physical and cognitive exertion may not be the only stressor. Some participants described emotional stressors which may have influenced and impacted fatigue and fatigability. Emotional fatigue was described as being affected by interpersonal and contextual factors that caused an alteration in the way they went about their lives. This description of fatigue would cause feelings of complete exhaustion where levels of concentration, energy, and functionality would dramatically decrease. The embodied action of fatigue should be further explored as the significance and association to emotional well-being and bodily implications are two interwoven aspects of fatigue that could reveal and deepen our understanding of fatigue as a whole. Moreover, consideration within the experimental protocol in relation to stigma and dignity, and its impact on ambulatory performance and fatigue, should be explored. As mentioned in claim 2, stigma and dignity were described to affect an individual’s functional ability on daily experiences, how they perceive and feel about themselves, and their body. This may have fundamentally flawed the experimental protocol in this study, as their view and attitude of themselves and how they think others see them, could have impacted how they performed and walked. Any level of psychological stress, conscious thought and awareness of their fatigue could, in itself, navigate their experience of fatigue. Most participants in this study stated the comfort of participating in a safe environment (familiar environment, flat floor for foot placement, and clear understanding of what is expected from them). From a generalised perspective, it could be argued that this caused little psychological stress to most of the participants, which may have resulted in little exacerbation of fatigue and/or fatigability. This could have been a flaw in the walking tests for this study. One suggestion to further investigate this could be the dual task paradigm. The dual task is conducted in experimental neuropsychology and is the ability to perform two tasks simultaneously to assess the performance compared to single task conditions [Hamilton et al., 2009]. Dual tasks with ‘walking and talking’ have been conducted in a MS cohort to investigate motor function and attention [Hamilton et al., 2009], postural performance [Jacobs & Kasser, 2012], memory impairment [D’Esposito et al., 1996], and muscle fatigue [Wolkorte et al., 2015]. It could be used to explore the interference, if any,

with fatigue in pwMS with different cognitive and motor tasks to exert a level of psychological stress. It could provide valuable insight into how pwMS process and experience fatigue. Overall, there may be many types of MS fatigue, including emotion-related fatigue, physical-related fatigue, and depression-related fatigue, that may be different from each other. The importance of understanding this could shape and tailor the direction of fatigue intervention programmes.

5) The importance of understanding disability and its association with fatigue was highlighted. As in previous research [Shema-Shiratzky et al., 2019; van der Linden et al., 2018], fatigability only became more apparent in individuals who were at least moderately disabled. As stated previously, fatigue may be experienced by all pwMS, but fatigability is increasingly likely to provoke a physiological response that only a small number of individuals in this research experienced. To understand the degree of disability, the rate of change or exertion, and its role in fatigability, in future studies, researchers should investigate each level of disability and its relationship to the exertion of fatigability.

10.3.3. Epistemological implications of naturalised phenomenology, the question of co-constitution[16]

How knowledge is acquired in different scientific disciplines varies depending on what is known to be true and how researchers determine this knowledge. Within MMR and naturalised phenomenology, a division of epistemic justification lies between the two paradigms and is still continuously debated within the field. Nevertheless, the understanding of human experience and behaviour have led to the development of a new scientific understanding of self-consciousness and the embodied self within naturalised phenomenology [Bitbol, 2012; Bockelman et al., 2013; Lutz et al., 2002, 2007; Reinerman-Jones et al., 2013; Thompson et al., 2005]. In this present PhD study, the usefulness of this methodology in investigating multiple aspects of fatigue from diverse disciplines was explored.

Emotional fatigue seems to emerge as the footbridge between physical processes and an instinctive feeling that is all-encompassing and therefore affects performance and wakefulness. Even though the findings from this research do not provide an explanation on how the footbridge between emotional stressors and the bodily implications of fatigue occurs, they do seem to indicate an additional aspect of MS fatigue that had not previously been established

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[16] For the first and third person, in this instance, to be used and work together, phenomenological and physiological research.

within the literature that is ripe for further exploration. This reflects the embodied action of fatigue, which Gallagher refers to as body image [2003]. Body image, in this regard, is a conscious image that is disintegrated but appears to be somewhat differentiated from its surrounding environment. Within this research, a few participants established the congruence between emotional stressors and a heightened sense of fatigue and fatigability that caused a change to their body image. Characteristics of frustration and anxiety were provoked either by interpersonal factors or the inability to process and perform simple tasks that caused stigma. The relationship between emotional well-being and bodily being is shifted by fatigue, which alters an individual's complete lifeworld. Phenomenological insights alongside experimental procedures could not only enrich our understanding of fatigue and its impact, but also aid in the development of management programmes and interventions for individuals who suffer from MS fatigue.

Through this and other studies [Shema-Shiratzky et al., 2019; van der Linden et al., 2018], another forethought on correlation runs between disability and fatigability. Accurate and clear measures of disability in relation to the degree and level of disability would ultimately create a clearer vision of fatigability and whether the degree of disability is associated with the impact of fatigability. Additionally, this would develop our understanding of fatigue and fatigability to gain further insight into the direct association between the two and grasp the significant, if any, with stigma and dignity to fatigue and fatigability. The data non significantly but subtly indicates elements of ambulatory fatigability biomarkers through velocity and peak ω. However, future research is needed to elucidate the relationship between disability and fatigability to clarify the whole meaning of fatigue.

10.2.3.1. Co-constitution of first and third persons

For NP to evolve and progress within research, approaches to establish a co-constitution between the first- and third-person should be given due consideration. As discussed in Chapter Six, researchers have suggested various propositions to dissolve some implications of NP regarding frameworks and stances. Firstly, Mayoh & Onwueguzie [2013] proposed parallels within axiological and methodological frameworks of phenomenological and physiological research. Ethics play a key role in forming a research question and understanding the issue around the research topic [Biddle & Schafft, 2014]. Preunderstanding within an individual recognises the unconscious network of attitudes and beliefs which ultimately influence, to some degree, an individual irrespective of motive and theories. Therefore, an individual is never completely value-free. Methodologically, quantitative researchers attempt to minimise these values in order to focus on the hypothesis and increase validity. Descriptive phenomenologists follow a method of recognising and constraining the role of the researcher, reflecting on preunderstanding and a set of procedures to give primacy to the phenomenon without a theoretical influence, so that the data points to the phenomenon. Despite epistemological differences, the underlying value and methodological context can arguably provide justification for combining phenomenology and physiological measures. Useful parallels can be met between axiological and methodological frameworks and new insights can emerge, which was attempted in this research.

The Varelian stance was indicated by Bitbol [2012] as neuro-materialist and anti-physical, and an approach that attempts to lead to an epistemic abundance and immersion of a multidimensional practice of phenomenology and scientific inquiry. As stated above, to capture one single encompassing theory within a methodology would be done with great difficulty due to the different values and motives within science [Varela, 1996]. However, by widening the field of attention by considering a modification to our reflection, awareness, and perception of one’s present situation, our perception of science and rigidity of theories and practical training could change [Bitbol, 2012].

This research highlights the strengths within phenomenology and physiologically based science to understand the process of co-determination of the subjective and objective poles of fatigue within MS. Agreeing with Petitmengin et al. [2007], the future questions are not to try and eliminate subjectivity and objectivity, but to better observe how lived experiences intervene at all stages of the co-constitution. Proponents of NP aim to reveal the congruence between two sets of data, not suppress it. Fatigue in this study was found to be layered in multitudinous ways and is a multi-factorial process. Fatigue as experienced impacts aspects of fatigability, as embodiment was central to participants in this study, even though the direct relationship remains unknown. Bodily, emotional, cognitive, and psychosocial aspects all influence the performance of fatigue, depending on the individual and their stressors.

10.4. Attempting to integrate findings of fatigue as experienced and physiological measures.

It would be difficult to interpret the direct relationship between phenomenological and physiological data, due to the conceptual and methodological issues regarding first- and third-person accounts. However, to facilitate the range of experiences and physiological parameters of a fatigue, a continuum may help in the navigation of understanding of the congruence between the two (Figure 10.26). The overlapping circles in the continuum of phenomenological findings demonstrate the interconnectivity of experiences and how they intertwine with each other. The fluidity of described experiences is often not defined as a singular aspect, it was often reported with other influences and factors that infiltrate the different constituents of fatigue. The continuum should be looked upon as a point of emphasis that does not necessarily directly affirm classifications of fatigue but demonstrates fatigue and its many variants.

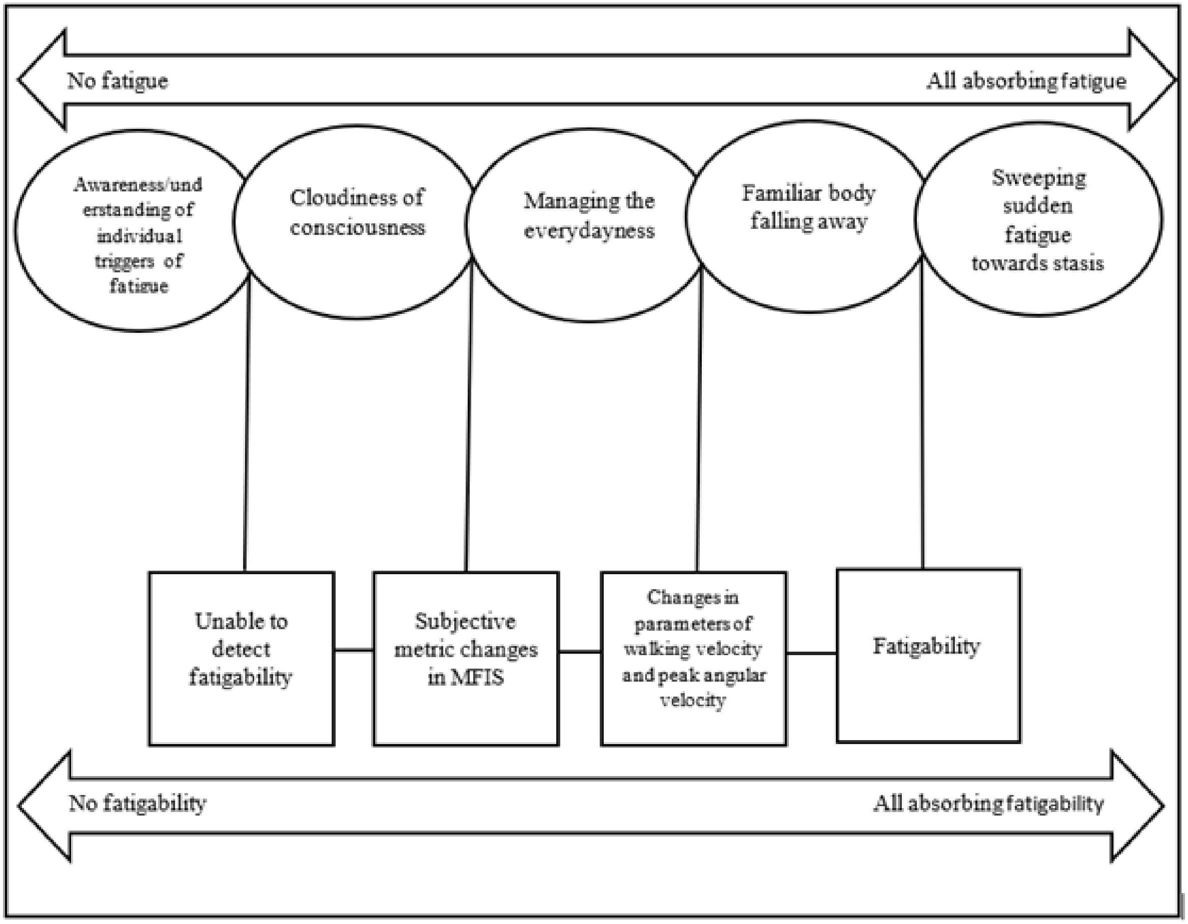


Figure 10.26.: Continuum line of phenomenological and physiological findings of fatigue.

The phenomenological findings grasped all constituents of fatigue as MS participants described their experiences of fatigue in depth and detail. The first dimension of the continuum was the awareness of individual triggers that were perceived as cause for any aspect of fatigue. An element of meta-awareness of fatigue was commonly reported in MS participants, as they learned over time to understand what their body and self-capacity were capable of before fatigue would affect them. Various forms of overstimulation would often trigger fatigue in a participant. Universally, it was agreed that numerous forms of physical exertion could exacerbate fatigue in all constituents. Sustained, continuous physical movement of standing upright or queuing for a prolonged period of time or after an exercise class would aggravate bodily fatigue and “brain fog” that was commonly described by the participants.

The processing of information continuously for a prolonged period of time was often described as a factor that would also cause “brain fog”. Social situations that typically had elevated external noises, of people talking or surrounding static noises, would require an increase in the level of concentration that ultimately would impact levels of fatigue. The time of day tended to exacerbate experiences of fatigue. Typically, heightened feeling of fatigue were reported in mid- to late-afternoon. At this stage of awareness, fatigability is undetectable. The body has not been exposed to motor exertion that causes considerable bodily weakness. However, the findings of this study indicate that pwMS gain a clear understanding of what exacerbates their fatigue and fatigability, irrespective of the “MS days” and “non-starter days”; pwMS generally have a grounded comprehension of their fatigue.

Cloudiness of consciousness influenced their ‘state of mind’ and the sense of being whole. Certain triggers would cause a level of inability to understand and think clearly. The cloudiness would impact judgment and some participants would avoid decision making until fatigue had subsided. The haziness described would cause simple tasks to be confusing and frustrating and would affect sustained attention. Subjective metrics of self-reported fatigue identified that MS participants were more likely to be impacted by cognitive fatigue in their everydayness. At this point on the continuum, only subjective reports of fatigue were quantifiable, suggesting fatigability does not occur at this stage. Interestingly, there were descriptions of feelings of fatigue after the performance of the 6MW in some participants. However, there was little illustration of this through the physiological measurements. As reiterated throughout this thesis, the 6MW was used and has been previously performed to elicit fatigability in pwMS [Goldman et al., 2008]. Hence, there was a component of fatigued experienced through physical exertion of sustained walking, albeit the walking test didn’t convey significant biomarkers of fatigability. Thus, the 6MW might not elicit fatigability in all mild to moderately disabled people, but it may elicit bodily-related fatigue and other aspects of fatigue.

Although participants were aware of the body alterations, their body imagery reflected fatigue in mannerisms that were sometimes out of their control. The unnatural movement of basic locomotion was typically described as a neglected sense of body detachment, that went from unconscious to conscious movement whilst experiencing fatigue. The body schema was often reported to have altered, as the automation of movement, such as walking, became visible for the individual. Some participants expressed the conscious prompting of leg placement that gave an experience of body detachment from the self and the body. The experience of little control over their lower extremity led some participants to feel as if they had to re-learn to walk, due to a disconnection between their bodily movement and self. Participants were generally aware of their body imagery regarding posture and general stance. Although almost hyper-aware of the perception of their body, participants expressed little control over their body. The unintentional change in body imagery shifted their body identity into being-in-the-world only as they know now. The body is more than an objective, physiological body, it is the centre of all systems coordinates. However, MS fatigue can disrupt the centre of systems as the orientation and bodily intentions can change unintentionally. The reduction in bodily control with daily tasks was described as a whole-body phenomenon.

The patient, Schneider, described by Gelb & Goldstein [Embree,1980] described body schema to play an important role. The patient was able to perform bodily movement successfully without concern, but with his eyes closed, he could not identify which part of his body was being touched, or the position of his limbs. The movement was only feasible when he could watch his movement and positioning [Embree, 1980]. According to Merleau-Ponty, a casual explanation of this functionality is not possible: “Behaviour is unity, and only from this viewpoint can the data be understood” [Merleau-Ponty & Landes, 2013]. The patient was lacking muscular movement intentionality, and it was not possible to appropriately understand the illness and patient from an objectivist or inductivist perspective. The illness cannot be objectified as a matter of fact that cannot be explained through a rationalistic explanation. It is better understood as a bodily one of being-in-the-world, where consciousness, body, and world are a unity. The aspect of “being” as the correlate of “being known” is a concept Merleau-Ponty discussed, to highlight how the body and world are interwoven [Tiemersma, 1982].

To do most everyday activities, the combination of real and abstract movement (the body schema and body image) come together to appropriately perform a movement for a task or activity. However, if one of these is compromised, the smooth orientation and adjustment for performing this task become disjointed and unbalanced [Wehrle, 2020]. To perform an abstract movement, one must be able to imagine and anticipate the movement. This was something Schneider was unable to do, as his body image does not anticipate all movements [Embree, 1980]. Hence, without the aspect of having a body and a sense of self-movement, body schema and real movement are limited.

Certain elements of fatigue could be considered in a similar light. There was an unknowing presence of fatigue with the participants, but this was somewhat invisible to others and pwMS. The invisibility lived through lived time was always present, but was bodily perceived as fallen away or lost. Fatigue would cause a disruption to an MS participant's movement. Participants were aware of their abstract movement and could anticipate putting one leg in front of the other, yet were unable to smoothly orientate their legs for walking without sole instruction and concentration. The body schema was impacted and did not function in the typical automated way. The complexity of the lived body in relation to lived time created a disrupted phenomenon for participants.

To further this thought, the "habit" explanation given by Merleau-Ponty incorporates the idea of having no hard division between pre-reflexive bodily knowledge and bodily context, which cannot be exclusively explained by neurological processes [Moya, 2014]. According to Merleau-Ponty, there is a unity of behaviour that aims to express intentionality between the two [Merleau-Ponty, 1963]. The lived body relates to a body that is incorporated into a world that carries out its operations. However, there is no representation established between the movement of the body and the world. There is a form of dialogue between the body and the world, in which each responds, depending on the environment and bodily state. The role of habits is to establish those behaviours and understand the habitual body (that of general and pre-reflexive existence) from the actual body (that of personal and reflexive existence) and the co-penetration with each other [Merleau-Ponty, 1963]. The behaviours of an individual with CNS damage are more likely to have a broken habitual and actual body dialogue. In this research, the inability to readjust the habitual and actual body is dislodged by fatigue as walking was disrupted.

For instance, learning to drive requires a continuous monitoring of actions that require an individual to process and think of each step required to drive and move a car. During this process, the individual is aware of each step they take to accomplish the task. Nevertheless, with practice, the new skill becomes embedded within the individual, and no longer requires thought of each action. This ability acquired "will lead to performance without explicit monitoring of bodily movement, the skill will be fully embodied and embedded within the proper context" [Gallagher & Zahavi, 2008]. The dialogue between the body and the world is now embedded in the individual whilst driving. However, the “sixth sense” between the body and the world for pwMS with fatigue is intangible, as the communication between thought and action is disrupted. This can be an extension of the concept of proprioception, the sense that lets us perceive location, movement, and action of the body is relative to body image. The control of the movement with fatigue is lost, as the body schema of walking is no longer performing in an automated motor-sensory way. The dislodging of body schema causes the individual to consciously reiterate operationalised movement of intentional walking. From a reductionist perspective the idea of having no hard division between pre-reflexive bodily knowledge and bodily context can be somewhat related to the theory of predictive coding of fatigue [Greenhouse-Tucknott et al., 2020]. From a basic understanding, predictive coding is proposed as multi-level cortical systems to transfer prediction and prediction error from higher to lower levels of the body to serve predictions and make informed judgments [Greenhouse-Tucknott et al., 2020; Rao & Ballard, 1999]. When an automated movement (from a prediction) is misjudged, an ‘error signal’ occurs, therefore not relying on an automation that was expected (for example, when you are catching a ball and it starts travelling slightly left of where you expect so you reflexively/subconsciously adjust your hand's position). The subconscious movement/prediction (moving your hand to catch the ball), becomes a conscious movement (readjusting the hand, by an accumulation of error signals, to catch the ball). The accumulation of error signals for pwMS could easily be fatiguing due to the constant conscious adjustment that cause ‘error signals’. The predictive model suggests the relationship between the perception of fatigue and effort may be associated; ‘error signals’ occur based on the perception of effort, which can generate the feeling of fatigue if continuously experienced. Therefore, similar to the discussion in section 10.3.2., the self-awareness of specific beliefs (stigma, dignity) will heighten the chance of ‘error signals’ in this model and generates the elevation of effort and fatigue.

Although approached tentatively, fatigue somehow unhinges the co-penetration between the habitual body and the actual body. To yield back to the physiological measurement used in this research, the specific measurement of walking velocity and peak ω fails to significantly identify the disconnection of the co-penetration that occurs with fatigue. As stated previously, it must not be discounted that the 6MW did not elicit fatigability in all participants, which resulted in nonsignificant findings. However, if fatigability was demonstrated in all participants through walking, would the relationship between the habitual and actual body be clearer?

At the upper constituent of the continuum is the sweeping sudden stasis of fatigue that participants experienced. The extremity of fatigue was often described with little reasonable explanation. The extreme and sudden limitation to most senses was commonly reported. The bodily movement was completely restricted, thoughts and intellectual responses were restrained, and all social activities had to be paused due to this overwhelming feeling. all PwMS (but not our healthy participants) occasionally referred to fatigue without an onset or trigger, which was described as a “non-starter” day. In this context, participants were unable to explain their reasoning or belief as to why they experienced this severity of fatigue. However, it could be closely related to the feelings participants described with fatigue. The overwhelming element of fatigue was close to exhaustion, as it consumed any energy a participant had and was intractable from their actual and habitual body. The all-absorbing nature was often reported with no preconception or awareness of embodiment. The wave of fatigue was typically described in conjunction with confusion followed by an element of stasis and motionless. There was a feeling of an almost catatonic state, as the dialogue between the habitual and actual body was evidently disrupted. There was also dramatic shift of adjustment from bodily familiarity, as a sense of losing control over fatigue as the whole body became unresponsive. The severity of experiencing this oppressive fatigue and its impact was often hard to palpate for participants, as it was often a debilitation of all senses.

Fatigue is seen as a barrier. The profound nature of fatigue and the invisibility of it makes it difficult to manage because of the lack of projection for others to understand, and it’s not something individuals can clearly perceive. Flensner et al. [2003] discussed the phenomenon of fatigue and found a variety of constructive and non-constructive perceptions. Fatigue was always present, and time-consuming. Even when not fatigued, it would always be on pwMS’ minds and was taken into consideration when going about their daily lives. Similarly, in the present study, participants found fatigue to feel unnatural, as the body either felt heavy or not quite awake. In this study, participants reported natural movement to become unnatural, as everyday activities such as walking required vigilance and constant monitoring. There were restrictions on life and a sense of dependency, as fatigue would not allow daily activities without disruption. Flensner et al. [2003] found pwMS had a desire for acceptance and structured daily living of the disturbance of fatigue. However, acceptance wasn’t necessarily a desire but a process in the present study. The process and acceptance were emphasised as important, as once the adaptation of selfhood and identity were familiar to the individual, fatigue levels reportedly improved and allowed for improved fatigue management. The uncertainty of fatigue on all levels, from pathophysiology to the mannerisms of everyday fatigue, may have accentuated the unreliable and capricious feeling of such a varying symptom (stigma).

Kluger et al. [2013] reported that fatigue remains fundamentally unclear in definition and terminology and this hinders the progression of management and interventions for fatigue. The investigation between the two, fatigue and fatigability, has mostly relied on self-reported questionnaires and objective measures of fatigue, but these lack the precise and reliable first-person accounts which phenomenology allows.

Reflecting phenomenological and physiological structures enabled the further clarification of fatigue in this research. The direct experience of general structures and objectivistic science is likely to lead to a better comprehension of the spatial character of the human body [Tiemersma, 1982]. Although both structures are still rough, they permit a certain correspondence between physiological measures and the subjective experience analysed. The cases of fatigue demonstrated solid aspects of fatigue as experienced through bodily changes and encounters that impacted participants in subtle but unique ways. This, to some degree, was exhibited in physiological measures, as some participants suggested ambulatory fatigability, but the bodily changes were small, vacillating and demonstrated inconsistency.

The cases of fatigue do highlight the significance of the deep disruption fatigue causes to pwMS and the assortment fatigue presents itself. The attempt in this research to establish footbridges between physiological and phenomenological data only enable the beginnings of detection from one side of fatigue to the other, from multiple aspects. They enable better fatigue anticipation and a full comprehension of mannerisms, in the hope to allow better measurement and management. The continuum aids further investigation of the range of manifestations of fatigue that could provide a more unified perspective of fatigue and its behaviour.

10.4.1. Limitations

10.4.1.1. Experimental limitations

Although briefly discussed at the beginning of the chapter, in terms of experimental limitations, a small cohort of pwMS does not truly represent a full MS population. Hence, any assumptions made in significantly smaller sample sizes may be inaccurate and skewed, which would not truly reflect the results. In this research, to gather data to appropriately identify and confirm gait deterioration, a small size would not suffice and confirm fatigue in gait deterioration.

Another limitation lies in the use of the self-administered EDSS (or EDSS-S). Although advantageous for time consumption, Bowen et al. [2001] observed EDSS-S consistently scored within a maximum range of one point higher than the physician-administered EDSS in more than 70% of cases. This could result in higher levels of disability scores, which could be interpreted as an inaccurate representation of disability severity. In this research, the average EDSS-S score was calculated at 5.13, but with different disability measurements a different output could have been calculated that could have affected the overall interpretation of disability and fatigue. Therefore, efficacy of disability measures would be required to further evaluate the sensitivity to changes in disability in relation to fatigue.

The inconsistent results may reflect on the inconsistency of pwMS in relation to the degree of disability, ambulatory ability, and variability of fatigue and, the potential of variability in the protocol. The inclusion criteria did not include pwMS who have established fatigue (with a specific measure of fatigue, for example, a fatigue questionnaire), although it was emphasised to participate if experiences of fatigue were common. The inclusion criterion were predominantly based on disability (EDSS-S), and their ability to walk 100m unaided, therefore, the inconsistencies could have stemmed from this. For most studies investigating fatigue, the inconsistencies within the experiences of fatigue as discussed in chapter seven may have affected the overall results. PwMS experience good and bad days ("non starter" or "MS" day) with an aspect of unpredictability for when these days occur. The uncertainty and wide array of experiences create further difficulty to grasp and comprehend fatigue. The experimental design had inconsistencies with the conduction of timing of day and format and timings of the walking tests themselves. Due to room availability, the conduction of the experiment was not consistent in relation to the time of day. As established in previous research [Iriarte et al., 2000], fatigue is likely to progress and worsen throughout the course of the day. With this in mind, participants who participated in morning experiments could have produced different results if they had participated in the afternoon. If all pwMS participated at the same time point in the afternoon, fatigability measures could have potentially been significantly produced. As suggested at the beginning of this chapter, the T25FW test may have been performed too late after the 6MW (1-3 minutes later), which may have resulted in individuals no longer experiencing fatigue.

Furthermore, the study was cross-sectional, which limits the efficient evaluation of the gait parameters used in monitoring fatigue and gait deterioration over a specified time period [Witchel et al., 2018].

10.4.1.2. Methodological limitations

According to Gallagher et al. [2015], “Neurophenomenology is a method like gathering grapes from different vineyards, tasting and comparing, and possibly blending to attain the best vintage. As it is used, it matures and attains more clarification.” Both phenomenology and physiology, bring about a unique set of tools to study a specific phenomenon; however, they both have different starting points and assumptions of which raise concern over methodological implications. The methodological division creates difficulty in establishing any congruence between physiological analysis and phenomenological description.

Ideally, phenomenological reflection should complement physiological analyses and provide insight into findings that traditional measures can sometimes overlook. However, without distinct findings, such as in the present research, the combination of both sets of data can become unclear and presents the challenge of how to truly relate phenomenology and natural physiological findings to one another. This conceptual issue, of the ability to report and integrate results, remains problematic.

Phenomenology is not something that can be solely reduced to mathematics, as it would lose its meaning as a methodology and its strength to grasp the fruitful description of a given experience. Nonetheless, Bockelman et al. [2013] suggested a degree of verification where interpreting the naturalised phenomenological data may add confidence to the basic findings. The idea of a sliding qualitative scale of effect after the conduction of the interviews could provide support to the textual analyses of the interviews. It could provide simple correlations and comparisons that initially bridge the datasets together. Using such a scale does not capture the full and unique lived experiences and should only be used in attempt to narrow the explanatory gap alongside phenomenological analysis. This approach may support and assist in resolving and narrowing part of the explanatory gap within naturalised phenomenology. These suggestions follow a similar approach to Northoff & Heinzel [2009], who investigated emotions using the combination of first- and third-person data. The continuous first-person experience can be obtained on a continuum scale between one to nine emotional manners. The transformation can then be directly related to neuronal states correlated as measured in fMRI. However, numerical values are not identical to emotional experience itself and the experience should not be disregarded.

Some critics may draw attention to another limitation that lies with the issue of epistemology, the concern of bias and distortion of an experience. Although phenomenologists hold that only our experience of the world, direct and subjective human experience is comprehensible, other scientific perspectives may counter argue that first-person accounts raise epistemological issues about meta-awareness to first order experience. For instance, it has been discussed in experimental psychology that human memory is not an exact reproduction of past experiences, but instead can be a flawed process that is susceptible to various errors and distortions [Brainerd & Reyna, 2008].

In addition to this, in research involving fatigue, especially in circumstances where an individual may be experiencing fatigue, some could argue that a participant's memory of an experience may be distorted. Reflecting on the present study, the process may have caused new or misleading reflections on a participant’s experience of fatigue due to the experimental design of the study (ambulation assessment followed by a phenomenological interview). That is unknowingly focussing on how participants were physically and bodily affected by fatigue. However, from a phenomenological perspective, it is believed the experience in itself is the most direct and ‘knowable’ source to understand the given experience of fatigue.

Proponents of naturalised phenomenology aim to avoid predefined categories by reducing external biases and using the participant’s experience as a genuine source of data [Gallagher et al., 2015]. Descriptive phenomenologists aim to bracket all previous judgment and previous knowledge of the phenomenon under investigation in order for the researcher to focus attention on the pure experiences of the participants. However, as stated above, the interviews were conducted after the assessment to appropriately reflect on their experiences of fatigue. This in itself could have affected, consciously or unconsciously, the participants’ judgments on what to reflect on. This distortion may have caused imperfect reflections on experiences of fatigue. However, participants could independently show greater coherence than others between self-affective states and awareness of experiences. Therefore, first-person experiences still hold great value and importance in the study of human experience and behaviour.

As this was intended as an exploratory study, the key constituents that have emerged within the data are interpretations of MS fatigue experiences. The researcher is aware of and acknowledges that different researchers may interpret the data in different ways and therefore, although the findings are inconclusive, believes they contribute significantly to the identification of areas for further investigation. However, by staying close to participants’ experiences, the interpretations do offer provocative insights into the experiences of MS fatigue as described by the participants.

There remain significant challenges regarding methodological issues, but there is reason to believe, based on the findings, that naturalised phenomenology can contribute to providing a better understanding of complex human experiences. As a researcher, I believe that by adopting phenomenological approaches, researchers can open up clarifications and classifications that are not captured in physiological approaches. Used together, these approaches can offer a new methodology to assist in the development of new research, particularly for MS fatigue as well as other experiences.

Chapter Eleven: Conclusion

This PhD comprises research exploring contextualised observations of fatigue as experienced, compared to gait changes in velocity and peak ω in pwMS. In the thesis, the phenomenological and ambulatory literature was methodically explored to devise and construct a naturalised phenomenological study.

The objective was to conduct a trifold experiment:

1) To grasp the constituents of MS fatigue through rich phenomenological reflection. Through the phenomenological interview and analysis, all aspects of participants' everydayness was grasped, allowing for an all-encompassing description of the foundations of fatigue through the lens of pwMS themselves.
2) To measure the velocity and peak ω throughout the execution of the 6MW at the thigh and ankle. Through gait assessment, the changes of each consecutive minute was evaluated to develop an objective marker of fatigability in pwMS.
3) The sets of data were then formed into fatigue case examples, so that the similarities and differences between holistic "subjective" reports of fatigue and "objective" ambulatory measurements could be explored.

The identification of fatigability through ambulation was not possible in this research, which consequently led to an insufficient integration of results. However, bodily changes to imagery and perception of fatigue to centralise and impact a pwMS' selfhood was revealed. Before elaborating and directing towards future research, in this concluding chapter will serve as a guide through the relevant chapters that intrinsically led the reader to this chapter.

11.1. Summary of chapters

Two scoping literature reviews were conducted to investigate fatigue within the two disciplines of research incorporated in this thesis. In Chapter Two, the current experiences of fatigue through the lens of pwMS was summarised. There was agreement in the literature regarding the unpredictable nature of fatigue and the multiple layers that affected pwMS' everydayness in many bodily, cognitive, psychological, and social aspects.

Fatigue was seen as a barrier. Bodily changes of motor weakness, cognitive changes of a decline in speed and alertness, and social alterations of increased self-isolation due to certain limitations caused a reduction in social activity.

PwMS considered perceived fatigue and the perception of others of significant importance. Their self-identity of such was divided into two aspects: identifying and highlighting their MS and fatigue to others, and wanting to keep their body imagery to others prior to diagnosis. In this chapter, a clear understanding of pwMS' experiences of physicality and bodily implications of fatigue was established. This directed the researched to question movement and bodily function approaches, and explore the factors that could aid the development of improving body and body imagery within and as observed.

In Chapter Three, ambulatory fatigue in pwMS was investigated with the use of wearable sensor technology to explore gait changes. A variety of parameters were found to be used in attempt to objectively identify fatigue. However, no gold standard was established in the current literature due to inconsistencies and factors impacting results.

The 6MW was commonly used to assess fatigability, where alterations and gait deterioration in the lower extremity ROM, cadence, velocity, warp, and DTW scores decreased in moderately disabled pwMS [Engelhard et al., 2016; Moon et al., 2017; Motta et al., 2016; Shema-Shiratzky et al., 2019]. Researchers highlighted that disease severity and experimental design could have impacted their overall results. The degree of disability was pinpointed to have a level of association with fatigue [Shema-Shiratzky et al., 2019]. It is expected that mild, moderate, and severe levels of disability are all impacted differently in relation to ambulatory fatigue. Also, walk surfaces with treadmills and walkways varying in length could all influence gait characterisations and the overall analysis and interpretations of results. Consequently, the direct comparison between studies was increasingly difficult due to the difference in methods and data analysis. Nevertheless, overall gait deterioration was found in parameters of velocity, step length and time, lower extremity ROM, and DTW pathology in the majority of studies [Engelhard et al., 2016; Moon et al., 2017; Motta et al., 2016; Shema-Shiratzky et al., 2019]. It was concluded that there was inconsistency within objective markers of motor ambulatory fatigue. Thus, qualitative research may assist in ironing out factors impacting fatigue that could guide the direction of accurate and precise measurement. Both reviews were used to guide the development of the experiential components of fatigue through fatigue as experienced and the association with gait parameters.

In Chapter Four, it was found that in a limited number of studies, the direct relationship between patient-reported experiences and physiological measures of ambulatory fatigue were explored. It is suggested in the literature that there is a degree of correspondence between descriptions of fatigue and walking capacity, but this is weak and inconsistent [Dalgas et al., 2018; Loy et al., 2017]. It remains unclear whether fatigue directly affects walking or vice versa [Dalgas et al., 2018; Filli et al., 2018; Hebert & Corboy, 2013; Kempen et al., 2012; Sacco et al., 2011; Socie et al., 2013]. Although these studies illustrate aspects of an individual's experience of fatigue, questionnaires arguably do not fully reflect the lived experiences of fatigue and provide a limited explanation of the variance of experiences. Thus, the whole phenomenon of fatigue is not conveyed. This informed the development of this research, to unravel a clearer picture to gauge the congruence between first-person accounts (fatigue) to third-person accounts (fatigability).

This study was novel due to the methodological approach which enabled the exploration of fatigue in two diverse disciplines of research. By adopting a naturalised phenomenological approach, the researcher aimed to highlight the strengths of both sets of data, and establish new light on the whole phenomenon under investigation. Fatigue in this study was explored phenomenologically and through motor, ambulatory fatigue, to gain both "subjective" and "objective" viewpoints. Phenomenologically, fatigue was experienced and broken down into four constituents: 1) familiar body falling away, 2) sweeping sudden fatigue towards stasis, 3) cloudiness of consciousness, and 4) managing the everydayness. Fatigue was described considerably through the lived body as embodiment infused participants in their everydayness. Bodily function was impacted by all aspects of physical, cognitive, psychological, and social elements of their lives. It was described as a journey of acceptance between fatigue, fatigability, and the ever-present impacting aspects that effectively changed their everydayness, body image, and perception. Embodiment was centralised in participants as their interactive processes were often disrupted. Physical projections of swaying, scuffing of feet, and leg dragging were frequently described to disrupt everydayness.

At the extreme side and heaviness of fatigue, the constituent of sweeping sudden fatigue was discovered. Fatigue often caused a feeling of temporary debilitation to most senses. The management of such extremity was only dealt with by participants understanding their own individual limits before a wave of fatigue was triggered. An element of body disengagement as a dislodge from the self and a dislocation from the body made participants hyper-aware of the feeling of instructing their body to move. A simple task would suddenly be of great difficulty and often there was an inability to do anything but rest.

As well as bodily impairment, participants described a degree of intellectual and emotional fatigue. Haziness of sustained attention, memory, speed, and flexibility were affected by everyday fatigue. Participants’ state of mind, and consequently their sense of being whole ,was altered as daily activities that involved comprehension, decision-making and judgment could unwillingly and unpredictably change the course of their day. The inability to not fully comprehend a task, process, or activity often caused an emotional fatigue. Frustration from this disruption caused a hindrance in going about their daily activities.

The final theme engaged the everydayness of fatigue with MS. Time management was key: all participants agreed lifestyle adaptation of dietary, work, and exercise changes were necessary. The consensus of managing daily fatigue was often strategic and required a level of acceptance and adaptation in order to cope with all other lifeworlds. Without management strategies, there was a level of fear and anxiety of exacerbating their fatigue. Knowing, and understanding the limit of all bodily, mental, and emotional elements that pwMS are able to do without fatigue, as without it, fatigue would infiltrate their everydayness. Overall, fluctuating bodily alterations affected participants’ selfhood, and they had to accept a new identity. A mixture of emotions was caused by the portrayal of others and how they acted and viewed them with this new identity. It revealed embodiment and selfhood at the core of the fatigue continuum of experiences.

Fatigability was sought through ambulatory measurement that identified velocity and peak ω. The 6MW did illustrate signs of gait deterioration in peak ω values in the thigh, but this was not demonstrated in all participants. Parameters were determined at each consecutive minute of the 6MW that analysed peak ω of the thigh and ankle of each minute compared to the first to identify the deviation from minute one. Further fatigability measures were composed of walking velocity measures of distance covered in minute one to minute six of the 6MW, and duration of T25FW pre- and post-6MW. On average, participants only demonstrated a subtle 0.08 second difference slower in T25FW post 6MW and covered 4m less in distance from the first to last minute. In comparison to the older healthy cohort, MS participants had a significantly reduced peak ω at the thigh and ankle, whilst their inter-step interval was higher as they took longer to perform each inter-step. Overall, the results indicated a subtle rate of change in velocity and peak ω. Nevertheless, the results were not significant and further research involving a larger cohort of pwMS is needed to establish a biomarker for fatigability.

In order to explore gait characterisations in pwMS, TD methods were conducted. TD characterisations in three signals in NGIMU sensors (x-io) were explored in Chapter Eight. TD was used as part of the process to investigate ambulatory fatigue in order to eliminate the turns to appropriately analyse gait velocity and peak ω changes in MS participants. The three signals were magnetometry and accelerometer signals compared to gyroscopy methods (used as the ground truth method) in older healthy and MS populations. In this sub-study, there was recognition of magnetometry signals for both the older healthy and MS cohorts located at the sternum compared to gyroscopy signals was 99.85% and 98.66% accurate, respectively. The findings indicated that magnetometry can be used in conjunction with gyroscopy methods for 180-degree TD in older healthy and MS populations.

The integrative key finding was centralised around how the perception of fatigue can impact the experiences of fatigue. Embodiment is a multilevel phenomenon: it is an interplay between the body, components of the body, and the world the body lives in [Krieger, 2005]. It can be defined slightly differently depending on the discipline of science. Psychologists would explain embodiment as the congruence of the brain and the body's physiological processes, whereas philosophers see embodiment as the concept that binds an intentional object and phenomena [Moya, 2014]. It enables the exploration of our bodily context of being, our awareness, and subjective states that shape the way we are as human beings.

In this research, fatigue may have projected through bodily functions without necessarily causing debilitating, all engrossing fatigue. Emotional and cognitive triggers are described as experiences of fatigue through an individual's perception and their feelings linked to fatigue. However, occasionally conceptual and emotional stressors that predominantly occur as abstract can influence and cause fatigability with both bodily and cognitive debilitation. The suggestion of the characteristic of embodiment intertwines through layers of physical, cognitive, and psychosocial aspects in MS fatigue. Embodiment could be seen as of central concern in fatigue as a whole and should be explored further to focus on the congruence between emotional, psychological and physical states of fatigue.

Although the study found no statistical significance in the objective measurement for ambulatory fatigue and there continues to be no gold standard for a biomarker for fatigue in MS (predominantly due to the study being underpowered with a small sample size to detect a difference between groups). There may be clinical significance from the PhD study. The range of manifestations highlighted the impact of emotional-related fatigue and the intertwined nature of fatigue. This alone could increase the effectiveness of clinical measurement for pwMS with questionnaires such as the MFIS. The usefulness of an effective questionnaire in clinical practice and research could indicate the impact of a treatment success. The study highlights the association between fatigue, stigma, and dignity which demonstrates the significance of an individual's perceptions and beliefs.

11.2. Contributions to fatigue

Fatigue has commonly been operationalised in studies investigating partial views of fatigue. However, in this research, the whole phenomenon of fatigue was explored from "subjective" and "objective" viewpoints from fatigue as experienced to measures of ambulatory fatigue. In the phenomenological study, it was identified that all descriptions of fatigue as experienced and the effects of bodily function and experience were significant processes of comprehension and acceptance to participants.

In this present research, many types of fatigue-related factors that may all be different variants from each other were established. This reiterates fatigue categorisation as 'an umbrella term' that encompasses many unarticulated and unexplored dimensions of the phenomenon. In line with previous findings, physical and cognitive stressors were apparent in participants' descriptions. However, it was also found that emotional stressors of interpersonal factors seem to trigger and exacerbate fatigue. This study shed light on the congruence of fatigue, stigma, and dignity. Participants described a change to how they see, feel, and believe in themselves due to their experiences of fatigue. Therefore, any level of psychological stress could exacerbate fatigue that subsequently affects how pwMS function and move. Due to the nature of this study that was conducted in a "safe environment" (familiar surroundings, flat floor for foot placement and a clear understanding what is expected from them), as the majority of participants stated; arguably this caused little to no psychological stress to trigger stigma that may have resulted in little fatigability demonstrated in this study. Practically, for healthcare professionals, in particular therapists, emotional-related fatigue, psychological stress and stigma may significantly contribute to how they explore, examine, and manage fatigue in pwMS. Emotional related fatigue will also be unique to each individual. Nevertheless, identifying and understanding emotional stressors may give therapists and subsequently pwMS a better understanding to manage fatigue. Additionally, pwMS have developed a meta-awareness about their fatigue, how it functions in every aspect in their lifeworlds. The taken-for-granted experiences that were once unconscious and unaware for most pwMS are now conscious as they are aware of all facets of bodily and self aspects that are interwoven and affected by fatigue. The heightened awareness and established recognition of their pre-reflexivity to fatigue provides insight for therapists and how pwMS experience fatigue. Therapists can learn to better understand these unconscious experiences to assist in more effective management. Currently this is overlooked in practice altogether.

The body feeling separate from self, as suggested by Merleau-Ponty [1968], was indicated in this study. The perception of the body reflected fatigue in mannerisms out of participants' control. There was a feeling of body detachment that came alongside fatigue as participants experienced no control over different parts of their body. There was a sensation of disconnection from the whole embodied self however, the confluence between the perception and bodily impacts of fatigue are yet to be fully established. A connection remains between the two, as the perception and concept of fatigue can affect physical functional ability and, as Merleau-Ponty [1968] stated, “the subject and object are correlated in an inseparable way”. From a practical perspective, in relation to the management of fatigue, this connection between the feelings and actions of fatigue should be considered and integrated in for example, physiotherapy interventions. These findings highlight the importance of the connection and inseparable relation between the different stressors to exacerbate fatigue, including the emotional and physical states of pwMS. Identifying and becoming more aware of the potential interaction and the unity of behaviour between the two could be an effective way to enhance treatment outcomes in physiotherapeutic practice and increase positive management of fatigue in pwMS. Fatigue is not a linear experience and is often not described in a singular mannerism. In this present research, it was identified that the current measurement does not always reflect upon such aspects of fatigue and is very partial. From a phenomenological investigation, the continuum of fatigue was established in Chapter Ten (see Figure 10.26) that begins to illustrate the range of manifestations that could enable future investigation for a more holistic or unified perspective of fatigue. The range and variants of fatigue established from this phenomenological investigation could be used to further the effectiveness and usefulness of self-reported measures that are used in a clinical setting. For example, a questionnaire, the MFIS, and the addition of the impact of emotional-related fatigue and well-being for pwMS to grasp and understand all the constituents of fatigue. Gaining validated measures for ambulatory and motor fatigue will not only increase awareness of the impact of fatigue, but it will help identify how fatigue affects movement and coordination that will develop and assist the management for fatigue and improve their quality of life.

There continues to be no gold standard for physiological biomarkers for fatigue in pwMS. Although nonsignificant results were found within peak ω throughout each minute of the 6MW, the most promising measure was the peak ω in the dominant thigh of pwMS with a decline in peak ω value in the last minute of the 6MW. Repeated measures conducted with a larger cohort and moderately disabled pwMS could help establish the usefulness of the measurement. Nevertheless, this study reconfirms no new fatigability measures.

11.3. Contribution to methods of turn detection

In Chapter Nine, the usefulness of TD was detected, comparing gyroscope signals (El-Gohary's method) to magnetometry signals in both older healthy and MS cohorts. The recognition of magnetometry signals at the sternum were 99.85% accurate in the older healthy group and 98.66% accurate in pwMS in comparison to El-Gohary's method [2014]. This suggests magnetometry signals located at the sternum can be used for 180-degree TD in older healthy and MS populations. This method of analysis can be useful for detecting turn characterisations, behaviours and patterns in different populations (e.g. Parkinson's) but also to eliminate turns so gait analysis can be sucessfully executed. In this study, it was established that the detection of turns can be effectively done using magnetometry and gyroscopy signals located at the sternum in both populations and could be used in future studies.

11.4. Insights from an attempt to apply naturalised phenomenology

No previous studies have been conducted using a naturalised phenomenological study to explore MS fatigue. Until the present study, this topic had not been explored using this methodology nor been investigated within a phenomenological approach in conjunction with physiological measurement.

Naturalised phenomenology is a method that is used to explore a phenomenon from a "subjective" and "objective" viewpoint. This was deemed appropriate for this research, as MS fatigue is multifaceted in nature. The methodological approach provided a footbridge to begin a continuum of fatigue, that begins to detect one facet of fatigue to another. Although complete integration of the two sets of data were not possible due to methodological and epistemological differences (the aim of the method is to reveal the interaction of two sets of data), the use of naturalised phenomenology brought to light the range of manifestations and types of fatigue that pwMS experience and convey and points to directions for further investigation.

The methodology is suitable for an exploratory study, such as in this PhD study, as it allows data to emerge and reveal itself through first- and third-person experiences. As stated above, exploration of fatigue was performed as a whole, from both perspectives. Many types of fatigue were found, where naturalised phenomenology suggested fatigue and fatigability to be distinct and potentially independent from each other, even though there reportedly is an association between them.

Nonetheless, as there were many facets of fatigue that were described, in this PhD research, only the measurement of ambulatory fatigue from a third person perspective was focussed on. This may have not been enough to capture fatigability (as some participants described different types of bodily fatigue). Other motor functions that cause fatigability, such as muscular or cognitive fatigue, may prove useful to encompass aspects of fatigability that were not conducted in this study. As a result of this, it could be argued that the whole phenomenon of motor fatigue was not explored.

Another consideration on the application of naturalised phenomenology is the experimental design of the study. The continuity of the assessment was tiring for some participants, who displayed symptoms of tiredness in their interview (slurred speech and verbal confirmation of tiredness). This may have resulted in a lack of full reflection and description from some participants. Although dependent on the study under investigation, in this study, in some cases, conducting the interview after the physical assessment was a mild inconvenience for participants experiencing tiredness and fatigue.

A naturalised phenomenological approach brought awareness of the richness of the lived experiences of fatigue. By taking the experiences into account, it enabled a mutual enrichment of understanding fatigue to develop quantifying and comprehending fatigue as a whole.

11.5. Philosophical approach to healthcare

The philosophical concept derived from Merleau-Ponty’s [1963] embodied consciousness and habit explains the unity of behaviour between bodily and intelligent conduct, where there is no hard separation between the two. This concept may be considered to be applied to some healthcare models to provide a more philosophical and holistic approach to healthcare for phenomena deemed more complex and multifaceted. Carel [2010] discussed this philosophical application of the body as a central role, acknowledging the primacy of perception, to medicine and healthcare. She suggested this approach could narrow the gap between the objective assessments of wellbeing in illness to the subjective experience of illness, to develop a more attuned dialogue, and would illuminate Merleau-Ponty's concepts of the habitual body [Carel, 2010]. Becoming more aware of the co-penetration that exists between the subject and the world may benefit many management interventions including fatigue in MS.

11.6. Lines of enquiry

As proposed by Kluger et al. [2013], a taxonomy of fatigue may assist in establishing the complexity of the domains and components that fall under the umbrella term "fatigue". Classifying groups based on characteristics and associations could resolve confusion within the literature and illustrate a more definite distinction, but also illustrate the connections across all characteristics of fatigue, and its confluence to stigma and dignity, to grasp the whole phenomenon of fatigue. Although the literature within MS fatigue is growing, the lack of definition and terminology remains problematic. Phenomenologically, fatigue has been fruitfully described as a continuum and the distinction between fatigue and fatigability has been highlighted. A taxonomy would further provide a foundational component of both ends of the continuum that has not yet been successfully established. This could then be used to devise and develop more accurate measurements and management interventions for an improvement in QOL in ambulation and fatigue as experienced.

An essential aspect in relation to rehabilitation programmes in MS fatigue is to understand how fatigability declines throughout the entire disease process. The conflicting results of this research and previous studies may indicate fatigue and fatigability do not progress linearly [Dalgas et al., 2018; Loy et al., 2017]. This suggests that even within each specific level/category of disability, pwMS may perform differently in terms of gait deterioration and characterisations. This could arguably explain the inconsistent results within the majority of the ambulatory fatigue literature. Identifying the physical characterisations of fatigability and the subtle levels of disability may assist in determining fatigability more consistently, which could ultimately be used as an indicator for management interventions within the MS community. In future, researchers should focus on the clear pathway of disability level and fatigability changes and how fatigue as experienced can impact pwMS' perception of both.

Some researchers have suggested fatigue and fatigability as separate entities [Kluger et al., 2013]. This doesn't imply that both entities should be researched without consideration of the aspects of embodiment, as there appears to be a degree of association between the two and their effect on one another. As suggested in Chapter Ten, both fatigue and fatigability fluctuate on a continuum of experience and this does not follow a linear pattern. The rate of change in both continuums and its impacting factors may be affected by proprioception from a habitual and actual bodily aspect. Merleau-Ponty [1963] discussed the indistinct division between pre-reflexive bodily knowledge and bodily context, a form of dialogue that is likely disrupted from CNS damage.

The dislodge of fatigue between the habitual and actual body leaves a discontinuous sense of perception and movement. Proprioception provides an unconscious ability to sense location, movement and action (primarily communicated through the cerebellum) [Radák, 2018]. It allows the body to perform simultaneous actions without stopping to think of each individual action. With disruption to proprioception, individuals have to methodically process each action consciously, which requires vigilance and constant monitoring that consequently may be a reason why tasks can be so tiring.

Fatigue is described to unanimously alter unconscious actions of bodily movement and impact embodiment in a similar mannerism to proprioception disruption. Although in this thesis the disruption of embodiment in the habitual and actual body has only begun to be explored, the association between fatigue, fatigability and proprioception may also guide a more comprehensive understanding of the behaviour of fatigue. Physiological fatigue and the perception of fatigue in relation to proprioception could provide an explanation to the sense of the habitual and actual state of the body. Furthermore, due to proponents of phenomenology focussing on the structures of consciousness, neurophysiological measurement and phenomenology could be used to insightfully investigate the embodiment of fatigue and proprioception in an attempt to explore internal and conscious states of experience. This may shine new light on fatigue from a multidisciplinary perspective and enlighten fatigue research into new directions.

11.7. Reflections on the study

Within all research studies, there are challenges and objectives to overcome; this PhD was no different. Logistically, problems arose with a change in rooms halfway through the PhD, (for data collection) which created amendments to ethics proposal and a delay in data collection. However, this did not cause any major complications and further provided more opportunity for recruitment. Furthermore, fatigue is an undesirable experience for pwMS, therefore, encouraging individuals to participate became challenging as the 6MW is a test used to typically exacerbate their fatigue. Not only this but finding potential participants within local organisations that were able to walk 100m unaided was difficult; commonly, I found individuals to be moderately to severely disabled (<6 EDSS) to attend local MS organisations and centres and, therefore, unable to participate in the study.

Similar to other MMR studies, the issue of collecting, handling, reporting, analysing and interpreting first and third person data was challenging, especially with two diverse datasets such as phenomenology and sensor-derived data. The integration chapter was difficult to conduct mainly due to the way qualitative and quantitative research is presented. If presented on a continuum, the phenomenological field sits on the opposing end to physiological and sensor-derived research; the language and the epistemological approaches differ considerably. This created difficulty in how to integrate the two together and, it caused a very large dataset to overall analyse. Nevertheless, I learnt to overcome the difficulty in integration by reflection and reflect on the two diverse disciplines for an insightful approach that provided new reflections that would not have been highlighted without a naturalised phenomenological approach.

I have learnt how different fields of research approach and conduct a study, which I believe has broadened my understanding and knowledge on conducting research. I have had the opportunity to present at national and international conferences that was insightful and more importantly, enjoyable! I have learnt the vast range of manifestation fatigue presents itself with. Fatigue is a complex phenomenon, that is interwoven into all lifeworld perspectives, that has shifted my knowledge in fatigue (in comparison to the beginning of my PhD).

Due to the size of this PhD study, there were areas of data that could have been used and interpreted but were not. The nature of the study aimed to explore the global phenomenon of fatigue, to entice the many facets fatigue presents itself with. A simple additional measure could have explored the cognitive domain in both pwMS and the ‘healthy’ cohort with questionnaires such as the MFIS and its cognitive aspect of fatigue. Additional objective cognitive measurements (reaction time or memory tests) could have been used to directly compare ambulation measurement. This could have given a more globally picture of fatigue that may have given a more complete representation of fatigue in pwMS. Other simple metrics such as cadence and stride time could have been used; these could have explored and possibly justified the insignificance of the ambulatory fatigue findings.

11.8. To conclude

The findings from this research support the view that fatigue within MS is dissimilar to universal tiredness that the general population is most likely to experience. MS fatigue has a variety of characteristics of impacting factors and domains of fatigue that creates a complex phenomenon.

This research represents a multidisciplinary approach to MS fatigue. The overall objective of this research was to investigate the congruence between fatigue and fatigability, and to explore the confluence between an individual's perception, feeling, and experience of fatigue, to quantifiable and physiological fatigue in ambulation. The PhD aimed to establish the overarching phenomenon of fatigue, to grasp full, rich descriptions of an individual's experiences. Through a phenomenological lens, fatigue was established as a continuum, ranging from mild to sudden, all-absorbing fatigue. There are many phenomena of fatigue, and this research demonstrates a whole range of MS fatigue experiences from unconscious and conscious components of an individual's life. The invisibility of fatigue created an illusion of a fit body to others, unless an all-absorbing fatigue was experienced which caused temporary debilitation to most senses. Fatigue centralised the disengagement of bodily function and cloudiness of conscious and caused a deep disruption to daily rhythm.

The evaluation of ambulatory fatigue using inertial wearable sensors during the 6MW concluded insignificant in this study. There was little association between measures of ambulatory fatigue, walking velocity and peak ω at the thigh and ankle. However, it is suspected that only a few participants displayed fatigability from the 6MW in this research study. Additionally, it was not possible to measure fatigability in all the participants using these performance-based measurements, due to the nature of the activity, the sample size and the question of disability severity and measurement. However, a promising approach using magnetometry signals for the use of 180 degree turn detection in an older healthy and MS cohort was established in this study. Magnetometry signals alongside gyroscopy signals, should be considered for future use of turn detection in both cohorts to provide an effective method to eliminate turns for straight walkway gait analysis. Additionally, it could provide turn behaviour and patterns analysis to explore the characterisations in different populations.

Although still unclear, there was a confluence of embodiment between fatigue as experienced and fatigability, which further supports fatigue as a multifaceted phenomenon. It was prominent that fatigue impacts pwMS and, there is an overlap in the impact of fatigue within bodily and cognitive experiences, however, quantifiable ambulatory fatigue was not ubiquitous in all participants. The inseparable congruence between the subject and the object relay deeply with fatigue as the multitude of variants demonstrate in this study. Reflecting on phenomenological and physiological structures enables further clarification from one side of fatigue to the other (in terms of the continuum) and, assists in grasping the whole phenomenon. The study brought to light the congruence with fatigue, stigma and dignity; it demonstrated the further significance of an individual's perception and belief and how this affects the experiences of fatigue and fatigability. Without this clear comprehension, it hinders the progress of interventions and management for fatigue. Fatigue was found to impact all aspects of a pwMS' life and their lifeworlds, it is a global and complex phenomenon that ranges dramatically dependent on the individual, activity and management of fatigue.

This is an attempt to use a naturalised phenomenological approach and to assess its usefulness in this area of research. Naturalised phenomenology was a fruitful method used to explore fatigue from multiple perspectives, shedding light on the overall experience of fatigue. It explored fatigue from a more holistic and global viewpoint; of which, with further research, incorporating this methodology, will allow us to further understand the behaviour and characteristics of fatigue, and grasp a clearer measurement of fatigue. Through phenomenological reflection, detail of experimental design and practice could perhaps be tailored to investigate and gain further precision on measurement and management. Furthermore, the full, rich descriptions of experiences could assist and tailor self-reported measures, such as the MFIS, to provide the full phenomenon of fatigue and a more precise measurement.

The use of this methodology provided a global understanding of fatigue and indicated the approach to fatigue in terms of research, measurement and management needs to be addressed in order to fully establish fatigue and all its variants. Naturalised phenomenology has enabled us to begin doing this and has immense promise in establishing intricate and complex phenomena, such as fatigue in MS.

References

Al-Obaidi, S., Wall, J. C., Al-Yaqoub, A., & Al-Ghanim, M. (2003). Basic gait parameters: A comparison of reference data for normal subjects 20 to 29 years of age from Kuwait and

Scandinavia. *Journal of Rehabilitation Research and Development*, *40*(4), 361–366. https://doi.org/10.1682/JRRD.2003.07.0361

Andreasen, A. K., Jakobsen, J., Petersen, T., & Andersen, H. (2009). *Fatigued patients with multiple sclerosis have impaired central muscle activation*. *November 2008*, 818–827.

Ashworth, P. D. (2016). The lifeworld – enriching qualitative evidence. *Qualitative Research in Psychology*. https://doi.org/10.1080/14780887.2015.1076917

Barker, A. B., Smale, K., Hunt, N., Lincoln, N. B., & das Nair, R. (2019). Experience of identity change in people who reported a diagnosis of multiple sclerosis: A qualitative inquiry. *International Journal of MS Care*, *21*(5), 235–242. https://doi.org/10.7224/1537-2073.2018-069

Barth, J., Oberndorfer, C., Pasluosta, C., Schülein, S., Gassner, H., Reinfelder, S., Kugler, P., Schuldhaus, D., Winkler, J., Klucken, J., & Eskofier, B. M. (2015). Stride segmentation during free walk movements using multi-dimensional subsequence dynamic time warping on inertial sensor data. *Sensors (Switzerland)*. https://doi.org/10.3390/s150306419

Beatty, A., Schiller, N. B., & Whooley, M. (2012). Six-minute walk test as a prognostic tool in stable coronary heart disease: data from the Heart and Soul Study. *Arch Intern Med, 172*(14), 1096–1102. https://doi.org/10.1001/archinternmed.2012.2198.

Beckerman, H., Eijssen, I. C., van Meeteren, J., Verhulsdonck, M. C., & de Groot, V. (2020). Fatigue Profiles in Patients with Multiple Sclerosis are Based on Severity of Fatigue and not on Dimensions of Fatigue. *Scientific Reports*, *10*(1), 1–10. https://doi.org/10.1038/s41598-020-61076-1

Beech, I. (1999). Bracketing in phenomenological research. *Nurse Researcher*, *6*(3), 35–51. https://doi.org/10.7748/nr1999.04.6.3.35.c6086

Berkovich-Ohana, A., Dor-Ziderman, Y., Trautwein, F. M., Schweitzer, Y., Nave, O., Fulder, S., & Ataria, Y. (2020). The Hitchhiker’s Guide to Neurophenomenology – The Case of Studying Self Boundaries With Meditators. *Frontiers in Psychology*, *11*(July). https://doi.org/10.3389/fpsyg.2020.01680

Bertrand, R. M., & Willis, S. L. (1999). Everyday problem solving in Alzheimer’s patients: A comparison of subjective and objective assessments. *Aging and Mental Health*.

https://doi.org/10.1080/13607869956055

Biddle, C., & Schafft, K. A. (2014). Axiology and Anomaly in the Practice of Mixed Methods Work: Pragmatism, Valuation, and the Transformative Paradigm. *Journal of Mixed Methods Research*, *9*(4), 320–334. https://doi.org/10.1177/1558689814533157

Bitbol, M. (2012). Neurophenomenology, an ongoing practice of/in consciousness. *Constructivist Foundations*, *7*(3), 165–173.

Bitbol, M., & Petitmengin, C. (2017). Neurophenomenology and the Micro-phenomenological Interview. In *The Blackwell Companion to Consciousness*. https://doi.org/10.1002/9781119132363.ch51

Blaney, B. E., & Lowe-Strong, A. (2009). The impact of fatigue on communication in multiple sclerosis. The insider's perspective. *Disability and Rehabilitation*, *31*(3), 170–180. https://doi.org/10.1080/09638280701869629

Bockelman, P., Reinerman-Jones, L., & Gallagher, S. (2013). Methodological lessons in neurophenomenology: Review of a baseline study and recommendations for research approaches. *Frontiers in Human Neuroscience*. https://doi.org/10.3389/fnhum.2013.00608

Bohannon, Bubela, Magasi, W. and G. (2010). Sit-to-stand test: Performance and determinants across the age-span. *NIH*, *31*(9), 1713–1723. https://doi.org/10.1109/TMI.2012.2196707.Separate

Bowen, J., Gibbons, L., Gianas, A., & Kraft, G. H. (2001). Self-administered Expanded Disability Status Scale with functional system. *Multiple Sclerosis*, *August 2000*. https://doi.org/10.1177/135245850100700311

Brainerd, C. J., & Reyna, V. F. (2008). The Science of False Memory. In *The Science of False Memory*. https://doi.org/10.1093/acprof:oso/9780195154054.001.0001

Brodie, M. A. D., Beijer, T. R., Canning, C. G., & Lord, S. R. (2015). Head and pelvis stride-to-stride oscillations in gait: Validation and interpretation of measurements from wearable accelerometers. *Physiological Measurement*, *36*(5), 857–872. https://doi.org/10.1088/0967-3334/36/5/857

Brooks, J. (2015). Learning from the ' lifeworld ' Final author version. *The Psychologist*, *28*(August), 645–646. https://thepsychologist.bps.org.uk/volume-28/august-

2015/learning-lifeworld

Browne, P., Chandraratna, D., Angood, C., Tremlett, H., Baker, C., Taylor, B. V., & Thompson, A. J. (2014). Atlas of multiple sclerosis 2013: A growing global problem with widespread inequity. In *Neurology*. https://doi.org/10.1212/WNL.0000000000000768

Burschka, J. M., Keune, P. M., Menge, U., Oy, U. H., Oschmann, P., & Hoos, O. (2012). *An exploration of impaired walking dynamics and fatigue in Multiple Sclerosis*. 2–9.

Carel, H. (2010). *PHENOMENOLOGY AND ITS APPLICATION IN MEDICINE*. 1–18.

Cella, D. F., Dineen, K., Arnason, B., Reder, A., Webster, K. A., Karabatsos, G., Chang, C., Lloyd, S., Mo, F., Stewart, J., & Stefoski, D. (1996). Validation of the functional assessment of multiple sclerosis quality of life instrument. *Neurology*, *47*(1), 129–139. https://doi.org/10.1212/WNL.47.1.129

Charon, R. (1989). DOCTOR-PATIENT / READER-WRITER : Learning to Find the Text. *An Interdisciplinary Journal*, *72*(1), 137–152.

Chipchase, S. Y., Lincoln, N. B., & Radford, K. A. (2003). Measuring fatigue in people with Multiple Sclerosis. *Disability and Rehabilitation*, *25*(14), 778–784. https://doi.org/10.1080/0963828031000093477

Colombo, B., Martinelli, F., Paolo, B., Marco, R., & Comi, R. L. M. M. F. G. (2000). *MRI and motor evoked potential findings in nondisabled multiple sclerosis patients with and without symptoms of fatigue*. 506–509.

Colyer, S. L., Evans, M., Cosker, D. P., & Salo, A. I. T. (2018). A Review of the Evolution of Vision-Based Motion Analysis and the Integration of Advanced Computer Vision Methods Towards Developing a Markerless System. *Sports Medicine - Open*, *4*(1). https://doi.org/10.1186/s40798-018-0139-y

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

Creswell, J. . (2009). Mixed methods procedures. *Research Design: Qualitative, Quantitative and Mixed Methods Approaches*, 203–226. https://doi.org/10.4135/9781849208956

D'Esposito, M., Onishi, K., Thompson, H., Robinson, K., Armstrong, C., & Grossman, M. (1996). Working memory impairments in multiple sclerosis: Evidence from a dual-task paradigm. *Neuropsychology*, *10*(1), 51–56. https://doi.org/10.1037/0894-4105.10.1.51

Dahlberg, H., & Dahlberg, K. (2020). Open and Reflective Lifeworld Research: A Third Way. *Qualitative Inquiry*, *26*(5), 458–464. https://doi.org/10.1177/1077800419836696

Dalgas, U., Langeskov-Christensen, M., Skjerbæk, A., Jensen, E., Baert, I., Romberg, A., Santoyo Medina, C., Gebara, B., Maertens de Noordhout, B., Knuts, K., Béthoux, F., Rasova, K., Severijns, D., Bibby, B. M., Kalron, A., Norman, B., Van Geel, F., Wens, I., & Feys, P. (2018a). Is the impact of fatigue related to walking capacity and perceived ability in persons with multiple sclerosis? A multicenter study. *Journal of the Neurological Sciences*, *387*(November 2017), 179–186. https://doi.org/10.1016/j.jns.2018.02.026

Dalgas, U., Langeskov-Christensen, M., Skjerbæk, A., Jensen, E., Baert, I., Romberg, A., Santoyo Medina, C., Gebara, B., Maertens de Noordhout, B., Knuts, K., Béthoux, F., Rasova, K., Severijns, D., Bibby, B. M., Kalron, A., Norman, B., Van Geel, F., Wens, I., & Feys, P. (2018b). Is the impact of fatigue related to walking capacity and perceived ability in persons with multiple sclerosis? A multicenter study. *Journal of the Neurological Sciences*, *387*(November 2017), 179–186. https://doi.org/10.1016/j.jns.2018.02.026

Dalgas, U, Langeskov-christensen, M., Skjerbæk, A., Jensen, E., Baert, I., Romberg, A., Severijns, D., Bibby, B. M., Kalron, A., Norman, B., Geel, F. Van, Wens, I., & Feys, P. (2018). Is the impact of fatigue related to walking capacity and perceived ability in persons with multiple sclerosis ? A multicenter study. *Journal of the Neurological Sciences*, *387*(February), 179–186. https://doi.org/10.1016/j.jns.2018.02.026

Dalgas, Ulrik, Kjølhede, T., Gijbels, D., Romberg, A., Noordhout, B. M. De, Knuts, K., & Feys, P. (2014). *Aerobic intensity and pacing pattern during the six-minute walk test in PATIENTS WITH multiple sclerosis*. 59–66. https://doi.org/10.2340/16501977-1231

Dandu, S. R., Engelhard, M. M., Goldman, M. D., & Lach, J. (2016). Determining physiological significance of inertial gait features in multiple sclerosis. *BSN 2016 - 13th Annual Body Sensor Networks Conference*, 266–271. https://doi.org/10.1109/BSN.2016.7516271 de Vries, W. H. K., Veeger, H. E. J., Baten, C. T. M., & van der Helm, F. C. T. (2009). Magnetic distortion in motion labs, implications for validating inertial magnetic sensors. *Gait and Posture*, *29*(4), 535–541. https://doi.org/10.1016/j.gaitpost.2008.12.004

Devins, G. M., Edworthy, S. M., Paul, L. C., Mandin, H., Seland, T. P., Klein, G., Costello, C. G., & Shapiro, C. M. (1993). Restless sleep, illness intrusiveness, and depressive symptoms in three chronic illness conditions: Rheumatoid arthritis, end-stage renal disease, and multiple sclerosis. *Journal of Psychosomatic Research*, *37*(2), 163–170. https://doi.org/10.1016/0022-3999(93)90083-R

Dormans, J. P. (2015). Orthopedic management of children with cerebral palsy. *Pediatric Clinics of North America*, *40*(3), 645–657. https://doi.org/10.1016/S0031-3955(16)38556-X

Eatough, V., & Shaw, K. (2019). “It’s like having an evil twin”: an interpretative phenomenological analysis of the lifeworld of a person with Parkinson’s disease. *Journal of Research in Nursing*, *24*(1–2), 49–58. https://doi.org/10.1177/1744987118821396

Edwards, R. H., Hill, D. K., Jones, D. A., & Merton, P. A. (1977). Fatigue of long duration in human skeletal muscle after exercise. *The Journal of Physiology*, *272*(3), 769–778. https://doi.org/10.1113/jphysiol.1977.sp012072

Eilertsen, G., Ormstad, H., & Kirkevold, M. (2013). Experiences of poststroke fatigue: Qualitative meta-synthesis. *Journal of Advanced Nursing*, *69*(3), 514–525. https://doi.org/10.1111/jan.12002

El-Gohary, M., Pearson, S., McNames, J., Mancini, M., Horak, F., Mellone, S., & Chiari, L. (2014). Continuous monitoring of turning in patients with movement disability. *Sensors (Switzerland)*, *14*(1), 356–369. https://doi.org/10.3390/s140100356

Engelhard, Dandu, Patek, Lach, G. (2016). Quantifying Six-Minute Walk Induced Gait Deterioration with Inertial Sensors in Multiple Sclerosis Subjects. *Physiology & Behavior*, *176*(1), 139–148. https://doi.org/10.1016/j.physbeh.2017.03.040

Engelhard, M. M., Dandu, S. R., Patek, S. D., Lach, J. C., & Goldman, M. D. (2016). Quantifying six-minute walk induced gait deterioration with inertial sensors in multiple sclerosis subjects. *Gait and Posture*. https://doi.org/10.1016/j.gaitpost.2016.07.184

England, P. H. (2020). *Multiple sclerosis: prevalence, incidence and smoking status - data briefing*. https://www.gov.uk/government/publications/multiple-sclerosis-prevalence-incidence-and-smoking-status/multiple-sclerosis-prevalence-incidence-and-smoking-status-data-briefing

Federation, M. S. I. (2012). Fatigue and MS. *Mocus*, *January*.

Filli, L., Sutter, T., Easthope, C. S., Killeen, T., Meyer, C., Reuter, K., Lörincz, L., Bolliger, M., Weller, M., Curt, A., Straumann, D., Linnebank, M., & Zörner, B. (2018a). Profiling walking dysfunction in multiple sclerosis: Characterisation, classification and progression over time. *Scientific Reports*, *8*(1), 1–13. https://doi.org/10.1038/s41598-018-22676-0

Filli, L., Sutter, T., Easthope, C. S., Killeen, T., Meyer, C., Reuter, K., Lörincz, L., Bolliger, M., Weller, M., Curt, A., Straumann, D., Linnebank, M., & Zörner, B. (2018b). Profiling walking dysfunction in multiple sclerosis: Characterisation, classification and progression over time. *Scientific Reports*, *8*(1), 1–13. https://doi.org/10.1038/s41598-018-22676-0

Finlay, L. (2008). A dance between the reduction and reflexivity: Explicating the "phenomenological psychological attitude." *Journal of Phenomenological Psychology*, *39*(1), 1–32. https://doi.org/10.1163/156916208X311601

Fisk, J. D., Pontefract, A., Ritvo, P. G., Archibald, C. J., & Murray, T. J. (1994). The Impact of Fatigue on Patients with Multiple Sclerosis. *THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES*, *21*(1), 9–14.

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. *Clinical Infectious Diseases*. https://doi.org/10.1093/clinids/18.Supplement_1.S79

Flensner, G., Ek, A. C., & Söderhamn, O. (2003a). Lived experience of MS-related fatigue - A phenomenological interview study. *International Journal of Nursing Studies*, *40*(7), 707–717. https://doi.org/10.1016/S0020-7489(03)00010-5

Flensner, G., Ek, A. C., & Söderhamn, O. (2003b). Lived experience of MS-related fatigue - A phenomenological interview study. *International Journal of Nursing Studies*, *40*(7), 707–717. https://doi.org/10.1016/S0020-7489(03)00010-5

Flensner, G., & Lindencrona, C. (2002). *The cooling-suit : case studies of its influence on fatigue among eight individuals with multiple sclerosis*. 541–550.

Forbes, A., While, A., Mathes, L., & Griffiths, P. (2006). Health problems and health-related quality of life in people with multiple sclerosis. *Clinical Rehabilitation*, *20*(1), 67–78. https://doi.org/10.1191/0269215506cr880oa

Gallagher, S. (2003). *Neurophenomenological Research on Embodied experience*. *November*, 1–34.

Gallagher, S. (2006). How the Body Shapes the Mind. In *How the Body Shapes the Mind*. https://doi.org/10.1093/0199271941.001.0001

Gallagher, S. (2015). On the possibility of naturalizing phenomenology. *Oxford Handbook of Contemporary Phenomenology*, 70–93. https://doi.org/10.1515/ling-2016-0005

Gallagher, S. (2018). Rethinking Nature: Phenomenology and a Non-reductionist Cognitive Science. *Australasian Philosophical Review*, *2*(2), 125–137. https://doi.org/10.1080/24740500.2018.1552074

Gallagher, S., & Brøsted Sørensen, J. (2006). Experimenting with phenomenology. *Consciousness and Cognition*, *15*(1), 119–134. https://doi.org/10.1016/j.concog.2005.03.002

Gallagher, S., & Meltzoff, A. N. (1996). The earliest sense of self and others: Merleau-Ponty and recent developmental studies. *Philosophical Psychology*, *9*(2), 211–233. https://doi.org/10.1080/09515089608573181

Gallagher, S., Reinerman-Jones, L., Janz, B., Bockelman, P., & Trempler, J. (2015). A Neurophenomenology of Awe and Wonder. In *A Neurophenomenology of Awe and Wonder*. https://doi.org/10.1057/9781137496058

Gallagher, S., & Zahavi, D. (2008). *The Phenomenological Mind: An introduction to Philosophy of Mind and Cognitive Science*. *2002*. https://doi.org/10.4324/9780203086599

Gallagher, S., & Zahavi, D. (2012). The phenomenological mind. In *Choice Reviews Online* (Vol. 50, Issue 04). https://doi.org/10.5860/choice.50-1996

Galvin, K. T., & Todres, L. (2018). Eighteen kinds of well-being although there may be more: A conceptual framework illustrated with practical direction for caring. In *The Routledge handbook of well-being*.

Ganea, R., Paraschiv-Ionescu, A., Büla, C., Rochat, S., & Aminian, K. (2011). Multi-parametric evaluation of sit-to-stand and stand-to-sit transitions in elderly people. *Medical Engineering and Physics*. https://doi.org/10.1016/j.medengphy.2011.04.015

Ghajarzadeh, M., Jalilian, R., Eskandari, G., Sahraian, M. A., Azimi, A., & Mohammadifar, M. (2013). Fatigue in multiple sclerosis: Relationship with disease duration, physical disability, disease pattern, age and sex. *Acta Neurologica Belgica*, *113*(4), 411–414. https://doi.org/10.1007/s13760-013-0198-2

Giorgi, A. (1997). The theory, practice, and evaluation of the phenomenological method as a qualitative research procedure. *Journal of Phenomenological Psychology*. https://doi.org/10.1163/156916297X00103

Giorgi, A. P., Giorgi, B. M., & Morley, J. (2017). The Descriptive Phenomenological Psychological Method. *Qualitative Research in Psychology: Expanding Perspectives in Methodology and Design*, *July*, 243–273. https://doi.org/10.1037/10595-013

Glaser, B. (1965). *The Constant Comparative Method of Qualitative Analysis. 12*(4), 436–445.

Goldman, M. D., Marrie, R. A., & Cohen, J. A. (2008a). Evaluation of the six-minute walk in multiple sclerosis. *Multiple Sclerosis Journal*, *14*(July 2007), 383–390.

Goldman, M. D., Marrie, R. A., & Cohen, J. A. (2008b). *Evaluation of the six-minute walk in multiple sclerosis subjects and healthy controls*. *June 2007*, 383–390.

Goldman, M. D., Motl, R. W., Scagnelli, J., Pula, J. H., Sosnoff, J. J., & Cadavid, D. (2013). Clinically meaningful performance benchmarks in MS:Timed 25-Foot Walk and the real world. *Neurology*, *81*(21), 1856–1863. https://doi.org/10.1212/01.wnl.0000436065.97642.d2

Goverover, Y., Kalmar, J., Gaudino-Goering, E., Shawaryn, M., Moore, N. B., Halper, J., & DeLuca, J. (2005). The relation between subjective and objective measures of everyday life activities in persons with multiple sclerosis. *Archives of Physical Medicine and Rehabilitation*, *86*(12), 2303–2308. https://doi.org/10.1016/j.apmr.2005.05.016

Greene, B. R., McGrath, D., O’Neill, R., O’Donovan, K. J., Burns, A., & Caulfield, B.

(2010). An adaptive gyroscope-based algorithm for temporal gait analysis. *Medical and Biological Engineering and Computing*, *48*(12), 1251–1260. https://doi.org/10.1007/s11517-010-0692-0

Greene, B. R., Rutledge, S., McGurgan, I., McGuigan, C., O'Connell, K., Caulfield, B., & Tubridy, N. (2015). Assessment and Classification of Early-Stage Multiple Sclerosis with Inertial Sensors: Comparison Against Clinical Measures of Disease State. *IEEE Journal of Biomedical and Health Informatics*, *19*(4), 1356–1361. https://doi.org/10.1109/JBHI.2015.2435057

Gupta, A., Nagaraj, K., Prasad, C., Taly, A., & Christopher, R. (2013). Prevalence of fatigue in patients with multiple sclerosis and its effect on the quality of life. *Journal of Neurosciences in Rural Practice*, *4*(3), 278. https://doi.org/10.4103/0976-3147.118774

Hamill, C. (2010). Bracketing--practical considerations in Husserlian phenomenological research. *Nurse Researcher*. https://doi.org/10.7748/nr2010.01.17.2.16.c7458

Hamilton, F., Rochester, L., Paul, L., Rafferty, D., O'Leary, C. P., & Evans, J. J. (2009). Walking and talking: An investigation of cognitive-motor dual tasking in multiple sclerosis. *Multiple Sclerosis*, *15*(10), 1215–1227. https://doi.org/10.1177/1352458509106712

Hebert, J. R., & Corboy, J. R. (2013). The association between multiple sclerosis-related fatigue and balance as a function of central sensory integration. *Gait & Posture*, *38*, 37–42.

Heidegger, M. (1962). Being and Time (J. Macquarrie and E. Robinson, Trans.). In *Media*.

Heine, M., van den Akker, L. E., Blikman, L., Hoekstra, T., van Munster, E., Verschuren, O., Visser-Meily, A., Kwakkel, G., de Groot, V., Beckerman, H., Malekzadeh, A., van den Akker, L. E., Looijmans, M., Sanches, S. A., Dekker, J., Collette, E. H., van Oosten, B. W., Teunissen, C. E., Blankenstein, M. A., … Aarts, G. J. (2016). Real-Time Assessment of Fatigue in Patients With Multiple Sclerosis: How Does It Relate to Commonly Used Self-Report Fatigue Questionnaires? *Archives of Physical Medicine and Rehabilitation*, *97*(11), 1887-1894.e1. https://doi.org/10.1016/j.apmr.2016.04.019

Heinzel, A., & Northoff, G. (2009). Emotional feeling and the orbitomedial prefrontal cortex: Theoretical and empirical considerations. *Philosophical Psychology*, *22*(4), 443–464.

https://doi.org/10.1080/09515080903153592

Hjollund, N. H., Andersen, J. H., & Bech, P. (2007). Assessment of fatigue in chronic disease: A bibliographic study of fatigue measurement scales. *Health and Quality of Life Outcomes*, *5*, 1–5. https://doi.org/10.1186/1477-7525-5-12

Hobart, J. C., Riazi, A., Lamping, D. L., Fitzpatrick, R., & Thompson, A. J. (2003). Measuring the impact of MS on walking ability: The 12-item MS Walking Scale (MSWS-12). *Neurology*, *60*(1), 31–36. https://doi.org/10.1212/WNL.60.1.31

Hobart, J., Lamping, D., Fitzpatrick, R., Riazi, A., & Thompson, A. (2001). The multiple sclerosis impact scale (MSIS-29) a new patient-based outcome measure. *Brain*. https://doi.org/10.1093/brain/124.5.962

Holberg, C., & Finlayson, M. (2007). Factors influencing the use of energy conservation strategies by persons with multiple sclerosis. *American Journal of Occupational Therapy*, *61*(1), 96–107. https://doi.org/10.5014/ajot.61.1.96

Holtzer, R., Shuman, M., Mahoney, J. R., Lipton, R., & Verghese, J. (2011). Cognitive Fatigue defined in the context of attention networks. *Aging, Neuropsychology, and Cognition*, *18*(1), 108–128. https://doi.org/10.1080/13825585.2010.517826

Howe, K. R. (1988). Against the Quantitative-Qualitative Incompatibility Thesis or Dogmas Die Hard. *Educational Researcher*, *17*(8), 10–16. https://doi.org/10.3102/0013189X017008010

Huisinga, J. M., Filipi, M. L., Schmid, K. K., & Stergiou, N. (2011). Is there a relationship between fatigue questionnaires and gait mechanics in persons with multiple sclerosis? *Archives of Physical Medicine and Rehabilitation*, *92*(10), 1594–1601. https://doi.org/10.1016/j.apmr.2011.05.017

Husserl, E., & Findlay, J. N. (1970). Logical investigations. In *International library of philosophy and scientific method.* (Vol. 2). London : Routledge & Kegan Paul ; New York : Humanities Press, Inc. https://doi.org/10.4324/9780203879047

Jacobs, J. V, & Kasser, S. L. (2012). Effects of dual tasking on the postural performance of people with and without multiple sclerosis: a pilot study. *Journal of Neurology*, *259*(6), 166–176. https://doi.org/10.1007/s00415-011-6321-5

Jacquette, D. (2004). The Cambridge Companion to Brentano. In *The Cambridge Companion* *to Brentano*. https://doi.org/10.1017/CCOL0521809800

Janssen, W. G. M., Bussmann, J. B. J., Horemans, H. L. D., & Stam, H. J. (2008). Validity of accelerometry in assessing the duration of the sit-to-stand movement. *Medical and Biological Engineering and Computing*. https://doi.org/10.1007/s11517-008-0366-3

Kalron, A. (2015). The correlation between symptomatic fatigue to definite measures of gait in people with multiple sclerosis. *Gait and Posture*, *44*, 178–183. https://doi.org/10.1016/j.gaitpost.2015.12.014

Kaya Aygunoglu, S., Celebi, A., Vardar, N., & Gursoy, E. (2015). Correlation of Fatigue with Depression, Disability Level and Quality of Life in Patients with Multiple Sclerosis. *Noro Psikiyatri Arsivi*, *52*(3), 247–251. https://doi.org/10.5152/npa.2015.8714

Kelleher, K. J., Spence, W., Solomonidis, S., & Apatsidis, D. (2010). The characterisation of gait patterns of people with multiple sclerosis. *Disabil Rehabil*, *32*(15), 1242–1250. https://doi.org/10.3109/09638280903464497

Kempen, J. C. E., De Groot, V., Knol, D. L., Lankhorst, G. J., & Beckerman, H. (2012). Self-reported fatigue and energy cost during walking are not related in patients with multiple sclerosis. *Archives of Physical Medicine and Rehabilitation*. https://doi.org/10.1016/j.apmr.2011.12.013

Kempen, J., De Groot, V., Knol, D. L., Polman, C. H., Lankhorst, G. J., & Beckerman, H. (2011). Community walking can be assessed using a 10-metre timed walk test. *Multiple Sclerosis Journal*. https://doi.org/10.1177/1352458511403641

Keogh, E., & Ratanamahatana, C. A. (2005). Exact indexing of dynamic time warping. *Knowledge and Information Systems*. https://doi.org/10.1007/s10115-004-0154-9

Khan, F., Amatya, B., & Galea, M. (2014). *Management of fatigue in persons with multiple sclerosis*. *5*(September), 1–15. https://doi.org/10.3389/fneur.2014.00177

Kim, Lovera, J., Schaben, L., Melara, J., Bourdette, D. □, & Whitham, R. (2010). *Novel method for measurement of fatigue in multiple sclerosis: Real-Time Digital Fatigue Score*. *47*(5), 477–484. https://doi.org/10.1682/JRRD.2009.09.0151

Kirchhoff, M. D., & Hutto, D. D. (2016). Never mind the gap: Neurophenomenology, radical enactivism, and the hard problem of consciousness. *Constructivist Foundations*.

Kiverstein, J. (2005). NATURALISING PHENOMENOLOGY: USING PHENOMENOLOGY TO CLOSE THE EXPLANATORY GAP. In *Thesis*. https://doi.org/10.1088/1751-8113/44/8/085201

Klein, M. (1975). Love, guilt, and reparation, and other works, 1921-1945. In *The writings of Melanie Klein*.

Kluger, B. M., Krupp, L. B., & Enoka, R. M. (2013). Fatigue and fatigability in neurologic inllnesses. *Neurology*, *80*, 409–416.

Knaster, E. S., Yorkston, K. M., Johnson, K. L., McMullen, K. A., & Ehde, D. M. (2011). Perspectives on Self-Management in Multiple Sclerosis: A focus group study. *International Journal of MS Care*, *13*(3), 146–152. http://www.ijmsc.org/doi/pdf/10.7224/1537-2073-13.S3.1

Kos, D., Kerckhofs, E., Nagels, G., D'hooghe, M. B., & Ilsbroukx, S. (2008). Review article: Origin of fatigue in multiple sclerosis: Review of the literature. *Neurorehabilitation and Neural Repair*, *22*(1), 91–100. https://doi.org/10.1177/1545968306298934

Krieger, N. (2005). Embodiment: A conceptual glossary for epidemiology. *Journal of Epidemiology and Community Health*, *59*(5), 350–355. https://doi.org/10.1136/jech.2004.024562

Kroencke, D. C., Lynch, S. G., & Denney, D. R. (2000a). Fatigue in multiple sclerosis: relationship to depression, disability, and disease pattern. *Multiple Sclerosis Journal*, *6*(2), 131–136. https://doi.org/10.1177/135245850000600213

Kroencke, D. C., Lynch, S. G., & Denney, D. R. (2000b). *Fatigue in multiple sderosis : relationship to depression , disability , and disease pattern*. *00*, 131–136.

Krupp, L. B., Alvarez, L. A., Larocca, N. G., & Labe, C. (1988). Fatigue in Multiple Sclerosis. *Arch Neurol*, *45*.

Krupp, L. B., & Elkins, L. E. (2000). *Fatigue and declines in cognitive functioning in multiple sclerosis*. *5*.

Krupp, L. B., Larocca, N. G., Muir Nash, J., & Steinberg, A. D. (1989). The fatigue severity scale: Application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of Neurology*. https://doi.org/10.1001/archneur.1989.00520460115022

Langdridge, D. (2008). Phenomenology and Critical Social Psychology: Directions and Debates in Theory and Research. *Social and Personality Psychology Compass*. https://doi.org/10.1111/j.1751-9004.2008.00114.x

Le Van Quyen, M., Martinerie, J., Navarro, V., Boon, P., D'Havé, M., Adam, C., Renault, B., Varela, F., & Baulac, M. (2001). Anticipation of epileptic seizures from standard EEG recordings. *Lancet*, *361*(9361), 183–188. https://doi.org/10.1016/S0140-6736(03)12780-8

Learmonth, Y. C., Dlugonski, D., Pilutti, L. A., Sandroff, B. M., Klaren, R., & Motl, R. W. (2013). Psychometric properties of the Fatigue Severity Scale and the Modified Fatigue Impact Scale. *Journal of the Neurological Sciences*. https://doi.org/10.1016/j.jns.2013.05.023

Leone, C., Severijns, D., Doležalová, V., Baert, I., Dalgas, U., Romberg, A., Bethoux, F., Gebara, B., Santoyo Medina, C., Maamâgi, H., Rasova, K., Maertens De Noordhout, B., Knuts, K., Skjerbaek, A., Jensen, E., Wagner, J. M., & Feys, P. (2016). Prevalence of walking-related motor fatigue in persons with multiple sclerosis: Decline in walking distance induced by the 6-minute walk test. *Neurorehabilitation and Neural Repair*, *30*(4), 373–383. https://doi.org/10.1177/1545968315597070

Lerdal, A., Gulowsen Celius, E., Krupp, L., & Dahl, A. A. (2007). A prospective study of patterns of fatigue in multiple sclerosis. *European Journal of Neurology*, *14*(12), 1338–1343. https://doi.org/10.1111/j.1468-1331.2007.01974.x

Lobentanz, Asenbaum, Vass, & Sauter. (2004). *Factors influencing quality of life in multiple sclerosis patients : disability , depressive mood , fatigue and sleep quality*. *18*, 6–13. https://doi.org/10.1111/j.1600-0404.2004.00257.x

Lohne, V., Aasgaard, T., Caspari, S., Slettebø, Å., & Nåden, D. (2010). The lonely battle for dignity: Individuals struggling with multiple sclerosis. *Nursing Ethics*, *17*(3), 301–311. https://doi.org/10.1177/0969733010361439

Loy, B. D., Taylor, R. L., Fling, B. W., & Horak, F. B. (2017). Relationship between perceived fatigue and performance fatigability in people with multiple sclerosis: A systematic review and meta-analysis. *Journal of Psychosomatic Research*, *100*(February), 1–7. https://doi.org/10.1016/j.jpsychores.2017.06.017

Lublin, F. D., & Reingold, S. C. (1996). Defining the clinical course of multiple sclerosis: The 2013 revisions. *Neurology*, *84*(9), 963. https://doi.org/10.1212/01.wnl.0000462309.76486.c5

Lutz, A., Lachaux, J.-P., Martinerie, J., & Varela, F. J. (2002). Guiding the study of brain dynamics by using first-person data: Synchrony patterns correlate with ongoing conscious states during a simple visual task. *Proceedings of the National Academy of Sciences*. https://doi.org/10.1073/pnas.032658199

Lutz, Antoine. (2007). Neurophenomenology and the study of self-consciousness. *Consciousness and Cognition*, *16*(3), 765–767. https://doi.org/10.1016/j.concog.2007.08.007

MacAllister, W. S., & Krupp, L. B. (2005). Multiple sclerosis - Related fatigue. *Physical Medicine and Rehabilitation Clinics of North America*, *16*(2), 483–502. https://doi.org/10.1016/j.pmr.2005.01.014

Mackenzie, I. S., Morant, S. V., Bloomfield, G. A., MacDonald, T. M., & O'Riordan, J. (2013). Incidence and prevalence of multiple sclerosis in the UK 1990-2010: A descriptive study in the General Practice Research Database. *Journal of Neurology, Neurosurgery and Psychiatry*, *85*(1), 79–84. https://doi.org/10.1136/jnnp-2013-305450

Madgwick, S. O. H. (2010). Automated calibration of an accelerometers , magnetometers and gyroscopes - A feasibility study. *Tehc Rep, x-Io Technologies Limited, Bristol, UK*.

Mancini, M., Smulders, K., Cohen, R. G., Horak, F. B., Giladi, N., & Nutt, J. G. (2017). The clinical significance of freezing while turning in Parkinson's disease. *Neuroscience*. https://doi.org/10.1016/j.neuroscience.2016.11.045

Matsushima, A., Yoshida, K., Genno, H., Murata, A., Matsuzawa, S., Nakamura, K., Nakamura, A., & Ikeda, S. ichi. (2015). Clinical assessment of standing and gait in ataxic patients using a triaxial accelerometer. *Cerebellum and Ataxias*. https://doi.org/10.1186/s40673-015-0028-9

Mayoh, J., & Onwuegbuzie, A. J. (2013). Toward a Conceptualization of Mixed Methods Phenomenological Research. *Journal of Mixed Methods Research*, *9*(1), 91–107. https://doi.org/10.1177/1558689813505358

McGivern, P. (2008). Reductive levels and multi-scale structure. In *Synthese*.

https://doi.org/10.1007/s11229-007-9232-3

Mcintyre, R., & Smith, D. W. W. (1989). *Husserl's Phenomenology: A Textbook*. 147–179. http://www.csun.edu/~vcoao087/pubs/intent.pdf

McLoughlin, J. V., Barr, C. J., Patritti, B., Crotty, M., Lord, S. R., & Sturnieks, D. L. (2016). Fatigue induced changes to kinematic and kinetic gait parameters following six minutes of walking in people with multiple sclerosis. *Disability and Rehabilitation*, *38*(6), 535–543. https://doi.org/10.3109/09638288.2015.1047969

Merleau-Ponty. (1968). *The Visible and the Invisible*.

Merleau-Ponty, M. (1963). PHENOMENOLOGY OF PERCEPTION. *Philosophical Books*. https://doi.org/10.1111/j.1468-0149.1963.tb00795.x

Merleau-Ponty, M. (1964). The Primacy of Perception and Its Philosophical Consequences. In *The Primacy of Perception*.

Merleau-Ponty, M., & Landes, D. A. (2013). Phenomenology of perception. In *Phenomenology of Perception*. https://doi.org/10.4324/9780203720714

Mezini, S., & Soundy, A. (2019). A thematic synthesis considering the factors which influence multiple sclerosis related fatigue during physical activity. *Behavioral Sciences*, *9*(7). https://doi.org/10.3390/bs9070070

Middleton, A., Fritz, S. L., & Lusardi, M. (2015). Walking speed: The functional vital sign. *Journal of Aging and Physical Activity*, *23*(2), 314–322. https://doi.org/10.1123/japa.2013-0236

Miller, C. (1997). The Lived Experience of Relapsing Multiple Sclerosis: A Phenomenological Study. *Journal of Neuroscience Nursing*, *29*(5).

Mills, R. J., & Young, C. A. (2008). A medical definition of fatigue in multiple sclerosis. *Qjm*, *101*(1), 49–60. https://doi.org/10.1093/qjmed/hcm122

Mills, Roger J., & Young, C. A. (2010). The relationship between fatigue and other clinical features of multiple sclerosis. *Multiple Sclerosis Journal*, *17*(5), 604–612. https://doi.org/10.1177/1352458510392262

Mills, Roger J., Young, C. A., Pallant, J. F., & Tennant, A. (2010). Development of a patient reported outcome scale for fatigue in multiple sclerosis: The Neurological Fatigue Index

(NFI-MS). *Health and Quality of Life Outcomes*, *8*, 1–10. https://doi.org/10.1186/1477-7525-8-22

Mitchell, S. D. (2004). Why integrative pluralism? *E:CO Emergence: Complexity and Organization*, *6*(1–2), 81–91. https://doi.org/10.1023/a:1012990030867

Moon, Y., Mcginnis, R. S., Seagers, K., Motl, R. W., Sheth, N., Wright, A., Ghaffari, R., & Sosnoff, J. J. (2017). *Monitoring gait in multiple sclerosis with novel wearable motion sensors*. 1–19. https://doi.org/10.1371/journal.pone.0171346

Moon, Y., McGinnis, R. S., Seagers, K., Motl, R. W., Sheth, N., Wright, J. A., Ghaffari, R., & Sosnoff, J. J. (2017). Monitoring gait in multiple sclerosis with novel wearable motion sensors. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0171346

Moran, D. (2010). Husserl, Sartre and Merleau-Ponty on Embodiment, Touch and the 'Double Sensation.' In *Sartre on the Body*. https://doi.org/10.1057/9780230248519_3

Moriya, R., & Kutsumi, M. (2010). Fatigue in Japanese people with multiple sclerosis. *Nursing and Health Sciences*, *12*(4), 421–428. https://doi.org/10.1111/j.1442-2018.2010.00554.x

Morris, M. E., Cantwell, C., Vowels, L., & Dodd, K. (2002). *Changes in gait and fatigue from morning to afternoon in people with multiple sclerosis*. *2*, 361–365.

Motl, R. W., Balantrapu, S., Pilutti, L., Dlugonski, D., Suh, Y., Sandroff, B. M., Lane, A., & Fernhall, B. (2013). Symptomatic correlates of six-minute walk performance in persons with multiple sclerosis. *European Journal of Physical and Rehabilitation Medicine*.

Motl, Robert W., McAuley, E., Snook, E. M., & Gliottoni, R. C. (2009). Physical activity and quality of life in multiple sclerosis: Intermediary roles of disability, fatigue, mood, pain, self-efficacy and social support. *Psychology, Health and Medicine*, *14*(1), 111–124. https://doi.org/10.1080/13548500802241902

Motl, Robert W., Sandroff, B. M., Kwakkel, G., Dalgas, U., Feinstein, A., Heesen, C., Feys, P., & Thompson, A. J. (2017). Exercise in patients with multiple sclerosis. *The Lancet Neurology*, *16*(10), 848–856. https://doi.org/10.1016/S1474-4422(17)30281-8

Motl, Robert W., Sandroff, B. M., Suh, Y., & Sosnoff, J. J. (2012). Energy cost of walking and its association with gait parameters, daily activity, and fatigue in persons with mild multiple sclerosis. *Neurorehabilitation and Neural Repair*.

https://doi.org/10.1177/1545968312437943

Motl, Robert W, Sandroff, B. M., Suh, Y., & Sosnoff, J. J. (2012). *Energy Cost of Walking and Its Association With Gait Parameters , Daily Activity , and Fatigue in Persons With Mild Multiple Sclerosis*. https://doi.org/10.1177/1545968312437943

Motta, C., Palermo, E., Studer, V., Germanotta, M., Germani, G., Centonze, D., Cappa, P., Rossi, S., & Rossi, S. (2016a). Disability and fatigue can be objectively measured in multiple sclerosis. *PLoS ONE*, *11*(2), 1–12. https://doi.org/10.1371/journal.pone.0148997

Motta, C., Palermo, E., Studer, V., Germanotta, M., Germani, G., Centonze, D., Cappa, P., Rossi, S., & Rossi, S. (2016b). Disability and fatigue can be objectively measured in multiple sclerosis. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0148997

Moya, P. (2014). Habit and embodiment in Merleau-Ponty. *Frontiers in Human Neuroscience*, *8*(JULY), 1–3. https://doi.org/10.3389/fnhum.2014.00542

Myers, C. S., & Rabiner, L. R. (1981). A Comparative Study of Several Dynamic Time-Warping Algorithms for Connected-Word Recognition. *Bell System Technical Journal*, *60*(7), 1389–1409. https://doi.org/10.1002/j.1538-7305.1981.tb00272.x

Newland, P. K., Thomas, F. P., Riley, M., Flick, L. H., & Fearing, A. (2012). The use of focus groups to characterize symptoms in persons with multiple sclerosis. *Journal of Neuroscience Nursing*, *44*(6), 351–357. https://doi.org/10.1097/JNN.0b013e318268308b

Newton, G., Griffiths, A., & Soundy, A. (2016). The Experience of Fatigue in Neurological Patients with Multiple Sclerosis: A Thematic Synthesis. *Physiotherapy*. https://doi.org/10.1016/j.physio.2016.11.004

Nogueira, L. A. C., dos Santos, L. T., Sabino, P. G., Alvarenga, R. M. P., & Santos Thuler, L. C. (2013). Factors for Lower Walking Speed in Persons with Multiple Sclerosis. *Multiple Sclerosis International*, *2013*, 1–8. https://doi.org/10.1155/2013/875648

Nyström, M., & Dahlberg, K. (2001). Pre-understanding and openness - A relationship without hope? *Scandinavian Journal of Caring Sciences*, *15*(4), 339–346. https://doi.org/10.1046/j.1471-6712.2001.00043.x

O’Cathain, A., Murphy, E., & Nicholl, J. (2010). Three techniques for integrating data in mixed methods studies. *BMJ (Online)*. https://doi.org/10.1136/bmj.c4587

Olsson, M., Lexell, J., & Söderberg, S. (2004). The meaning of fatigue for women with multiple sclerosis. *Journal of Advanced Nursing*, *49*(1), 7–15. https://doi.org/10.1111/j.1365-2648.2004.03258.x

Pace Giannotta, A. (2017). Varela on the Pragmatic Dimension of Phenomenology. *Constructivist Foundations*.

Pearson, S., Mancini, M., El-Gohary, M., McNames, J., & Horak, F. (2013). Turn detection and characterization with inertial sensors. *IcSPORTS 2013 - Proceedings of the International Congress on Sports Science Research and Technology Support*. https://doi.org/10.5220/0004647000190022

Petitmengin, C., Navarro, V., & Le Van Quyen, M. (2007). Anticipating seizure: Pre-reflective experience at the center of neuro-phenomenology. *Consciousness and Cognition*, *16*(3), 746–764. https://doi.org/10.1016/j.concog.2007.05.006

Petticrew, M., & Roberts, H. (2006). *Systematic Reviews in the Social Sciences*. https://doi.org/10.1002/9780470754887

Phan-Ba, R., Calay, P., Grodent, P., Delrue, G., Lommers, E., Delvaux, V., Moonen, G., Nagels, G., & Belachew, S. (2012). A corrected version of the Timed-25 Foot Walk Test with a dynamic start to capture the maximum ambulation speed in multiple sclerosis patients. *NeuroRehabilitation*. https://doi.org/10.3233/NRE-2012-0754

Pittion-Vouyovitch, S., Debouverie, M., Guillemin, F., Vandenberghe, N., Anxionnat, R., & Vespignani, H. (2006). Fatigue in multiple sclerosis is related to disability, depression and quality of life. *Journal of the Neurological Sciences*, *243*(1–2), 39–45. https://doi.org/10.1016/j.jns.2005.11.025

Podsiadlo, D; Richardson, S. (1991). The Timed Up and Go: A Test of Basic Functional Mobility for Frail Elderly Persons. *Journal of the American Geriatrics Society*.

Psarakis, M., Greene, D. A., Cole, M. H., Lord, S. R., Hoang, P., & Brodie, M. (2018). Wearable technology reveals gait compensations, unstable walking patterns and fatigue in people with multiple sclerosis. *Physiological Measurement*, *39*(7). https://doi.org/10.1088/1361-6579/aac0a3

Psarakis1, M., Greene1, D. A., Cole1, P. M. H., Lord2, P. S. R., , PhD, Ds. P., Hoang1, 2, & , PhD; Matthew Brodie2, 3, P. (2018). Wearable technology reveals gait compensations, unstable walking patterns and fatigue in people with Multiple Sclerosis. *Physiological Measurement*.

Qureshi, A., Brandt-Pearce, M., & Goldman, M. D. (2016a). Relationship between gait variables and domains of neurologic dysfunction in multiple sclerosis using six-minute walk test. *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*, *2016-Octob*, 4959–4962. https://doi.org/10.1109/EMBC.2016.7591840

Qureshi, A., Brandt-Pearce, M., & Goldman, M. D. (2016b). Relationship between gait variables and domains of neurologic dysfunction in multiple sclerosis using six-minute walk test. *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*. https://doi.org/10.1109/EMBC.2016.7591840

Radák, Z. (2018). Fundamentals of Strength Training. *The Physiology of Physical Training*, 55–80. https://doi.org/10.1016/b978-0-12-815137-2.00004-8

Raggi, A., Covelli, V., Schiavolin, S., Scaratti, C., Leonardi, M., & Willems, M. (2016). Work-related problems in multiple sclerosis: A literature review on its associates and determinants. *Disability and Rehabilitation*, *38*(10), 936–944. https://doi.org/10.3109/09638288.2015.1070295

Rasmussen, T. H. (1997). *Kroppens Merleau-Ponty*. *3*.

Razazian, N., Shokrian, N., Bostani, A., Moradian, N., & Tahmasebi, S. (2014). *Sociodemographic and Clinical Variables in Patients With*. *19*(1), 38–42.

Reinerman-Jones, L., Sollins, B., Gallagher, S., & Janz, B. (2013). Neurophenomenology: An integrated approach to exploring awe and wonder. *South African Journal of Philosophy*, *32*(4), 295–309. https://doi.org/10.1080/02580136.2013.867397

Riley, P. O., Paolini, G., Della Croce, U., Paylo, K. W., & Kerrigan, D. C. (2007). A kinematic and kinetic comparison of overground and treadmill walking in healthy subjects. *Gait and Posture*. https://doi.org/10.1016/j.gaitpost.2006.07.003

Romani, A., Cosi, V., Neurofisiopatologia, S., Evocati, L. P., Mondino, I. N. C., Mondino, C., & Neurologiche, S. (2004). *Fatigue in multiple sclerosis : and response Alfonsi*. *February*, 462–468.

Rossier, P., & Wade, D. T. (2001). Validity and reliability comparison of 4 mobility measures in patients presenting with neurologic impairment. *Archives of Physical Medicine and Rehabilitation*. https://doi.org/10.1053/apmr.2001.9396

Roy, J.-M., Petitot, J., Pachoud, B., & Varela, F. J. (1999). Naturalizing Phenomenology: Issues in Contemporary Phenomenology and Cognitive Science. In *Naturalizing Phenomenology: Issues in Contemporary Phenomenology and Cognitive Science*.

Rudroff, T., Kindred, J. H., & Ketelhut, N. B. (2016). Fatigue in multiple sclerosis: Misconceptions and future research directions. *Frontiers in Neurology*, *7*(AUG), 1–6. https://doi.org/10.3389/fneur.2016.00122

Sacco, R., Bussman, R., Oesch, P., Kesselring, J., & Beer, S. (2011). Assessment of gait parameters and fatigue in MS patients during inpatient rehabilitation: A pilot trial. *Journal of Neurology*, *258*(5), 889–894. https://doi.org/10.1007/s00415-010-5821-z

Sartre, J. (1956). *Being and Nothingness*. Philosophical Library.

Savci, S., Inal-it, D., Artiw, W., Guclu-gunduz, A., & Armutlu, K. (2005). *Six-minute walk distance as a measure of functional exercise capacity in multiple sclerosis*. *27*(22), 1365–1371. https://doi.org/10.1080/09638280500164479

Scalzitti, D. A., Harwood, K. J., Maring, J. R., Leach, S. J., Ruckert, E. A., & Costello, E. (2018). Validation of the 2-minute walk test with the 6-minute walk test and other functional measures in persons with multiple sclerosis. *International Journal of MS Care*. https://doi.org/10.7224/1537-2073.2017-046

Schmid, S., Schweizer, K., Romkes, J., Lorenzetti, S., & Brunner, R. (2013). Secondary gait deviations in patients with and without neurological involvement: A systematic review. *Gait and Posture*, *37*(4), 480–493. https://doi.org/10.1016/j.gaitpost.2012.09.006

Schubert, M., Wohlfarth, K., Rollnik, J. D., & Dengler, R. (1998). Walking and fatigue in multiple sclerosis: The role of the corticospinal system. *Muscle & Nerve*, *21*(8), 1068–1070. https://doi.org/10.1002/(sici)1097-4598(199808)21:8<1068::aid-mus12>3.3.co;2-m

Schüssler, G. (1992). Coping strategies and individual meanings of illness. *Social Science and Medicine*, *34*(4), 427–432. https://doi.org/10.1016/0277-9536(92)90303-8

Schwartz, C. E., Coulthard-Morris, L., & Zeng, Q. (1996). Psychosocial correlates of fatigue in multiple sclerosis. *Archives of Physical Medicine and Rehabilitation*.

https://doi.org/10.1016/S0003-9993(96)90162-8

Schwartz, J. E., Jandorf, L., & Krupp, L. B. (1993). The measurement of fatigue: A new instrument. *Journal of Psychosomatic Research*, *37*(7), 753–762. https://doi.org/10.1016/0022-3999(93)90104-N

Schwid, Petrie, Murray, Leitch, Bowen, Alquist, Pelligrino, Roberts, Harper-Bennie, Milan, Guisado, Luna, Montgomery, Lamparter, Ku, Lee, Goldwater, Cutter, Webbon, & Group, N. C. S. (2003). *A randomized controlled study of the acute and chronic effects of cooling*.

Sehle, A., Mündermann, A., Starrost, K., Sailer, S., Becher, I., Dettmers, C., & Vieten, M. (2011). *Objective assessment of motor fatigue in multiple sclerosis using kinematic gait analysis : a pilot study*. 1–13.

Severijns, D., Zijdewind, I., Dalgas, U., Lamers, I., Lismont, C., & Feys, P. (2017). The Assessment of Motor Fatigability in Persons with Multiple Sclerosis: A Systematic Review. *Neurorehabilitation and Neural Repair*, *31*(5), 413–431. https://doi.org/10.1177/1545968317690831

Shahrbanian, S., Duquette, P., & Mayo, N. E. (2018). Impairment, disability and fatigue in multiple sclerosis. *Caspian Journal of Internal Medicine*, *9*(3), 244–251. https://doi.org/10.22088/cjim.9.3.244

Shanahan, C. J., Boonstra, F. M. C., & Lizama, L. E. C. (2018). *Technologies for Advanced Gait and Balance Assessments in People with Multiple Sclerosis*. *8*(February). https://doi.org/10.3389/fneur.2017.00708

Sharrack, B., & Hughes, R. A. C. (1999). The Guy's neurological disability scale (GNDS): A new disability measure for multiple sclerosis. *Multiple Sclerosis*, *5*(4), 223–233. https://doi.org/10.1177/135245859900500406

Shema-Shiratzky, S., Gazit, E., Sun, R., Regev, K., Karni, A., Sosnoff, J. J., Herman, T., Mirelman, A., & Hausdorff, J. M. (2019). Deterioration of specific aspects of gait during the instrumented 6-min walk test among people with multiple sclerosis. *Journal of Neurology*, *266*(12), 3022–3030. https://doi.org/10.1007/s00415-019-09500-z

Shirai, S., Yabe, I., Takahashi-Iwata, I., Matsushima, M., Ito, Y. M., Takakusaki, K., & Sasaki, H. (2019). The Responsiveness of Triaxial Accelerometer Measurement of Gait

Ataxia Is Higher than That of the Scale for the Assessment and Rating of Ataxia in the Early Stages of Spinocerebellar Degeneration. *Cerebellum*. https://doi.org/10.1007/s12311-019-01025-5

Skerrett, T. N., & Moss-Morris, R. (2006). Fatigue and social impairment in multiple sclerosis: The role of patients' cognitive and behavioral responses to their symptoms. *Journal of Psychosomatic Research*, *61*(5), 587–593. https://doi.org/10.1016/j.jpsychores.2006.04.018

Smith, C. M., Fitzgerald, H. J., & Whitehead, L. (2015). How fatigue influences exercise participation in men with multiple sclerosis. *Qualitative Health Research*, *25*(2), 179–188. https://doi.org/10.1177/1049732314551989

Smith, C., Olson, K., Hale, L. A., Baxter, D., & Schneiders, A. G. (2011). How does fatigue influence community-based exercise participation in people with multiple sclerosis? *Disability and Rehabilitation*, *33*(23–24), 2362–2371. https://doi.org/10.3109/09638288.2011.573054

Socie, M. J., Motl, R. W., Pula, J. H., Sandroff, B. M., & Sosnoff, J. J. (2013). Gait variability and disability in multiple sclerosis. *Gait and Posture*, *38*(1), 51–55. https://doi.org/10.1016/j.gaitpost.2012.10.012

Sokolowski, R. (1999). Introduction to Phenomenology. In *Introduction to Phenomenology*. https://doi.org/10.1017/cbo9780511809118

Spain, R. I., St. George, R. J., Salarian, A., Mancini, M., Wagner, J. M., Horak, F. B., & Bourdette, D. (2012). Body-worn motion sensors detect balance and gait deficits in people with multiple sclerosis who have normal walking speed. *Gait and Posture*, *35*(4), 573–578. https://doi.org/10.1016/j.gaitpost.2011.11.026

Spencer, L. A., Silverman, A. M., & Cook, J. E. (2019). Adapting to multiple sclerosis stigma across the Life Span. *International Journal of MS Care*, *21*(5), 227–234. https://doi.org/10.7224/1537-2073.2019-056

Stone, A. A., Schwartz, J. E., Broderick, J. E., & Shiffman, S. S. (2005). Variability of momentary pain predicts recall of weekly pain: A consequence of the peak (or salience) memory heuristic. In *Personality and Social Psychology Bulletin*. https://doi.org/10.1177/0146167205275615

Stuifbergen, A. K., & Rogers, S. (1997). The experience of fatigue and strategies of self-care among persons with multiple sclerosis. *Applied Nursing Research*, *10*(1), 2–10. https://doi.org/10.1016/S0897-1897(97)80023-7

Surakka, J., Romberg, A., Ruutiainen, J., Virtanen, A., Aunola, S., & Mäentaka, K. (2004). Assessment of muscle strength and motor fatigue with a knee dynamometer in subjects with multiple sclerosis: A new fatigue index. *Clinical Rehabilitation*, *18*(6), 652–659. https://doi.org/10.1191/0269215504cr781oa

Sweetland, J., Howse, E., & Playford, E. D. (2012). A systematic review of research undertaken in vocational rehabilitation for people with multiple sclerosis. *Disability and Rehabilitation*, *34*(24), 2031–2038. https://doi.org/10.3109/09638288.2012.669019

Taborri, J., Studer, V., Grossi, P., Brambilla, L., Ferrò, M. T., Mantegazza, R., & Rossi, S. (2019). Measuring changes in gait kinematics due to walking-related fatigue in patients with Multiple Sclerosis. *Medical Measurements and Applications, MeMeA 2019 - Symposium Proceedings*. https://doi.org/10.1109/MeMeA.2019.8802195

Tabuteau-Harrison, S. L., Haslam, C., & Mewse, A. J. (2016). Adjusting to living with multiple sclerosis: The role of social groups. *Neuropsychological Rehabilitation*, *26*(1), 36–59. https://doi.org/10.1080/09602011.2014.993403

Téllez, N., Río, J., Tintoré, M., Nos, C., Galán, I., & Montalban, X. (2005). Does the modified fatigue impact scale offer a more comprehensive assessment of fatigue in MS? *Multiple Sclerosis, 11*(2), 198–202. https://doi.org/10.1191/1352458505ms1148oa

Thompson, E., Lutz, A., & Cosmelli, D. (2005). Neurophenomenology: An introduction for neurophilosophers. In *Cognition and the Brain: The Philosophy and Neuroscience Movement*. https://doi.org/10.1017/CBO9780511610608.003

Tiemersma, D. (1982). ‘Body-Image’ and ‘Body-Schema’ in the existential phenomenology of Merleau-Ponty. *Journal of the British Society for Phenomenology*, *13*(3), 246–255. https://doi.org/10.1080/00071773.1982.11007591

Toombs, S. K. A. Y. (1993). *The Meaning of Illness: A Phenomenological Account of the Different Perspectives of Physician and Patient* (1st ed.). Springer Netherlands. https://doi.org/10.1007/978-94-011-2630-4

Turpin, M., Kerr, G., Gullo, H., Bennett, S., Asano, M., & Finlayson, M. (2018).

Understanding and living with multiple sclerosis fatigue. *British Journal of Occupational Therapy*, *81*(2), 82–89. https://doi.org/10.1177/0308022617728679

Valenzuela-Moguillansky, C., Vásquez-Rosati, A., & Riegler, A. (2017). Building a science of experience: Neurophenomenology and related disciplines. *Constructivist Foundations*, *12*(2), 131–138.

van der Linden, M. L., Andreopoulou, G., Scopes, J., Hooper, J. E., & Mercer, T. H. (2018). Ankle Kinematics and Temporal Gait Characteristics over the Duration of a 6-Minute Walk Test in People with Multiple Sclerosis Who Experience Foot Drop. *Rehabilitation Research and Practice*, *2018*, 1–6. https://doi.org/10.1155/2018/1260852

Varela, Francisco J, Thompson, Evan, & Rosch, E. (1995). Embodied Mind: Cognitive Science and Human Experience. *Leonardo*, *39*(3), 245–251.

Varela, F. J. (1996). *NEUROPHENOMENOLOGY A Methodological Remedy for the Hard Problem I: A Cartography of Approaches*.

Varela, F. J., Thompson, E., & Rosch, E. (1991). NOOO The embodied mind: Cognitive science and human experience. In *The embodied mind: Cognitive science and human experience.*

Varela, F. J., Thompson, E., Rosch, E., & Kabat-Zinn, J. (2016). The embodied mind: Cognitive science and human experience. In *The Embodied Mind: Cognitive Science and Human Experience*. https://doi.org/10.29173/cmplct8718

Vienne-Jumeau, A., Quijoux, F., Vidal, P. P., & Ricard, D. (2019). Value of gait analysis for measuring disease severity using inertial sensors in patients with multiple sclerosis: Protocol for a systematic review and meta-analysis. *Systematic Reviews*, *8*(1), 1–5. https://doi.org/10.1186/s13643-018-0918-z

Vijayasingham, L., Jogulu, U., & Allotey, P. (2017). Work Change in Multiple Sclerosis as Motivated by the Pursuit of Illness-Work-Life Balance: A Qualitative Study. *Multiple Sclerosis International*, *2017*, 1–7. https://doi.org/10.1155/2017/8010912

Vijayasingham, L., & Mairami, F. F. (2018). Employment of patients with multiple sclerosis : the influence of psychosocial – structural coping and context. *Degenerative Neurological and Neuromuscular Disease*, 15–24.

Vörös, S., Froese, T., & Riegler, A. (2016). Epistemological odyssey: Introduction to special issue on the diversity of enactivism and neurophenomenology. *Constructivist Foundations*, *11*(2), 189–203.

Ware, J. E., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (Sf-36): I. conceptual framework and item selection. *Medical Care*, *30*(6), 473–483. https://doi.org/10.1097/00005650-199206000-00002

Wehrle, M. (2020). Being a body and having a body. The twofold temporality of embodied intentionality. *Phenomenology and the Cognitive Sciences*, *19*(3), 499–521. https://doi.org/10.1007/s11097-019-09610-z

Weinshenker, B. G., Bass, B., Rice, G. P. A., Noseworthy, J., Carriere, W., Baskerville, J., & Ebers, G. C. (1989). The natural history of multiple sclerosis: A geographically based study: I. Clinical course and disability. *Brain*. https://doi.org/10.1093/brain/112.1.133

Welch, L., & Palmer, R. E. (1971). Hermeneutics, Interpretation Theory in Schleiermacher, Dilthey, Heidegger and Gadamer. *The Journal of Aesthetics and Art Criticism*. https://doi.org/10.2307/429547

Wertz, F. J. (2005). Phenomenological research methods for counseling psychology. In *Journal of Counseling Psychology*. https://doi.org/10.1037/0022-0167.52.2.167

Whittemore, R., Chase, S. K., & Mandle, C. L. (2001). Validity in qualitative research. *Qualitative Health Research*. https://doi.org/10.1177/104973201129119299

Wilkes, C., Kydd, R., Sagar, M., & Broadbent, E. (2017). Upright posture improves affect and fatigue in people with depressive symptoms. *Journal of Behavior Therapy and Experimental Psychiatry*. https://doi.org/10.1016/j.jbtep.2016.07.015

Witchel, H. J., Oberndorfer, C., Needham, R., Healy, A., Westling, C. E. I., Guppy, J. H., Bush, J., Barth, J., Herberz, C., Roggen, D., Eskofier, B. M., Rashid, W., Chockalingam, N., & Klucken, J. (2018). *Thigh-Derived Inertial Sensor Metrics to Assess the Sit-to-Stand and Stand-to-Sit Transitions in the Timed Up and Go (TUG) Task in Multiple Sclerosis*.

Wolkorte, R., Heersema, D. J., & Zijdewind, I. (2015). Reduced dual-task performance in ms patients is further decreased by muscle fatigue. *Neurorehabilitation and Neural Repair*. https://doi.org/10.1177/1545968314552529

Yorkston, K. M., Johnson, K., Klasner, E. R., Amtmann, D., Kuehn, C. M., & Dudgeon, B.

(2003). Getting the work done: A qualitative study of individuals with multiple sclerosis. *Disability and Rehabilitation*, *25*(8), 369–379. https://doi.org/10.1080/0963828031000090506

Yorkston, K. M., Klasner, E. R., & Swanson, K. M. (2001). Communication in Context: A Qualitative Study of the Experiences of Individuals with Multiple Sclerosis. *American Journal of Speech-Language Pathology*, *10*(2), 126–137. https://doi.org/10.1044/1058-0360(2001/013)

Zahavi, D. (2010). Handbook of Phenomenology and Cognitive Science. *Handbook of Phenomenology and Cognitive Science*. https://doi.org/10.1007/978-90-481-2646-0

Zahavi, D. (2019a). Applied phenomenology: why it is safe to ignore the epoché. *Continental Philosophy Review*, *0123456789*. https://doi.org/10.1007/s11007-019-09463-y

Zahavi, D. (2019b). Getting It Quite Wrong: Van Manen and Smith on Phenomenology. *Qualitative Health Research*, *29*(6), 900–907. https://doi.org/10.1177/1049732318817547

Zampieri, C., Salarian, A., Carlson-Kuhta, P., Nutt, J. G., & Horak, F. B. (2011). Assessing mobility at home in people with early Parkinson's disease using an instrumented Timed Up and Go test. *Parkinsonism and Related Disorders*. https://doi.org/10.1016/j.parkreldis.2010.08.001

Zellini, F., Niepel, G., Tench, C. R., & Constantinescu, C. S. (2009). Hypothalamic involvement assessed by T1 relaxation time in patients with relapsing—remitting multiple sclerosis. Multiple Sclerosis Journal, 15(12), 1442–1449. https://doi.org/10.1177/1352458509350306

Zhang, Y., Taylor, B. V., Simpson, S., Jr, Blizzard, L., & van der Mei, I. (2019). Patient-reported outcomes are worse for progressive-onset multiple sclerosis than relapse-onset multiple sclerosis, particularly early in the disease process. European journal of neurology, 26(1), 155–161. https://doi.org/10.1111/ene.13786

Ziemke, T., Zlatev, J., & Frank, R. (2007). Body, language, and mind (pp. 241- 263). Berlin: Mouton de Gruyter.

Zifko, U. A., Rupp, M., Schwarz, S., Zipko, H. T., & Maida, E. M. (2002). Modafinil in treatment of fatigue in multiple sclerosis. Results of an open-label study. Journal of neurology, 249(8), 983–987. https://doi.org/10.1007/s00415-002-0765-6

Appendices

Forthcoming work

1) Conference paper, middle author:
   Aiswarya Nagasubramony, Harry J. Witchel, Carina E I Westling, Rebecca F Player, and Kathleen T Galvin. (2020). Using wearable inertial sensors to detect different strategies for the sit-to-stand transition in multiple sclerosis. In 32nd European

Conference on Cognitive Ergonomics (ECCE 2020), October 6–9, 2020, SIENA, Italy. ACM, New York, NY, USA, 4 pages. https://doi.org/10.1145/3335082.3335115

2) First name author submitted, in the process of revisions:
   Rebecca F Player, Aiswarya Nagasubramony, Kathleen T Galvin, Harry J Witchel. (2021). Comparison of the detection of U-turns in a healthy and multiple sclerosis population using gyroscopy, magnetometry and accelerometry signals from wearable sensors located at the sternum and ankle. Sensors.
3) Co-authorship of a book chapter:
   Galvin, K., Thurlow, O. and Player, R., (2020). From Phenomenology to Practice: Theoretical foundations and phenomenological methods. In: K. Aranda, ed., Critical Qualitative Health Research: Exploring Philosophies, Politics and Practices, 1st ed. Abingdon, Oxon: Routledge.

Appendices A: Data transcriptions examples

A (i): M084: Transcript

For: Brighton University

Title:	M084
Type:	Interview
Convention:	Verbatim / Qualitative Analysis
Audio Length:	19 minutes

Transcriber:	EST/RY1
At:	Essential Secretary Ltd
Completion Date:	24.01.2019

Transcriber's Notes:

Any difficulties experienced, accents and general comments

number of unclears	0	**number of inaudibles**	0
spell check performed	Yes	**proofing performed**	Yes
audio quality	Clear		
speaker related issues	None		
equipment related issues	None		
terminology issues	None		
other comments	None		

Please find attached your completed transcript.

Whilst every effort is made to ensure that the attached transcript is an accurate record of your audio recording, sometimes difficulties are encountered in understanding technical words, people speaking with a foreign accent and in some cases when somebody is speaking from a crowded room with a lot of background noise and from mobile phones.

Where we have had difficulty understanding words we have indicated this as [unclear] with the appropriate time stamp, or simply attempted to spell the word phonetically but followed it with [ph].

[Start of recording]

INT: So can you discuss with me, your lived experiences about MS fatigue, you may start by reflecting on the assessment we've completed, it's up to you.

RES: I'd, I'd like to start from the beginning of my MS, which was twenty seven years ago, so at that time, I had a lot of attack, MS attacks, which I had had previously, but I hadn't actually been diagnosed until the end of, of that year. So ninety one, was when I was when I was diagnosed eventually, which was great. I had two little children, one of them was only born in the February of that year, the first one was born, um ninety eight, err ninety nine, sorry ninety nine, ninety one, so eighty nine, ninety one.

INT: Yeah.

RES: Um anyway so I had two little ones, two little tiny girls, and I also at the same time my father was diagnosed with um end stage cancer, and so I had to cope with, with him dying, me not being able to work anymore, because I was, when I, when I told them at work.

INT: Yeah.

RES: That I had MS and wanted to work in different places that weren't so hot as the Labour ward, which is where I was working and they said "No we can't do that, you've got to work where we want you to work, you can't, you can't, you can't decide where you want to work, we decide where we want". So I said "Well I can't cope with that then, I can't cope in this heat".

INT: Yeah.

RES: Therefore I was advised to take early retirement, which is what I did, which was great at the time, because I had two little children.

INT: Yeah.

RES: And it meant I could stay at home with them and then we had to move because there's no way that we could live where we were living, cos my, my income was half of, half of our outgoings if you like.

INT: Yeah.

RES: So if I couldn't go back to work, we couldn't carry on living where we were living, so and my husband went for um, (pause) move his job, so we had to move our house and everything too, there was a lot of, a lot of stress in that period.

INT: Um.

RES: And I you know, I was having such a lot of attacks, I couldn't feel from my chest downwards, all that stuff, but still had to carry on. And um at that time, my fatigue was really more up in my head.

INT: Okay.

RES: So I, I'd be trying to get you know, trying to walk the girls to school and that sort of thing, was hard work because I couldn't feel my legs, my feet, when they started to get the feeling back, it was like broken glass, and that went on for like months at a time.

INT: Okay.

RES: And how long it was lasting for, it was four years, before I could buy any new shoes, because I couldn't tell what my feet were doing.

INT: Because you couldn't feel them?

RES: I couldn't, if I could feel them, they were feeling wrong things, like they.

INT: Okay.

RES: Like the perception was so awry.

INT: Okay.

RES: That I couldn't tell, it felt like I had blisters on the back of my feet, or pebbles under my knees, all sorts of things like that.

INT: Okay.

RES: Um and that really plays with your mind, you know, when you have to keep checking your body to see if, it is okay and it takes, after a few years you, you do become accustomed to it, but the fatigue was.

INT: Okay yeah.

RES: Exacerbated by um very um, I don't know how you say, when the hormones are so involved as well.

INT: Yeah when they were high.

RES: They're going up and down, up and down, I used to have terrible um premenstrual tension.

INT: Okay yeah.

RES: I used to have very heavy bleeding and then I used, I used to be a monster for two out of four weeks you know, really horrible nasty person.

INT: Yeah.

RES: And that's very exhausting to be like that and to know you're being so horrible, it's really but that's aside, that's another thing.

INT: Oh yeah.

RES: But that also doesn’t help with the fatigue because I used to, if you know, take the girls to school and then I’d, when they would come home, I would be so tired, I’d just be lying down on the settee and they’d just talk to me but I’d just be lying down there completely prone and I, I would talk, but I just could not lift my head up.

INT: So you could talk physically?

RES: I could talk, I could communicate, but I could not get my body up to do anything, and that was a horrible time and I think my life started to get more normal after I had the menopause which came early, I was very lucky.

INT: Yeah.

RES: That’s when I was about fifty two I spose, and then I, I lost all that sort of fatigue and the only fatigue I have now is muscle fatigue, when we’re, my legs decide they’re not going to work anymore properly and then I, I sort of go, I don’t, I don’t have enough control over my body to be able to sit upright, like this, or stand up like, or get a water like this.

INT: Okay.

RES: And at the moment, I spend my life, when I’m standing up, telling my leg to straighten, stand straight instead of all, and when I do that.

INT: Okay.

RES: I can walk, you know, like I can walk here, but as long as I’ve got something safe around me I’m fine.

INT: Okay that’s interesting.

RES: So that’s it really.

INT: Can you um.

RES: That’s the end of my fatigue talk.

INT: And can you just tell me about, um so when you do get muscle fatigue, can you give like an example of when you did feel it and kind of?

RES: When I feel it, when it’s going, I, I, when it’s, when I feel as though my legs are going, I say “I’ve got to sit down now”.

INT: Uh huh.

RES: I have a saddle, a saddle stool in the kitchen which helps me a bit.

INT: Okay.

RES: But then when I drop things and I keep having to go down, and come up, I, I, it makes me kind of giddy, I dunno how, how else to explain it.

INT: Okay.

RES: Um and then when I do stand up, because I’ve been doing all, all that sort of bending down and what have you, then I can’t really get my balance properly, and that’s when I have to tell my leg to, to stay straight, because I have a tendency when I'm tired, just to not bother, I go over like this.

INT: Yeah.

RES: And then eventually my legs say I can't hold your body like that, don't be stupid, so I go down on the floor, get down and then pull myself up to sit in the other room, that's, that's what happens.

INT: Okay, yeah that's how you do it.

RES: And Dave gets very cross at me, he says "You've got, you've got your Quasimodo on again.

INT: (Chuckling).

RES: Well that's what I look like, you know, and it makes him feel really, it makes him feel really horrible.

INT: Um.

RES: He says "I can't bear this, stand up straight".

INT: Um can we just go back to when you said, when you first had it, when you were first getting symptoms but you weren't actually diagnosed, you said you had.

RES: Yes.

INT: Cognitive.

RES: I had um, the first diagnostics, the symptom I had, I also had pre, the um, two years previously, I, I kept having little attacks, it was optic neuritis.

INT: Okay.

RES: And I had some horrible um optic effects after that.

INT: Yeah.

RES: In the pursuing years, um but I've forgotten what the question is now sorry.

INT: Don't worry um, no I said can you go into a bit more detail, when you had the, you said it affected you mentally, the fatigue?

RES: Yes, yes it did yes.

INT: Yeah, can you explain, give anymore um description with that, so do you have an example of when you did feel like it affected you mentally?

RES: Mentally in sort of, when I say mentally.

INT: Yeah.

RES: I'm just trying, trying to process the thoughts.

INT: Okay.

RES: And the understanding of what was happening to me, it's, that's when I said it's a brain game, I always call it a brain game.

INT: Yeah, yeah.

RES: Because that's what it feels like, you have to, you can almost feel the cogs whirring.

INT: Yeah and then.

RES: You know, watching me do it and I, and then becoming um, what's the, see my, I can't, I can't.

INT: Don't worry, don't worry.

RES: I can't verbalise it anymore.

INT: Yeah.

RES: Um become, not becoming accustomed, becoming, accepting of the fact that, that um, things are not what they feel they are.

INT: Yeah.

RES: But it, it's just a sensation, just, just processing that all the time.

INT: Yeah, okay.

RES: It's very, very, it, it, it's a kind of, you know, you think oh for goodness sake, all the time.

INT: Yeah.

RES: It's sort of that.

INT: Yeah I understand.

RES: It's very clever of you to understand, I don't understand (chuckling).

INT: Um can you think of an experience where you did feel like with the whole, you know, you said you felt the cogs turning, can you feel, can you think back to a time when that happened and can you explain that experience?

RES: Um.

INT: So I think you mentioned before, you said you first felt it when you were walking.

RES: Well oh the optic neuritis is the easiest one to explain, when I couldn't, when I, when I had double vision with it, when I could see two precisely similar.

INT: Objects yeah.

RES: View, views of what was going on.

INT: Yeah.

RES: And then you're driving and you, you'd think oh which one do I follow.

INT: Yeah.

RES: So I, I ended up having to put a, a patch over that eye, simply so I could see straight to walk because.

INT: And that helped?

RES: At that time I had a different um, with the optic neuritis, that helped.

INT: Yeah.

RES: And, and it was quite a fun thing, because the girls would say “Oh mummy’s being a pirate today”.

INT: (Chuckling).

RES: To try, to try and make it easier for them, um, I don’t think I’m actually answering the question properly.

INT: No you are, you’re doing, and it’s really useful, um it’s just yeah that’s really good, so you’ve talked a little bit about how it affects your um thought process.

RES: You have, yes, it’s just how to explain it to other people, I found really hard and therefore.

INT: Yeah.

RES: That’s when I tended to become very insular.

INT: Okay.

RES: Um I found it easier not to go out, and I didn’t want to explain things, because when you concentrate on, on the self, it’s very difficult to escape that horrible.

INT: Yeah.

RES: A horrible thing you’ve become, its not, for me it was not a good thing to have to concentrate on the way that my body was working.

INT: Yeah.

RES: I’d prefer to go back to the time when I was concentrating on the world outside.

INT: Okay.

RES: And that err, yeah I got, I got dragged down in that sort of being aware of myself, just simply because of all the things that were happening, the symptoms.

INT: Yeah and do you still feel that you have to concentrate on yourself all the time?

RES: Well yes because that’s one of the reasons why I don’t walk without, without having a frame or.

INT: Yeah.

RES: Or cane or anything.

INT: Yeah.

RES: I can walk, as you can see I can walk.

INT: Yeah.

RES: But if I haven't got something to make sure that I don't fall over when I trip on a paving slab, or whatever, I don't want to do it, because it's too much of an effort to try and explain to people, "Just leave me here on the floor".

INT: Yeah.

RES: "Whilst I get my equilibrium back, until I'm ready to walk by myself", because how can you say that to people, they're trying to help you.

INT: Um.

RES: And if they tried to help, they'll be pulling your arm up or something and that would just automatically make me, not be able to stand on your feet. So I'm, I'm afraid that I've just, I've spoiled my capacity of exercising, just by not wanting to ask people for help.

INT: Okay.

RES: It's bad enough my husband helping.

INT: And you don't want to ask him for help because.

RES: No, because they don't understand that I've got to come, I've got to readjust, I've got to get my headspace right before I can get my body space right.

INT: Yep, okay so you almost have to plan.

RES: So I need some time yeah.

INT: Yeah okay that's interesting.

RES: And it, it's one of those horrible, you see I'm fidgeting all the time.

INT: It's fine.

RES: Because I don't like it, I'm trying to escape from it, from the conversation yeah.

INT: Sorry.

RES: It's alright, it's not your fault (chuckling).

INT: And one last thing, um can you just reflect, it doesn't matter how little or how big, on the assessment, that you've just had, how did that make you feel?

RES: Oh the assessment is great, I felt.

INT: Yeah in terms of your fatigue I mean?

RES: No, it was no problem, because I felt safe, there were chairs everywhere.

INT: Yeah.

RES: I didn't feel as though I've been put under any undue stress at all.

INT: Good, good.

RES: It was great, yeah and it's very easy.

INT: Good and did you feel any fatigue at any point or not?

RES: I started to feel as though my legs were getting a bit draggy at the end, but because everything.

INT: Okay.

RES: Felt safe, there was no problem.

INT: Good yes.

RES: I, I think you know, worried to go out, I mean, it was really nice when, when I had Dave come with me to time my walking, and he came on my little motor scooter next to us.

INT: Right, yeah.

RES: He, he was timing me, and then when he saw that my legs were dragging, he said "Okay, get off the scooter now".

INT: Okay.

RES: So it was really, really nice to do it like that.

INT: Yeah.

RES: And again sometimes when I go walking, just with the frame, and he, he'll come on his little pull out cycle, he's got one of these things that he can put in the boot at the same time as that.

INT: That's very handy.

RES: Yes it's really nice.

INT: (Chuckling) um.

RES: So yeah that's nice to do that.

INT: Good and do you have anything else to add in terms of um MS and fatigue with you?

RES: I think, that the, the mental fatigue is what.

INT: Uh huh.

RES: Causes most problems.

INT: And why do you think that?

RES: Because it's very difficult to think when you're fatigued, that's it really.

INT: Um okay, yeah that's good.

RES: I think, that's all I've got to say.

INT: Okay thank you, (long pause) let me just note, eighteen minutes, twenty four seconds.

[End of Recording]

A (ii): M089: Transcript

For:	Brighton University
Title:	M089
Type:	Interview
Convention:	Verbatim / Qualitative Analysis
Audio Length:	19 minutes
Transcriber:	EST/RY1
At:	Essential Secretary Ltd
Completion Date:	29.03.2019

Transcriber's Notes:

Any difficulties experienced, accents and general comments

number of unclears	0	**number of inaudibles**	0
spell check performed	Yes	**proofing performed**	Yes
audio quality	Clear		
speaker related issues	None		
equipment related issues	None		
terminology issues	None		
other comments	None		

Please find attached your completed transcript.

Whilst every effort is made to ensure that the attached transcript is an accurate record of your audio recording, sometimes difficulties are encountered in understanding technical words, people speaking with a foreign accent and in some cases when somebody is speaking from a crowded room with a lot of background noise and from mobile phones.

Where we have had difficulty understanding words we have indicated this as [unclear] with the appropriate time stamp, or simply attempted to spell the word phonetically but followed it with [ph].

[Start of recording]

INT: So can you describe in as much detail as possible, about your lived experiences of fatigue?

RES: Okay um well normally living my everyday life um, around the house, it's very difficult, I, I cleaning, I, I while cleaning, so I tend to do it in two lots now, I do upstairs first and then you know, do downstairs. Sometimes um I have to take a rest in between you know, after activity of half an hour or an hour, it depends on how much um I've, I found on a particular day but normally um, I, it's not a great problem. Um.

INT: And when you say you rest, um how long do you rest for, in the in between?

RES: Oh it just depends, I mean, I, usually, um, let's say if I go for a walk, err sometimes in the summer especially, you know, if it's nice, I do, I do walk as much as I can, I go along the seafront and err, before I, I sort of go back home, I, I need to sit down and, and rest.

INT: Um.

RES: Um it depends on how fatigued I am, and also what's happening at a particular time, so but I tend to recover fairly quickly, within twenty minutes, half, you know, it's usually enough to carry on, but sometimes obviously you know, I sit down and rest longer.

INT: Yeah um so can you think of any situation in particular that stands out for you, where you felt really fatigued um and can you, if possible just go into it, just in as much detail and describe how it made you feel err?

RES: Well heat affects me, if it's very hot.

INT: Yeah.

RES: Then I get err, my legs get very, very heavy let's say.

INT: Okay.

RES: Um err the coordination goes much more quickly err and I can't function that well in the heat or, I love it, I love the sun and all that, but I can't function very well, so that really affects me quite badly. Um, I can also remember back in before I was diagnosed, before I knew what was wrong with me, um, I was fine for most activities, but if I exerted that bit high, like, I used to do the London to Brighton, Brighton bike ride.

INT: Fabulous.

RES: But Turners Hill and Ditching Beacon I absolutely dread it, because I didn't know but I suddenly.

INT: Yeah.

RES: It, it's that little extra, on the level fine, you know.

INT: Okay.

RES: Because you can just push and, and go.

INT: Yeah.

RES: Err we got to err, I can, it's, you know, everything that I could do at a good steady rate, it's not so stressful.

INT: Yeah, yeah.

RES: But as soon as little changes and you have to do more, it gets difficult and Turners Hill, oh, I remember gritting my teeth and trying to get up and Ditchling Beacon even worse of course, I did it about four times and since, but that's, but it's now thirty years ago.

INT: Okay.

RES: Um and, and before that as well, ever, whenever I did something that was just a bit harder than the normal steady exertion, I felt it.

INT: Yeah okay and when you mean you felt it, is it just that it, you suddenly felt exhausted or?

RES: Well it's the leg weight that pull you back, you can hardly err you know, move on, um, err, I remember I used to cycle around Brighton and going over you know, in front of the University, err, Codeine Lane, err up the hill there.

INT: Yeah, yeah.

RES: And, and places, places like that, always have been, and, and I blamed myself, I was like oh my God, I'm not fit enough, I must lose weight and you know, I must try harder and all that but it was fatigue setting in.

INT: Yeah oh okay um and when you said, I just want to go back, the heat affects you, and heat affects you in fatigue, um you said that your legs get heavy?

RES: Well my coordination also, again with fatigue, I, I, again my leg, it's my right leg that's affected, the left leg is fine, it's my right leg mainly.

INT: Okay yeah.

RES: And that becomes, I call it "mushy", it doesn't, you know, it doesn't, you know, I can't control it anymore.

INT: Okay so yeah, so you feel not in control of it, you feel you can't move as well?

RES: Yeah, yeah.

INT: Yeah okay.

RES: Well I really you know, sometimes have to sit down, I can't move anymore.

INT: Yeah.

RES: And then I also get pain um.

INT: Okay.

RES: Um it, it gets painful in my leg, you know, apart from that, I also have some problems with my spine of course, you know, you have that sort of problem, so it all works together and then it makes then impossible for me to carry on.

INT: Okay, okay um.

RES: Or very, very difficult let's say.

INT: Yeah.

RES: If, if the life depended, you can do a little extra (chuckling).

INT: Yeah um so how has, so say fatigue affects you with your balance.

RES: Yes.

INT: And your, your you exert yourself a bit more, so with the coordination, um so with your balance for example, how would you say that's affected when you get fatigued and what?

RES: Um well I mean I'm always affected my, my balance, I err, I, I can't walk in a straight line.

INT: Uh huh.

RES: I don't know whether you've noticed that?

INT: You're fine (chuckling).

RES: Um I can't stand up on, on one leg, you know, I can walk, I can't run, I think it's because when you're running, you have, your feet often aren't, for too long, so my balance I can't cope with that um.

INT: Okay.

RES: Um I can't walk up and down stairs, I mean I can walk up and down any stair, as long as I can hold onto something, so I always need a rail, a hand rail then I'm fine, um I don't, err, especially walking down, it's very uncomfortable for me, because you know, my sense of balance, I feel I'm falling.

INT: Okay interesting.

RES: Um walking, I have to walk with a stick now, I mean not here, err you know, I, I can see what the path is like, I, I know, I always have to prepare myself where I'm going to go and have to use a stick.

INT: Okay.

RES: Because any unevenness, and I'm, I forget to think of my feet, and I'm, I'm gone.

INT: Yeah.

RES: I don't want to injure myself.

INT: So you take the stick when you don't really know the terrain that much, what to expect?

RES: If I go into town, if I do anything now, I, I always have my stick.

INT: Okay.

RES: And that's been increasingly necessary over the last few years.

INT: And do you think, do you think that helps with the fatigue a little bit or not?

RES: It does help with the fatigue as well, because I, I do support myself a bit on it, but it's more for balance, it's not so much for toppling [ph] myself let's say.

INT: Okay that's good.

RES: But it does help to take the strain off this leg.

INT: Yeah um and can you think of any different scenario or situation where you have felt tired, and fatigued um throughout your diagnosis? So you've mentioned like it affects your walking, does lack of balance affect anything else or?

RES: No it's just when I, you know, the heat does affect it, but that's from the outside, but otherwise it's just extra activity, then, then I get fatigued yeah but not.

INT: Okay.

RES: Not in any other way, I mean the first time, I mean I had a, a, you know, I only realised that now, after I, you know, was diagnosed when I was nineteen, I um, I was going to work and I was from the bus stop to the entrance, I was working in a hospital in fact, it's about three hundred metres, something like that.

INT: Yeah.

RES: Well I can't remember exactly but you know that kind of distance.

INT: Yeah.

RES: And there was a bit of an incline, I was nineteen, I don't remember exactly, it wasn't the summer, but it was, it was quite hot as well.

INT: Okay.

RES: And I walked with some colleagues and I remember having to grit my teeth to walk up the distance there.

INT: Oh really.

RES: And that was the first time.

INT: Interesting.

RES: I think that was my first err relapse.

INT: Yeah.

RES: And that lasted for about two weeks.

INT: And when you said you grit your teeth was it because you, was it because you couldn't walk on it or?

RES: I, I couldn't, you know, I had, I didn't want to show that.

INT: Yeah.

RES: I couldn't walk.

INT: Yeah.

RES: But I had to, I had, had to put such an effort in, into not showing, err and, and trying to pretend that I was walking normally.

INT: Yeah.

RES: And you know, just to make the distance up there.

INT: Okay.

RES: And that lasted two weeks and I remember like, you know, as clearly as anything, and I always, it's always been in my mind, as like what happened there, what happened there? And now I know that's what it was.

INT: Yeah.

RES: And now I know that's what it was.

INT: Yeah.

RES: It was a, a you know, a period of fatigue.

INT: So in that, you said it lasted for two weeks, in those two weeks, do you remember any other um, scenarios?

RES: No it just came on, nothing.

INT: So then for, for those two weeks, do you remember, like cos you were at University did you say?

RES: No, no I was working in a hospital yeah.

INT: Okay um did that affect your working?

RES: No, no it was just.

INT: No.

RES: That extra effort of.

INT: Okay.

RES: Because there was, it was a bit of an incline walking, I mean on the level I wouldn't have noticed it.

INT: Yeah.

RES: But as soon as I had to walk a bit up, although it wasn't very steep.

INT: Oh dear, yeah.

RES: You know, I just suddenly you know it’s like, attaching lead weights.

INT: Yeah, yeah.

RES: Big lead weights and you’re trying to, trying to drag yourself along.

INT: Yeah.

RES: And not sure, like you have lead weights on your legs, and walk in, “Hello, good morning”.

INT: Yeah I can imagine that’s very hard.

RES: Yeah it, I still remember it.

INT: Okay um.

RES: So it’s that kind of thing you know, you, you’re dragged down, you, you have to make a super effort to do the normal thing.

INT: And did you just fell it in your legs, the lead, did you feel it anywhere else?

RES: No, no it’s just.

INT: Just in your legs?

RES: Yeah just, holding it down.

INT: Yeah okay.

RES: Although my arms have never been affected no, apart from poor coordination, err you know.

INT: Okay.

RES: I, yeah I knock things over, my husband always moves the glasses and things on the table, my husband always clears them out of my way, just puts everything away (chuckling), because I go like this. You know, I think it’s, (sighing), I don’t know whether it’s the actual eye to think, I don’t know, that I don’t judge the distance properly.

INT: Eye to hand yeah.

RES: But I, I think it’s, I do judge the distance, but I don’t then actually, I think my you know, there must be something with my arm as well, I think my arm is here, but it’s you know, because I, your brain tells your, your foot or your you know, you, you learnt how, you know, when you’re sort of, how you stretch and how far you have to go to get that glass.

INT: Yeah.

RES: But I probably think it’s already there, then I’ll do this.

INT: Okay.

RES: It’s likely that with, with, with the leg, my, you learn to walk and then you don’t think about walking anymore do you?

INT: Yeah.

RES: While I have to actually um err relearn you know, every time I'm walking I have to think of my feet.

INT: Yeah so you have to reteach yourself almost like.

RES: Yeah and this is very, very difficult.

INT: Yeah.

RES: Cos I've always been a person who takes ten things all at once and plan the twelfth.

INT: Yeah.

RES: And you have to then stop doing that, and it's not easy.

INT: Yeah, I can imagine.

RES: So I, I have to sort of look at my feet, think of my feet all that, am I lifting my foot, you know, go up, go up you know, I mean.

INT: Yeah.

RES: I could never, I couldn't for example, I could never do window shopping you know.

INT: Okay.

RES: Where you either walk along and have a look at a window, can't.

INT: Yeah you can't do that.

RES: I have to stop and look at the window and then carry on.

INT: Because you can't focus your feet and?

RES: No, no because um as soon as my head is turned.

INT: Yeah.

RES: My, my balance and everything goes out.

INT: Okay that's interesting.

RES: And that's one, yeah also sometimes you know, once I fell at home, you know, about when I was standing at my counter, cooking something and then I wanted to go um, you know, like I say and you turn over and what you do is you move that leg, and then that leg round, and I was gonna turn over to get something from over there, and err, err you know, this leg.

INT: Yeah.

RES: I thought I turned, I.

INT: Yeah.

RES: And but it hadn't actually turned, this, this leg was still there and this leg came over here.

INT: Yeah.

RES: While this one is still there, and.

INT: So you just fell yeah.

RES: Yeah I really fell badly, so it, it's, it's that kind of thing, you, you, your coordination.

INT: Yeah.

RES: Err but what you do naturally, what you've learnt to do as a baby is.

INT: It's difficult yeah I get what you're saying, err, do you find um when you have, so you said sometimes you feel sort of clumsy and your husband moves everything.

RES: A safe distance yeah (chuckling).

INT: Yeah do you find um that's different when you're slightly fatigued um?

RES: Oh yeah, yeah, yeah.

INT: Yeah.

RES: Yeah fatigue would, would affect it all and.

INT: And how?

RES: Then I know I have to sit down and rest.

INT: And how would it affect it, would it just?

RES: Well I get clumsy.

INT: Okay so it would make it worse, okay.

RES: Yeah.

INT: Okay and you have um, mildly mentioned the fact that it's hard to focus on two things at once, so you have to, if you're walking or walking and you can't window shop.

RES: Yeah.

INT: Um do you find that that's the same with a lot of things, so err with your mind, do you find?

RES: Oh no, if, if I'm sitting down.

INT: Yeah.

RES: Um if I don't have to rely on my balance.

INT: Yeah.

RES: Then that's fine.

INT: Okay.

RES: No, no I, I, I don't think, (sighing) apart from getting older and, and things get a bit slower in your head (chuckling) um no, I, I mentally I'm not affected as far as I know.

INT: Okay that’s good um and with the assessment we’ve just done, did you find that you were tired at any point or um fatigued, or did you feel a physical affect?

RES: When I was walking the six minutes.

INT: Yeah.

RES: I felt um, I was getting a little less err, a little wobblier let’s say.

INT: Okay.

RES: So my, my coordination [ph] was not as good at the end as it was in the beginning.

INT: Okay.

RES: But I didn’t feel sort of particularly fatigued.

INT: Yeah.

RES: But I think I, I, I was affected yeah.

INT: Okay and that was affected with your walking, you felt it makes?

RES: Yeah I mean you know, I’m not, you know, I get wobblier.

INT: Okay, and your legs feel heavier or is it just that?

RES: No, just wobblier yeah.

INT: Thank you that’s fine, um, anymore, like anymore err situations that you can remember where you did feel fatigued, um?

RES: Just if I walk a lot.

INT: Yeah so you were just, you are predominantly affected with fatigue when you do a lot of like physical activities?

RES: Yeah.

INT: Okay.

RES: I’ve just been on holiday.

INT: Pardon?

RES: I’ve just been on holiday, I did a lot of walking there.

INT: Nice.

RES: Yeah.

INT: And was it hot where you went?

RES: Err no, no.

INT: No okay.

RES: I’ve been to India, but it wasn’t very hot but you know, my husband looks after me so he, he is, he is very good, he knows when I need him.

INT: Okay.

RES: So he's take my arm when I need to hold on and.

INT: Yeah, okay.

RES: He's good.

INT: Yeah, yeah that sounds great, um.

RES: So we do a lot of walking, but we do sightseeing, we stop again, and look at this and look at that, and then you carry on walking, so it wasn't, although there, there were some days when I thought, I'm glad, you know, the culture, I can sit down, but I did manage it.

INT: Yeah.

RES: Did walk a lot of steps I must say.

INT: Good, good um is there anything else that you'd like to add um, about your experience of fatigue and how, how it makes you feel um before we?

RES: No I realise as I say, I think that I'm on the whole relatively lucky so far, my progress has been, you know relatively slow so you know, um, I hope to get a few more holidays in before it's too late (chuckling).

INT: Yeah definitely okay, okay yeah if that's, if that's all you have, then we can switch off?

RES: Um, yeah.

INT: Thank you.

[End of Recording]

A (iii): M090: Transcript

For:	Brighton University
Title:	MO90
Type:	Interview
Convention:	Verbatim / Qualitative Analysis
Audio Length:	31 minutes
Transcriber:	EST/JI1
At:	Essential Secretary Ltd
Completion Date:	14.08.2019

Transcriber's Notes:

Any difficulties experienced, accents and general comments

number of unclears	3	**number of inaudibles**	2
spell check performed	Yes	**proofing performed**	Yes

audio quality	Good – tapping sound in background on occasions.
speaker related issues	As above
equipment related issues	None
terminology issues	None
other comments	None

Please find attached your completed transcript.

Whilst every effort is made to ensure that the attached transcript is an accurate record of your audio recording, sometimes difficulties are encountered in understanding technical words, people speaking with a foreign accent and in some cases when somebody is speaking from a crowded room with a lot of background noise and from mobile phones.

Where we have had difficulty understanding words we have indicated this as [unclear] with the appropriate time stamp, or simply attempted to spell the word phonetically but followed it with [ph].

[Start of recording]

INT: Okay, so can you discuss with me, erm, in as much description you can your lived experiences with fatigue and MS?

RES: Okay, well, erm, I was, er, had the symptoms, first symptoms of MS in May 96, the same year I became pregnant with my son. I had an MRI in the September and, erm, it was confirmed I had multiple sclerosis. The consultant told me (laughs) to go home and not worry about it and concentrate on my baby, so that was fine. So all through the pregnancy I was tired, but it could have been the MS, it could have been the pregnancy. I had a healthy son and, er, from 1997, when he was born until 2002, erm, I didn't have any relapses at all or any significant symptoms. I used to get tingles in random parts of my body and the consultant thought it might be nerve memory, he didn't think it was significant.

INT: Okay, what in that timeframe you just said?

RES: Er, 97 to 2002.

INT: Yeah.

RES: November 2002, my life has got very stressful, erm, work was very challenging, there were many individuals at work that, I was a senior manager and ...

INT: Okay.

RES: ... there were manager partners, they were in chaos (laughs) ...

INT: Yeah, okay (laughs).

RES: ... and things were falling apart and I split up with my son's dad and in the November 2002 I started to feel like pins and needles all over my body ...

INT: Okay.

RES: ... and, erm, I kept going to work because his dad was in London and I was just with my six year old starting a new school and new home in Sheffield ...

INT: Yeah.

RES: ... and the tingles got worse and worse and worse and by the (pause), by the beginning of January, I woke up and it felt like there were a million ants crawling over my hair ...

INT: Okay.

RES: ... and I was so exorcised by it that I got a pair of scissors and cut all my hair off to ...

INT: Wow.

RES: ... get some relief because I thought is it sclerosis or is it the MS and if it's the MS obviously it's not the scalp ...

INT: Yeah.

RES: ... but the, the fact that it was cooler made it a lot more tolerable. Anyway, I was.

INT: Was it just on your head?

RES: Er, the tingles ...

INT: Yeah.

RES: ... were all over ...

INT: Okay.

RES: ... and it got worse and worse and worse and, erm, but I forced myself to go to work and I went to work and then beginning of the February I got, er, an infection and, erm, I woke up in the morning and I could not force myself to get up to go to work or to get my son up, so, erm, I called, er, his friend's mum and said will you collect Jack from the door cos I can't get to school today …

INT: Yeah.

RES: … so she said that's fine. Erm, his dad was still in London, erm, and I was struggling to get up in the morning to get Jack ready for school and it was just terrible. Anyway, Jack's grandma came to visit us and, erm, she said this can't go on, you need to go to hospital cos his dad was still in London, he'd come up every now and again, but he was working down there and, erm, things weren't great …

INT: Okay.

RES: … and, er, so I went to the hospital, but I couldn't walk, I had to be pushed in a wheelchair and, er.

INT: Because of how?

RES: Fatigue.

INT: Yeah, okay.

RES: Fatigue, crippling fatigue. It’s not tiredness, it’s like treading treacle, you know you can hardly move your limbs. Anyway, I mean the final straw at work, I was chairing a meeting, a quite important meeting and I was so tired in this meeting that I excused myself, I said could somebody take over the chair for a few minutes, I need to just do something …

INT: Yeah.

RES: … and this was a university in, er, Sheffield and I found a room and it was empty cos …

INT: Yeah.

RES: … it was out of term time and I crawled under the desks and I laid there for about ten minutes.

INT: Bloody hell.

RES: It was absolutely awful, just awful and this is my memory you see of fatigue, that I know how bad it can get for me.

INT: Yeah.

RES: So, er, anyway, so I went up to the hospital and I saw the consultant who was totally wonderful, he was a lovely man …

INT: Okay.

RES: … and I got a shed load of steroids to shift the relapse …

INT: Yeah.

RES: … cos this is my first significant relapse really apart from the very first one where I got double vision and I couldn’t walk and it was all funny …

INT: Okay.

RES: … er, but that only lasted a while, a few weeks whereas this was, that was November now we’re talking about March …

INT: Okay.

RES: … erm, and, er, I didn’t go back to work.

INT: Okay.

RES: So I was (sighs), er, his dad left his job in London, his Nan told him, she came over to look after me while he was still in London and she said you’ve got to come back and live in the house and look after Alison and Jack, so, er, he did and I went to bed essentially, I mean I did, I went to bed, I did not get up at all …

INT: Um.

RES: … and the symptoms, as the weeks went on I got less tingles, but my vision [unclear-05:22] …

INT: Yeah.

RES: … so it got darker and darker and darker and darker until I could not see at all.

INT: Wow.

RES: So all I did was I just lay, well my brain, you know your brain works you know, er, perhaps less effectively nowadays. Anyway, erm, I listened to the radio all the time. I couldn't hold a book. I find a little notebook, I tended to write, I tend to write things at the end of the day …

INT: Um.

RES: … and I found this notebook from that time and the writing has disappeared, you can't read the words and that was my last venture, that was sort of March 2003.

INT: Oh, wow.

RES: So I was in bed from the February essentially apart from that trip to the hospital, er, and then I got, I call it blindness, I had no vision, I couldn't see anything for several months …

INT: Gosh.

RES: … er, and I wasn't out of bed. I mean I'm very, er, er, modest and I don't like anything to do with you know, erm, going to the toilet, I'm very private.

INT: Yeah.

RES: So I crawled to the toilet, I wouldn't have anybody to you know …

INT: Okay.

RES: … have any of that, I crawled, but …

INT: (Coughs).

RES: … everybody, I mean I did nothing, I just was in bed. So by about the November, erm, work were really quite good, they sort of kept in touch. I was on you know full pay, then half pay like if you're, like a Government officer, it's all tied by that, it's fine and, er, so the end of 2003 my boss came to see me and she said it doesn't really look like things are moving are they Alison and …

INT: Um.

RES: … you, oh, I lost my speech as well and I was (making noises).

INT: What around the same time as your vision?

RES: Yeah, yeah.

INT: Oh, my gosh.

RES: I mean it was a shit time, I'll tell you, it was really awful. I felt so sorry for my son because I hadn't ever told him I'd got MS you see, so I think, erm, I think he was a bit, erm, well never really talked about it much, but I was very worried about him.

INT: Yeah.

RES: Anyway, er, my boss came to see me and she set in motion ill health retirement from work, er, and, erm, I just let her do it, I mean very efficient, good woman, very efficient nurse, she sorted it all out. Erm, so, erm, I officially retired from work 31st of March, er, 2004 …

INT: Okay.

RES: … so from like the February 2000, well November 2002 to February …

INT: Yeah.

RES: … 2003, February through to the Christmas, I didn't get up for Christmas, but I think I got up for Jack's birthday which was March, so I was essentially in bed for a year …

INT: Wow.

RES: … and a lot of that time was very, very sensory deprived, erm, (sighs).

INT: Sorry, so how long did you have, er, problems with your speech for?

RES: (Long pause). Probably weeks.

INT: Okay.

RES: Might even have been months. Erm (pause). Everybody came to see me, it was. My sister came, she, er, she blew into my room like a rose.

INT: (Laughs).

RES: Yeah, family came to me you know. Anyway so, er, by about the March 2000 and, no, no. Yeah, by about the March I was sitting up, so the deputation came from work in my living room and it was horrible, and they were really kind, there was my union rep, there was my boss, there was the HR guy, it was, you know little family, little meeting …

INT: Yeah.

RES: … and I wasn't dressed, I was in my dressing gown, I hadn't got dressed for months, erm, and towards the end of it I burst into tears and said so I'm just useless then and they were so sweet. Anyway, so they basically said no, you're not useless and hot foot it out of there (laughs). So that year sort of trundled on and I was getting up a bit and I was sleeping a lot, my vision was okay and my speech returned, so I tried to do bits and bats and then, oh, I got a bit depressed cos …

INT: Um, yeah.

RES: … you know you never think of yourself as not a robust person, but you kind of feel well you let yourself down there Alison, you know it's a bit obvious getting depressed cos you've lost your career you know, but I did, I got depressed and in the October I went to see my consultant, Doctor Jordan and essentially (laughs) I just burst into tears in front of him for about ten minutes, it was so embarrassing and he was so sweet, he said Alison, I think you're depressed and he gave me anti-depressants. He said I know you don't wanna take them, but it just takes the edge off and it gets you to a state where you can start to cope with the things that are upsetting you …

INT: Yeah.

RES: … cos it's acute [ph] and I don't know what, the terms they use these days, but in mine it was endogenous reaction cos [unclear-10:19] reaction becomes depression.

INT: Yeah.

RES: Erm, so, er, so that was that, that was that, that was 2004. 2005 I'm getting up a little bit; I was generally at home, so I'm retired …

INT: Yeah.

RES: … and I'm not doing very much, erm.

INT: Can we, erm, just quickly, can we go back to, erm, obviously when you were bedbound …

RES: Yeah.

INT: … for about a year.

RES: Yeah.

INT: Erm, can you just describe what it was like, erm, why you couldn't get up, erm?

RES: I couldn't get up cos I hadn't got the energy …

INT: Okay.

RES: … to get up.

INT: Yeah.

RES: Erm, although I was, I mean I did lie in bed, but sometimes I hadn't got the energy to just lift my hands to hold the book when I could see. I was just so utterly exhausted …

INT: Okay.

RES: … and all I wanted to do was just lie there and sleep it off …

INT: Yeah.

RES: … you know just sleep it off cos when I saw an MS nurse or the consultant because this was the most, this is the most important bit about fatigue for me.

INT: Okay.

RES: Okay, so 2005 trundled on …

INT: Yeah.

RES: … and then, erm, I did a little project with my son in the summer, for the summer holidays because I thought you know he's gonna be bored, so I called it on our doorstep …

INT: Right.

RES: … so we, who comes to our door, you know the postman, the bin man, you know all that and then what's down our street, what's in our neighbourhood, what, you know so we did, he did a book like that, you know a lever arch, we did it all through the summer on our doorstep, it was for writing practise as well, but generally …

INT: Yeah.

RES: … you know it was messing about and, er, I made a little medal for him at the end of the summer and we had a little ceremony presenting a certificate and a medal …

INT: Oh, nice.

RES: … and I told the teacher about it and she said you should bring it in and he got the Head Teacher's award.

INT: (Laughs). Nice.

RES: Anyway, that was great. So September I'm up, I'm positive you know …

INT: Yeah.

RES: … I'm great and then, erm, in the October I'm in bed with his dad, it's midnight, I'd been starting to feel a bit sort of wobbly, like jelly like, I didn't really understand it, not MSC cos MSC is (sighs) like that, but this was weird. Anyway, I woke his dad up at midnight, I said why is somebody digging up the road at this time of night, he said what you talking about, I said what's that banging and it was my heart. I went to the doctors the next day and, er, said I feel terrible, I feel wretched and she said it's your MS, I said, and I did say to her, I said it doesn't feel like MS, it feels something different. Anyway, she took some bloods and said go home and rest.

INT: Yeah.

RES: That afternoon they phoned me and said you need come down to the surgery now, er, yeah cos they've got the bloods back because she rushed it through for some reason.

INT: Yeah.

RES: I'd developed graves disease. Have you heard of graves disease?

INT: Yeah, I have heard of graves disease.

RES: Yeah, it's actually thyroid.

INT: Yeah.

RES: So I had graves disease which went on for a few months, er, but fortunately, fortunately I'm very anti conventional medicine …

INT: Uh-huh.

RES: … animal tests and all that stuff and I mean I'm not an idiot, you know doctors (laughs) …

INT: No, no (laughs). No, way.

RES: … and all the rest of it, but, but anyway a close friend of mine who's also vegan, we've been vegan together a long time, both [inaudible-13:46], erm, she had graves disease and she, er, dealt with it and treated it …

INT: Uh-huh.

RES: … and finished with it through a herbal, herbalist.

INT: Okay.

RES: So I went down to this herbalist in Sheffield and they'd given me three tablets, Prednisolone …

INT: Yeah.

RES: … something beginning with L and another thing, I got three different, I mean I think I was quite anaemic anyway, but they gave me three different types of tablets, so I was taking something for the thyroid, this graves condition. Anyway, so I went to the herbalist and she, we had a long interview and da-de-da and she gave me this, so I went home, stopped the tablets, took this and then I, my levels went way up again and she (laughs), she told me off, she said no, no, no, you, herbs take a long time, so your conventional herb, that's what you do.

INT: Yeah, gradual.

RES: And she said if you don't keep taking them I won't treat you. Anyway, so over the course of six months, erm, Sodalite is apparently the crystal to protect your, er, thyroid so I used, I got a sodalite thing there, that's why I like to have things like there almost, I got sodalite and, erm, because do you know what the treatment is for graves disease?

INT: No.

RES: Right, they, erm, they give you thyroxin, they try and increase your thyroid …

INT: Yeah.

RES: … which makes you hyper, hyper …

INT: Yeah.

RES: … I think I had the hot one. They give you an, a radioactive tablet which knocks out your thyroid …

INT: Okay.

RES: … and you take thyroxin or you have surgery. Now I didn't have any of that, I've protected my, I'm like this …

INT: Yeah.

RES: … with it. Anyway, so it got a bit complicated with the MS, but because I'd had this summer with Jack and I felt positive, I thought you know perhaps I can think about going back to work and then slump (sighs). So I got better from the graves and then the MS wasn't really an issue and what I found was when I get tingles and I get them in random parts of the body, often across my shoulders or here, when I feel I'm getting tingles …

INT: Right.

RES: … the MS nurse said you go to bed for two weeks and then you'll be fine and that's.

INT: MS nurse said that?

RES: An MS nurse said that …

INT: Yes, okay.

RES: … in Sheffield.

INT: Yeah.

RES: Doctor Jordan has set up a wonderful MS department, he was a fabulous. Ironically he got a brain tumour [tapping noise in background] [inaudible-16:10], got a brain tumour and had died.

INT: No.

RES: He was a wonderful man, really, really wonderful. So then, oh, dear me, dear, dear me.

INT: (Laughs).

RES: Anyway, so for years, erm, after this terribly awful relapse …

INT: Yeah.

RES: … erm, I've tried to really take quite good care of myself. So I stopped smoking [ph], well I didn't stop, I stopped drinking, I tried to eat a healthier vegan diet. Erm, I did go gluten free for a while which I think helps, but I've lapsed, but I am now gluten free.

INT: Okay.

RES: Erm, so you know life went on, I had a full-time job, I had my son, I had my partner and it, there was ups and downs, but when I felt myself getting a little bit tingly …

INT: Uh-huh.

RES: … I'd just say to them I'm going to bed …

INT: Okay.

RES: … and that was in the context of a proper working life, but for (sighs). Well we, erm, we lived in Sheffield, then we moved to Brighton and, er, yeah, I got my, I went back to work as a social worker …

INT: Yeah.

RES: … for a year to see if I could do it in 2006 and it was fine, I got the qualification that I did and so I applied for another manager's job and I got the post, I managed the social work service at the county hospital …

INT: Nice.

RES: … which is, er, oh, no, I got the learning disability job. No, no, that was before. Er, I managed the people at the hospital. That was a good job, nice crowd. Terribly, awful environment to work in.

INT: I bet it, yeah.

RES: I mean bank nurses, a very stressful job for lots of people. Anyway, I have had a number of relapses. So I went to work there in 2007 and I think the stress of my personal relationship with my son's dad …

INT: Yeah.

RES: … precipitated the majority of the, well precipitated all the, all the relapses …

INT: Oh, wow.

RES: … was the main factor cos it was very difficult. Anyway, so I had a relapse in 2009 and then one in 2010, this is when I'd be off work eight weeks. So in 2000 and, yeah that was just tiredness, I was just.

INT: What the 2009?

RES: 2009 was just tiredness; I did not feel I could.

INT: Tiredness in what way?

RES: Erm, everything was such an effort. The idea of getting dressed was appalling …

INT: Okay, yeah.

RES: … you know just standing up and (sighs), yeah. I mean it's sort of, it's the emotional part of it as well I think, but just the idea of just not feeling, as if you've been run over by a steamroller, you know it was just …

INT: Yeah.

RES: … and then 2010 I had another relapse, but that affected my vision. I got awful, erm, like popliar [ph], erm.

INT: Oh, er, neuritis?

RES: Yeah, I've got neuritis and double-vision and I tried to conceal it at work that I wasn't falling into a relapse because I just, I was, felt guilty I suppose. Anyway, I had to wear a patch, an eye patch and it got, cos I was doing this in meetings and people were saying so what you doing Alison and I thought, oh, so I was wearing an eye patch and I wore that eye patch for five months. So that relapse really affected my eyes …

INT: yeah.

RES: … and, er, as well as the [unclear-19:31] fatigue and then (pause) 2000.

INT: Did you find the eye patch helped?

RES: Yeah, cos you …

INT: Yeah.

RES: … just move one eye, you wouldn't have to, you wouldn't be looking like that all the time.

INT: Okay.

RES: It's very disturbing you know. I get it very occasionally when I'm really tired at night and I look at the, in the, well the laptop and it …

INT: Yeah.

RES: … oh, there's two Vera's (laughs). Erm, 2013, so I'm back at work and I have to go into a different area because, erm, er, and I think my boss wanted me to do something different. Erm, I think they thought I couldn't really go back to the hospital. A lot of people had moved. Erm, I didn't particularly want to go back to the hospital, it was very, very stressful.

INT: Um.

RES: So I moved into a different job, it was still a difficult job; it's about hospital discharges and finding home helps which is not easy, not easy.

INT: Yeah.

RES: Anyway, I did that for a couple of years and then in 2013 I had a relapse of about seven weeks and this is not great for my health record, you know my work record …

INT: Yeah.

RES: … it's not good at all. Anyway, erm, and that was just, I ground to a halt at work and, erm, I just said to, er, I said to my colleagues, I couldn't see my boss, I said I'm gonna have to go home, so I don't know if you know Bartholomew House in Brighton, but say to walk from here to that house …

INT: Yeah.

RES: … okay, so that was my office …

INT: Okay.

RES: … to the bus stop.

INT: So about …

RES: That took me an hour.

INT: … fifty metres?

RES: That took me an hour.

INT: Wow.

RES: I just, cos I was walking so slowly …

INT: Yeah.

RES: … and I was holding on. I didn't, and if you come with me I was so ashamed …

INT: Okay.

RES: … you know, I mean it's ridiculous. Anyway, 20.

INT: So (coughs) was it because you felt that in your body or was it, erm, that in your head you couldn't walk?

RES: Walk. Er, it's my body.

INT: Okay.

RES: It was just too much effort to do that and that is normally how I walk, I rush around you know. I mean I, pace is the worst word in the English language …

INT: (Laughs).

RES: … I used to hate that when I first got the diagnosis, I don't want pace; I want to be you [ph]. Anyway, so, er, yeah, 20, it wasn't 2013, it was 2014 and then, erm, 2013 I got, er, 2014 I got a relapse which again was a lot of tingles and a lot of fatigue and a lot of stress and, erm.

INT: Was it fatigue in the same sense as prior?

RES: Yeah, it was getting that way. It was getting pretty grim …

INT: Okay.

RES: … and I just, I just phoned up work and said I can't come in, I'm not well and I did not go back to work.

INT: Okay.

RES: So I was off work for a year …

INT: Uh-huh.

RES: … trying to get better, you know I was trying to get better, but it didn't, nothing happened and I saw Doctor, you know the consultants a few times and I had tests and this and that and another MRI who …

INT: Okay.

RES: … if you have one just tip, shut your eyes, just close your eyes.

INT: Yeah, people say that (laughs).

RES: Anyway, erm, I was, there was another meeting in 2015, May, March actually to say that, erm, I wasn't able to come. Occupational Health did a report …

INT: Uh-huh.

RES: … so I had to go. So then I retired from work and most of 2015 I spent half in bed and half out of bed, but at this time my son and I were living alone together, his dad …

INT: Okay.

RES: … I don't exactly know where he was.

INT: Okay.

RES: Oh, yeah cos there was a longstanding feud between me and his dad, he, erm, he defraud, he stole several thousand pounds from me and I tried to get it back from him and he promised to pay it when he sold something and when he sold something he bought something else, so. Yeah, when he sold his flat he said I'd get the thousands then and he sold the flat, he bought a house up north and so I said I'm gonna take you to court, I can't have you do this, big mistake, never go to small claims court, it's so expensive, so I was struggling financially and I think that contributed to the stress and the fatigue, so …

INT: Yeah.

RES: … it's all mixed up isn't it? Anyway, so since 2015, now 2015 I was in bed, but, erm, I don't know, when you lose your career, you know what you've done forever it's quite hard. I mean I do enjoy doing different things, but, erm, I don't feel I have a sense of purpose anymore.

INT: Okay.

RES: I was talking to the MS nurse about it and I wasn't sure if last year I was just being lazy cos, yeah cos like 2016 was quite a good year because I got somebody to do the garden and so we have lots of fruit and veg growing and it was really nice …

INT: Nice.

RES: … and I did some lovely walks in the spring in the woods and Downs, nice walks, erm …

INT: Yeah.

RES: … but.

INT: And were the walks okay? You didn't feel?

RES: Yeah. No, the walks were fine.

INT: Yeah.

RES: The walks were absolutely fine. So I think 2016 I probably was quite strong, then we had some issues, er, with my son's girlfriend and, erm, that all got a bit difficult cos she was living with us.

INT: Okay.

RES: Er, but it's really hard now to describe (sighs).

INT: Yeah.

RES: MS is difficult because if you don't look like you've got anything and generally you cope alright, it's like what's it about …

INT: Yeah, it is hard.

RES: … you know, yeah.

INT: It's.

RES: But, so when I get tingles …

INT: Yeah.

RES: … if I ignore them I know that there's a likelihood that I will get worse because MS isn't like, you know when people say well just push through it, you can't do that with MS …

INT: No.

RES: … you push through you go down in my experience.

INT: Yeah.

RES: Other people might be different …

INT: Yeah.

RES: … but, er, yeah.

INT: Okay, that's good. Erm, I'm trying to think about other things that you've said. The, when you said, erm, the MS nurse said when you get pins and needles go to bed and rest.

RES: Yeah, yeah.

INT: Erm, is that because the pins and needles, erm, would lead to fatigue or is that just because then all symptoms would get worse?

RES: Well no, I think it's. In my experience and my, er, in my experience of MS and of my own illness, if you like, or disease, whatever you wanna call it is that if I get tingles usually, inevitably that means that I'm gonna get fatigued …

INT: Okay.

RES: … it's kind of this little trigger.

INT: Yeah, okay.

RES: So basically I think the tingles are to say you're doing too much …

INT: Yeah.

RES: … you know, but sometimes I do ignore it and that's not good either …

INT: Yeah.

RES: … cos then I do get not very well, so it's a bit boring you know spending your life in bed, but hey ho (laughs).

INT: I know (sighs). Erm.

RES: Well I try not to, but you know.

INT: Yeah, well I think you're doing well …

RES: (Laughs).

INT: … you're doing really good (laughs). Erm, okay, er, trying to think of other descriptions you've said (pause). Erm, yes, when you had your first meeting when you were in senior management and, erm, you said that you paused for, got someone to take over the meeting …

RES: Yeah.

INT: … and you went into the other room and crawled under the table.

RES: Um, um, I know, disgraceful.

INT: Can you describe a bit like, describe that just a little bit more?

RES: Erm, well I was. I was at that head of the table and the door was there …

INT: Okay.

RES: … and it felt like I was a bit on fire, the tingles …

INT: Okay.

RES: … were really, really severe you know and I couldn't concentrate and I thought if I don't lie down, like a real intense need, if I don't lie down I'm not gonna be well you know and that's what gets you with, when you're, with my fatigue …

INT: Um.

RES: … so I thought I have to lie down, if I don't lie down I'm gonna, I wouldn't think I'm gonna fall down, but I think I'm not gonna be well, something's you know, so, er, and I probably dozed off. I can sleep anywhere, I can sleep on a sixpence me, like the Duke of Wellington, he catnapped.

INT: Yeah (laughs).

RES: I can catnap, like to now, when I go back to Peacehaven on bus I shall probably be asleep before I even get to the South Downs Way (laughs).

INT: (Laughs).

RES: Right, so yeah …

INT: That's good.

RES: … it felt like I was on fire and then I lay down and that and, er, I must have dozed off cos I thought, oh, I better get going now. So I managed to get up and I, you know had the, I finished the meeting and we got various resolutions passed, so it was, you know it was a reasonable meeting …

INT: Yeah.

RES: … but it wasn't as good as it could have been, but I think, but I want to go back to the tiredness is that sometimes you get so tired it's like it hurts, it's really hard to explain, but it's like it's so overwhelming, but only inside you that, I don't know, it's weird.

INT: And when you say inside of you, do you mean in your body or in your …

RES: Yeah, yeah.

INT: … head?

RES: Yeah, all over the body.

INT: Yeah, all over?

RES: All over, yeah, yeah …

INT: Okay.

RES: … and it's like it hurts (laughs) you know. It's, you can't imagine being tired hurts, but it feels like it hurts, you know it just gets so heavy and like that expression treading treacle, I used that for years after I got the MS because when I was trying to get better after the big relapse it was like, if you can imagine what treading treacle is like …

INT: Yeah.

RES: … or pushing your, all your legs through sand …

INT: Yeah.

RES: … that's what it's like, it's just, oh, it's the pits really (laughs).

INT: [Unclear-29:35]. Oh, yeah, that's (coughs). Yeah, I can imagine that being really heavy.

RES: Um, yeah.

INT: Erm, yeah, okay. Erm, if you have, erm, any other things to mention, any other, anything else that you'd want to say about fatigue, erm, then you can now?

RES: I think you know you've got MS fatigue when you go to sleep exhausted and you wake up exhausted.

INT: Okay.

RES: So, like I say, I mean I do make a bit of a joke of it, but I do actually spend at least fifty percent of the week in bed and sometimes I'll just wake up and I'll be like this and I'll just say Jack, because his bedroom's across the way, I'm not getting up today, you'll have to look after yourself and I just know I have to stay there.

INT: Right.

RES: In fact in the week the only two things that get me out, I go and visit an old lady who's bedbound, I'm a library volunteer, so I visit her a couple of weeks, every couple of weeks, but we don't talk about it, literally we just gossip …

INT: (Laughs).

RES: … and chat.

INT: Right.

RES: She's a nice woman. She's been bedbound for twenty odd years, so I get up for her …

INT: Oh.

RES: … and I get up for Italian, so next week whoo (laughs).

INT: (Laughs).

RES: So you know yesterday Italian, next week Italian finishes, yeah.

INT: And what is that, a complete end? Does it not start again in the?

RES: Oh, yeah, there'll be next year as well.

INT: Um.

RES: Um, in two minds, yeah.

INT: Okay. Okay, I think we'll stop there.

[End of Recording]

Appendices B: Progression tables from transcriptions examples

B (i): M084 data analysis progression table

Meaning Units	**Transferred meaning units**	**Moving towards the phenomenon**
I'd, I'd like to start from the beginning of my MS, which was twenty seven years ago, so at that time, I had a lot of attack, MS attacks, which I had had previously, but I hadn't actually been diagnosed until the end of, of that year. So ninety one, was when I was when I was diagnosed eventually, which was great. I had two little children, one of them was only born in the February of that year, the first one was born, um ninety eight, err ninety nine, sorry ninety nine, ninety one, so eighty nine, ninety one. Um anyway so I had two little ones, two little tiny girls, and I also at the same time my father was diagnosed with um end stage cancer, and so I had to cope with, with him dying, me not being able to work anymore, because I was, when I, when I told them at work.	At her time of diagnosis, she had to deal with multiple issues all at once with numerous attacks, two small child and attempting to find a coping strategy with the diagnosis of her fathers end stage cancer, his death and herself not being able to work anymore due to her MS.	Multi-faceted events causing a strain on her life with the addition and complexity of the MS-fatigue and its new diagnosis.
That I had MS and wanted to work in different places that weren't so hot as the Labour ward, which is where I was working and they said "No we can't do that, you've got to work where we want you to work, you can't, you can't, you can't decide where you want to work, we decide where we want". So I said "Well I can't cope with that then, I can't cope in this heat". Therefore I was advised to take early retirement, which is what I did.	Stressing she wanted to change her work environment due to the heat in the labour ward after her diagnosis, she took up on the offer to take an early retirement as work strictly expressed no change to her work environment.	Selfhood- her concern of feeling uncomfortable in a situation and not being able to change the inflexibility of her work environment forced a big life change and decision.
which was great at the time, because I had two little children. And it meant I could stay at home with them and then we had to move because there's no way that we could	Not being able to physically work caused an early retirement and produced more stress. This meant her	Economic consequences. Knock on effect of an early retirement caused

live where we were living, cos my, my income was half of, half of our outgoings if you like. So if I couldn't go back to work, we couldn't carry on living where we were living, so and my husband went for um, (pause) move his job, so we had to move our house and everything too, there was a lot of, a lot of stress in that period.	income was half which caused her husband to move jobs and for the family to move to a new house.	consequences for her and her family with more stress, vicious cycle.
And I you know, I was having such a lot of attacks, I couldn't feel from my chest downwards, all that stuff, but still had to carry on. And um at that time, my fatigue was really more up in my head. So I, I'd be trying to get you know, trying to walk the girls to school and that sort of thing, was hard work because I couldn't feel my legs, my feet, when they started to get the feeling back, it was like broken glass, and that went on for like months at a time. And how long it was lasting for, it was four years, before I could buy any new shoes, because I couldn't tell what my feet were doing. I couldn't, if I could feel them, they were feeling wrong things, like they. Like the perception was so awry. That I couldn't tell, it felt like I had blisters on the back of my feet, or pebbles under my knees, all sorts of things like that	Physical numbness from the chest down affecting the sensation in her legs and feet impacting how she proceeded with daily activities. Expressing the continuous altered bodily sensations as 'broken glass' and 'pebbles under her knees'. She thought fatigue was all in her head.	Embodiment implications as she felt a misalignment with her perception of her body, and sensations in the world. For example, she described her feet feeling like broken glass and pebbles under her knees. New bodily sensations that brought discomfort.
Um and that really plays with your mind, you know, when you have to keep checking your body to see if, it is okay and it takes, after a few years you, you do become accustomed to it, but the fatigue was. Exacerbated by um very um, I don't know how you say, when the hormones are so involved as well. They're going up and down, up and down, I used to have terrible um premenstrual tension. I used to have very heavy bleeding and then I used, I used to be a monster for two out of four weeks you know, really horrible nasty person. And that's very exhausting to be like that and to	Regularly checking her own body to see if everything was okay really played with her mind. The impact physiologically, especially on her premenstrual cycle, made her temperament fluctuate a lot. The fact she knew she was being horrible to her family was exhausting.	Mood, sociality- Aware of her mood and temperament fluctuations from physiological changes (menstrual cycle), she understood but found it exhausting how it affected others around her.

know you're being so horrible, it's really but that's aside, that's another thing.		
But that also doesn't help with the fatigue because I used to, if you know, take the girls to school and then I'd, when they would come home, I would be so tired, I'd just be lying down on the settee and they'd just talk to me but I'd just be lying down there completely prone and I, I would talk, but I just could not lift my head up. I could talk, I could communicate, but I could not get my body up to do anything, and that was a horrible time and I think my life started to get more normal after I had the menopause which came early, I was very lucky. That's when I was about fifty two I spose, and then I, I lost all that sort of fatigue.	The physiological and temperament changes did not help with the MS-fatigue as she would be physically exhausted after collecting her children from school. She was unable to do much physical movement so would have to lie prone and talk to her girls that way. However, she expressed gratitude for her menopause coming early as the type of physical fatigue she was experiencing went.	Temporality felt flattened as she was unable to physical move or do anything due to exhaustion. Yet the timing and early onset on her menopause caused this type of physical fatigue to never be experienced again, which she was thankful for. Feeling depletes to the extent of not being able to move.
The only fatigue I have now is muscle fatigue, when we're, my legs decide they're not going to work anymore properly and then I, I sort of go, I don't, I don't have enough control over my body to be able to sit upright, like this, or stand up like, or get a water like this. And at the moment, I spend my life, when I'm standing up, telling my leg to straighten, stand straight instead of all, and when I do that. I can walk, you know, like I can walk here, but as long as I've got something safe around me I'm fine. So that's it really. That's the end of my fatigue talk. When I feel it, when it's going, I, I, when it's, when I feel as though my legs are going, I say "I've got to sit down now". I have a saddle, a saddle stool in the kitchen which helps me a bit. But then when I drop things and I keep having to go down, and come up, I, I, it makes me kind of giddy, I dunno how, how else to explain it. Um and then when I do stand up, because I've been doing all, all that sort of bending down and what have you, then I can't really get my balance properly, and that's when I have to tell my leg to, to stay straight, because I have a tendency when I'm	Now she only feels muscular fatigue where she feels little control over her body. She is consciously aware that she has to tell her legs to straighten to walk, but as long as she feels she is in a safe environment, she can walk fine. To help with this 'lack of control' she has tools that help her out (the saddle stool in the kitchen). Although she still reports tiredness to affect her legs, bending down and balance in the kitchen. When this is the case, she rests and sits down in the other room.	She is very aware of her body spatially, including the lack of control of her body, hence the use of tools that help her out. Conscious 'control' of her body by instructing body parts, she feels her body is not reliable.

tired, just to not bother, I go over like this. And then eventually my legs say I can’t hold your body like that, don’t be stupid, so I go down on the floor, get down and then pull myself up to sit in the other room, that’s, that’s what happens.		
And Dave gets very cross at me, he says “You’ve got, you’ve got your Quasimodo on again. Well that’s what I look like, you know, and it makes him feel really, it makes him feel really horrible. He says “I can’t bear this, stand up straight”.	She reports her husband can get agitated at her for her posture and general stance when fatigued, although she knows he dislikes commenting on it.	Agitated/frustration felt within herself and others close to her- ‘you’ve got your Quasimodo on again’. Family has negative reaction to her body.
I had um, the first diagnostics, the symptom I had, I also had pre, the um, two years previously, I, I kept having little attacks, it was optic neuritis. And I had some horrible um optic effects after that. In the pursuing years, um but I’ve forgotten what the question is now sorry.	Her initial symptoms were optic neuritis which was horrible. She forgot what she was talking about in the interview.	Tiredness affecting her thought process in the interview illustrated her description of how fatigue disrupts her mentally.
Mentally in sort of, when I say mentally. I’m just trying, trying to process the thoughts. And the understanding of what was happening to me, it’s, that’s when I said it’s ***a brain game***, I always call it a brain game. Because that’s what it feels like, you have to, you can almost feel the cogs whirring. You know, watching me do it and I, and then becoming um, what’s the, see my, I can’t, I can’t. I can’t verbalise it anymore. Um become, not becoming accustomed, becoming, accepting of the fact that, that um, things are not what they feel they are. But it, it’s just a sensation, just, just processing that all the time. It’s very, very, it, it, it’s a kind of, you know, you think oh for goodness sake, all the time.	Fatigue affects her mentally with her thought process. She states the feeling of her mind processing information all the time, knowing there is a delay to her thought process. This process seems to be very frustrating and tiring for her.	The sensation of continuously processing thoughts and information is frustrating and tiring for her.
Well oh the optic neuritis is the easiest one to explain, when I couldn’t, when I, when I had double vision with it, when I could see two precisely similar. View, views of what was going on. And then you’re driving and you, you’d think oh	Her optic neuritis gave her symptoms of unclear and double vision which caused her confusion. However, wearing an eye patch seemed to help symptoms.	Optic neuritis caused double vision however wearing an eye patch helps.

which one do I follow. So I, I ended up having to put a, a patch over that eye, simply so I could see straight to walk because at that time I had a different um, with the optic neuritis, that helped.		
And, and it was quite a fun thing, because the girls would say “Oh mummy’s being a pirate today”. To try, to try and make it easier for them, um, I don’t think I’m actually answering the question properly. You have, yes, it’s just how to explain it to other people, I found really hard and therefore.	Her children would find her eye patch amusing which she thought made it easier for them. She expresses the difficulty in explaining her thoughts into words.	Mood- Creating amusement for her children by lightening her condition with her eye patch.
That’s when I tended to become very insular. Um I found it easier not to go out, and I didn’t want to explain things, because when you concentrate on, on the self, it’s very difficult to escape that horrible. A horrible thing you’ve become, its not, for me it was not a good thing to have to concentrate on the way that my body was working.	She found herself becoming more isolated by not socializing because she did want to explain herself regularly to other people. Expressing annoyance and the unpleasantness of constantly focusing on her body movements and sensations. Bodily dominance.	Sociality was affected by becoming more isolated due to the concept of consistently focusing on how her body should move (embodiment) and feeling the need to continuously clarify this to other people around her. An element of bodily dominance.
I’d prefer to go back to the time when I was concentrating on the world outside. And that err, yeah I got, I got dragged down in that sort of being aware of myself, just simply because of all the things that were happening, the symptoms. Well yes because that’s one of the reasons why I don’t walk without, without having a frame or cane or anything. I can walk, as you can see I can walk. But if I haven’t got something to make sure that I don’t fall over when I trip on a paving slab, or whatever, I don’t want to do it, because it’s too much of an effort to try and explain to people, “Just leave me here on the floor”. “Whilst I get my equilibrium back, until I’m ready to walk by myself”, because how can you say that to people, they’re trying to help you. And if they tried to help, they’ll be pulling your arm up or something and that would just automatically make me, not	She is very aware of her symptoms and this is one of the reasons why she doesn’t walk without support. On the event that she does fall over, people trying to help her seems to make her symptoms worse. Her ‘equilibrium’ must be restored, readjust her mind then her body and then she is usually ready to walk by herself. This constant adjust is frustrating, she feels like she is trying to escape from it all the time. Self-imposed constraints for ease due to unreliable body and effort.	Spatial awareness is heightened with symptoms needing physical support unless confidence is felt in the surrounding environment. On the event of falling, ‘equilibrium’ must be restored with both her cognitive and physical state. This is taxing as she feels ensnared by this. Self-imposed constraints for ease due to unreliable body and effort.

be able to stand on your feet. So I'm, I'm afraid that I've just, I've spoiled my capacity of exercising, just by not wanting to ask people for help. It's bad enough my husband helping. No, because they don't understand that I've got to come, I've got to readjust, I've got to get my headspace right before I can get my body space right. So I need some time yeah. And it, it's one of those horrible, you see I'm fidgeting all the time. Because I don't like it, I'm trying to escape from it, from the conversation yeah.		
Oh the assessment is great, I felt. No, it was no problem, because I felt safe, there were chairs everywhere. I didn't feel as though I've been put under any undue stress at all. It was great, yeah and it's very easy. I started to feel as though my legs were getting a bit draggy at the end, but because everything. Felt safe, there was no problem.	The assessment was good, she felt safe and not under any stress at all. However, her legs started to feel tired towards the end of the assessment.	Felt little fatigue throughout the assessment, only lower extremity fatigue towards the end- 'legs getting a bit draggy'.
I, I think you know, worried to go out, I mean, it was really nice when, when I had Dave come with me to time my walking, and he came on my little motor scooter next to us. He, he was timing me, and then when he saw that my legs were dragging, he said "Okay, get off the scooter now". So it was really, really nice to do it like that. And again sometimes when I go walking, just with the frame, and he, he'll come on his little pull out cycle, he's got one of these things that he can put in the boot at the same time as that.	Expressing worry about going out, however her husband would regularly monitor her walking and tell her to use aid (a scooter or frame) when visible symptoms of fatigue would appear when walking.	Self hood in her environment was projected with concern about ambulation. Illustrates the support and positivity of close relationships that help monitor and aid her with day to day activities.
I think, that the, the mental fatigue is what. Causes most problems. Because it's very difficult to think when you're fatigued, that's it really. I think, that's all I've got to say.	Mental fatigue causes most of her problems as it is very difficult to think when fatigued.	Cognitive fatigue predominantly affects her.

B (ii): M089 data analysis progression table

Meaning Units	**Transferred meaning units**	**Moving towards the phenomenon**
Okay um well normally living my everyday life um, around the house, it's very difficult, I, I cleaning, I, I while cleaning, so I tend to do it in two lots now, I do upstairs first and then you know, do downstairs. Sometimes um I have to take a rest in between you know, after activity of half an hour or an hour, it depends on how much um I've, I found on a particular day but normally um, I, it's not a great problem. Um. Oh it just depends, I mean, I, usually, um, let's say if I go for a walk, .err sometimes in the summer especially, you know, if it's nice, I do, I do walk as much as I can, I go along the seafront and err, before I, I sort of go back home, I, I need to sit down and, and rest. Um it depends on how fatigued I am, and also what's happening at a particular time, so but I tend to recover fairly quickly, within twenty minutes, half, you know, it's usually enough to carry on, but sometimes obviously you know, I sit down and rest longer.	Everyday activities can be difficult, cleaning the house is usually divided into two sessions with a rest in between dependent on the quantity of cleaning. She enjoys going for walks in the summer time, however sits down and rests for 20 minutes before she walks to head home, dividing up her time to make sure she can carry on.	Pre-planning rest breaks with daily activities (cleaning, walks) so energy can be maintained and controlled so she is able to continue with the rest of the day.
Well heat affects me, if it's very hot. Then I get err, my legs get very, very heavy let's say. Um err the coordination goes much more quickly err and I can't function that well in the heat or, I love it, I love the sun and all that, but I can't function very well, so that really affects me quite badly.	Heat affects the way she functions physically with her coordination, leg sensation and movement - 'legs get very heavy'. Although, she loves the sun, but can't.	An increase in temperature (heat) affects physical function in terms of coordination, leg sensation and movement- 'legs get very heavy'.
Um, I can also remember back in before I was diagnosed, before I knew what was wrong with me, um, I was fine for most activities, but if I exerted that bit high, like, I used to do the London to Brighton, Brighton bike ride. But Turners Hill and Ditching Beacon I absolutely dread it, because I didn't know but I suddenly. It, it's that little extra, on the level fine,	Before she was diagnosed she felt something was wrong when exerting herself with physical activities. She would really feel that extra push, it would make her grit her teeth- 'I remember gritting my teeth trying to get up'.	Prior diagnosis awareness of conflicting bodily movement with exertion of exercise- 'I remember gritting my teeth trying to get up'. Forcing things to work.

you know. Because you can just push and, and go. Err we got to err, I can, it's, you know, everything that I could do at a good steady rate, it's not so stressful. But as soon as little changes and you have to do more, it gets difficult and Turners Hill, oh, I remember gritting my teeth and trying to get up and Ditchling Beacon even worse of course, I did it about four times and since, but that's, but it's now thirty years ago. Um and, and before that as well, ever, whenever I did something that was just a bit harder than the normal steady exertion, I felt it.		
Well it's the leg weight that pull you back, you can hardly err you know, move on, um, err, I remember I used to cycle around Brighton and going over you know, in front of the University, err, Codeine Lane, err up the hill there. And, and places, places like that, always have been, and, and I blamed myself, I was like oh my God, I'm not fit enough, I must lose weight and you know, I must try harder and all that but it was fatigue setting in.	She describes the feeling in her legs, the weight will pull her down when exerting herself. She blames herself for not being fit enough, however now she realizes it was the fatigue setting in.	The feeling of blame and self-doubt with the limitation of exercise. A physical gravitational pull affects the legs with any sort of strenuous exercise. Her legs felt heavy, the feeling of dragging them around.
Well my coordination also, again with fatigue, I, I, again my leg, it's my right leg that's affected, the left leg is fine, it's my right leg mainly. And that becomes, I call it "mushy", it doesn't, you know, it doesn't, you know, I can't control it anymore. Well I really you know, sometimes have to sit down, I can't move anymore.	Her right leg gets affected by fatigue describing it as 'mushy' because she will feel the of lack of control. Sometimes she must sit down due to this feeling in her leg as she can't move it anymore.	The description of a leg 'feeling mushy' due to lack of motor control. Uncontrollable body/ unpredictability.
And then I also get pain um. Um it, it gets painful in my leg, you know, apart from that, I also have some problems with my spine of course, you know, you have that sort of problem, so it all works together and then it makes then impossible for me to carry on. Or very, very difficult let's say. If, if the life depended, you can do a little extra (chuckling).	She gets pain in her legs and problems in her spine which makes it difficult to carry on with her daily activities. However, she expressed- 'if the life depended on it, you can do a little extra'.	Physical issues create difficulty to continue with daily activities, however, expresses a sense of agency, 'if the life depended on it, you can do a little extra'. Has the need for everything to work and function like before diagnosis.
Um well I mean I'm always affected my, my balance, I err, I, I can't walk in a straight line. I don't know whether you've	Fatigue affects her balance noting that she rarely walks in a straight line, stands on one leg or runs anymore as	Spatiality- without physical support, walking and balance is unnerving.

noticed that? Um I can't stand up on, on one leg, you know, I can walk, I can't run, I think it's because when you're running, you have, your feet often aren't, for too long, so my balance I can't cope with that um. Um I can't walk up and down stairs, I mean I can walk up and down any stair, as long as I can hold onto something, so I always need a rail, a hand rail then I'm fine, um I don't, err, especially walking down, it's very uncomfortable for me, because you know, my sense of balance, I feel I'm falling. Um walking, I have to walk with a stick now, I mean not here, err you know, I, I can see what the path is like, I, I know, I always have to prepare myself where I'm going to go and have to use a stick. Because any unevenness, and I'm, I forget to think of my feet, and I'm, I'm gone. I don't want to injure myself. If I go into town, if I do anything now, I, I always have my stick. And that's been increasingly necessary over the last few years.	her feet aren't on the floor for too long. She can walk stairs if there is some level of support (railing), however, dislikes walking downstairs as she gets the sense of falling, knocking her balance. She always walks with a stick now (the last couple of years) unless she knows or can see the exact route because otherwise forgetting to think about her feet and the unevenness of the ground means she is highly likely to fall.	
It does help with the fatigue as well, because I, I do support myself a bit on it, but it's more for balance, it's not so much for toppling [ph] myself let's say. But it does help to take the strain off this leg. No it's just when I, you know, the heat does affect it, but that's from the outside, but otherwise it's just extra activity, then, then I get fatigued yeah but not. Not in any other way, I mean the first time, I mean I had a, a, you know, I only realised that now, after I, you know, was diagnosed when I was nineteen, I um, I was going to work and I was from the bus stop to the entrance, I was working in a hospital in fact, it's about three hundred metres, something like that. Well I can't remember exactly but you know that kind of distance. And there was a bit of an incline, I was nineteen, I don't remember exactly, it wasn't the summer, but it was, it was quite hot as well. And I walked with some colleagues and I remember having to grit my teeth to walk up	The support of a walking stick helps with fatigue, balance and taking the strain off her leg (right). Heat and extra activities exacerbate her fatigue. Reflecting to working in a hospital, the walk from the bus stop to work would be difficult, she used to grit her teeth to get herself to work (200m walk with a gentle incline, weather was hot). She didn't want to show any sign of struggle and attempted to walk normally. This phase lasted for two weeks, which she believes to be her first relapse. She had to fight the relapse, embattled.	The struggle of attempting to act normal at work, embattled as she had to fight the relapse.

the distance there. And that was the first time. I think that was my first err relapse. And that lasted for about two weeks. I, I couldn't, you know, I had, I didn't want to show that, I couldn't walk. But I had to, I had, had to put such an effort in, into not showing, err and, and trying to pretend that I was walking normally. And you know, just to make the distance up there. And that lasted two weeks and I remember like, you know, as clearly as anything, and I always, it's always been in my mind, as like what happened there, what happened there? And now I know that's what it was. And now I know that's what it was. It was a, a you know, a period of fatigue. No it just came on, nothing.		
No, no I was working in a hospital yeah. No, no it was just. That extra effort of. Because there was, it was a bit of an incline walking, I mean on the level I wouldn't have noticed it. But as soon as I had to walk a bit up, although it wasn't very steep. You know, I just suddenly you know it's like, attaching lead weights. Big lead weights and you're trying to, trying to drag yourself along. And not sure, like you have lead weights on your legs, and walk in, "Hello, good morning". Yeah it, I still remember it. So it's that kind of thing you know, you, you're dragged down, you, you have to make a super effort to do the normal thing. Yeah just, holding it down.	The very slight incline in gradient caused her to struggle walking in that time frame. She described her legs as lead, dragging them along whilst working, making an effort to walk normal.	Physical description of her 'legs feeling like lead' due to them dragging. Body as baggage with the dragging body.
Although my arms have never been affected no, apart from poor coordination, err you know. I, yeah I knock things over, my husband always moves the glasses and things on the table, my husband always clears them out of my way, just puts everything away (chuckling), because I go like this. You know, I think it's, (sighing), I don't know whether it's the actual eye to think, I don't know, that I don't judge the distance properly. But I, I think it's, I do judge the distance,	Coordination is affected as she can be clumsy, her husband makes sure to clear items to reduce knocking things over. She is unsure whether its her hand eye coordination or her spatial awareness although she is very aware of her movements so can get confused how she can trip/knocks things over.	Spatiality- spatial awareness is affected with upper and lower extremity. Perception and judgement.

but I don't then actually, I think my you know, there must be something with my arm as well, I think my arm is here, but it's you know, because I, your brain tells your, your foot or your you know, you, you learnt how, you know, when you're sort of, how you stretch and how far you have to go to get that glass. But I probably think it's already there, then I'll do this.		
It's likely that with, with, with the leg, my, you learn to walk and then you don't think about walking anymore do you? While I have to actually um err relearn you know, every time I'm walking I have to think of my feet. Yeah and this is very, very difficult. Cos I've always been a person who takes ten things all at once and plan the twelfth. And you have to then stop doing that, and it's not easy. So I, I have to sort of look at my feet, think of my feet all that, am I lifting my foot, you know, go up, go up you know, I mean.	She has to relearn walking every time because she has to think of every phase of her leg movement whilst walking. Expresses frustration with this as she used to be able to multi task regularly, however now she focusses on one thing at a time.	The sense of relearning to walk every time.
I could never, I couldn't for example, I could never do window shopping you know. Where you either walk along and have a look at a window, can't. I have to stop and look at the window and then carry on. No, no because um as soon as my head is turned. My, my balance and everything goes out. And that's one, yeah also sometimes you know, once I fell at home, you know, about when I was standing at my counter, cooking something and then I wanted to go um, you know, like I say and you turn over and what you do is you move that leg, and then that leg round, and I was gonna turn over to get something from over there, and err, err you know, this leg. I thought I turned, I. And but it hadn't actually turned, this, this leg was still there and this leg came over here. While this one is still there, and Yeah I really fell badly, so it, it's, it's that kind of thing, you, you, your coordination. Err but what you do naturally, what you've learnt to do as a baby is. *(int) so you said sometimes you feel sort of clumsy and your husband*	She has to focus on one thing at a time, if she is walking then she to stop to look at shop windows because of her balance. Sometimes her body doesn't move even after she has told it to, she has to think of things you do naturally, what you've learnt as a baby. She must rest otherwise she can get clumsy. The natural unconscious movement no longer works.	Sense of control is weakened where she can not multi-task. Natural movements that once were taken for granted, now are more difficult, the natural unconscious movement no longer works.

moves everything. A safe distance yeah (chuckling). Yeah fatigue would, would affect it all and Then I know I have to sit down and rest Well I get clumsy.		
(int) you have um, mildly mentioned the fact that it's hard to focus on two things at once, so you have to, if you're walking or walking and you can't window shop. Um do you find that that's the same with a lot of things, so err with your mind, do you find? Oh no, if, if I'm sitting down. Um if I don't have to rely on my balance. Then that's fine. No, no I, I, I don't think, (sighing) apart from getting older and, and things get a bit slower in your head (chuckling) um no, I, I mentally I'm not affected as far as I know.	Sitting down her balance is not affected, she says things naturally get a bit slower mentally as we get older.	Spatiality is not affected when seated due to balance not being an issue.
(int) with the assessment we've just done, did you find that you were tired at any point or um fatigued? When I was walking the six minutes. I felt um, I was getting a little less err, a little wobblier let's say. So my, my coordination [ph] was not as good at the end as it was in the beginning. But I didn't feel sort of particularly fatigued. But I think I, I, I was affected yeah. Yeah I mean you know, I'm not, you know, I get wobblier.	During the six minute walk she felt she her coordination was not as good towards the end as she felt more wobbly walking. However, didn't feel any significant fatigue.	Embodiment issues with coordination during the end of the six minute walk, although did not subjectivity report fatigue.
(int) um, anymore, like anymore err situations that you can remember where you did feel fatigued, um? Just if I walk a lot. I've just been on holiday. I've just been on holiday, I did a lot of walking there. I've been to India, but it wasn't very hot but you know, my husband looks after me so he, he is, he is very good, he knows when I need him. So he's take my arm when I need to hold on and He's good. So we do a lot of walking, but we do sightseeing, we stop again, and look at this and look at that, and then you carry on walking, so it wasn't, although there, there were some days when I thought, I'm glad, you know, the culture, I can sit down, but I did manage it. Did walk a lot of steps I must say.	She gets fatigued if she walks a lot. In India, they did a lot of walking, however her husband is really good and looks after her in terms of taking things at her pace.	She gets fatigued if she walks a lot, however expresses gratitude of her husbands understanding.

(int) Good, good um is there anything else that you'd like to add um, about your experience of fatigue and how, how it makes you feel um before we? No I realise as I say, I think that I'm on the whole relatively lucky so far, my progress has been, you know relatively slow so you know, um, I hope to get a few more holidays in before it's too late (chuckling).		

B (iii): M090 data analysis progression table

Meaning Units	**Transferred meaning units**	**Moving towards a phenomenon**
Okay, well, erm, I was, er, had the symptoms, first symptoms of MS in May 96, the same year I became pregnant with my son. I had an MRI in the September and, erm, it was confirmed I had multiple sclerosis. The consultant told me (laughs) to go home and not worry about it and concentrate on my baby, so that was fine. So all through the pregnancy I was tired, but it could have been the MS, it could have been the pregnancy. I had a healthy son and, er, from 1997, when he was born until 2002, erm, I didn't have any relapses at all or any significant symptoms. I used to get tingles in random parts of my body and the consultant thought it might be nerve memory, he didn't think it was significant. November 2002, my life has got very stressful, erm, work was very challenging, there were many individuals at work that, I was a senior manager and there were manager partners, they were in chaos (laughs) ...... and things were falling apart and I split up with my son's dad and in the November 2002 I started to feel like pins and needles all over my body ...... and, erm, I kept going to work because his dad was in London and I was just with my six year old starting a new school and new home in Sheffield... and the tingles got worse and worse and worse and by the (pause), by the beginning of January, I woke up and it felt like there were a million ants crawling over my hair ...... and I was so exorcised by it that I got a pair of scissors and cut all my hair off to ...... get some relief because I thought is it sclerosis or is it the MS and if it's the MS obviously it's not the scalp ...... but the, the fact that it was cooler made it	She experienced her first symptoms the same year as she became pregnant with her son, so she was unsure whether the tiredness could have been from the pregnancy or the MS. She did not have any significant symptoms or relapses with only tingling sensations in random parts of her body. After splitting up with her husband and additional stress at work, she began feeling intense pins and needles all over her body to the point where she actively cut off her hair to get some relief from the feeling of *'ants crawling'*. This made her head cooler, making the symptom more tolerable. The sensations got worse overtime however, she forced herself to go to work until she got an infection and could not get up to take her son to school. She continued to experience high levels of fatigue at work, excusing herself from important meetings for minutes of peace '*crawled under the desks and I laid there for about ten minutes'*. She then made the decision to go to the hospital in a wheelchair due to the crippling fatigue, which she described as *'treading treacle'* because of the lack of ability to move any limbs. This was her first significant relapse which lasted an estimated five months, so the consultant gave her some steroids to attempt to shift the relapse. She did not return to work. She is driven to carry on with work, despite it all with radical strategies to cope with her fatigue.	A sense of physical embodiment from her symptoms of severe scalp pins and needles described as *'ants crawling'* and, the altered sensation of whole-body movement difficulty described as *'treading treacle'*. The physicality of these caused her to actively cut off her hair and occasionally use a wheelchair. Finding minutes of peace at work by crawling under a desk to lie in silence by oneself, to shut off from everything. She is driven to carry on with work, despite it all with radical strategies to cope with fatigue. 'It's not tiredness, it's like treading treacle, you know you can hardly move your limbs'.

a lot more tolerable. Anyway, I was. the tingles were all over. ... and it got worse and worse and worse and, erm, but I forced myself to go to work and I went to work.		
and then beginning of the February I got, er, an infection and, erm, I woke up in the morning and I could not force myself to get up to go to work or to get my son up, so, erm, I called, er, his friend's mum and said will you collect Jack from the door cos I can't get to school today …… so she said that's fine. Erm, his dad was still in London, erm, and I was struggling to get up in the morning to get Jack ready for school and it was just terrible. Anyway, Jack's grandma came to visit us and, erm, she said this can't go on, you need to go to hospital cos his dad was still in London, he'd come up every now and again, but he was working down there and, erm, things weren't great …… and, er, so I went to the hospital, but I couldn't walk, I had to be pushed in a wheelchair and, er.[int: Because of how?] Fatigue, crippling fatigue. It's not tiredness, it's like treading treacle, you know you can hardly move your limbs. Anyway, I mean the final straw at work, I was chairing a meeting, a quite important meeting and I was so tired in this meeting that I excused myself, I said could somebody take over the chair for a few minutes, I need to just do something …… and this was a university in, er, Sheffield and I found a room and it was empty cos … it was out of term time and I crawled under the desks and I laid there for about ten minutes. It was absolutely awful, just awful and this is my memory you see of fatigue, that I know how bad it can get for me. So, er, anyway, so I went up to the hospital and I saw the consultant who was totally wonderful, he was a lovely man …… and I got a shed load of steroids to shift the relapse …… cos this is my first		

significant relapse really apart from the very first one where I got double vision and I couldn't walk and it was all funny …… er, but that only lasted a while, a few weeks whereas this was, that was November now we're talking about March …er, and I didn't go back to work.		
So I was (sighs), er, his dad left his job in London, his Nan told him, she came over to look after me while he was still in London and she said you've got to come back and live in the house and look after Alison and Jack, so, er, he did and I went to bed essentially, I mean I did, I went to bed, I did not get up at all …… and the symptoms, as the weeks went on I got less tingles, but my vision [unclear-05:22] …… so it got darker and darker and darker and darker until I could not see at all. So all I did was I just lay, well my brain, you know your brain works you know, er, perhaps less effectively nowadays. Anyway, erm, I listened to the radio all the time. I couldn't hold a book. I find a little notebook, I tended to write, I tend to write things at the end of the day …… and I found this notebook from that time and the writing has disappeared, you can't read the words and that was my last venture, that was sort of March 2003. So I was in bed from the February essentially apart from that trip to the hospital, er, and then I got, I call it blindness, I had no vision, I couldn't see anything for several months …… er, and I wasn't out of bed. I mean I'm very, er, er, modest and I don't like anything to do with you know, erm, going to the toilet, I'm very private. So I crawled to the toilet, I wouldn't have anybody to you know …… have any of that, I crawled, but everybody, I mean I did nothing, I just was in bed.	Her husband came back and lived with her as she was bedbound for months until the symptoms of tingling and fatigue lessened and subsided. She began writing things down in a notebook at the end of each day, however, her vision worsened and darkened until she essentially could not see for months, so just lay in bed listening to the radio. She held onto her modesty, as she explained the difficulty of crawling to the toilet whilst her vision was impaired.	Bedbound due to the inability to move the body at all. The loss of a sense and sight temporarily created complete restriction and a sense of darkness for her, with only the radio as company. The statement '*I mean I just did nothing, I just was in bed'*, suggests time became static for her. Her spatiality of losing sight altered and distorted her physical actions and activities (going to the toilet with more difficulty etc). However, her sense of self and modesty remained.
So by about the November, erm, work were really quite good, they sort of kept in touch. I was on you know full	Her work visited her to discuss and agree for an ill health retirement. She articulated embarrassment	(Self-hood)

pay, then half pay like if you're, like a Government officer, it's all tied by that, it's fine and, er, so the end of 2003 my boss came to see me and she said it doesn't really look like things are moving are they Alison and …… you, oh, I lost my speech as well and I was (making noises).I mean it was a shit time, I'll tell you, it was really awful. I felt so sorry for my son because I hadn't ever told him I'd got MS you see, so I think, erm, I think he was a bit, erm, well never really talked about it much, but I was very worried about him. Anyway, er, my boss came to see me and she set in motion ill health retirement from work, er, and, erm, I just let her do it, I mean very efficient, good woman, very efficient nurse, she sorted it all out. Erm, so, erm, I officially retired from work 31st of March, er, 2004 … … so from like the February 2000, well November 2002 to February …… 2003, February through to the Christmas, I didn't get up for Christmas, but I think I got up for Jack's birthday which was March, so I was essentially in bed for a year …… and a lot of that time was very, very sensory deprived, erm, (sighs). [int: Sorry, so how long did you have, er, problems with your speech for?]. (Long pause). Probably weeks, might even have been months. Erm (pause). Everybody came to see me, it was. My sister came, she, er, she blew into my room like a rose. Yeah, family came to me you know. Anyway so, er, by about the March 2000 and, no, no. Yeah, by about the March I was sitting up, so the deputation came from work in my living room and it was horrible, and they were really kind, there was my union rep, there was my boss, there was the HR guy, it was, you know little family, little meeting …… and I wasn't dressed, I was in my dressing gown, I hadn't got dressed for months, erm, and towards the end of it I burst	and uselessness as she hadn't gotten properly dressed for months and burst into tears towards the end of the visit. She expressed feeling sorry and worried for her son due to the lack of communication and understanding about her illness, and his own health and well-being.	Her own identity with work colleagues and family had changed, a tone of embarrassment and uselessness as she felt out of control. Worried about the impact of her illness on her son due to the lack of communication and understanding of her illness. -family support? -work context? She's not doing much, 'trundling on'.

into tears and said so I'm just useless then and they were so sweet. Anyway, so they basically said no, you're not useless and hot foot it out of there (laughs).		
So that year sort of trundled on and I was getting up a bit and I was sleeping a lot, my vision was okay and my speech returned, so I tried to do bits and bats and then, oh, I got a bit depressed cos …… you know you never think of yourself as not a robust person, but you kind of feel well you let yourself down there Alison, you know it's a bit obvious getting depressed cos you've lost your career you know, but I did, I got depressed and in the October I went to see my consultant, Doctor Jordan and essentially (laughs) I just burst into tears in front of him for about ten minutes, it was so embarrassing and he was so sweet, he said Alison, I think you're depressed and he gave me anti-depressants. He said I know you don't wanna take them, but it just takes the edge off and it gets you to a state where you can start to cope with the things that are upsetting you …… cos it's acute [ph] and I don't know what, the terms they use these days, but in mine it was endogenous reaction cos [unclear-10:19] reaction becomes depression. Erm, so, er, so that was that, that was that, that was 2004. 2005 I'm getting up a little bit; I was generally at home, so I'm retired …… and I'm not doing very much, erm.	Throughout the year her vision and speech returned, however she slept a lot, and after a neurological consultation, she got prescribed anti-depressive medication to initially help her to cope with her diagnosis and life changes. She mentions the initial reluctancy to taking the medication. She describes doing very little in those two years, states she is retired and not doing very much.	The process, adaptation and decisions she had to make from the secondary affects of the illness, like depression caused discourse in her life so she was able to very little.
[int: Can we, erm, just quickly, can we go back to, erm, obviously when you were bedbound …] … for about a year. [int: Erm, can you just describe what it was like, erm, why you couldn't get up, erm?] I couldn't get up cos I hadn't got the energy to get up. Erm, although I was, I mean I did lie in bed, but sometimes I hadn't got the energy to just lift my hands to hold the book when I could see. I was just so utterly exhausted. … and all I wanted to	The lack of energy, to occasionally even lift her hand up, made her want to just lie in bed, still, and sleep it off due to feeling '*utterly exhausted'*.	Her complete lack of energy and utter exhaustion impacts her body, with considerable effort to even lift her hand up.

do was just lie there and sleep it off …… you know just sleep it off cos when I saw an MS nurse or the consultant because this was the most, this is the most important bit about fatigue for me.		
Okay, so 2005 trundled on. … and then, erm, I did a little project with my son in the summer, for the summer holidays because I thought you know he's gonna be bored, so I called it on our doorstep …… so we, who comes to our door, you know the postman, the bin man, you know all that and then what's down our street, what's in our neighbourhood, what, you know so we did, he did a book like that, you know a lever arch, we did it all through the summer on our doorstep, it was for writing practise as well, but generally …… you know it was messing about and, er, I made a little medal for him at the end of the summer and we had a little ceremony presenting a certificate and a medal …… and I told the teacher about it and she said you should bring it in and he got the Head Teacher's award. Anyway, that was great. So September I'm up, I'm positive you know …	She enjoyed an active summer with her son, creating a little project called '*our doorstep'*, of which made her feel positive as her son shared his summer experience at school where he received the headteachers award.	She spoke fondly of positive memories of the summer spent doing a project with her son, when her illness did not fully impact her daily life activities.
… I'm great and then, erm, in the October I'm in bed with his dad, it's midnight, I'd been starting to feel a bit sort of wobbly, like jelly like, I didn't really understand it, not MSC cos MSC is (sighs) like that, but this was weird. Anyway, I woke his dad up at midnight, I said why is somebody digging up the road at this time of night, he said what you talking about, I said what's that banging and it was my heart. I went to the doctors the next day and, er, said I feel terrible, I feel wretched and she said it's your MS, I said, and I did say to her, I said it doesn't feel like MS, it feels something different. Anyway, she took some bloods and said go home and rest. That afternoon they	A month later she began feeling physically unstable *'sort of wobbly, like jelly'*. After a disorientating sensation of loud banging, the feeling of somebody digging up the road, she got diagnosed with graves disease. She combined conventional medicine with herbal and found over the course of six months her symptoms improved a lot. The feeling of annoyance was expressed as she was starting to feel better after a summer with her son, considering work again, and then another complication arose. Although now she only gets the sensation of pins and needles in random parts of her	Annoyance of a secondary diagnosis following the feeling of positivity after the summer with her son. Her experience of embodiment was changed again as she felt physically unstable *'like jelly'* and *'loud banging as if somebody is digging up the road'*. Openness to trying variety of treatments as responded by the doctor but stopped, she does not rely on anti-depressants.

phoned me and said you need come down to the surgery now, er, yeah cos they've got the bloods back because she rushed it through for some reason. I'd developed graves disease. Have you heard of graves disease? [int: yes I have heard of Graves disease]. Yeah, it's actually thyroid. So I had graves disease which went on for a few months, er, but fortunately, fortunately I'm very anti conventional medicine …… animal tests and all that stuff and I mean I'm not an idiot, you know doctors (laughs) …… and all the rest of it, but, but anyway a close friend of mine who's also vegan, we've been vegan together a long time, both [inaudible-13:46], erm, she had graves disease and she, er, dealt with it and treated it …… and finished with it through a herbal, herbalist. So I went down to this herbalist in Sheffield and they'd given me three tablets, Prednisolone …… something beginning with L and another thing, I got three different, I mean I think I was quite anaemic anyway, but they gave me three different types of tablets, so I was taking something for the thyroid, this graves condition. Anyway, so I went to the herbalist and she, we had a long interview and da-de-da and she gave me this, so I went home, stopped the tablets, took this and then I, my levels went way up again and she (laughs), she told me off, she said no, no, no, you, herbs take a long time, so your conventional herb, that's what you do. And she said if you don't keep taking them I won't treat you. Anyway, so over the course of six months, erm, Sodalite is apparently the crystal to protect your, er, thyroid so I used, I got a sodalite crystal there, that's why I like to have things like there almost, I got sodalite and, erm, because do you know what the treatment is for graves disease? [int: no]. Right, they, erm, they give you thyroxin, they try and increase your	body, of which she was advised to go to bed for two weeks by the MS nurse.	

thyroid …… which makes you hyper, hyper. I think I got the hot one They give you an, a radioactive tablet which knocks out your thyroid …… and you take thyroxin or you have surgery. Now I didn't have any of that, I've protected my, I'm like this with it. Anyway, so it got a bit complicated with the MS, but because I'd had this summer with Jack and I felt positive, I thought you know perhaps I can think about going back to work and then slump (sighs). So I got better from the graves and then the MS wasn't really an issue and what I found was when I get tingles and I get them in random parts of the body, often across my shoulders or here, when I feel I'm getting tingles.… the MS nurse said you go to bed for two weeks and then you'll be fine and that's. An MS nurse said that in Sheffield. Doctor Jordan has set up a wonderful MS department, he was a fabulous. Ironically he got a brain tumour [tapping noise in background] [inaudible-16:10], got a brain tumour and had died. He was a wonderful man, really, really wonderful. So then, oh, dear me, dear, dear me.		
Anyway, so for years, erm, after this terribly awful relapse … erm, I've tried to really take quite good care of myself. So I stopped smoking [ph], well I didn't stop, I stopped drinking, I tried to eat a healthier vegan diet. Erm, I did go gluten free for a while which I think helps, but I've lapsed, but I am now gluten free. Erm, so you know life went on, I had a full-time job, I had my son, I had my partner and it, there was ups and downs, but when I felt myself getting a little bit tingly. I'd just say to them I'm going to bed. … and that was in the context of a proper working life, but for (sighs). Well we, erm, we lived in Sheffield, then we moved to Brighton and, er, yeah, I got my, I went back to work as a social worker …… for a year to see if I could do	Now, she is on a vegan diet and gluten free, which she thinks helps. She went back to work, as a social worker and another management job after moving down to Brighton from Sheffield.	Other factors like a vegan and gluten free diet are thought to help her symptoms. She was able to return to work after moving down to Brighton.

it in 2006 and it was fine, I got the qualification that I did and so I applied for another manager's job and I got the post, I managed the social work service at the county hospital …… which is, er, oh, no, I got the learning disability job. No, no, that was before. Er, I managed the people at the hospital. That was a good job, nice crowd. Terribly, awful environment to work in. I mean bank nurses, a very stressful job for lots of people.		
Anyway, I have had a number of relapses. So I went to work there in 2007 and I think the stress of my personal relationship with my son's dad …… precipitated the majority of the, well precipitated all the, all the relapses … was the main factor cos it was very difficult. Anyway, so I had a relapse in 2009 and then one in 2010, this is when I'd be off work eight weeks. So in 2000 and, yeah that was just tiredness, I was just.2009 was just tiredness; I did not feel I could Erm, everything was such an effort. The idea of getting dressed was appalling …… you know just standing up and (sighs), yeah. I mean it's sort of, it's the emotional part of it as well I think, but just the idea of just not feeling, as if you've been run over by a steamroller, you know it was just …… and then 2010 I had another relapse, but that affected my vision. I got awful, erm, like popliar [ph], erm. [int: Oh, er, neuritis?] Yeah, I've got neuritis and double-vision and I tried to conceal it at work that I wasn't falling into a relapse because I just, I was, felt guilty I suppose. Anyway, I had to wear a patch, an eye patch and it got, cos I was doing this in meetings and people were saying so what you doing Alison and I thought, oh, so I was wearing an eye patch and I wore that eye patch for five months. So that relapse really affected my eyes …… and, er, as well as	She thinks the majority of her relapses were precipitated by her husband and her relationship with him. Had a relapse in 2009 and 2010 which is when she had two months off work. The 2009 relapse was described as *'just tiredness'*, different from 2000. Emotionally and physically tired, the feeling *'as if you've been run over by a steamroller'*. The 2010 relapse she experienced neuritis and double vision, however wanted to conceal it at work, so she could continue working, but also expressed feeling guilty about this. She had to wear an eye patch to help her symptoms for five months. She changed job roles to make a slightly less stressful working environment, yet one day she sent herself home where a 50 metre walk to the bus stop, took her an hour. She was very ashamed by this.	She was aware that her symptoms and relapses were exacerbated by external factors, such as her relationship with her husband. The 2009 relapse was described as *'as if you've been run over by a steamroller'*. She experienced neuritis and double vision with her relapse in 2010, however tried to conceal it at work to continue working, expressing guilt about this. She wore an eyepatch to aid her symptoms for five months. To lower the stress, she changed job roles, however one day she sent herself home where a 50 metre walk to the bus stop took her an hour.

the [unclear-19:31] fatigue and then (pause) 2000 [int: did the eye patch help?] Yes, coz … just move one eye, you wouldn't have to, you wouldn't be looking like that all the time. It's very disturbing you know. I get it very occasionally when I'm really tired at night and I look at the, in the, well the laptop and it …… oh, there's two Vera's (laughs). Erm, 2013, so I'm back at work and I have to go into a different area because, erm, er, and I think my boss wanted me to do something different. Erm, I think they thought I couldn't really go back to the hospital. A lot of people had moved. Erm, I didn't particularly want to go back to the hospital, it was very, very stressful. So I moved into a different job, it was still a difficult job; it's about hospital discharges and finding home helps which is not easy, not easy. Anyway, I did that for a couple of years and then in 2013 I had a relapse of about seven weeks and this is not great for my health record, you know my work record …… it's not good at all. Anyway, erm, and that was just, I ground to a halt at work and, erm, I just said to, er, I said to my colleagues, I couldn't see my boss, I said I'm gonna have to go home, so I don't know if you know Bartholomew House in Brighton, but say to walk from here to that house … okay, so that was my office… to the bus stop. That took me an hour [int: fifty metres?] I just, cos I was walking so slowly … and I was holding on. I didn't, and if you come with me I was so ashamed you know, I mean it's ridiculous.		
[int: So (coughs) was it because you felt that in your body or was it, erm, that in your head you couldn't walk?]. Walk. Er, it's my body. It was just too much effort to do that and that is normally how I walk, I rush around you know. I mean I, pace is the worst word in the English	She felt the fatigue in her whole body, it was a lot of effort to walk in comparison to normal. *' I mean I, pace is the worst word in the English language…*'.	Fatigue affects her whole body, even with simple movements like walking. She mentions other stressful factors, personal and financially that were thought to affect her fatigue.

language. … I used to hate that when I first got the diagnosis, I don't want pace; I want to be you [ph]. Anyway, so, er, yeah, 20, it wasn't 2013, it was 2014 and then, erm, 2013 I got, er, 2014 I got a relapse which again was a lot of tingles and a lot of fatigue and a lot of stress and, erm. [int: Was it fatigue in the same sense as prior?]. Yeah, it was getting that way. It was getting pretty grim. … and I just, I just phoned up work and said I can't come in, I'm not well and I did not go back to work. So I was off work for a year … trying to get better, you know I was trying to get better, but it didn't, nothing happened and I saw Doctor, you know the consultants a few times and I had tests and this and that and another MRI who …… if you have one just tip, shut your eyes, just close your eyes. Anyway, erm, I was, there was another meeting in 2015, May, March actually to say that, erm, I wasn't able to come. Occupational Health did a report …… so I had to go. So then I retired from work and most of 2015 I spent half in bed and half out of bed, but at this time my son and I were living alone together, his dad …… I don't exactly know where he was. Oh, yeah cos there was a longstanding feud between me and his dad, he, erm, he defraud, he stole several thousand pounds from me and I tried to get it back from him and he promised to pay it when he sold something and when he sold something he bought something else, so. Yeah, when he sold his flat he said I'd get the thousands then and he sold the flat, he bought a house up north and so I said I'm gonna take you to court, I can't have you do this, big mistake, never go to small claims court, it's so expensive, so I was struggling financially and I think that contributed to the stress and the fatigue, so …… it's all mixed up isn't it?	She did not return back to work after this relapse, as rest did not seem to help. There was additionally stress from her husband with financial disputes and disagreements which ultimately, she went to small claims court for, however this got her into financial difficulties. ' I don't want pace; I want to be you'.	' I don't want pace; I want to be you'.

Anyway, so since 2015, now 2015 I was in bed, but, erm, I don't know, when you lose your career, you know what you've done forever it's quite hard. I mean I do enjoy doing different things, but, erm, I don't feel I have a sense of purpose anymore. I was talking to the MS nurse about it and I wasn't sure if last year I was just being lazy cos, yeah cos like 2016 was quite a good year because I got somebody to do the garden and so we have lots of fruit and veg growing and it was really nice …… and I did some lovely walks in the spring in the woods and Downs, nice walks, erm …[int: And were the walks okay? You didn't feel?]. Yeah. No, the walks were fine. The walks were absolutely fine. So I think 2016 I probably was quite strong, then we had some issues, er, with my son's girlfriend and, erm, that all got a bit difficult cos she was living with us. Er, but it's really hard now to describe (sighs). MS is difficult because if you don't look like you've got anything and generally you cope alright, it's like what's it about …you know its hard… But, so when I get tingles. … if I ignore them I know that there's a likelihood that I will get worse because MS isn't like, you know when people say well just push through it, you can't do that with MS. … you push through you go down in my experience. Other people might be different, but yeh. [int: Okay, that's good. Erm, I'm trying to think about other things that you've said. The, when you said, erm, the MS nurse said when you get pins and needles go to bed and rest. Erm, is that because the pins and needles, erm, would lead to fatigue or is that just because then all symptoms would get worse?]. Well no, I think it's. In my experience and my, er, in my experience of MS and of my own illness, if you like, or disease, whatever you wanna call it is that if	Since 2015 she has not been working, she has other activities she enjoys (vegetable patch in the garden and walks), however she feels she doesn't have a sense of purpose anymore due to losing her career. She expresses the image of some MS symptoms being invisible, which can make It difficult to explain. It is unlike other experiences, you can not just push through it if you are experiencing symptoms. She would state that if she starts getting *'the tingles'* then if she didn't address it and rest, that would lead to fatigue. It is the trigger.	Self-identify was questioned as she felt little sense of purpose due to no active occupation. Some MS symptoms are invisible, which creates difficulty with acceptance and understanding from others. MS fatigue is not something you can ignore and push through.

I get tingles usually, inevitably that means that I'm gonna get fatigued …… it's kind of this little trigger. So basically I think the tingles are to say you're doing too much… you know, but sometimes I do ignore it and that's not good either… cos then I do get not very well, so it's a bit boring you know spending your life in bed, but hey ho (laughs).[int: Yeah, well I think you're doing well …].		

[int: Erm, okay, er, trying to think of other descriptions you've said (pause). Erm, yes, when you had your first meeting when you were in senior management and, erm, you said that you paused for, got someone to take over the meeting …… and you went into the other room and crawled under the table Can you describe a bit like, describe that just a little bit more?]. Um, um, I know, disgraceful. Erm, well I was. I was at that head of the table and the door was there … and it felt like I was a bit on fire, the tingles … were really, really severe you know and I couldn't concentrate and I thought if I don't lie down, like a real intense need, if I don't lie down I'm not gonna be well you know and that's what gets you with, when you're, with my fatigue …… so I thought I have to lie down, if I don't lie down I'm gonna, I wouldn't think I'm gonna fall down, but I think I'm not gonna be well, something's you know, so, er, and I probably dozed off. I can sleep anywhere, I can sleep on a sixpence me, like the Duke of Wellington, he catnapped. I can catnap, like to now, when I go back to Peacehaven on bus I shall probably be asleep before I even get to the South Downs Way (laughs). … it felt like I was on fire and then I lay down and that and, er, I must have dozed off cos I thought, oh, I better get going now. So I managed to get up and I, you know had the, I finished the meeting and we got various resolutions passed, so it was, you know it was a reasonable meeting … but it wasn't as good as it could have been, but I think, but I want to go back to the tiredness is that sometimes you get so tired it's like it hurts, it's really hard to explain, but it's like it's so overwhelming, but only inside you that, I don't	Referring back to the time she crawled under the table at work, she described the sensation of severe pins and needles like '*fire'*, she couldn't concentrate due to the severity, so she had to lie down. '*I can sleep anywhere, I can sleep on a sixpence me, like the Duke of Wellington, he catnapped. I can catnap, like to now, when I go back to Peacehaven on bus I shall probably be asleep before I even get to the South Downs Way'*. Sometimes she gets so tired it can physically hurt, it is so over whelming, all over the body feels so heavy, expressing 'treading treacle'. She describes in attempt to get better post relapse, that she feels like she is treading through treacle, all in her legs feel like she is walking through sand.	The physicality of fatigue can be so overwhelming it is described as pain. The feeling of bodily heaviness was expressed as *'treading treacle'*. The severity of her physical embodiment implications of the pins and needles impacted her cognition as well as physically. She describes in attempt to get better post relapse, that she feels like she is treading through treacle, all in her legs feel like she is walking through sand.

know, it's weird. [int: And when you say inside of you, do you mean in your body or in your head?]. Yeah, all over the body … and it's like it hurts (laughs) you know. It's, you can't imagine being tired hurts, but it feels like it hurts, you know it just gets so heavy and like that expression treading treacle, I used that for years after I got the MS because when I was trying to get better after the big relapse it was like, if you can imagine what treading treacle is like …… or pushing your, all your legs through sand… that's what it's like, it's just, oh, it's the pits really (laughs).		
[int: Erm, yeah, okay. Erm, if you have, erm, any other things to mention, any other, anything else that you'd want to say about fatigue, erm, then you can now?]. I think you know you've got MS fatigue when you go to sleep exhausted and you wake up exhausted. So, like I say, I mean I do make a bit of a joke of it, but I do actually spend at least fifty percent of the week in bed and sometimes I'll just wake up and I'll be like this and I'll just say Jack, because his bedroom's across the way, I'm not getting up today, you'll have to look after yourself and I just know I have to stay there. In fact in the week the only two things that get me out, I go and visit an old lady who's bedbound, I'm a library volunteer, so I visit her a couple of weeks, every couple of weeks, but we don't talk about it, literally we just gossip … She's a nice woman. She's been bedbound for twenty odd years, so I get up for her …… and I get up for Italian, so next week whoo (laughs). So you know yesterday Italian, next week Italian finishes, yeah Oh, yeah, there'll be next year as well.	To have MS fatigue is going to bed exhausted and you wake up exhausted. Even though she jokes about it, she spends an estimated 50% of her time in bed. Currently there are only two things that get her out of bed, Italian classes and she visits a lady who is bed bound to gossip. She gets out of bed to help others.	Coping mechanism-joking? Her recognition of MS fatigue is the feeling of persistent fatigue, with or without sleep/rest. Due to the fatigue, only certain motives/activities get her out of bed. She gets out of bed to help others.

Appendices C: Protocol for assessment day

C (i): MS protocol

SAVE THIS PAPER COPY AFTER EXPERIMENT – it contains crucial data written on it

Volunteer Number ________________ Date/time _________________

Emergencies, Health and Safety

Harry Witchel	0771 284 5470 01273 697 917 Terri 01273 873 549 Trafford witcheloffice@gmail.com	Univ Sussex online reporting	Bsms1973@sussex.ac.uk
Rebecca Player	07491977740 rplayer3.rp@googlemail.com	Uni of Brighton rfp14@brighton.ac.uk reporting	
Emergency on Darley road Eastbourne campus	01273 642222		
Ambulance Eastbourne district general hospital	999	Police (Brighton) Kings Dr, Eastbourne BN21 2UD	999 or 101

All accidents must be reported to someone.

Injury: More serious injuries are those eliciting blood, pain that will not subside, or anything requiring hospital treatment. If there is blood or an injury where someone gets hurt (such as a fall resulting in a twisted ankle), this will have to be reported. In the first instance, report everything to Rebecca so I can help clean up and sort out things. If neither I nor Harry are available, you can contact the university emergency number at Eastbourne campus, or the responsible party at the venue where you are working (e.g. at the hospital). If a person hurts themselves and is bleeding profusely or has serious pain that does not abate (a burn wound or potentially a broken arm), go to the hospital to check it out. When possible, round up the equipment and just throw it (without organisation) into the cupboard or a locked room (while waiting for ambulance or taxi); the receptionist in the Robert Dodd building may be able to temporarily lock a room for you. If a volunteer is injured, either you or someone at the health science school should always stay with them. You should accompany the volunteer to the hospital, and once they are admitted (i.e. someone is looking after them), leave them, sort out the equipment, and then go back to the hospital and check on how they are doing. Money is provided for taxis.

Fluid spill: If there is a spill, we have to clean it up, but if there is a major spill we may need to contact the authority at the venue where the problem has occurred. If a piece of equipment has been dropped, you must report that to Rebecca.

Theft: If something is stolen (and you did not see it being stolen), report it to Rebecca. We may or may not be insured depending on where it occurred.

Robbery, aggressive behaviour: If a person(s) acts threatening to you, grabs something and takes it away (robbery), or attacks you, report to Rebecca, and we may report it to the police. Photographing the person may help, but do NOT aggravate the person by threatening them.

Day Before

- Telephone call to volunteer (or email if phone does not work
    - Remind volunteer to wear trousers – do NOT wear a dress or skirt
    - Ask volunteer for shoe size
    - If volunteer is a patient, ask for physician's name
- Charge sensors via USB (x-io)
- Format all Micro SD Cards
- Print all sheets and forms:
    - Patient Information Sheet
    - Consent Form
    - This Protocol
    - Demographics Form
    - EDSS-S – Self-assessed Extended Disability Status Scale
    - MSWS-12 – Multiple Sclerosis Walking Scale
    - MFIS – Modified Fatigue Impact Scale

- Bring sheets in plastic wallet
- Pack equipment: camera, laptop, sensors, thigh straps, money, paperwork, shoes, dynamometer.

On the Day

Unpack and Set Up Electrical devices (15 mins)

- Set up Floor lines and distances with tape
    - Mark every 5 feet in 25 feet distance (with BOTH tape and colourful cups)
        - The cups should be placed so that:
        - The participant does not bump into them
        - The cups are easily seen by the camera (ie faraway cups should be red or a colour that contrasts with the floor)
        - There is room to walk/manoeuvre around the cups when turning around
    - Place solid items to walk around at the beginning and end of the T25FW
- Place chair with no arms for sit to stand test.
    - 43.5cm height to seat.

Synchronise ALL Clocks to master clock

- Green digital clock facing laterally
- Green digital clock facing forward
- To set the green digital clocks: shift to **'set time'**. There are 3 buttons (mode, down and up). Use **'mode'** to shift from hours to mins etc. and up and down to change the numbers. The seconds cannot be changed so in order to sync the clocks, press up or down (half a second beforehand) when setting the minutes as the time hits the next minute on the other clocks.
- Stimulus computer
- Sensor computer

- Set visual (green numbers) clock according to radio clock (silver)
    - Place visual clock in FOV of camera
    - Sit clock on top of its box

    - Make sure the volunteer number (eg 'M061') is visible
- Set up 1 camera
    - Verify memory in card is in camera and has enough memory
    - Place camera on tripod
    - Check camera
        - Check light (make sure that clock is not obscured by reflections)
        - Is clock and all of the runway in the field of view of camera. Can you see the numbers clearly?
- Place a label with the volunteer code (e.g. **M045**) in view of the camera
    - should be within 6 feet of camera, on the wall or next to the green clock

Wearable Inertial Sensors

- Equipment needed:
- Wearable sensors (x8 plus master in hand)
- Use “thigh” sensors for wrists, and use ankles
- Use "waist" sensor for chest (on harness)
- Memory stick with SD card port
- Micro USB cable (for connecting sensors to PC)
- PC with sensor programmes installed

SENSOR EMERGENCIES: IF COMPUTER DOES NOT CONNECT TO SENSORS

There are only 3 things to go wrong if the computer does not connect to the sensor: the computer, the sensor or the wire. The most likely problem is the computer, but FIRST

- Test the easy stuff.
- Swap to another sensor, and see if that helps
    - If the sensors fail, they should fail one at a time (unless you have sequentially screwed up all of them)
    - Note: the sensor should have a constant green light on, and a constant yellow light, a possible white light and a red light, only when plugged in.
    - If the lights are not correct, then there is a sensor problem.
    - If the yellow light is never on, either you have not put the micro SD card in, the micro SD card is in but facing the wrong way or incorrectly seated, the micro SD card was not formatted correctly.

- If changing sensors does not help, swap the USB wire
- If changing the sensor AND changing the wire does not work, the problem is almost certainly the computer.
- If you think the problem is the computer:
    - First, just see if you can do the entire process on another computer
    - If another computer is not available, attempt to reboot the computer
    - Then look at what the NGIMU says the problem is

Formatting / Clearing the old data from Micro SD cards

- Not essential: Clear/format each SD card data (must be done before every experiment):

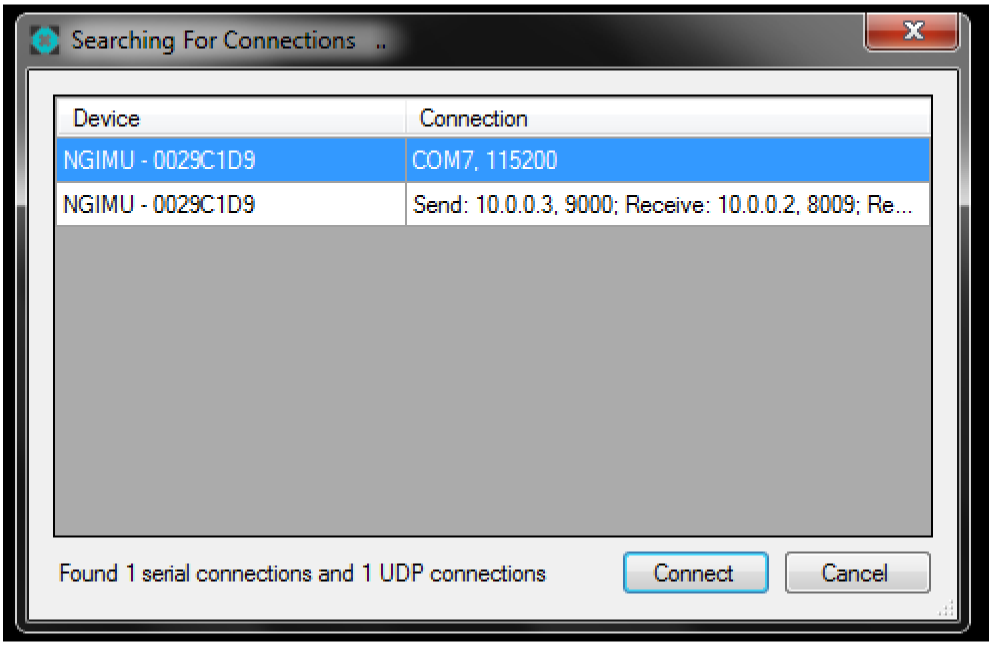
(Note: this can be done the day before. Best done with the sensors on)

- Line up sensors
- Turn all sensors on
- Select one sensor and move it in front of the computer (ie out of the line)
- Connect sensor to computer via micro USB
- The computer should immediately tell you with **autoplay** that a new drive is available. **Autoplay** should state the volume name of the card
- Close this **autoplay** window
- Double click on **SDformatter** programme
- The programme should show the name of the SD card in the box marked **volume label**
- If not, hit the **refresh** button
- If you still cannot see the volume name, you have a problem a poor connection between the drive and the card
- Try moving the card in and out slightly, or wiggling it
- IMPORTANT – check that correct drive is opened (e.g. ‘5B17’, size 14 GB)
- Click **format**
- Normally we use **quick format**, but when there are problems with sensor later, reformat card using the full format (Erase)

- To make a full format (which takes much longer), click on the **option** button in **SDformatter** and select **full format (erase)** in the **format type** window
- Click **OK** for both questions about whether you want to make changes and whether you want to continue
- When completed, close close **SDformatter**
- Safely eject USB connection from computer
- Remove SD card and place back into sensor (black-side up)

Sensors set up

- Connect the sensor to the USB port
    - If you get a spontaneous **Autoplay Removable Disk**, click on **cancel**
- Open NGIMU GUI.exe
    - Version 1.11: Currently working
    - In Sakmann: Located in D:\Sensors\NGIMU-Software-v1.11\NGIMU GUI
    - Xio symbol is a black X inside a blue diamond in a black square:
    - Double click on it.
    - It will immediately start looking for sensors to connect to:

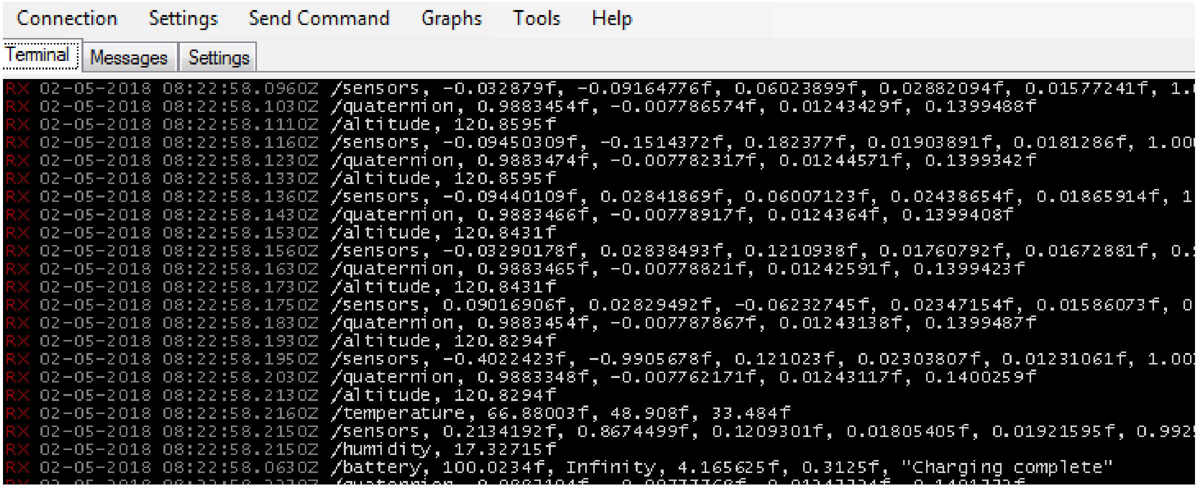


Device	Connection
NGIMU - 0029C1D9	COM7, 115200
NGIMU - 0029C1D9	Send: 10.0.0.3, 9000; Receive: 10.0.0.2, 8009; Re...

Found 1 serial connections and 1 UDP connections

- Select the correct sensor.

- Each sensor has a serial number (above image, the serial number is **0029C1D9**)
- It will usually show TWO possible connections to each sensor that it can detect: a USB connection (the one marked "**COM7**", or some other number), which is followed by the "baud" (transmission) rate, and 2) a wifi connection, which is identified by the words "send" and "receive", along with the local IP address (10.0.0.3 in the image above).
- If you don't see one or either of those, you will have to troubleshoot (see discussion later).

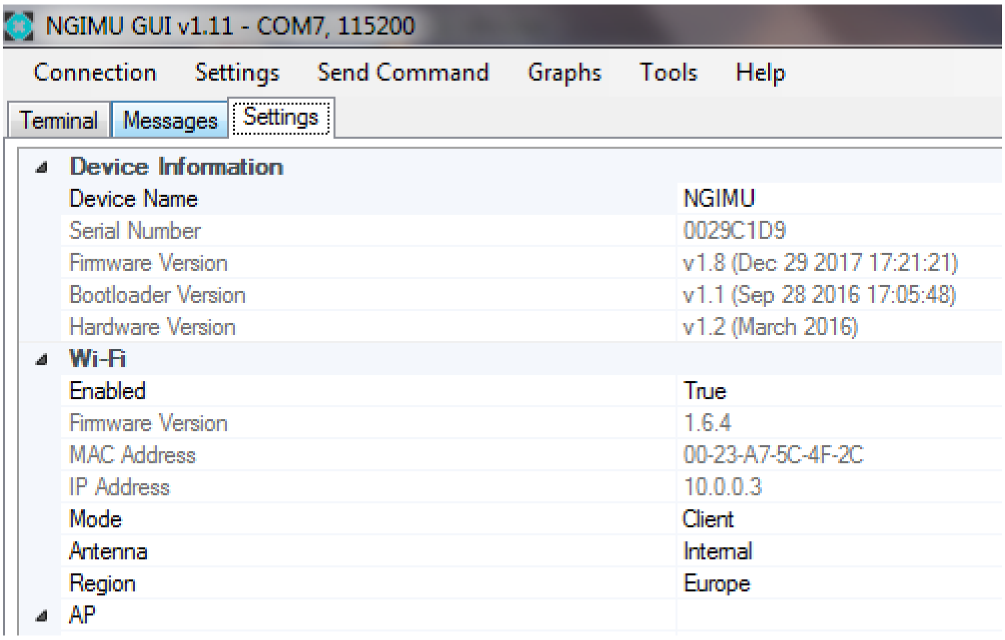
- For now, select the USB connection (click on it), then click on **Connect**.
    - You will then be taken to the main sensor GUI screen in the terminal frame, which will look like millions of numbers flying upward like in the Matrix movie.
    - 

```
RX 02-05-2018 08:22:58.0960Z /sensors, -0.032879f, -0.09164776f, 0.06023899f, 0.02882094f, 0.01577241f, 1.
RX 02-05-2018 08:22:58.1030Z /quaternion, 0.9883454f, -0.007786574f, 0.01243429f, 0.1399488f
RX 02-05-2018 08:22:58.1110Z /altitude, 120.8595f
RX 02-05-2018 08:22:58.1160Z /sensors, -0.09450309f, -0.1514372f, 0.182377f, 0.01903891f, 0.0181286f, 1.00
RX 02-05-2018 08:22:58.1230Z /quaternion, 0.9883474f, -0.007782317f, 0.01244571f, 0.1399342f
RX 02-05-2018 08:22:58.1330Z /altitude, 120.8595f
RX 02-05-2018 08:22:58.1360Z /sensors, -0.09440109f, 0.02841869f, 0.06007123f, 0.02438654f, 0.01865914f, 1
RX 02-05-2018 08:22:58.1430Z /quaternion, 0.9883466f, -0.00778917f, 0.0124364f, 0.1399408f
RX 02-05-2018 08:22:58.1530Z /altitude, 120.8431f
RX 02-05-2018 08:22:58.1560Z /sensors, -0.03290178f, 0.02838493f, 0.1210938f, 0.01760792f, 0.01672881f, 0.
RX 02-05-2018 08:22:58.1630Z /quaternion, 0.9883465f, -0.00778821f, 0.01242591f, 0.1399423f
RX 02-05-2018 08:22:58.1730Z /altitude, 120.8431f
RX 02-05-2018 08:22:58.1750Z /sensors, 0.09016906f, 0.02829492f, -0.06232745f, 0.02347154f, 0.01586073f, 0
RX 02-05-2018 08:22:58.1830Z /quaternion, 0.9883454f, -0.007787867f, 0.01243138f, 0.1399487f
RX 02-05-2018 08:22:58.1930Z /altitude, 120.8294f
RX 02-05-2018 08:22:58.1950Z /sensors, -0.4022423f, -0.9905678f, 0.121023f, 0.02303807f, 0.01231061f, 1.00
RX 02-05-2018 08:22:58.2030Z /quaternion, 0.9883348f, -0.007762171f, 0.01243117f, 0.1400259f
RX 02-05-2018 08:22:58.2130Z /altitude, 120.8294f
RX 02-05-2018 08:22:58.2160Z /temperature, 66.88003f, 48.908f, 33.484f
RX 02-05-2018 08:22:58.2150Z /sensors, 0.2134192f, 0.8674499f, 0.1209301f, 0.01805405f, 0.01921595f, 0.992
RX 02-05-2018 08:22:58.2150Z /humidity, 17.32715f
RX 02-05-2018 08:22:58.0630Z /battery, 100.0234f, Infinity, 4.165625f, 0.3125f, "Charging complete"
```

    - If the numbers are not flying upward, or if there is a red list of failures on the screen, you will have to troubleshoot.

- Pull down menu **Send Command / Set date and time**
    - This is ESSENTIAL. Otherwise the sensors may not line up later.

- Click on the **Settings** tab, and you will see this:

- 

Device Information	
Device Name	NGIMU
Serial Number	0029C1D9
Firmware Version	v1.8 (Dec 29 2017 17:21:21)
Bootloader Version	v1.1 (Sep 28 2016 17:05:48)
Hardware Version	v1.2 (March 2016)
Wi-Fi	
Enabled	True
Firmware Version	1.6.4
MAC Address	00-23-A7-5C-4F-2C
IP Address	10.0.0.3
Mode	Client
Antenna	Internal
Region	Europe
AP	

- Click on **F5** key, OR from the pull down menu select **Settings** / **Read from Device**
  - This is good practise. It is not strictly necessary.
  - This prevents you from accidentally looking at information from the previous sensor.
- Check that the settings are correct
  - Most of this information is for troubleshooting and checking the communication protocols.
  - The sections you will be immediately interested in are **Send Rates**, **Synchronisation Master**, and **AHRS**).
  - The current send rates we use:
  - Sensors 100
  - Quaternion 100
  - Altitude 100
  - Temperature1
  - Humdity 1
  - Battery 1
  - RSSI 2
  - All other send rates are 0.
- Change the settings that are wrong:

  - Type a new number in (or pull down a selection). If you type in a number, you must press **<Enter/Return>** key after it, or it does not register.
  - When you are done making all changes, send the changes to the sensor
  - Hit <**F6**> key or pull down **Settings** / **Write to Device**
- For settings **Synchronisation Master**
  - **Enable** should be **False** for all sensors except serial number 29C 35C
  - Only one sensor should be the synchronisation master. It is the boss sensor.
- For Settings **AHRS**, Ignore magnetometer should be **False**
  - For some locations where the magnetic interference is high, you may choose to ignore the magnetometers (true) because they can screw up the recordings.
- If you have changed anything, pull down **Settings** / **Write to Device** (OR hit <**F6**> again)
  - If you accidentally hit <F5>, you immediately erase all the changes you just made, so you will have to start again with the settings.
- Initialise the directions of the sensor
  - Place the sensor flat on the table, with the arrow that shows Y pointing directly away from you
    - It is arbitrary what direction you place the sensors, but all the sensors must be pointing in the same direction, and they must be on a flat surface.
    - Note that the two large holes for the external I/O are now facing you, and the single large I/O is opposite you.
  - Adjust the **3-D view**, so that the avatar is in the identical orientation to the real sensor.
    - Launch the **3-D view** from the pull down menu **Graphs** / **3-D view**
    - It may already be launched, in which case switch windows to see the 3-D view using <alt><Tab>
    - Use the mouse to drag the image into the correct orientation
    - Once it is in the correct orientation, it should work for all sensors, but you should check any way
    - Check the **3-D view**'s response by picking up the sensor and turning it in various directions. The sensor and the 3-D view should move in tandem.
    - If the 3-D view moves in the opposite direction from the sensor, you need to use the mouse to drag the 3-D view into the correct orientation.
  - Put the sensor back on the table in the standard direction (Y arrow pointing away)

- From the pull down menu: **Send command / AHRS initialise**
- <F4> or pulldown Connection /disconnect

- <F3> or pull down Connection / search for Connections

- Connect to the wifi connection for this sensor
- Check the 3-D view while tilting the sensor; it should still be aligned properly
- Physically disconnect the sensor from the USB.

Welcome PwMS/ volunteer

Hello, my name is Rebecca Player, I am a PhD researcher here at the university. Please call me Becky. How do you prefer to be addressed?

Today we will be making some measurements of your walking and coordination using some sensors to determine how your legs are moving while you are walking. Please note that these measurements will provide us with a way of better understanding how diseases of walking affect people.

What these measurements entail is as follows. We will fit the sensors on you by having you wear special shoes with sensors, and then using elasticated bands to fit the sensors to your ankles, thighs, sternum and waist. You will then be asked to perform various short tasks that involve walking specific distances.. You will also be asked to fill in some questionnaires. Whenever we ask you to walk, please make the first step forward with your right leg.

If at any time you feel you need a rest or you need to sit down, you may ask to do so. If you feel like you might lose your balance, you may ask for help immediately. If you feel that you cannot finish any more, you may ask to stop, and we will stop all the measurements immediately. Sometimes the straps around the thighs can become too tight when you sit down. If they are too tight, simply let me know and we can loosen them while you are sitting. Sometimes the straps can become too loose around the thighs. If they do please let us know and we can tighten them for you.

For some of the walking tasks we would like to film your legs; we will not film the rest of your body or ever show the film to anyone else. Filming the legs helps us quite a lot when we analyze the data. However, if you would prefer, we will not film your legs.

After the physical assessment, we will give you a rest and break whilst I set up the interview. We will then have an informal chat about your experiences of fatigue.

These measurements are NOT a treatment, and will not affect any treatment you may or may not be having.

We estimate that the entire procedure, including time for resting will take 1h30 to 2hrs.

- Hand out participant information
- Consent form
- Demographics form
- Weigh the participant on the scales (without shoes) and fill info on demographics form

Weight of patient (kg)	

Fill in forms whilst finalising sensors/set up

Now we planned 15 or so minutes for you to fill in some questionnaires.

Time of rest (start / stop)	

- Patient fills in the following MSWS-12, MFIS, demographics, sign consent form.

Synch inertial sensors in front of a recording camera

- Wake up all sensors while they remain on the synch stick
- Press grey command button on each
- The LEDs should be:
- Green on all the time (making measurements)
- Orange flashing about once per second (recording data to memory card)
- Red off (not charging)
- Blue off (not transmitting bluetooth)

At what time did you start unsleeping the sensors	
Were there any unusual events or false starts	

Synchronisation block protocol (3 mins) – this may be a repeat of the previous section

- Start camera recording/ record synchronisation
- Place synch stick in front of a recording camera
- Make your plan to synch the sensors
- Wake up xio-sensors
- Record time in notebook when you will make first movement

When are you going to use the LED light synch	
Were there any unusual events or false starts	

When are you going to bang the synch stick	
Were there any unusual events or false starts	

- Leave sensors absolutely still for at least 30 seconds
- Gently whack the synch stick at the planned synch start time
- Wait 5 seconds
- Turn stick vertical and replace it X3
- Wait 5 seconds
- Drop stick onto a hard surface from a height of 1 cm X3 in rapid succession
- Wait 5 seconds
- Turn stick vertical and replace it X3
- Leave sensors absolutely still for at least 30 seconds
- Do not move the synchronization block for 30 seconds
- Say loudly to camera, "Synchronisation to begin at:" [and say the expected time you will hit it]
- At appointed time:
    - HIT THE BLOCK sideways with a clipboard

    - If not forceful enough, record as a problem (above), wait 30 seconds and hit block again
- Pause for 10 seconds
- tilt block (manually pull up one side) to 30 degrees rapidly
- Move down to flat (drop last cm to get a clear accelerometer transient)
- Pause for 10 seconds
- Raise whole block by 2 cm and let if fall 3 times directly one after another
- Pause for 10 seconds
- At appointed time: tilt block (manually pull up one side) to 30 degrees rapidly
- Move down to flat (drop last cm to get a clear accelerometer transient)
- Pause for 10 seconds

Fit sensors onto volunteer (3 mins)

Now I am going to fit the sensors onto you. Please let me know if any are uncomfortable or need readjusting..

- Always use the same sensor on the same body part and in the same orientation
        - Fit to volunteer while they are standing
    - Always x-axis pointing upwards!
    - Left shoe: 082 → onto lateral aspect of shoe clip
    - Right shoe: B82
    - Left ankle: 91E → on lateral aspect, just above shoe
    - Right ankle: 7CC
    - Left thigh: 7AF→ on lateral aspect
        - Use gaffer tape, belt and clips to hold it in place
    - Right thigh: 1D9
        - Use gaffer tape, belt and clips to hold it in place
    - Right hip: A53 → at small of back / middle of lower back
        - Tape in place so that sensor does not slip upward
- Sternum: 29DE89.

- Check sensor positions and orientations / streaming lights

Sensors and their Locations

Body Placement (eg Left Wrist)	**Sensor Name (e.g. E441)**	**Problems During Exp.**

Identify Sensors Protocol

At what time did the participant start these movements (move their arm forward)	
Were there any unusual events or false starts	

- While seated:
- Move left arm in front of the body for 3 seconds
- Move right arm directly up for 3 seconds
- Lift left thigh up and down twice
- Lift right thigh up and down four times
- Rotate left foot without moving thigh twice
- Rotate right foot without moving thigh four times

BE AWARE OF FRONTAL AND LATERAL CAMERAS, DO NOT STAND IN FRONT DURING TESTING.

T25FW (10 mins)

- Remove chair
- Change positions of walking cups so they are on each side of the finish line

In a moment I am going to ask you to perform the following task. I'm going to ask you to walk 25 feet as quickly as possible, but safely. You will start from a standing position here behind this line and walk until you have passed that line over there. Please do not slow down until after you've passed the finish line. When you start walking, please start with your right leg. I shall now demonstrate the task. We will ask you to perform this test 3 times.

- Demonstrate it, walk 25 feet, toward the camera

Begin timing when the lead foot is lifted and crosses the starting line. The examiner should walk along with the patient as he/she completes the task (not essential for healthy volunteers and for people who have good balance). Stop timing when the lead foot crosses the finish line. The examiner should then record the subject's walk time to within 0.1 second, rounding as needed.

- Run T25FW **practice** (do not tell the volunteer it is practise), timing it with stopwatch

Time T25FW **practice** start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

- Run T25FW movement 1, timing it with stopwatch

Time T25FW movement 1 start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

Now we will repeat the same task, walking 25 feet toward the camera, without saying anything

- Run T25FW movement 2, timing it with stopwatch

Time T25FW movement 2 start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

REST (If needed) (5 MINS)

6MW (7 mins)

The next test would be a six-minute walking test. If you feel fatigued or if for any reason you do not feel confident that you can walk continuously for six minutes now, let me know. We can scale this down to a two minute walk, or we can skip this test. Do you feel strong enough to walk continuously for six minute now?

The object of this test is to walk at a comfortable speed for six minutes back and forth in this 25 feet course, so that you cover as much ground as possible. When you start walking, please start with your right leg. When you get to the end of the walking area, you should turn around the cups and walk back in the opposite direction, as if you were walking laps. You may slow down if necessary. If you stop, I want you to continue to walk again as soon as possible. You will be kept informed of the time and you will be encouraged to do your best. Your goal is to walk as far as possible in six minutes. Please do not talk during the test unless you have a problem or if I ask you a question. You must let me know if you have any chest pain or dizziness. When the six minutes is up I will ask you to stop where you are. I shall now demonstrate the task.

- Run 6MW movements timing it with a stopwatch WHILE
- Count laps – count every other lap by recording the minutes and seconds
- Monitor the patient for untoward signs and symptoms.

- *At minute one: "Five minutes remaining. Do your best!"*

- *At minute two: "Four minutes remaining. You're doing well - keep it up!"*
- *At minute three: "Half way point. Three minutes remaining. Do your best!"*
- *At minute four: "Two minutes remaining. You're doing well - keep it up!"*
- *At minute five: "One minute remaining. Do your best!"*

Time 6 minute walk start (hh:mm:ss)	
6 minute walk distance laps (count laps by writing minutes:seconds at each double-lap)	
6 minute walk distance feet	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

T25FW (2 mins)

I'm going to ask you to walk 25 feet as quickly as possible, but safely.

- Run T25FW movement 3, timing it with stopwatch

Time T25FW movement 3 start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

Now we will repeat the same task, walking 25 feet toward the camera, without saying anything

- Run T25FW movement 4, timing it with stopwatch

Time T25FW movement 4 start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

Synchronisation block protocol (3 mins)

- Place all sensors on synchronization block
- Record time in notebook when you will make first movement
- exactly the same procedure as in first synchronization block

When are you going to use the LED light synch	

Were there any unusual events or false starts	

First Movement (whack stick): (hh:mm:ss)	
Unexpected events / problems	

Turn off sensors - For each sensor:

- Press command button (x-io) to close files on SD-card

Sleep sensors: (hh:mm:ss)	
Unexpected events / problems	

- Make sure each sensor is in sleep mode (green light flashing every 3 seconds) (x-io)
- Switch off each sensor with slider switch ten minutes later (x-io)

(**REST 5-10 MINUTES)**

Interviews (30 minutes – 60 minutes)

- Set up room with two chairs and a table/desk to place the digital voice recorder on.
- Make sure all doors are shut so the interview can be private.

In a moment we are going to have a discussion on your lived experiences of fatigue with Multiple Sclerosis. There are no right or wrong answers to this interview. It is an open-ended discussion therefore there is no set questions. I would just like you to discuss in as much detail as you can about your experience of MS fatigue and how it has or hasn't affected your life and how this makes you feel. You may discuss and relate back to the assessment just completed to begin with if you like. Please answer freely, you may answer only what you want to answer and can leave at any given time.. You can say as much or little as you like. If at any point, you would like to stop the discussion, please do say and I will stop the digital recorder and then we can continue when you are ready. Do you have any questions?

Start recording, press record.

- When you feel the participant has finished with the discussion then stop the interview.

Stop recording.

Q: Can you discuss with me your lived experiences about MS fatigue? You may start by reflecting on the assessment you have just completed.

- Thank the volunteer for participating
- Offer to answer questions
- Offer to pay for travel expenses (fill in financial receipt)

Transfer and Backup All Data

- Line up sensors on the right side of the computer
- Select one sensor and move it in front of the computer (ie out of the line)
- Connect sensor to computer via micro USB cable
- Use Windows commander to copy files from the microSD card to the computer
    - On left window at top, instead of drive C, **select theNameOfYourSensor**
    - On the right window at top, navigate to drive **C/1_harry/Multiple Sclerosis or C/Becky/Multiple Sclerosis**
    - Create a new folder inside **Multiple Sclerosis** named the volunteer's code (eg **M072**) by hitting the F7 key
    - Inside the above directory, create a new directory named the sensor's namecode (eg E43E) by once again clicking on **F7** key
    - Copy the big **xio log** file with the data (should be about 30 Megabytes of data) from the SD card into the sensor folder (**E43E**)
        - clicking once on the **xio** file (this selects it) and
        - then press the **F5** key (copy)
        - If there is more than one **xio** file, the small files were recorded at the beginning of the day before you **sleep**ed the sensors. You want to copy the giant **xio** file with 30-60 megabytes of data, which is your experimental data
- Safely remove the USB cable from the computer
    - We do not erase the data from the card at this point. We copy it.
    - Standard practise is that we like to have data in at least three locations before we are sure that the data is safe. Thus, if the computer dies, then the data can be recovered from the card.
- Place the sensor in the new line of sensors that are "done" to the left of the computer
- Repeat this process for all 9 sensors

Transform the data from binary (xio) to csv format

- Launch sensor GUI (graphical user interface programme)

- Called **NGIMU GUI.exe**
- Located in **c:\1_Harry\sensors\X_IMU_Seb_Madgwick\GUI xio\ ….**
- Click on "**cancel**" in the **autoconnecting** window, while GUI looks for an attached sensor (there isn't one)
- Click on the tab on top **SD card**
- Click on **Browse** to find where you saved each individual bin file with data.
    - Should be inside the **C/1_harry/Multiple Sclerosis/M060**
- Click once on the **xio** file you want
- Click on **open**
- The **browse** window should disappear. Now click on **convert**. It should take about 30 seconds to convert the data into about 10 **csv** files.

Make sure to have hand written copy of KG measurements from dynamometer on the protocol.

Pack Up All Devices

Copy your new volunteer file (M052) to a portable hard disk, and take that home

- or make sure Harry has a copy of the files

C (ii): Older healthy protocol

SAVE THIS PAPER COPY AFTER EXPERIMENT – it contains crucial data written on it

Volunteer Number ________________ Date/time _________________

Emergencies, Health and Safety

Harry Witchel	0771 284 5470 01273 697 917 Terri 01273 873 549 Trafford witcheloffice@gmail.com	Univ Sussex online reporting	Bsms1973@sussex.ac.uk
Rebecca Player	07491977740 rplayer3.rp@googlemail.com	Uni of Brighton rfp14@brighton.ac.uk reporting	
Emergency on Darley road Eastbourne campus	01273 642222		
Ambulance Eastbourne district general hospital	999	Police (Brighton) Kings Dr, Eastbourne BN21 2UD	999 or 101

All accidents must be reported to someone.

Injury: More serious injuries are those eliciting blood, pain that will not subside, or anything requiring hospital treatment. If there is blood or an injury where someone gets hurt (such as a fall resulting in a twisted ankle), this will have to be reported. In the first instance, report everything to Rebecca so I can help clean up and sort out things. If neither I nor Harry are available, you can contact the university emergency number at Eastbourne campus, or the responsible party at the venue where you are working (e.g. at the hospital). If a person hurts themselves and is bleeding profusely or has serious pain that does not abate (a burn wound or potentially a broken arm), go to the hospital to check it out. When possible, round up the equipment and just throw it (without organisation) into the cupboard or a locked room (while waiting for ambulance or taxi); the receptionist in the Robert Dodd building may be able to temporarily lock a room for you. If a volunteer is injured, either you or someone at the health science school should always stay with them. You should accompany the volunteer to the hospital, and once they are admitted (i.e. someone is looking after them), leave them, sort out the equipment, and then go back to the hospital and check on how they are doing. Money is provided for taxis.

Fluid spill: If there is a spill, we have to clean it up, but if there is a major spill we may need to contact the authority at the venue where the problem has occurred. If a piece of equipment has been dropped, you must report that to Rebecca.

Theft: If something is stolen (and you did not see it being stolen), report it to Rebecca. We may or may not be insured depending on where it occurred.

Robbery, aggressive behaviour: If a person(s) acts threatening to you, grabs something and takes it away (robbery), or attacks you, report to Rebecca, and we may report it to the police. Photographing the person may help, but do NOT aggravate the person by threatening them.

Day Before

- Telephone call to volunteer (or email if phone does not work
    - Remind volunteer to wear trousers – do NOT wear a dress or skirt
    - Ask volunteer for shoe size
    - If volunteer is a patient, ask for physician's name
- Charge sensors via USB (x-io)
- Format all Micro SD Cards
- Print all sheets and forms:
    - Patient Information Sheet
    - Consent Form
    - This Protocol
    - Demographics Form
    - EDSS-S – Self-assessed Extended Disability Status Scale
    - MSWS-12 – Multiple Sclerosis Walking Scale
    - MFIS – Modified Fatigue Impact Scale
- Bring sheets in plastic wallet
- Pack equipment: camera, laptop, sensors, thigh straps, money, paperwork, shoes.

On the Day

Unpack and Set Up Electrical devices (15 mins)

- Set up Floor lines and distances with tape
    - Mark every 5 feet in 25 feet distance (with BOTH tape and colourful cups)
        - The cups should be placed so that:
        - The participant does not bump into them
        - The cups are easily seen by the camera (ie faraway cups should be red or a colour that contrasts with the floor)
        - There is room to walk/manoeuvre around the cups when turning around
    - Place solid items to walk around at the beginning and end of the T25FW
- Place chair with no arms for sit to stand test.
    - 43.5cm height to seat.

Synchronise ALL Clocks to master clock

- Green digital clock facing laterally
- Green digital clock facing forward
- To set the green digital clocks: shift to **'set time'**. There are 3 buttons (mode, down and up). Use **'mode'** to shift from hours to mins etc. and up and down to change the numbers. The seconds cannot be changed so in order to sync the clocks, press up or down (half a second beforehand) when setting the minutes as the time hits the next minute on the other clocks.
- Stimulus computer
- Sensor computer

- Set visual (green numbers) clock according to radio clock (silver)
    - Place visual clock in FOV of camera
    - Sit clock on top of its box
    - Make sure the volunteer number (eg 'M061') is visible
- Set up 1 camera
    - Verify memory in card is in camera and has enough memory

    - Place camera on tripod
    - Check camera
        - Check light (make sure that clock is not obscured by reflections)
        - Is clock and all of the runway in the field of view of camera. Can you see the numbers clearly?
- Place a label with the volunteer code (e.g. **M045**) in view of the camera
    - should be within 6 feet of camera, on the wall or next to the green clock

Wearable Inertial Sensors

- Equipment needed:
    - Wearable sensors (x8 plus master in hand)
    - Use “thigh” sensors and use ankle sensors
    - Use "waist" sensor for right hip
    - Use sensor for chest (on harness)
    - Memory stick with SD card port
    - Micro USB cable (for connecting sensors to PC)
    - PC with sensor programmes installed

SENSOR EMERGENCIES: IF COMPUTER DOES NOT CONNECT TO SENSORS

There are only 3 things to go wrong if the computer does not connect to the sensor: the computer, the sensor or the connection (wire or wifi). The most likely problem is the computer or wifi, but FIRST

- Test the easy stuff.
- Swap to another sensor, and see if that helps
    - If a sensor fails, only one should fail (unless you have sequentially screwed up all of them)
    - Note: the sensor should have a constant green light on (power and sensing), and a constant yellow light (recording onto card), a possible white light (a form of wifi, but not necessarily to your computer), and a red light, only when plugged in.
    - If the lights are not correct, then there is a sensor problem.
    - If the yellow light is never on, either you have not put the micro SD card in, the micro SD card is in but facing the wrong way or incorrectly seated, or the micro SD card was not formatted correctly.

        - Try: turning off that sensor, pop the card out and then put it in again
- If changing sensors does not help, swap the USB wire
- If changing the sensor AND changing the wire does not work, the problem is almost certainly the computer.
- If you think the problem is the computer:
    - First, just see if you can do the entire process on another computer
    - If another computer is not available, attempt to reboot the computer
    - Then look at what the NGIMU says the problem is

Formatting / Clearing the old data from Micro SD cards

- Not essential: Clear/format each SD card data (must be done before every experiment):

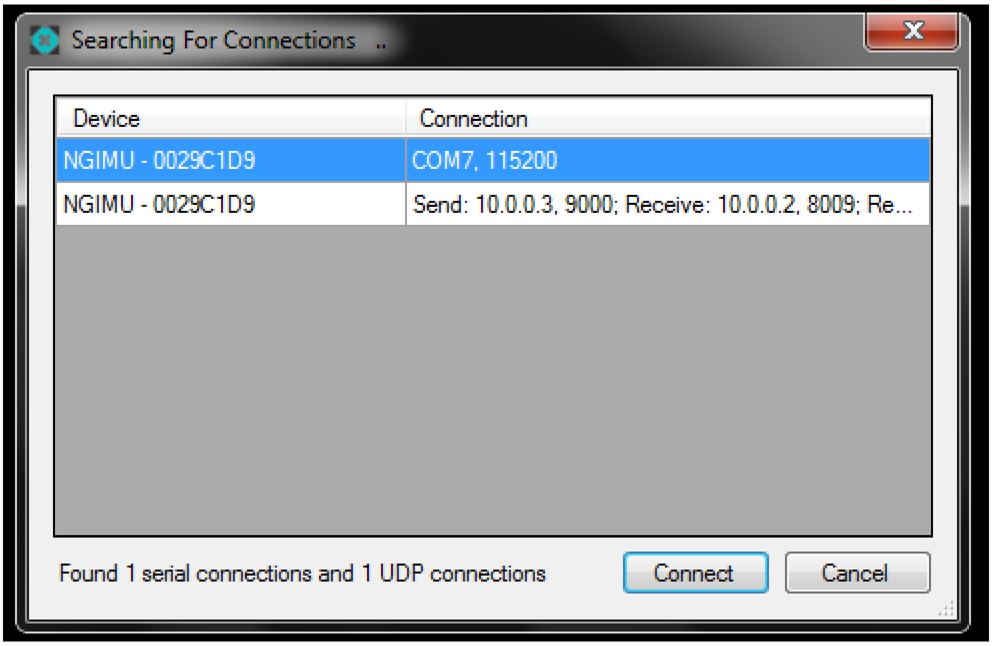
(Note: this can be done the day before. Best done with the sensors on)

- Line up sensors
- Turn all sensors on
- Select one sensor and move it in front of the computer (ie out of the line)
- Connect sensor to computer via micro USB
- The computer should immediately tell you with **autoplay** that a new drive is available. **Autoplay** should state the volume name of the card
- Close this **autoplay** window
- Double click on **SDformatter** programme
- The programme should show the name of the SD card in the box marked **volume label**
- If not, hit the **refresh** button
- If you still cannot see the volume name, you have a problem a poor connection between the drive and the card
- Try moving the card in and out slightly, or wiggling it
- IMPORTANT – check that correct drive is opened (e.g. ‘5B17’, size 14 GB)
- Click **format**
- Normally we use **quick format**, but when there are problems with sensor later, reformat card using the full format (Erase)

- To make a full format (which takes much longer), click on the **option** button in **SDformatter** and select **full format (erase)** in the **format type** window
- Click **OK** for both questions about whether you want to make changes and whether you want to continue
- When completed, close close **SDformatter**
- Safely eject USB connection from computer
- Remove SD card and place back into sensor (black-side up)

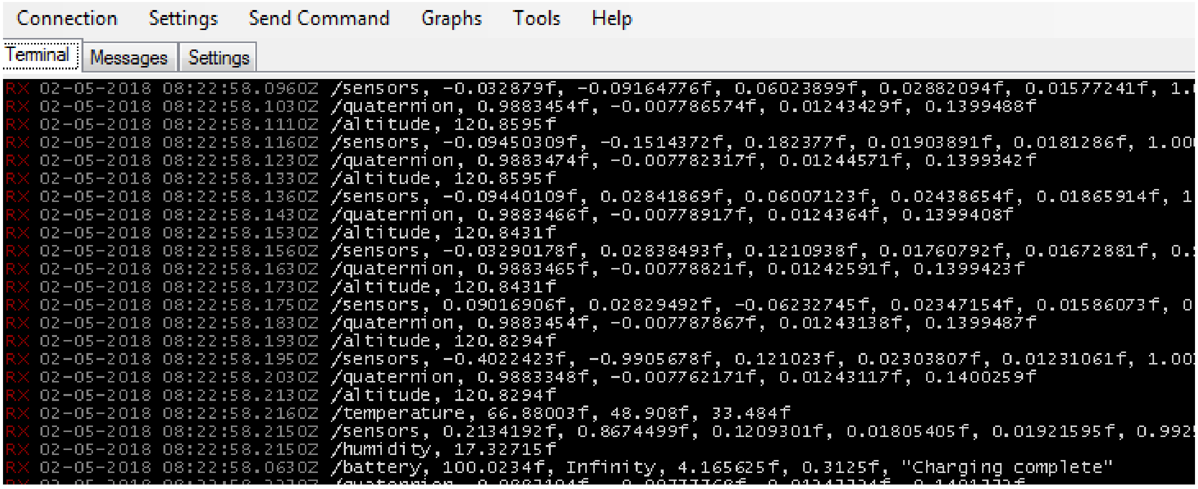
Sensors set up

- Turn on the sensor with its switch
- Connect the sensor to the USB port
  - If you get a spontaneous **Autoplay Removable Disk**, click on **cancel**
- Open NGIMU GUI.exe
  - Version 1.11: Currently working
  - In Sakmann: Located in D:\Sensors\NGIMU-Software-v1.11\NGIMU GUI
  - Xio symbol is a black X inside a blue diamond in a black square:
  - Double click on it.
  - It will immediately start looking for sensors to connect to:


Searching For Connections ..

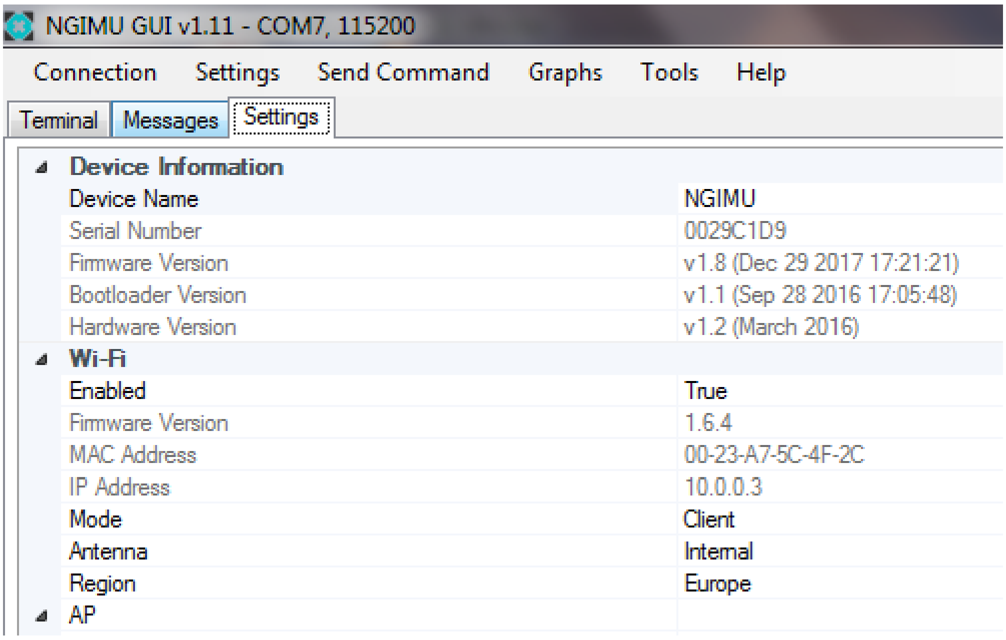
Device	Connection
NGIMU - 0029C1D9	COM7, 115200
NGIMU - 0029C1D9	Send: 10.0.0.3, 9000; Receive: 10.0.0.2, 8009; Re...

Found 1 serial connections and 1 UDP connections

- Select the correct sensor.
  - Each sensor has a serial number (above image, the serial number is **0029C1D9**)
  - It will usually show TWO possible connections to each sensor that it can detect: a USB connection (the one marked “**COM7**”, or some other number), which is followed by the “baud” (transmission) rate, and 2) a wifi connection, which is identified by the words “send” and “receive”, along with the local IP address (10.0.0.3 in the image above).
  - If you don’t see one or either of those, you will have to troubleshoot (see discussion later).
- For now, select the USB connection (click on it), then click on **Connect**.
  - You will then be taken to the main sensor GUI screen in the terminal frame, which will look like millions of numbers flying upward like in the Matrix movie.
  - 

```
RX 02-05-2018 08:22:58.0960Z /sensors, -0.032879f, -0.09164776f, 0.06023899f, 0.02882094f, 0.01577241f, 1.
RX 02-05-2018 08:22:58.1030Z /quaternion, 0.9883454f, -0.007786574f, 0.01243429f, 0.1399488f
RX 02-05-2018 08:22:58.1110Z /altitude, 120.8595f
RX 02-05-2018 08:22:58.1160Z /sensors, -0.09450309f, -0.1514372f, 0.182377f, 0.01903891f, 0.0181286f, 1.00
RX 02-05-2018 08:22:58.1230Z /quaternion, 0.9883474f, -0.007782317f, 0.01244571f, 0.1399342f
RX 02-05-2018 08:22:58.1330Z /altitude, 120.8595f
RX 02-05-2018 08:22:58.1360Z /sensors, -0.09440109f, 0.02841869f, 0.06007123f, 0.02438654f, 0.01865914f, 1
RX 02-05-2018 08:22:58.1430Z /quaternion, 0.9883466f, -0.00778917f, 0.0124364f, 0.1399408f
RX 02-05-2018 08:22:58.1530Z /altitude, 120.8431f
RX 02-05-2018 08:22:58.1560Z /sensors, -0.03290178f, 0.02838493f, 0.1210938f, 0.01760792f, 0.01672881f, 0.
RX 02-05-2018 08:22:58.1630Z /quaternion, 0.9883465f, -0.00778821f, 0.01242591f, 0.1399423f
RX 02-05-2018 08:22:58.1730Z /altitude, 120.8431f
RX 02-05-2018 08:22:58.1750Z /sensors, 0.09016906f, 0.02829492f, -0.06232745f, 0.02347154f, 0.01586073f, 0
RX 02-05-2018 08:22:58.1830Z /quaternion, 0.9883454f, -0.007787867f, 0.01243138f, 0.1399487f
RX 02-05-2018 08:22:58.1930Z /altitude, 120.8294f
RX 02-05-2018 08:22:58.1950Z /sensors, -0.4022423f, -0.9905678f, 0.121023f, 0.02303807f, 0.01231061f, 1.00
RX 02-05-2018 08:22:58.2030Z /quaternion, 0.9883348f, -0.007762171f, 0.01243117f, 0.1400259f
RX 02-05-2018 08:22:58.2130Z /altitude, 120.8294f
RX 02-05-2018 08:22:58.2160Z /temperature, 66.88003f, 48.908f, 33.484f
RX 02-05-2018 08:22:58.2150Z /sensors, 0.2134192f, 0.8674499f, 0.1209301f, 0.01805405f, 0.01921595f, 0.992
RX 02-05-2018 08:22:58.2150Z /humidity, 17.32715f
RX 02-05-2018 08:22:58.0630Z /battery, 100.0234f, Infinity, 4.165625f, 0.3125f, "Charging complete"
```

  - If the numbers are not flying upward, or if there is a red list of failures on the screen, you will have to troubleshoot.
- Pull down menu **Send Command / Set date and time**
  - This is ESSENTIAL. Otherwise the sensors may not line up later.
- Click on the **Settings** tab, and you will see this:

- 

Device Information	
Device Name	NGIMU
Serial Number	0029C1D9
Firmware Version	v1.8 (Dec 29 2017 17:21:21)
Bootloader Version	v1.1 (Sep 28 2016 17:05:48)
Hardware Version	v1.2 (March 2016)
Wi-Fi	
Enabled	True
Firmware Version	1.6.4
MAC Address	00-23-A7-5C-4F-2C
IP Address	10.0.0.3
Mode	Client
Antenna	Internal
Region	Europe
AP	

- Click on **F5** key, OR from the pull down menu select **Settings** / **Read from Device**
  - This is good practise. It is not strictly necessary.
  - This prevents you from accidentally looking at information from the previous sensor.
- Check that the settings are correct
- (you can usually skip this step for most of the sensors, but you should always do it for the first sensor)
  - Most of this information is for troubleshooting and checking the communication protocols.
  - The sections you will be immediately interested in are **Send Rates**, **Synchronisation Master**, and **AHRS**).
  - The current send rates we use:
  - Sensors 100
  - Quaternion 100
  - Altitude 2
  - Temperature1
  - Humdity 1
  - Battery 1
  - RSSI 2
  - All other send rates are 0.

- Change the settings that are wrong:
  - Type a new number in (or pull down a selection). If you type in a number, you must press **<Enter/Return>** key after it, or it does not register.
  - When you are done making all changes, send the changes to the sensor
  - Hit <**F6**> key or pull down **Settings** / **Write to Device**
- For settings **Synchronisation Master**
  - **Enable** should be **False** for all sensors except serial number 29C 35C
  - Only one sensor should be the synchronisation master. It is the boss sensor.
- For Settings **AHRS**, Ignore magnetometer should be **False**
  - For some locations where the magnetic interference is high, you may choose to ignore the magnetometers (true) because they can screw up the recordings.
- If you have changed anything, pull down **Settings** / **Write to Device** (OR hit <**F6**> again)
  - If you accidentally hit <F5>, you immediately erase all the changes you just made, so you will have to start again with the settings.
- Initialise the directions of the sensor
  - Place the sensor flat on the table, with the arrow that shows Y pointing directly away from you
    - It is arbitrary what direction you place the sensors, but all the sensors must be pointing in the same direction, and they must be on a flat surface.
    - Note that the two large holes for the external I/O are now facing you, and the single large I/O is opposite you.
  - Adjust the **3-D view**, so that the avatar is in the identical orientation to the real sensor.
    - Launch the **3-D view** from the pull down menu **Graphs** / **3-D view**
    - It may already be launched, in which case switch windows to see the 3-D view using <alt><Tab>
    - Use the mouse to drag the image into the correct orientation
    - Once it is in the correct orientation, it should work for all sensors, but you should check any way
    - Check the **3-D view**'s response by picking up the sensor and turning it in various directions. The sensor and the 3-D view should move in tandem.
    - If the 3-D view moves in the opposite direction from the sensor, you need to use the mouse to drag the 3-D view into the correct orientation.

- Put the sensor back on the table in the standard direction (Y arrow pointing away)
- From the pull down menu: **Send command / AHRS initialise**
- <F4> or pulldown Connection /disconnect

- <F3> or pull down Connection / search for Connections

- Connect to the wifi connection for this sensor
- Check the 3-D view while tilting the sensor; it should still be aligned properly
- Physically disconnect the sensor from the USB.

Welcome PwMS/ volunteer

- *Hello, my name is Rebecca Player, I'm working at Brighton and Sussex Medical School and I am the medical researcher for this study. Please call me Becky. How do you prefer to be addressed?*
- *Today we will be making some measurements of your walking, and we will be using sensors to determine how your legs are moving while you are walking. Please note that these measurements will provide us with a way of better understanding how diseases of walking affect people. These measurements are NOT a treatment, and whether you choose to participate or not will have NO BEARING on the treatment you will receive from your doctor and from the NHS.*
- *What these measurements entail is as follows. We will fit the sensors on you by having you wear special shoes with sensors, and then using elasticated bands to fit the sensors to your ankles, thighs, sternum and waist. You will then be asked to perform various short tasks that involve walking specific distances.. You will also be asked to fill in some questionnaires. Whenever we ask you to walk, please make the first step forward with your right leg.*
- *If at any time you feel you need a rest or you need to sit down, you may ask to do so. If you feel like you might lose your balance, you may ask for help immediately. If you feel that you cannot finish any more, you may ask to stop, and we will stop all the measurements immediately. Sometimes the straps around the thighs can become too tight when you sit down. If they are too tight, simply let me know and we can loosen them while you are sitting.*
- *For some of the walking tasks we would like to film your legs; we will not film the rest of your body or ever show the film to anyone else. Filming the legs helps us quite a lot when we analyze the data. However, if you would prefer, we will not film your legs.*
- *We estimate that the entire procedure, including time for resting will take 45 minutes.*

- Hand out participant information
- Consent form
- Demographics form
- Weigh the participant on the scales (without shoes) and fill info on demographics form

Weight of patient (kg)	

Fill in forms whilst finalising sensors/set up

Now we planned 15 or so minutes for you to fill in some questionnaires.

Time of rest (start / stop)	

- Patient fills in the following MSWS-12, MFIS, demographics, sign consent form.

Synch inertial sensors in front of a recording camera

Wake up all sensors while they remain on the synch stick

Press grey command button on each

The LEDs should be:

Green on all the time (making measurements)

Orange flashing about once per second (recording data to memory card)

Red off (not charging)

Blue off (not transmitting bluetooth)

At what time did you start unsleeping the sensors	
Were there any unusual events or false starts	

Synchronisation block protocol (3 mins) – this may be a repeat of the previous section

- Start camera recording/ record synchronisation

Place synch stick in front of a recording camera

Make your plan to synch the sensors

- Wake up xio-sensors
- Record time in notebook when you will make first movement

When are you going to use the LED light synch	
Were there any unusual events or false starts	

When are you going to bang the synch stick	
Were there any unusual events or false starts	

Leave sensors absolutely still for at least 30 seconds

Gently whack the synch stick at the planned synch start time

Wait 5 seconds

Turn stick vertical and replace it X3

Wait 5 seconds

Drop stick onto a hard surface from a height of 1 cm X3 in rapid succession

Wait 5 seconds

Turn stick vertical and replace it X3

Leave sensors absolutely still for at least 30 seconds

- Do not move the synchronization block for 30 seconds
- Say loudly to camera, "Synchronisation to begin at:" [and say the expected time you will hit it]
- At appointed time:
    - HIT THE BLOCK sideways with a clipboard
    - If not forceful enough, record as a problem (above), wait 30 seconds and hit block again

- Pause for 10 seconds
- tilt block (manually pull up one side) to 30 degrees rapidly
- Move down to flat (drop last cm to get a clear accelerometer transient)
- Pause for 10 seconds
- Raise whole block by 2 cm and let if fall 3 times directly one after another
- Pause for 10 seconds
- At appointed time: tilt block (manually pull up one side) to 30 degrees rapidly
- Move down to flat (drop last cm to get a clear accelerometer transient)
- Pause for 10 seconds

Fit sensors onto volunteer (3 mins)

Now I am going to fit the sensors onto you. Please let me know if any are uncomfortable or need readjusting.

- Always use the same sensor on the same body part and in the same orientation
        - Fit to volunteer while they are standing
    - Always x-axis pointing upwards!
    - Left ankle: 29C91E → on lateral aspect, just above shoe
    - Right ankle: 29C7CC
    - Left thigh: 29D7AF → on lateral aspect
        - Use gaffer tape, belt and clips to hold in place.
    - Right thigh: 29C1D9
        - Use gaffer tape, belt and clips to hold in place
    - Rip hip: 29CA53 → Just above greater trochanter.
        - Tape in place so that sensor does not slip upward
    - Put sensors onto shoes
    - Left Shoe: 29C082
    - Right Shoe: 29CB82
        - but do NOT wear shoes yet
- Check sensor positions and orientations / streaming lights

Sensors and their Locations

Body Placement (eg Left Wrist)	Sensor Name (e.g. E441)	Problems During Exp.

Identify Sensors Protocol

At what time did the participant start these movements (move their arm forward)	
Were there any unusual events or false starts	

While seated

Move left arm in front of the body for 3 seconds

Move right arm directly up for 3 seconds

Lift left thigh up and down twice

Lift right thigh up and down four times

Rotate left foot without moving thigh twice

Rotate right foot without moving thigh four times

Lean forward three times

BE AWARE OF THE FRONTAL AND LATERAL CAMERAS, DO NOT STAND INFRONT OF THEM DURING TESTING.

T25FW (10 mins)

- Remove chair
- Change positions of walking cups so they are on each side of the finish line

- *In a moment I am going to ask you to perform the following task. I'm going to ask you to walk 25 feet as quickly as possible, but safely. You will start from a standing position here behind this line and walk until you have passed that line over there. Please do not slow down until after you've passed the finish line. When you start walking, please start with your right leg. I shall now demonstrate the task. We will ask you to perform this test 3 times.*

- Demonstrate it, walk 25 feet, toward the camera

Begin timing when the lead foot is lifted and crosses the starting line. The examiner should walk along with the patient as he/she completes the task (not essential for healthy volunteers and for people who have good balance). Stop timing when the lead foot crosses the finish line. The examiner should then record the subject's walk time to within 0.1 second, rounding as needed.

- Run T25FW **practice** (do not tell the volunteer it is practise), timing it with stopwatch

Time T25FW **practice** start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

- Run T25FW movement 1, timing it with stopwatch

Time T25FW movement 1 start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

Now we will repeat the same task, walking 25 feet toward the camera, without saying anything

- Run T25FW movement 2, timing it with stopwatch

Time T25FW movement 2 start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

REST (If needed) (5 MINS)

6MW (7 mins)

The next test would be a six-minute walking test. If you feel fatigued or if for any reason you do not feel confident that you can walk continuously for six minutes now, let me know. We can scale this down to a two minute walk, or we can skip this test. Do you feel strong enough to walk continuously for six minute now?

The object of this test is to walk at a comfortable speed for six minutes back and forth in this 25 feet course, so that you cover as much ground as possible. When you start walking, please start with your right leg. When you get to the end of the walking area, you should turn around the cups and walk back in the opposite direction, as if you were walking laps. You may slow down if necessary. If you stop, I want you to continue to walk again as soon as possible. You will be kept informed of the time and you will be encouraged to do your best. Your goal is to walk as far as possible in six minutes. Please do not talk during the test unless you have a problem or if I ask you a question. You must let me know if you have any chest pain or dizziness. When the six minutes is up I will ask you to stop where you are. I shall now demonstrate the task.

- Run 6MW movements timing it with a stopwatch WHILE
- Count laps – count every other lap by recording the minutes and seconds
- Monitor the patient for untoward signs and symptoms.

- *At minute one: “Five minutes remaining. Do your best!”*

- *At minute two: "Four minutes remaining. You're doing well - keep it up!"*
- *At minute three: "Half way point. Three minutes remaining. Do your best!"*
- *At minute four: "Two minutes remaining. You're doing well - keep it up!"*
- *At minute five: "One minute remaining. Do your best!"*

Time 6 minute walk start (hh:mm:ss)	
6 minute walk distance laps (count laps by writing minutes:seconds at each double-lap)	
6 minute walk distance feet	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

T25FW (2 mins)

I'm going to ask you to walk 25 feet as quickly as possible, but safely.

- Run T25FW movement 3, timing it with stopwatch

Time T25FW movement 3 start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

Now we will repeat the same task, walking 25 feet toward the camera, without saying anything

- Run T25FW movement 4, timing it with stopwatch

Time T25FW movement 4 start (hh:mm:ss)	
Duration (s, ms)	
Unexpected events / problems	
Did you use the light to indicate start & finish	
How accurate were the signals?	

Remove sensors from Volunteer and debrief (2 mins)

- Thank the volunteer for participating
- Offer to answer questions
- Offer to pay for travel expenses (fill in financial receipt)
- Ask participant:

1. "Do you think the exercises you have done with us today will cause you to be more fatigued than usual at some point today?

2. If so, at what time (or times) is this fatigue likely to appear?

3. "What form will the fatigue take?

4. "Can you explain or describe how fatigued these exercises (or the six minute walk) will make you, such as by giving an example?"

Synchronisation block protocol (3 mins)

- Place all sensors on synchronization block
- Record time in notebook when you will make first movement
- exactly the same procedure as in first synchronization block

When are you going to use the LED light synch	
Were there any unusual events or false starts	

First Movement (whack stick): (hh:mm:ss)	
Unexpected events / problems	

Turn off sensors - For each sensor:

- Press command button (x-io) to close files on SD-card

Sleep sensors: (hh:mm:ss)	
Unexpected events / problems	

- Make sure each sensor is in sleep mode (green light flashing every 3 seconds) (x-io)
- Switch off each sensor with slider switch ten minutes later (x-io)

Transfer and Backup All Data

Line up sensors on the right side of the computer

Select one sensor and move it in front of the computer (ie out of the line)

Connect sensor to computer via micro USB cable

Use Windows commander to copy files from the microSD card to the computer

1. On left window at top, instead of drive C, **select theNameOfYourSensor**
2. On the right window at top, navigate to drive **C/1_harry/Multiple Sclerosis or C/Becky/Multiple Sclerosis**
3. Create a new folder inside **Multiple Sclerosis** named the volunteer's code (eg **M072**) by hitting the F7 key
4. Inside the above directory, create a new directory named the sensor's namecode (eg E43E) by once again clicking on **F7** key

5. Copy the big **xio log** file with the data (should be about 30 Megabytes of data) from the SD card into the sensor folder (**E43E**)
    1. clicking once on the **xio** file (this selects it) and
    2. then press the **F5** key (copy)
    3. If there is more than one **xio** file, the small files were recorded at the beginning of the day before you **sleep**ed the sensors. You want to copy the giant **xio** file with 30-60 megabytes of data, which is your experimental data

Safely remove the USB cable from the computer

6. We do not erase the data from the card at this point. We copy it.
7. Standard practise is that we like to have data in at least three locations before we are sure that the data is safe. Thus, if the computer dies, then the data can be recovered from the card.

Place the sensor in the new line of sensors that are "done" to the left of the computer

Repeat this process for all 9 sensors

Transform the data from binary (xio) to csv format

Launch sensor GUI (graphical user interface programme)

Called **NGIMU GUI.exe**

Located in **c:\1_Harry\sensors\X_IMU_Seb_Madgwick\GUI xio\ ….**

Click on "**cancel**" in the **autoconnecting** window, while GUI looks for an attached sensor (there isn't one)

Click on the tab on top **SD card**

Click on **Browse** to find where you saved each individual bin file with data.

8. Should be inside the **C/1_harry/Multiple Sclerosis/M060**

Click once on the **xio** file you want

Click on **open**

The **browse** window should disappear. Now click on **convert**. It should take about 30 seconds to convert the data into about 10 **csv** files.

Make sure to have hand written copy of KG measurements from dynamometer on the protocol.

Pack Up All Devices

Copy your new volunteer file (M052) to a portable hard disk, and take that home

or make sure Harry has a copy of the files

Appendices D: Participant Information Sheet

D (i): Participation Information Sheet MS

Title: *'**Fatigue in Multiple Sclerosis**: Comparing objective metrics of ambulation and activity (biomarkers) to the patient's perspective'*

We would like to invite you to take part in our research project. Before you decide, it is important to understand why the research is being done and what it will involve.

Please take time to read the following information carefully.

If anything is not clear or you would like more information, please do not hesitate to ask the researchers (details at the bottom). Take your time to decide whether you wish to take part or not.

What is the purpose of the study?

To investigate fatigue for people with mild to moderate multiple sclerosis using different measurement tools and compare to people's personal experiences and feelings.

What will happen if I agree to take part?

After reading the *Brief outline sheet* and *Participant information sheet*, if you decide to take part the primary researcher will ask you to read and sign a written consent form. Please note, your decision does not have to be instant; you can contact the primary researcher once you have made your decision.

You will then be sent an email with a survey attached asking you a variety of questions about your body functions on an average day. This form should be completed and sent back to the primary researcher who will check your functioning ability to see whether you are suitable for the study.

If you fall within the study's criteria, you will be contacted by the primary researcher and invited to participate in the study. If you do not fall in the criteria, the primary researcher will still contact you and be thanked for your time.

If you would prefer the survey to be sent via post/mail, this can also be arranged.

What is the study's criteria?

This project is using a scale called the Patient Administered Expanded Disability Severity Scale (EDSS-S) to assess your functional and daily activities. The scale is ranked from 0 – 10. For this study, anyone who falls into 1.0 – 5.5 on this scale will be invited to participate.

Will I be paid for taking part?

You will not be paid for participating in this study. However, you can be reimbursed for your travel expenses. All you have to do is fill out a form and hand it into the research team.

Do I have to do anything prior to the day?

The primary researcher will call you the day before to confirm your visit. She will remind you of the date and time of your visit, what to bring and wear, and she will ask for your shoe size.

Brief outline on what to expect on the day

The research study will involve one visit to MS Sussex Centre in Southwick. The day is designed so you will have plenty of time to do each section at your own pace, rest periods will be given (see below).

Participate to fill out questionnaires and demographics.
Physical tests
BREAK (anything up to 10 minutes)
Physical tests
BREAK for 10-15 MINUTES whilst we remove sensors.
Interview
Debrief

You will be asked to complete:

- 2 questionnaires,
- 2 walking tests,
- 1 interview

Please note, we will ask you to perform all tests twice (except the six-minute walk test). The assessments collectively test your mobility and fatigue.

During the physical assessments, we will require you to wear trainers which will be provided by the primary researcher. Wearable sensors will be placed on your back, hip, thigh and ankle to collect information and data. The sensors are small and will be Velcro strapped on top of your clothing to your comfort. Please note, you should wear comfortable clothing for walking (women should wear jeans or trousers rather than a skirt or dress). For accurate data collection, we will also be video recording throughout the physical assessment. Please note, we will only video record after consent has been given. The video recorder will be placed so your face will not be shown at any given time.

The interview is an opportunity to discuss and express how you felt during the physical tests. It is also an opportunity to talk about your previous experiences and feelings with fatigue. It is an open interview, you can say as little or as much as you please.

The whole procedure will last approximately 2 hours, depending on the length of the interview at the end.

If you are interested in knowing the type of questionnaires and assessments that will be used, you can read the list below. The questionnaires can be provided in advance if you wish.

Will my participation be kept confidential?

The researcher will have a duty of confidentiality to you, no information revealing your identities will be disclosed outside the research team. The assessment data will be anonymised, stored on a password protected computer and locked in a secure filing cabinet. All data will be kept anonymised and confidential throughout the project. **What are the possible risks of taking part?**

This project will not interfere or affect any treatment or medication.

The interview will ask about your personal feelings and experiences. This may potentially trigger stressful memories or emotions. If at any point during the interview you feel distressed, we can stop the interview until you are happy to continue. If you feel you need confidential advice, please ask to seek guidance from the university well-being team or contact the support number provided below.

- **University well-being centre**, Eastbourne, Trevin Towers Student Centre, **01273 643845**
- **MS support line 0808 800 8000-** Provides emotional support and details of support groups, helplines, agencies and counsellors throughout the UK for people with MS.

The physical assessment will be performed at your own pace. In the unlikely event of an injury does occur and you should fall or trip, there will be a first aider on site and will be reported to the research team.

What are the potential advantages to participating?

- This research is about assessment tools and technology that are used for the measurement of fatigue. These tools are not a cure, nor are they treatment. Although this research will not directly help alleviate any symptoms you have associated with multiple sclerosis, in the future it could result in more accurate techniques for effectively monitoring fatigue in persons with multiple sclerosis.
- You will learn how to assess fatigue and gain knowledge on the variety of tools available to analysing fatigue.
- This project will allow you to talk about your experiences of fatigue and reflect on how you feel and manage such experiences. It is a good opportunity to express what fatigue means to you.

Overall improving the monitoring of multiple sclerosis functional status is necessary to individualise treatment and rehabilitation programmes.

What will happen if I do not wish to continue with taking part?

Participants may withdraw at any time without giving a reason. However, data that has already been collected and processed may not necessarily be withdrawn from the analysis unless you specifically request this.

What will happen to the results in the study?

The results of the research will be analysed, written up and may be published in academic journals. If you wish, the primary researcher can provide you with the summary of the findings of your assessment after the entire testing is complete.

Who has reviewed the study?

Approval was given from the University Research Ethics Committee, University of Brighton.

Please keep hold of this information sheet if you wish to remind yourself on what to expect on the day.

What if there is a problem?

If you have any problems, complaints, concerns, or questions prior to, during or after participation in this research study please do not hesitate to contact the study team below. If you remain dissatisfied, you can contact the Appeal and Complaints office, which details are below. **Contact details**

Primary Investigator

Rebecca Player: Village Way, Brighton, BN1 9PH Email: rfp14@brighton.ac.uk Contact number: 07491977740 **Supervisors for Project**

- **Prof. Kate Galvin**: Village Way, School of Health Sciences, Brighton, BN1 9PH Email: k.galvin@brighton.ac.uk Contact number: +44 (0)1273 644028 - **Dr Harry Witchel**: Trafford Centre, Brighton and Sussex Medical School, Falmer, Brighton BN1 9RY Email: H.Witchel@bsms.ac.uk Contact number: +44 (0)1273 873549

Appeals and Complaints Office

Mithras House, University of Brighton, Lewes Road, Brighton BN2 4AT. Email: Complaints@brighton.ac.uk Contact number: 01273 642 895

D (ii): Participation Information Sheet Healthy

Title: *‘**Fatigue in Multiple Sclerosis**: Comparing objective metrics of ambulation and activity (biomarkers) to the patient’s perspective’*

We would like to invite you to take part in our research project. Before you decide, it is important to understand why the research is being done and what it will involve.

Please take time to read the following information carefully.

If anything is not clear or you would like more information, please do not hesitate to ask the researchers (details at the bottom). Take your time to decide whether you wish to take part or not.

What is the purpose of the study?

To investigate fatigue for people with mild to moderate multiple sclerosis using different measurement tools.

What will happen if I agree to take part?

After reading the *Brief outline sheet* and *Participant information sheet*, if you decide to take part the primary researcher will ask you to read and sign a written consent form. Please note, your decision does not have to be instant; you can contact the primary researcher once you have made your decision.

Why have I been invited to participate?

You are over the age of 18, have no serious illnesses and can walk atleast 100m without assistance.

Will I be paid for taking part?

You will not be paid for participating in this study. However, you can be reimbursed for your travel expenses.

Do I have to do anything prior to the day?

The primary researcher will call you the day before to confirm your visit. She will remind you of the date and time of your visit, what to bring and wear, and she will ask for your shoe size.

Brief outline on what to expect on the day

The research study will involve one visit to the MS Sussex Centre in Southwick. The day is designed so you will have plenty of time to do each section at your own pace, rest periods will be given (see below).

Participate to fill out questionnaires

You will be asked to complete:

- 2 questionnaires, 2 walking tests, & 1 interview.

Please note, we will ask you to perform all tests twice (except the six-minute walk test). The assessments collectively test your mobility and fatigue.

During the physical assessments, we will require you to wear trainers which will be provided by the primary researcher. Wearable sensors will be placed on your back, hip, thigh and ankle to collect information and data. The sensors are small and will be Velcro strapped on top of your clothing to your comfort. Please note, you should wear comfortable clothing for walking (women should wear jeans or trousers rather than a skirt or dress). For accurate data collection, we will also be video recording throughout the physical assessment. Please note, we will only video record after consent has been given. The video recorder will be placed so that your face will not be shown at any given time.

Physical tests
BREAK (anything up to 10 minutes)
Physical tests
BREAK for 10 minutes to remove sensors
Debrief

The duration of the whole procedure will last approximately 1 hour.

If you are interested in knowing the type of questionnaires and assessments that will be performed, you can read the list below. The questionnaires can be provided in advance if you wish.

Will my participation be kept confidential?

The researcher will have a duty of confidentiality to you, no information revealing your identities will be disclosed outside the research team. The assessment data will be anonymised, stored on a password protected computer and locked in a secure filing cabinet. All data will be kept anonymised and confidential throughout the project. **What are the possible risks of taking part?**

The physical assessment will be performed at your own pace. If an injury does occur and you should fall or trip, there will be a first aider on site and should be reported to the research team.

What are the potential advantages to participating?

- We need healthy volunteers for research projects like this, so we can compare data with people diagnosed with chronic conditions. This will develop research with the aim to provide better quality of life for people with multiple sclerosis.
- You will learn how to assess fatigue and gain knowledge on the variety of tools available for analysing fatigue.
- This research is about technology and assessment tools that are used for the measurement of fatigue. These tools are not a cure, nor are they treatment. Although this research will not directly help alleviate any symptoms of multiple sclerosis, in the future it could result in more accurate techniques for effectively monitoring fatigue in persons with multiple sclerosis. The project will contribute to research and new knowledge in this field.

Overall improving the monitoring of multiple sclerosis functional status is necessary to individualise treatment and rehabilitation programmes.

What will happen if I do not wish to continue with taking part?

Participants may withdraw at any time without any given reason before the analysis stage of the study. Data that has already been collected and processed may not necessarily be withdrawn from the analysis due to anonymised data and not being able to identify the data for withdrawal.

What will happen to the results in the study?

The results of the research will be analysed, written up and may be published in academic journals. If you wish, the primary researcher can provide you with the summary of the findings of your assessment after the entire testing is complete.

Who has reviewed the study?

Approval was given from the University Research Ethics Committee, University of Brighton.

Please keep hold of this information sheet, if you wish to remind yourself on what to expect on the day.

What if there is a problem?

If you have any problems, complaints, concerns, or questions prior to, during or after participation in this research study please do not hesitate to contact the study team below. If you remain dissatisfied, you can contact the Appeal and Complaints office, which details are below.

Contact details Primary Investigator

Rebecca Player: Village Way, Brighton, BN1 9PH Email: rfp14@brighton.ac.uk Contact number: 07491977740

Supervisors for Project

- **Prof. Kate Galvin**: Village Way, School of Health Sciences, Brighton, BN1 9PH Email: k.galvin@brighton.ac.uk Contact number: +44 (0)1273 644028 - **Dr Harry Witchel**: Trafford Centre, Brighton and Sussex Medical School, Falmer, Brighton BN1 9RY Email: H.Witchel@bsms.ac.uk Contact number: +44 (0)1273 873549

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Appendices E: Assessment day forms

E (i): Consent form

University of Brighton *Principle Researcher: Rebecca Player*

'Fatigue in Multiple Sclerosis: Comparing objective metrics of ambulation and activity (biomarkers) to the patient's perspective'

Please read below before signing the consent form.

1. **I have read and understood all the information on the participant information sheet about the research for this study and agree to participate in all activities.**
2. **I have been given the opportunity to consider my participation and asked questions about the research project.**
3. **I understand and agree to be video recorded without my face being shown at any given time.**
4. **I understand that the results will be used for research purposes only.**
5. **I understand that taking part is entirely voluntary and that I am free to withdraw at any time without any given reason before the analysis stage of the study.**
6. **I have been informed that the data I provide will be confidential unless the researcher believes there to be a risk to myself or the public.**

Number 7 applies to people with multiple sclerosis only.

7. **I agree that unidentified quotes from my interview *may* be used in the write up of the study, which may be published.**

…….

(Name of Participant, Date, Signature)

…….

(Name of Researcher, Date, Signature)

E (ii): Demographics form MS

Demographic Questionnaire (MS)

Name: ____

Contact Information
(phone/address/email):____
____

Volunteer #: ___________________________________

Date: ____

Demographic Information

Date of Birth (DD / MM / YYYY) __ __ / __ __ / __ __ __ __ Age ____ Gender

Occupation ____________

Height (in cm if possible) _______

Height at greater trochanter (cm) __________________

Shoe size ______________________________________

Weight (kg) ___________________________________

Highest Level of education completed or currently registered in? (circle one: grade school, some GCSE/ O Levels, A Levels, trade school, some university, BS/BA, some graduate school, Masters Degree, Doctorate, Professional Degree, other) If other, explain:
____

Are you a native English speaker?
Yes No

If no, at what age did you begin formal education in English ______________________

Estimated year (or age) of first symptoms _________________________________

Year (or age) of receiving an MS diagnosis ________________________________

Type of MS (if known) ____

Do you have a dominant leg? If so, please mark which leg.

Left Right

Name of your neurologist/GP ____

Medication____

Emergency contact information (name and phone)

E (iii): Demographics form Healthy

Demographic Questionnaire (H)

Name: ____

Contact Information
(phone/address/email):____
____

Volunteer #: ___________________________________

Date: ____

Demographic Information

Date of Birth (DD / MM / YYYY) __ __ / __ __ / __ __ __ __ Age ____ Gender______

Occupation_________________________ ______________

Height (in cm if possible)________________________ _______

Height at greater trochanter (cm) ___________________

Shoe size ______________________________________

Weight (kg)_____________________________________

Highest Level of education completed or currently registered in? (circle one: grade school, some GCSE/ O Levels, A Levels, trade school, some university, BS/BA, some graduate school, Masters Degree, Doctorate, Professional Degree, other) If other, explain:
____

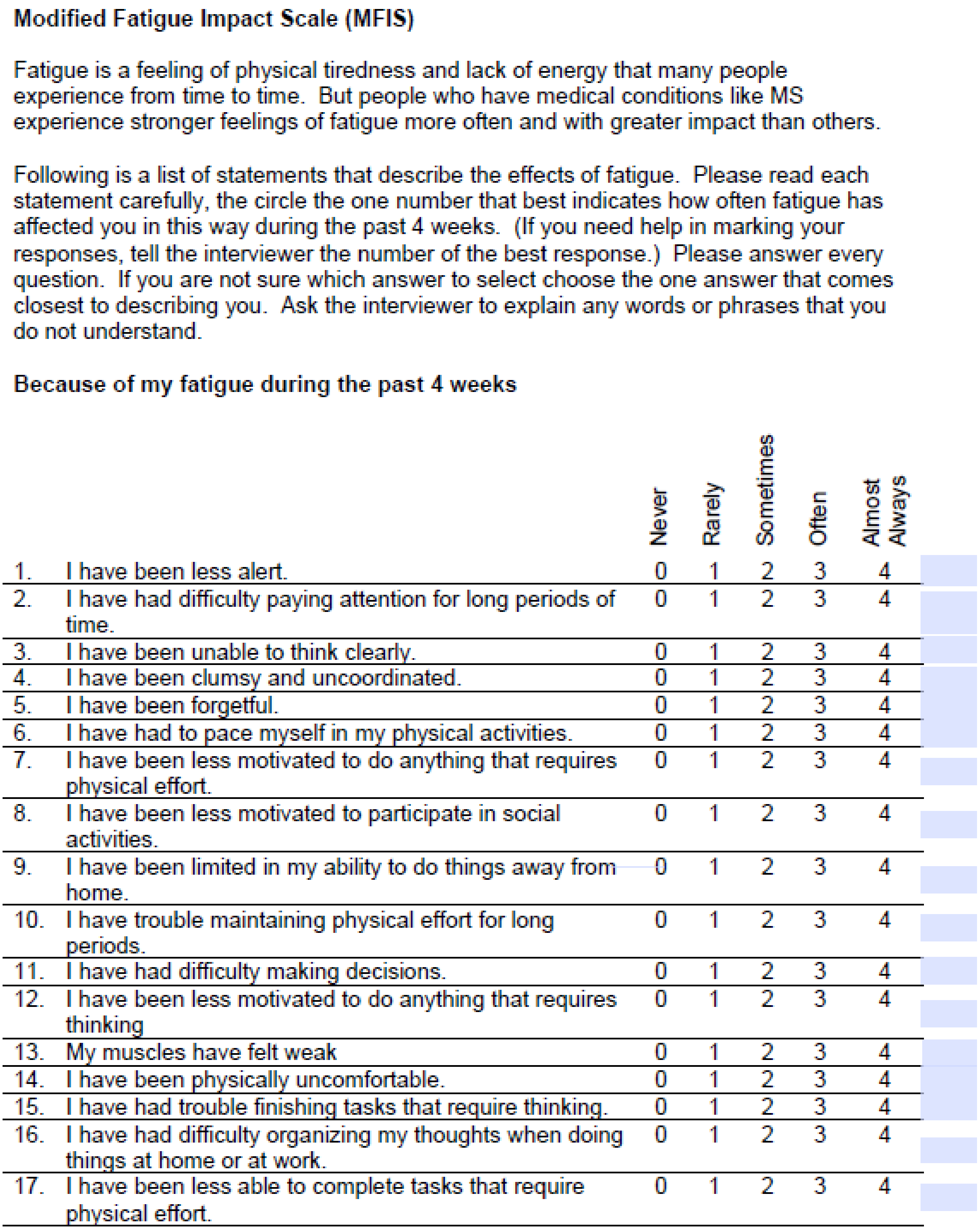
Health conditions____

Are you a native English speaker?
Yes No

If no, at what age did you begin formal education in English ________________________

Emergency contact information (name and phone)
____
____

E (iv): Modified Fatigue Impact Scale



Modified Fatigue Impact Scale (MFIS)

Fatigue is a feeling of physical tiredness and lack of energy that many people experience from time to time. But people who have medical conditions like MS experience stronger feelings of fatigue more often and with greater impact than others.

Following is a list of statements that describe the effects of fatigue. Please read each statement carefully, the circle the one number that best indicates how often fatigue has affected you in this way during the past 4 weeks. (If you need help in marking your responses, tell the interviewer the number of the best response.) Please answer every question. If you are not sure which answer to select choose the one answer that comes closest to describing you. Ask the interviewer to explain any words or phrases that you do not understand.

Because of my fatigue during the past 4 weeks

		Never	Rarely	Sometimes	Often	Almost Always
1.	I have been less alert.	0	1	2	3	4
2.	I have had difficulty paying attention for long periods of time.	0	1	2	3	4
3.	I have been unable to think clearly.	0	1	2	3	4
4.	I have been clumsy and uncoordinated.	0	1	2	3	4
5.	I have been forgetful.	0	1	2	3	4
6.	I have had to pace myself in my physical activities.	0	1	2	3	4
7.	I have been less motivated to do anything that requires physical effort.	0	1	2	3	4
8.	I have been less motivated to participate in social activities.	0	1	2	3	4
9.	I have been limited in my ability to do things away from home.	0	1	2	3	4
10.	I have trouble maintaining physical effort for long periods.	0	1	2	3	4
11.	I have had difficulty making decisions.	0	1	2	3	4
12.	I have been less motivated to do anything that requires thinking	0	1	2	3	4
13.	My muscles have felt weak	0	1	2	3	4
14.	I have been physically uncomfortable.	0	1	2	3	4
15.	I have had trouble finishing tasks that require thinking.	0	1	2	3	4
16.	I have had difficulty organizing my thoughts when doing things at home or at work.	0	1	2	3	4
17.	I have been less able to complete tasks that require physical effort.	0	1	2	3	4

	Never	Rarely	Sometimes	Often	Almost Always	
18. My thinking has been slowed down.	0	1	2	3	4	
19. I have had trouble concentrating.	0	1	2	3	4	
20. I have limited my physical activities.	0	1	2	3	4	
21. I have needed to rest more often or for longer periods.	0	1	2	3	4	

Instructions for Scoring the MFIS

Items on the MFIS can be aggregated into three subscales (physical, cognitive, and psychosocial), as well as into a total MFIS score. All items are scaled so that higher scores indicate a greater impact of fatigue on a person's activities.

Physical Subscale

This scale can range from 0 to 36. It is computed by adding raw scores on the following items: 4+6+7+10+13+14+17+20+21.

0

Cognitive Subscale

This scale can range from 0 to 40. It is computed by adding raw scores on the following items: 1+2+3+5+11+12+15+16+18+19.

0

Psychosocial Subscale

This scale can range from 0 to 8. It is computed by adding raw scores on the following items: 8+9.

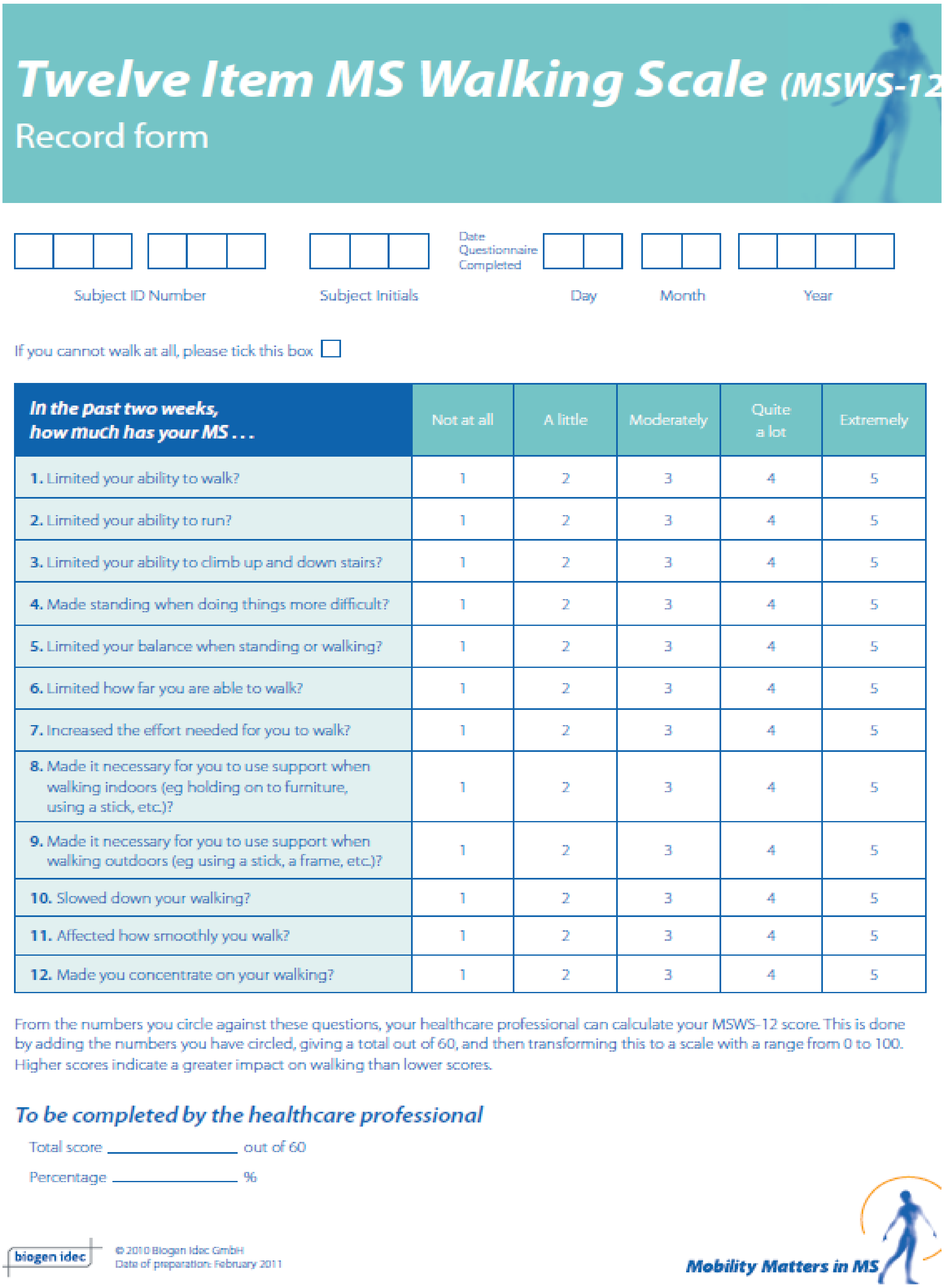
0

Total MFIS Score

The total MFIS score can range from 0 to 84. It is computed by adding scores on the physical, cognitive, and psychosocial subscales.

0

E (v): Multiple Sclerosis Walking Scale-12



Twelve Item MS Walking Scale (MSWS-12

Record form

Subject ID Number ☐☐☐ ☐☐☐

Subject Initials ☐☐☐

Date Questionnaire Completed: Day ☐☐ Month ☐☐ Year ☐☐☐☐

If you cannot walk at all, please tick this box ☐

In the past two weeks, how much has your MS . . .	Not at all	A little	Moderately	Quite a lot	Extremely
1. Limited your ability to walk?	1	2	3	4	5
2. Limited your ability to run?	1	2	3	4	5
3. Limited your ability to climb up and down stairs?	1	2	3	4	5
4. Made standing when doing things more difficult?	1	2	3	4	5
5. Limited your balance when standing or walking?	1	2	3	4	5
6. Limited how far you are able to walk?	1	2	3	4	5
7. Increased the effort needed for you to walk?	1	2	3	4	5
8. Made it necessary for you to use support when walking indoors (eg holding on to furniture, using a stick, etc.)?	1	2	3	4	5
9. Made it necessary for you to use support when walking outdoors (eg using a stick, a frame, etc.)?	1	2	3	4	5
10. Slowed down your walking?	1	2	3	4	5
11. Affected how smoothly you walk?	1	2	3	4	5
12. Made you concentrate on your walking?	1	2	3	4	5

From the numbers you circle against these questions, your healthcare professional can calculate your MSWS-12 score. This is done by adding the numbers you have circled, giving a total out of 60, and then transforming this to a scale with a range from 0 to 100. Higher scores indicate a greater impact on walking than lower scores.

To be completed by the healthcare professional

Total score ____________ out of 60

Percentage ____________ %

biogen idec

Date of preparation: February 2011

Mobility Matters in MS

E (vi): Patient-administered Expanded Disability Status Scale

Patient Administered
Expanded Disability Status Scale
EDSS©

University of Washington

Department of Neurology
Multiple Sclerosis Research Center

Developed for research purposes in Multiple Sclerosis (1999)

We would like to know how well your body functions on an average day, not your worst days and not your best days. Please check the box that most closely matches your abilities.

Walking distances: On an **average** day I can:

1. ☐ Walk more than 3 tenths of a mile without stopping to rest. (This is a little further than 5 football field lengths.)

   I would need ☐ no help ☐ a cane ☐ two canes ☐ a walker

2. ☐ Walk 2 tenths of a mile without stopping to rest. (This is a little further than 3 football field lengths.)

   I would need ☐ no help ☐ a cane ☐ two canes ☐ a walker

3. ☐ Walk 600 feet without stopping to rest. (This is 2 football field lengths.)

   I would need ☐ No help ☐ A cane ☐ Two canes ☐ A walker

4. ☐ Walk 300 feet without stopping to rest. (This is 1 football field length.)

   I would need ☐ No help ☐ A cane ☐ Two canes ☐ A walker

5. ☐ Walk 60 feet without stopping to rest.

   I would need ☐ No help ☐ A cane ☐ Two canes ☐ A walker

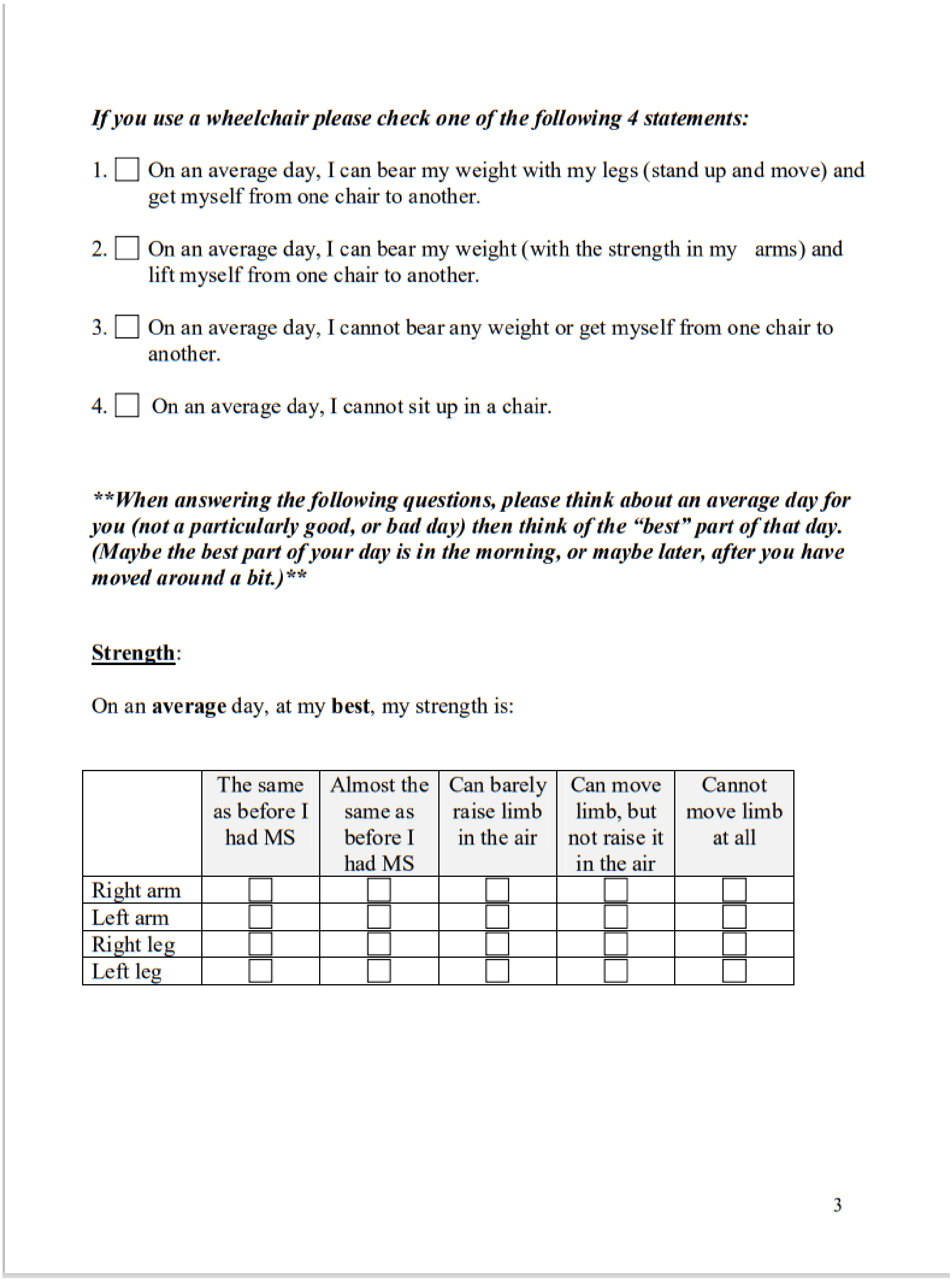
6. ☐ Walk 15 feet without stopping to rest

   I would need ☐ No help ☐ A cane ☐ Two canes ☐ A walker

7. ☐ Walk a few steps.

   I would need ☐ No help ☐ A cane ☐ Two canes ☐ A walker

8. ☐ Use a wheelchair



If you use a wheelchair please check one of the following 4 statements:

1. ☐ On an average day, I can bear my weight with my legs (stand up and move) and get myself from one chair to another.

2. ☐ On an average day, I can bear my weight (with the strength in my arms) and lift myself from one chair to another.

3. ☐ On an average day, I cannot bear any weight or get myself from one chair to another.

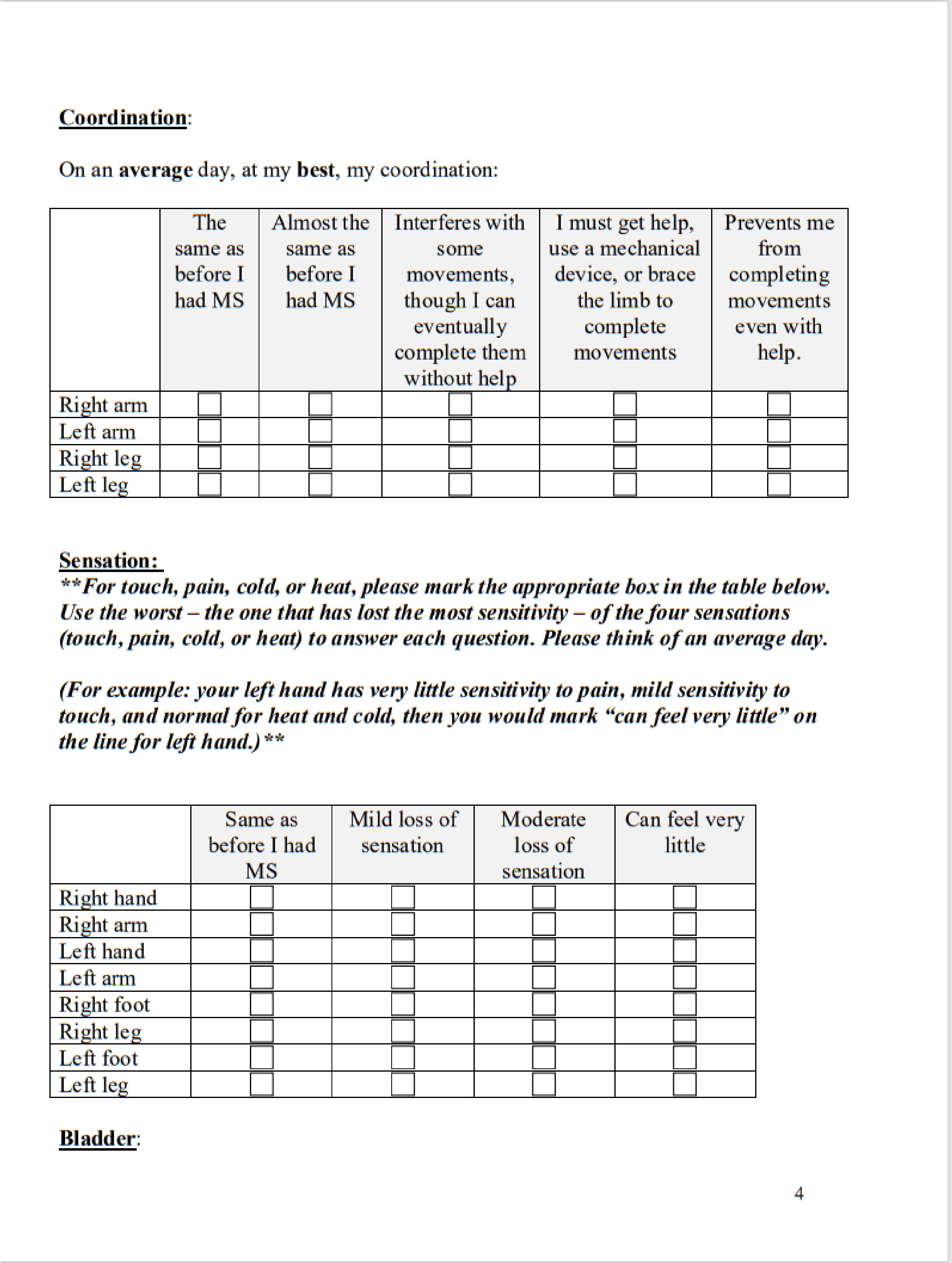
4. ☐ On an average day, I cannot sit up in a chair.

*****When answering the following questions, please think about an average day for you (not a particularly good, or bad day) then think of the "best" part of that day. (Maybe the best part of your day is in the morning, or maybe later, after you have moved around a bit.)*****

Strength:

On an **average** day, at my **best**, my strength is:

	The same as before I had MS	Almost the same as before I had MS	Can barely raise limb in the air	Can move limb, but not raise it in the air	Cannot move limb at all
Right arm	☐	☐	☐	☐	☐
Left arm	☐	☐	☐	☐	☐
Right leg	☐	☐	☐	☐	☐
Left leg	☐	☐	☐	☐	☐



Coordination:

On an **average** day, at my **best**, my coordination:

	The same as before I had MS	Almost the same as before I had MS	Interferes with some movements, though I can eventually complete them without help	I must get help, use a mechanical device, or brace the limb to complete movements	Prevents me from completing movements even with help.
Right arm	☐	☐	☐	☐	☐
Left arm	☐	☐	☐	☐	☐
Right leg	☐	☐	☐	☐	☐
Left leg	☐	☐	☐	☐	☐

Sensation:

*****For touch, pain, cold, or heat, please mark the appropriate box in the table below. Use the worst – the one that has lost the most sensitivity – of the four sensations (touch, pain, cold, or heat) to answer each question. Please think of an average day.***

(For example: your left hand has very little sensitivity to pain, mild sensitivity to touch, and normal for heat and cold, then you would mark "can feel very little" on the line for left hand.)**

	Same as before I had MS	Mild loss of sensation	Moderate loss of sensation	Can feel very little
Right hand	☐	☐	☐	☐
Right arm	☐	☐	☐	☐
Left hand	☐	☐	☐	☐
Left arm	☐	☐	☐	☐
Right foot	☐	☐	☐	☐
Right leg	☐	☐	☐	☐
Left foot	☐	☐	☐	☐
Left leg	☐	☐	☐	☐

Bladder:

On an **average** day, I have:

Yes	No	
☐	☐	A normal bladder
☐	☐	Urgency (once I need to go I have a hard time holding it)
☐	☐	Hesitancy (I feel I need to go but nothing happens)
☐	☐	Accidents (incontinence) occasionally but once a week or less
☐	☐	Accidents (incontinence) twice a week or more, but less than daily
☐	☐	Accidents (incontinence) daily
☐	☐	Use self catheterization
☐	☐	Use continuous catheter (indwelling or condom catheter)

Vision:

1. Which line is the smallest that you can read (you can use glasses if needed).

Left eye only	Right eye only	Both eyes together	
☐	☐	☐	937826
☐	☐	☐	428365
☐	☐	☐	374258
☐	☐	☐	428365
☐	☐	☐	Cannot read any of the lines above

2. I see double (two things, where there is really only one) :

☐ Never ☐ About once a week ☐ Almost daily ☐ Constantly

3. On an average day, my eye movements are unsteady

☐ Never ☐ Only when looking to the side ☐ All the time

Speech:

On an average day, my speech is:

☐ Is the same as before I had MS
☐ Slightly Slurred
☐ Moderately Slurred
☐ Severely Slurred

Swallowing:

On an average day, my swallowing is:

☐ Normal
☐ Occasional choking
☐ Unable to swallow

Thinking:

On an average day, my thinking and memory is:

Although some people may wish to consider thinking and memory separately, we need you to combine them and check one box below.

☐ Is the same as before I had MS
☐ Is almost the same as before I had MS
☐ Occasionally causes a problem in my daily life
☐ Frequently causes a problem in my daily life
☐ Others have to help me manage my affairs

Appendices F: Tier 2 Cross-School Research Ethics Committee (CREC) Application Form

Please note that review by a Tier 2 CREC is only required for proposals that present more than minimal ethical risk. For lower risk proposals, please complete the Tier 1 form and submit it to your School Research Ethics Panel. The Tier 1 form includes a checklist to help determine the level of review required. If it is unclear whether your proposal requires Tier 1 or Tier 2 review, please complete the Tier 1 form and checklist in the first instance. If your proposal has been referred up to the CREC by your Tier 1 School Research Ethics Panel, please attach a copy of the completed Tier 1 form to this application. Please do not include any other forms or documents with your application, other than those listed in the checklist in section 11.

Please adhere to the indicated word counts on this form. Any application that exceeds the word counts will not be considered by the CREC.

1 Applicant details

Project title	**‘Fatigue in Multiple Sclerosis: Comparing objective metrics of ambulation and activity (biomarkers) to the patient’s perspective’**
Proposed start and end date of project	**1 Apr 2018 - 1 Oct 2020**
Name of researcher	**Rebecca Player**
School	**Health Sciences & BSMS**
Level (UG/Taught PG/PGR/Staff)	**PhD**
Address	**Village way, Brighton, BN1 9PH**
Phone	**07491977740**

Email (please use University email address)	**rfp14@brighton.ac.uk**
Funder (if applicable)	**University funded studentship**

2 Student details

Course/Module/Unit name/number	**PHD Health Sciences**
Name of supervisor/tutor	**Professor Kathleen Galvin** **Doctor Harry Witchel**
Supervisor contact details	**Prof. Kate Galvin** **School of Health Sciences** **Westlain House** **Falmer** **Brighton BN1 9PH** **Telephone: +44 (0)1273 644028** **Email: K.Galvin@brighton.ac.uk** **Dr Harry Witchel** **Room 204 Trafford Centre for Medical Research, BSMS,** **University of Sussex,** **BN1 9RY** **Telephone: +44 (0)1273 873549** **Email: H.Witchel@bsms.ac.uk**

3 Introduction (Maximum 500 words)

Please provide a brief background to the research, including context and rationale and the purpose of the research and aims of the study/hypothesis to be tested.

Introduction

Multiple sclerosis (MS) is a chronic, inflammatory, neurodegenerative disease affecting an estimated 2.5 million people worldwide, with approximately 75-90% of individuals reported to suffer from MS related fatigue itself [Dua & Rompani, 2008]. Alongside depression and disability, fatigue is considered to be one of the most prevalent and debilitating symptoms in people with MS (pwMS) [Flensner, Ek & Soderhamn, 2003]. It is a symptom that allows for multiple facets of definition which can be difficult to describe and portray. Some, but not all, pwMS have reported fatigue to be always present and 'a feeling that the body could not escape or control' [Flensner, Ek & Soderhamn, 2003]. Conventional objective measurements of fatigue and fatigability (and clinical observation) have not always corresponded with subjective reports from patients [Surakka et al., 2004]. Fatigue is a physical, psychological, social and even existential dimension of a patient's life, which makes its measurement problematic [Calsius et al., 2015].

A considerable amount of research has been conducted on subjective and objective measurements of MS fatigue exploring interviews, questionnaires, types of scans, and gait analysis. However, to our knowledge, the interdisciplinary methodology of neurophenomenology has never been conducted for MS, creating an opportunity to approach this gap in the literature to attempt to understand how fatigue is embodied [Gallagher et al., 2015]. Current research highlights the lack of progression and management on MS related fatigue; thus, engaging in exploring a variety of subjective and objective measurement tools will allow further understanding of the multidimensional symptom. Within this project, the focus will be assessing fatigue on mild to moderate pwMS through comparing phenomenological interviewing, gait analysis and variability, muscle strength, patient reported questionnaires. This will bridge different aspects of fatigue and help develop more accurate measurements for fatigue.

Aims and Objectives

1.Improve clinical measurement by using physiological parameters to assess ambulatory fatigue and gait variability impairment (expanding biomarkers). Furthermore, by gaining extensive insight from first-person perspective using a phenomenological approach, to grasp the foundations of fatigue from lived experiences.

2.Find the correspondences between subjective and objective fatigue to seek further utility of mixed methods approach for the measurement and treatment of MS related fatigue.

3.Enable health professionals and researchers to evaluate treatments and adapt them according to the course of the disease as experienced through developing improved fatigue assessments.

Rationale

This project will draw together two very different disciplines to bridge physiological assessment with first person accounts. Few teams have the cross-disciplinary expertise to pursue this. It will increase public and professional engagement by using an array of measuring tools to enhance clinical measurement and progress towards making a positive difference for people with MS related fatigue.

As stated above, to our knowledge there are no studies for MS related fatigue using neurophenomenology; given the novelty and ambition of the methodology, the project is exploring the prospect of bridging research methods together to create an exciting interdisciplinary study.

4 Research approach and methods (Maximum 1,000 words)

Please outline the research approach and methods to be used including:

- How is the research to be conducted – what is the design?
- How, where and when will data be collected (please include copies of any questionnaires to be used, or sample interview questions)?
- What research methods (statistical or qualitative) will be used? Please demonstrate an understanding of procedures to be used and/or training undertaking in research methods.
- How will the results be analysed and by whom?
- How will the analysis achieve the purpose of the study?
- What facilities/resources will be required and who will provide them?

Neurophenomenology is a mixed methods methodology aiming to bridge physiological data and accounts of first-person experience using phenomenology [Varela, 1996]. This research project will be a mixed methods convergent parallel approach. The idea is to compare the qualitative responses from the pwMS as to their fatigue to the quantitative results that may highlight differences between actual and perceptive fatigue. The first phase will be a quantitative one: a prospective cohort study measuring walking fatigue using validated walking, balance and coordiniation assessment tools. The second phase will be a phenomenological study to explore the experiences of pwMS about fatigue and their health and related treatments.

Phenomenology is essentially a style of thinking that involves theoretical principles and foundations to develop an understanding of everydayness and ordinary existence of a person. Its methodology involves the 'bigger picture' of extracting real-life experiences in relation to cognitive, emotional, physical and social related fatigue through an interview. The methodology does not technically 'solve' research but seeks to unveil the lived experience of an individual [Paley, 2005].

The qualitative phase

The objectives are to understand and explore:

a. The perception of fatigue in pwMS

b. The times when fatigue is greater and the degree of that fatigue

c. The knowledge and practices that are employed to cope with fatigue

d. Produce reflections that may be useful in determining and changing practices in involving pwMS who suffer from fatigue.

Data collection and analysis

PwMS will be invited to participate in conversational style individual taped interviews. The interviews will be conducted by the principal investigator. The principal investigator has experience of interviewing for research purposes. The interviews will be confidential unless there is an overriding need to share information in accordance with GCP procedures. The participants will be told that they can terminate the interview at any time, and they do not have to answer all the questions.

This study will use descriptive phenomenology using the five stages of data analysis suggested by Ashworth [2003]:

Stage 1: Record interviews using a digital recorder, followed by transcribing thoroughly. The recordings will be performed by the primary researcher, of which she will then select 15 interviews to be recorded. This will be sent to a professional transcriber. The professional transcriber will be aware of identifiable data.

Stage 2: Identify units of information from the data.

Stage 3: Use of phenomenological reduction and eidetic induction through interpretation.

Stage 4: The units of information to be synthesised into a situated structure as a synopsis (for each interview/individual).

Stage 5: Use Ashworth's seven fractions of the lifeworld to interrogate the meaning of the text/data.

These seven fractions of lifeworld are as follows: (1) Self-hood, (2) Sociality, (3) Embodiment, (4) Temporality, (5) Spatiality, (6) Project and (7) Discourse.

The quantitative phase

Objectives to be explored will be:

a. To measure tasks representing walking and everyday living in pwMS before and after fatigue.

b. To assess which tool or combination of tools best measure fatigue in pwMS.

c. To compare the fatigue levels as measured by the tools with the results from the qualitative data.

d. To compare the measures of fatigue in pwMS to those without MS.

The biomechanical methods involve the use of physiological measures to understand gait function, mobility and muscular strength to fatigue in pwMS using wearable sensors. Please find the seven tests listed in the table that will be used. These clinical tests alone will allow the assessment of endurance, balance and strength. Along with these tests, inertial sensors, which have been validated for the use of people with motor impairments and are the most widely used wearable systems for gait and balance analysis [Bugane, Benedetti, D'Angeli, & Leardino, 2014; Tien, Glaser & Aminoff, 2010]. Inertial sensors will detect subtle clinical gait changes that will allow more precise and accurate measurement than using just time alone. The sensors capture spatiotemporal data (space and time), kinematic data including joint angles, velocity, orientation and gravitational forces. It will also eliminate ceiling and floor effects. For example, the derived metric from the Romberg's test is the time taken before falling; in our past experience with pwMS (EDSS < 6), the pwMS never fall during Romberg's test, even with their eyes closed. These measurements will be important when comparing time to distance in relation to fatigue. For example, the six-minute walk (6MW) has illustrated that after two minutes of walking, step length and cadence are normally reduced, with leg swing angular velocity reduced [Motl et al., 2017].

Previous work on assessing pwMS walking has been performed using wearable sensors (Oberndorfer et al., 2015; Witchel et al., 2017; Needham, Naemi & Chockalingham, 2014).

Taking into consideration the EDSS severity range, participants categorised between 3.0-5.5 are anticipated to be able to manage with these tests, with given rest periods. The layout of the assessment day for pwMS and the healthy volunteers is shown below.

People with MS
physical tests
BREAK (anything up to 10 minutes)
physical tests
BREAK (anything up to 10 minutes)
physical tests
BREAK for 30 MINUTES whilst participate fills out the questionnaires
Interview
End

Healthy volunteers
physical tests
BREAK (anything up to 10 minutes)
physical tests
BREAK (anything up to 10 minutes)
physical tests
BREAK for 30 MINUTES whilst participate fills out the questionnaires
End

All tests will be timed with a stop watch and recorded on paper.

All tasks except for the 6MW are performed at least three times. The first time is a practice run, then one repetition is performed before the 6MW, and one repetition is performed afterward. The knee flexion test and Rombergs test do not have a practise run. The T25FW has two repetitions before and after the 6MW due to the nature of the test (best of two walks is selected). The TTW has three practise runs because of its well know learning effect.

Test	Function & rationale	Repetition of test	Metrics	Estimated duration (including explanations)
Timed 25 foot walk (T25FW)	To assess coordination and walking speed. The T25FW is considered be to the best characterised objective measure of walking disability in MS [Kieseier & Pozzilli, 2012]. This will be used to assess gait velocity but also to compare against other walking tests such as the six minute	4	Velocity, temporal variables (including variability), jerk pitch angular velocities, coupling angles in sagittal plane.	2 minutes

	walk to measure walking fatigue.			
Timed up and go (TUG)	To assess balance, functional mobility, daily use extensor strength/coordination. The Timed Up and Go (TUG) is different from other walking tests as it requires sitting to standing and standing to sitting. Not only is this relevant to daily activities, yet also involves the assessment of balance and lower extremity muscular strength which is an important factor in relation to walking.	3	Jerk pitch angular velocities, coupling angles in sagittal plane.	1-2 minutes
Three meter timed tandem (TTW)	To assess dynamic balance and motor function. This test is used routinely in clinical practice. TTW has better ability to detect motor/cerebellar symptoms in mildly disabled MS than the T25FW [Stellmann, Vettorazzi, Poettgen & Heesen, 2014]. We can gain validity and more accurate results by comparing the TTW, chair rise, TUG and rombergs test which all assess aspects of balance. Including the TTW, chair rise and rombergs test in the project allows us to have a broader understanding of how fatigue is likely to affect different	5	Jerk pitch angular velocities, coupling angles in sagittal plane.	3 minutes

	functions of a person including balance.			
Chair rise X5	To assess motor function, balance and lower extremity strength (muscle fatigue). Measures daily use extensor strength/coordination (may be superior/cleaner to TUG). The chair rise, also known as the sit to stand test (STS) has been extensively used in clinical practice to measure lower extremity strength. The test requires muscles to generate forces to accelerate/decelerate the body's mass through a distance against the pull of gravity (Bohannon, Bubela, Magasi, Wang & Gershon, 2010). Again, it assesses sit-to-stand and stand-to-sit which is important to measure for fatigue due to its function being part of everyday activities.	3	Jerk pitch angular velocities, coupling angles in sagittal plane.	1-2 minutes
Chair rise X1	To assess motor function, balance and lower extremity strength (muscle fatigue). Measures daily use extensor strength/coordination (may be superior/cleaner to TUG).	3	Jerk pitch angular velocities, coupling angles in sagittal plane.	1 minute
Rombergs	To assess static balance (eyes open vs closed)	4 (2+2)	Spectral power of sternal attitude.	3 minutes

	Rombergs is a clinical test that is widely used in the suite of tests to assess balance and vestibular function. Along with TUG, chair rise and TTW, the test will assess balance and allow validity to the project by using multiple balance assessments. ***Please note, force plates will not be used due to the primary investigators previous experience with functional test and lack of experience with force plates.***			
Six minute walk (6MW)	To assess gait and motor fatigue. The 6MW allows walking fatigue and endurance to be more specifically measured in relation to the other shorter walking assessments [King et al., 2010].	1	Temporal variables (velocity stride time), variabilities, deceleration index.	7 minutes
Dynamometer	To assess muscle strength and muscle fatigue. Measuring left vs right) The hand held dynamometer will be tested in the lower extremity due to the nature of the project assessing functions of the lower limb (walking tests etc). A standardised grip hand held device will not specifically measure muscular strength and fatigue in the lower extremity.	4 (2+2)	Maximum strength (newtons)	2 minutes

	Additionally, the use of a gold standard biodex dyanamometer can not be used due to the facilities and the lack of training the primary investigator has.			

The physical assessment will be performed in a laboratory setting with the participants walking along a 25 foot distance. The inertial sensors will be attached above clothing on a participant's shoes, ankle, thigh and lower back. Seven sensors will be placed in total. The sensors will be attached whilst the participant is standing, with a semi elastic velcro strap to securely fit the sensors. The ankle sensors will be attached on the outer aspect of the ankle, just above the shoe. The thigh sensors will be placed above the knee on the outer aspect of the thigh. The lower back sensor will be placed centrally on the back, just above the waist (please see photos below). All participants will wear standardised running shoes (Lonsdale) of the correct shoe size, in order to correct for differences in gait due to shoe stiffness or heels. The research team have a collection of different sizes to fit all participants.

Figure A

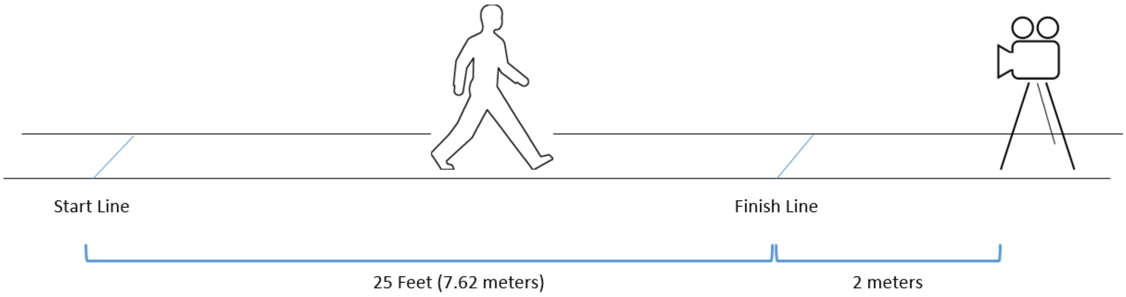
The dynamometer will be a hand-held device that will be tested on the lower extremity (knee flexion test), which will be performed twice. The dynamometer will be placed on the participants calf muscle, above clothing, whilst seated in a chair.

Time alignments between sensors with other measurements and the camera recordings will be performed. The camera recordings and data from the sensors should align in timings of movement with the participant. The camera will be placed on a tripod facing the walking strip on the opposite end of the starting point of all walking tests. The camera will be placed two metres after the measured 25-foot strip to avoid risk of tripping or affecting data. Please see the diagram below.

Figure B

Figure B shows a participant walking with sensors attached along a 25foot walkway, marked out with cones and tape. The researcher is positioned aside the participant with a clipboard. Please note, this is not the official walkway for the proposed project.

Figure C



The camera is placed so the participants shoulders and below are on show. No faces will be shown on the camera. The camera will be recording throughout the entire physical assessment.

Data Analysis

The sensor and camera recordings data will be transferred onto the password protected university computer. The data from the sensors will be stored and analysed in MATLAB of which kinematic and temporal variables will be generated.

The physical assessment will then be analysed using unpaired inferential statistic tests using MATLAB (unpaired t-tests for normal distribution and rank sum tests for non-parametric samples). The mean, median, standard deviation, standard error of the mean and median of absolute deviation (for non-parametric) will be calculated for all outcome measures. The final analysis will look at linear regression (general linear model).

Using these methods of analysis, the primary researcher will then compare all data, studying subjective and objective fatigue looking for similarities and differences.

All the results will be collected and analysed by the primary researcher with supervision of Prof Galvin for phenomenological analysis and Dr Witchel for the physical assessment analysis.

The project will be based at Eastbourne campus, University of Brighton in the Robert Dodd building. For the physical assessment the human movement lab, annexe two will be used for all assessments which is fully insured and equipped for testing. The interviews will also take place in annexe two, in the office room section attached to the human movement lab. The rooms can be booked in the HML calendar via staff central which has to formally be booked by a supervisor.

The primary researcher is, and will continue to attend masterclasses on qualitative and quantitative research, gaining knowledge on statistical analysis, phenomenological methods and learning the strengths and limitations of interdisciplinary research.

The possible burden on participants throughout the day:

- Making sure the participants feel comfortable with being video recorded from the shoulders down. The participants will be asked before the camera is switched on whether they are okay with this. If the scenario arises of the participants face to be shown due to the participant falling, or from camera movement, we will inform the participant and inform them of our data protection and security regulations. If the participant is unhappy with this, we will destroy the camera recording of this participant.

- If the sensors feel uncomfortable on the participant. The sensors will be Velcro strapped to the participant with added tape if necessary. The primary researcher will not begin the physical assessment until the participant agrees they are comfortable, able to move freely and happy with the positioning of the sensors on them.
- If the participants feel too tired to continue a test, the primary researcher will give a rest period of 10 minutes. If after this 10 minutes the participant still feels unable to continue, another 10 minutes will be given. If the participant feels they can no longer continue with the assessment, the primary researcher will re-schedule a day to perform the other tests.
- The primary researcher will walk with the participants and will be close enough to help in the case that balance is lost. In the unlikely event of a fall the primary researcher will report and document the accident. If there is blood or an injury (e.g. a sprained ankle), the first aider will be contacted. If the injury is more serious (e.g. the bleeding won't stop or a suspected broken ankle), the participant will be accompanied to the hospital by the primary researcher or a member of the research team.
- If the participant feels emotionally distressed during the physical test or interview, time out will be given to the participant. If after these 10 minutes the participant still feels distressed, the primary researcher will seek advice from the well-being centre. We will also provide contact details of the MS helpline 0808 800 8000.

5a Participants and recruitment: general information (Maximum 500 words)

What sort of participants (age range, ethnicity, number, gender) are to be recruited? Will any vulnerable groups of people or individuals be involved? Consider the concept of 'vulnerability' in its broadest sense.

What inclusion/exclusion criteria will be used? Is exclusion from the research likely to deny an individual access from services that would otherwise have been provided?

How will initial contact be made? Include details of gatekeepers and others who are to be approached? Please supply a copy of any means of advertising, such as posters, leaflets, emails, web pages or letters.

Participants: inclusion and exclusion criteria -

The number of people estimated to participate is 60 total (30 pwMS, and 30 age- and gender-matched healthy volunteers). There will be no gender preference, although the project may recruit more women as statistically twice as many women to men are diagnosed with MS [Ahlgren et al., 2011]. The inclusion criteria include that patients (1) must have a definitive diagnosis of MS according to the McDonald criteria (verified by their GP or neurologist). All participants must be able to (2) walk for at least 100m, and (3) have the absence of other conditions that affect function including cognitive and gait impairment [Mcdonald et al., 2001]. (4) PwMS must have an EDSS scoring of 3.0-5.5 and (5) age range of 18+. This project requires no specificity to ethnicity; however statistically, MS sufferers are mainly from Western Caucasian background [Marrie, 2004]. All participants must (6) UK based and be able to (7) understand and speak fluent English. (8) PwMS must be comfortable with performing in depth, descriptive interviews.

Participants will be excluded from the project if (1) informed consent is not given or if they are unable to give written consent due to the cognitive impairment. However, cognitive impairment is unlikely for pwMS categorised 3.0 – 5.5 on the EDSS scale.

It is important to consider pwMS may be vulnerable. This project has been designed in consideration of this: (1) breaks in between assessments, (2) extra time allocated within the day for all participants if or/and when needed and, (3) first aider and counsellor onsite if needed for participants. Participants may be vulnerable with specific topics whilst being interviewed. The primary researcher will seek guidance from the well-being centre if the participant becomes distressed.

Healthy participants should be 18+, no systemic or musculoskeletal conditions (or temporary illnesses) that will affect gait function and ability and, be willing to perform and complete the questionnaires and physical assessment with given informed consent. The primary researcher will begin recruitment via email. The healthy and Multiple Sclerosis volunteers will be identified through email and posters through purposive sampling. This type of sampling has been chosen due to: a) the multiple sclerosis volunteers must lie within 3.0-5.5 of the EDSS and, b) the healthy volunteers have to be age-matched to the multiple sclerosis volunteers. The ages do not have to be identify, however within a similar range of a couple of years. (Please see attached file for participant recruitment process flowchart for people with Multiple Sclerosis and healthy volunteers). The sampling strategy reflects earlier studies [Witchel et al., 2017].

Please see attached files of posters and email templates.

A copy of any relevant materials used to recruit participants should be attached to this application

5b Participants and recruitment: payments to participants (Maximum 500 words)

Will participants be reimbursed or paid for their expenses and/or time? If so, please provide details of any payments or vouchers to be offered, or other incentives such as being entered into a prize draw (you should ensure that any payment does not constitute an inappropriate inducement to take part).

The participants will be made aware that their participation for this study is voluntary. Travel expenses will be offered to all participants.

The primary researcher has £1500 per annum in research costs which will be go towards travel expenses for participants. All participants will be asked to complete a TS5 form (see attached) and they will be reimbursed directly. The money is held by the school on the primary researcher's behalf, so the claim forms should be submitted to the school. Participants may claim back travelling as follows:

(1) Travelling by car: 45p per mile

(2) Travelling by train: Price of ticket, with evidence of receipt.

(3) Travelling by taxi (only covered if coming from Eastbourne rail station to Robert Dodd building): estimated £4-5 each way.

(4) Travelling by bus from Brighton or Eastbourne: £5-day ticket

For participants driving, parking permits are available. The primary researcher must book on the school of health sciences website HML calendar, select estates and facility management then, select parking permit. The participant must give their car registration number 48 hours before. (The primary researcher herself can't book the lab on staff central, therefore one of the supervisors will be asked).

The budget for transcribing will be under the same research costs of the primary researcher annual research costs budget. An example of the cost is as follows: £1.17 per minute of audio, (a maximum of 60 minutes per interview) 1.17 x 60 = 70.2. (15 participants will be transcribed), 70.2 x 15 = £1053. (information from www.academic-transcription.html)

6 Potential ethical issues including risks, benefits, outcomes and impacts of the research beyond participant recruitment and vulnerabilities (Minimum 200 words)

Referring to the Tier 1 checklist, please outline the key ethical issues in this research and discuss how potential issues are to be addressed and how any negative impact(s) will be minimised. Please ensure where relevant that you have completed a risk assessment form and (for students) it has been signed by your course leader, and attach it with this application.

Are there any expected benefits or positive impacts of the research on participants or their communities? Possible impacts might include psychological, health, social, economic or political changes or ramifications, either at the time the research is carried out or in the future.

Potential ethical issues	**How ethical issues will be addressed**
(1) Coercion	(1) It is solely the participants choice if they want to participate or not. Throughout the recruitment stage the participant will be informed and re-informed that they can withdraw from the project at any given time, without any given reason. They will also be reminded that the project is voluntary and no form of payment for

	participating will be done for performing the assessment, only travel reimbursement.
(2) Exclusion after pre-assessment	(2) If the participant is not in in the EDSS scoring range of 3.0-5.5, they will be informed via their choice of contact (phone, email or SMS). They will be thanked, informed of their scoring if they wish and familiarised with the data protection act (1998) about their assessment data.
(3) Shoe wear	(3) We will supply the trainers for the physical assessments, which are suitable for the surface and allow good movement for walking. We will not allow them to use their own shoe wear for health and safety regulations. We have a set of 9 different identical trainers of various sizes. shoes will be regularly sprayed with agents to guarantee hygiene.
(4) If participant becomes too tired to perform a physical test	(4) We will give a rest period of 10 minutes initially with all sensors and cameras to remain active. After the 10 minutes we will ask the participant if they are ready to proceed. If yes, we will proceed and re-do the test if paused half way through. If no, we will give the participant another 10 minutes. We will repeat the procedure until the participant is ready to continue with the assessment.
	(5) The camera will be positioned so the participants face will not be shown. The camera will show the participants shoulders and down. The participants will be asked before the camera is switched on whether they are okay with this. If the scenario arises of the participants face to be shown due to the participant falling, or from camera movement, we will inform the participant and inform them of our data protection and security regulations. If the participant is unhappy with this, we will

(5) The camera and the participants identity	destroy the camera recording of this participant. The cameras will be used to add additional analysis for assessing walking and balance and as back up data if a sensor fails. The participants face will not be identified by the camera.
(6) If a participant trips, falls or gets injured	(6) The primary researcher will walk with the participants and will be close enough to help in the case that balance is lost. In the unlikely event of a fall the primary researcher will report and document the accident. If there is blood or an injury (e.g. a sprained ankle), the first aider will be contacted. If the injury is more serious (e.g. the bleeding won’t stop or a suspected broken ankle), the participant will be accompanied to the hospital by the primary researcher or a member of the research team. Money will be provided for taxis.
	(7) This is unlikely, as our protocol does not use fluids. We will clean it up immediately, but if there is a major spill we may need to contact the authority at the venue where the problem has occurred.
	(8) The sensors will be Velcro strapped to the participant with added tape if necessary. If the sensors come off during assessment, the assessment will be stopped, and the person will be re-strapped. After the participant confirms the strap is secure and allows easy movement, the test will be re-done.
	(9) Before the interview is recorded, the primary researcher will explain to the participant the structure of the interview, clarifying if the participant is comfortable with the procedure. If they are not comfortable discussing any topics, they will not be pressurised into talking about it. If a topic arises where the participant feels distressed the distress protocol adapted by Draucker et al., 2009 will be used and the primary researcher will seek advice from the well-being centre (see appendices). We

	will also provide contact details of the MS helpline 0808 800 8000.
(7) If there is a fluid spill in the lab	(10) The participants will be assured on research confidentiality, notifying them at any point they can turn the Dictaphone on and off during the interview. During the interview or physical assessments, the participants may become identifiable, yet measures will be taken to ensure secure storage of information. The participants will be allocated a number for the physical assessments, of which will be used for the duration of the project as their identity. All records of participants' identity and details will comply with the data protection act (1998) and will be destroyed after ten years.
(8) if the wearable sensors fall off during an assessment	(11) As stated before, breaks will be given in the physical assessment (five-minute slots quarterly and an extra 10 minutes if requested by participant). However, if the participant feels they are unable to perform the interview after a given 30 minutes break, an offer of returning the following day will be given. Allocated time will be given each day to allow for this.
(9) Any discussion of emotional distress	(12) The project assessment and interview will be conducted by the same researcher, the primary researcher. This minimises unfair practice and assessment which also allows the data of not being biased.

(10) Anonymity and Confidentiality (11) If a participant is tired after the physical assessment and unable to do the interview. (12) Potential unfair assessment	

7 Participant information and consent (Maximum 500 words)

Please outline how participants will be informed (both orally and in writing) about the research and their participation in the study. How will you ensure that information is provided in a format/language suitable for the target audience? Please describe how written consent will be obtained, or if you are working with participants who cannot give written consent, an explanation of the reason for seeking oral consent and details of the procedure to be adopted.

If consent is not being sought, or will not be sought until after data has been collected (e.g. if it involves covert observation), please say why consent will not be sought or why the delay is necessary, and what steps will be taken (if any) to debrief participants and obtain consent afterwards.

Local MS organisations and charities will be emailed basic information about the project, giving an opportunity to meet to discuss the project further. If an organisation accepts advertising/participation recruitment (in writing) in the project, the participants will have the opportunity to be shown a poster which will be put up in their building. The participants will also be offered the poster by hand to keep, if they choose to contact the primary researcher for more information. This poster will be available to pick up from the organisation by the centre manager. They will further be informed about the project (if they decide to participate), with a brief outline form and participant information sheet.

Participants will be given a consent form twice. Once before completing the EDSS assessment. Secondly, as informed consent for the project including all the tests, interviews and questionnaires.

The participant information sheet will have an email and phone number for the participants to use if they decide to participate. The participants are not expected to make a decision immediately and should be allowed time before acting on their decision. All participants will receive a poster, information sheet, consent form and a brief outline sheet. On the information and consent form, it will be made clear to the participants of withdrawal at any given time. All information given to participants is reader friendly but with professional and relevant writing and information.

Please see attached files for consent form, brief outline sheet and participant information sheets.

Copies of consent forms, participant information sheets and any other information for participants should be attached to this application

8 Confidentiality and data storage (Maximum 500 words)

Please describe measures that will be taken to ensure anonymity, privacy, confidentiality and data protection. This should include:

- How participants will be identified without breach of the data protection act and to guard against invasion of privacy (e.g. if you plan to access personal information to identify potential participants)?
- What steps will be taken to anonymise data (this may include removing identifying information in addition to names)

- How data (both physical and digital) will be collected, handled, transferred and stored
- Who will have access to the data other than the researcher (eg supervisors, transcribers etc)
- How long data will be retained, and how it will eventually be destroyed
- Where the research data will be published (eg essay, dissertation, academic paper, exhibition, online) and who will have access to the results

The primary researcher has a duty of confidentiality, no information revealing data or identities will be disclosed outside the research team. Compliant to the Data Protection Act of England and Wales [1998] and the Freedom of Information Act [2002], the researcher will handle, process, store and destroy the data correctly.

All data will be collected by the primary researcher. The participants' consent forms, questionnaires and paper files from the physical assessment will be secured in a locked cabinet in Westlain building of Brighton University. The personal details of the participants (name, contact details, diagnostic information) will be stored in separate files in a different locked cabinet. Only the research team will have access to the cabinet. A single master key document will be used to store details of the participants. To maximally secure this information, each participant will be allocated an identifier code, which will then be locked in to the filing cabinet which only the research team will have access to. The digital recordings from the sensors, questionnaires and interviews will be kept secure on a password protected computer in the University, no personal laptops will be used. The primary researcher and the supervisors will be the only researchers to have access to the electronic information on the computers.

The physical information from the participants (questionnaires and consent form) will be collected solely from the primary researcher after they have completed each form. This information will then be placed into a secure briefcase by the primary researcher and transported by herself to the locked cabinet in the Westlain building.

To ensure confidentiality, during the transcription process, all references to names, places or services will be removed and anonymised and replaced by descriptions. The data will be analysed and collected for thesis publication. All the data after ten years will be deleted from the computer and the paper files will be shredded.

9 Other ethical issues

Please outline any other ethical issues that have not already been discussed in the sections above and describe how these will be addressed.

The full assessment day will take anytime from 2-2.5 hours. The assessment days are organised to allocate two participants per day, with extra time given for participants who request it. There will be also be time given at the end of the day for an interview slot, just in case a participant is unable to perform the interview on their allocated day of the physical assessment. This option will not affect the project.

A PPI group will be formed in terms of the design of the research, undertaking the research, and dissemination of the research. It will give the primary researcher advice and guidance at any stage of the project. A PPI group will be formed by members of the organisations (both staff and pwMS) and meeting with some members of the University of Brighton's Research Development Service.

Please see attached risk assessment form with the other potential risks and hazards.

10 Supervisor sign-off (for student research only)

I confirm that I have checked the application and that the student has addressed the relevant ethical issues, has received training in ethics as part of their module or programme and has the necessary skills and experience to carry out the proposed research.

Kathleen Galvin 18/01/2018

Supervisor: ________________________ Date: __________

11 Checklist for accompanying documents

Please ensure you have attached copies of any of the following documents where relevant, and please do not include any other forms with your application.

- ☐ Tier 1 form (where proposal has been referred up from School Research Ethics Panel)
- ☐ Information sheets
- ☐ Consent forms
- ☐ Advertising or recruitment materials
- ☐ Sample questionnaires or interview questions
- ☐ Risk assessment forms
- ☐ Letters of support from external organisations involved in the research
- ☐ List of references cited in the application

Please also note that the application must be complete and please ensure that it has been checked for accuracy, grammar and spelling.

Please return this form and all accompanying documentation to the Secretary of the Cross-School Research Ethics Committees (Kate Connolly, k.connolly2@brighton.ac.uk)