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MS and Physical Activity



Self-efficacy, Physical Activity and QOL in People with MS

Abstract

Self-Efficacy is part of the social-cognitive theory defined as the belief that one can successfully cope with challenging situations and attain certain goals. It has been suggested this principle can be applied to physical and psychological quality of life in individuals with Multiple Sclerosis (MS).

Objective: To examine if self-efficacy and physical activity have relationships with quality of life (QOL) in individuals with MS.

Methods: 109 individuals with MS participated in this study. Each individual completed the Multiple Sclerosis Self-Efficacy scale (MSSE), the Multiple Sclerosis Impact Scale (MSIS-29), and the Good in Leisure-Time Exercise Questionnaire (GLTEQ). Pearson product moment correlation coefficients were computed for self-efficacy, physical activity and QOL.

Results: The sample (n=109) was composed as follows, females (75%), relapsing remitting form of MS (81%), married (68%), employed (44%). Time since MS diagnosis was 7.6 years (SE=0.62). There were moderately high negative correlations between MSSE and QOL physical component ($r=-0.65$, $p<0.01$) and psychological component ($r=-0.63$, $p<0.01$), indicating that individuals with increased sense of self-efficacy experienced less psychological issues and an increased level of participation in physical tasks. There was a low negative but significant correlation between total time spent in leisure activity and QOL physical component ($r=-0.21$, $p<0.05$), but not for QOL psychological component. Physical activity has a negative correlation with physical impact of QOL ($r=-0.21$, $p<0.05$) and no correlation with psychological component ($p>0.05$).

Conclusion: The results of this study demonstrate that with increased self-efficacy there is an increase in QOL on both physical and psychological components, which is important for increased independence and functionality in individuals with MS.

Keywords: Multiple sclerosis; Self-efficacy; Quality of life; Physical activity

Introduction

Multiple Sclerosis (MS) is an immune-mediated disease of the central nervous system (CNS) with both inflammatory and degenerative components. It can present with an array of symptoms such as visual disturbances, motor and sensory deficits, bladder and sexual dysfunction, and psychological issues to include depression, anxiety, and cognitive dysfunction [1].

The diagnosis of MS, given the chronic nature of the disease and the fact that it implies an un-predictable path to variable degrees of disability, can have a great psychological impact and a distressing effect on quality of life (QOL). Given the variety and severity of symptoms in MS, often not visible to other people, coping mechanisms may be compromised and disrupt many aspects of life from personal (family and relationships) to professional (employment). This may impact an individuals' self-efficacy.

Self-efficacy in MS

Self-Efficacy is part of the social-cognitive theory that involves beliefs that one can successfully cope with challenging situations and have the ability to overcome them [2]. An individual's level of self-efficacy is often influenced by their accomplishments or capacity of performance, verbal persuasion, and the interpretation of psychological and affective states [2]. Individuals with strong self-efficacy beliefs will more likely set higher personal goals believing they will successfully achieve them. In contrast, someone with low self-efficacy beliefs will be more likely to set lower personal goals, as they do not believe they will be able to achieve high objectives. In the context of a chronic illness, their beliefs may affect their own perception of the condition, the impact the

illness will have on their life, and to which capacity they are able to handle the disease. Previous studies have shown high self-efficacy to be a predictor of health related behavior such as adherence to medication [3,4], decreased depression [5,6] and increased participation in physical activity [7-11]. Self-efficacy has been demonstrated to be a predictor of psychological improvement in individuals with chronic diseases such as cancer [12], rheumatoid arthritis [13,14], fibromyalgia [15] and MS [16,17].

Physical activity in MS

Participation in physical activity (PA) of individuals diagnosed with MS is generally low [18], especially in those that complain of multiple or worsening of symptoms [9,19] and those that report high levels of fatigue or difficulty walking [20]. In the past, individuals diagnosed with MS were recommended not to engage in any physical activity in order to avoid even a slight increase in core body temperature which may worsen neurological function, known as Uhthoff's phenomenon [21]. More recently it has been demonstrated that individuals with MS benefit from physical activity in a similar way to the non-diseased

population [22] and experience improvement in their fatigue levels [23]. Participation in physical activity can be greatly compromised in the MS population as the disease presents with both physical (spasticity, muscle weakness, ataxia, fatigue, and pain), and psychological (emotional state, anxiety and depression) symptoms that decrease the ability and willingness to do so.

Quality of life in MS

Quality of life (QOL) is affected in a large number of individuals living with chronic diseases like MS [24,25]. The unpredictable clinical course and absence of a curative treatment in MS greatly affect the psychological QOL, with about 50% of individuals experiencing depression at some point during the course of the disease [26]. Individuals with self-reported more rapidly progressive types of MS usually experience greater disability and impairment, and thus often have lower QOL [27]. However, one study showed that duration of disease positively correlated with better QOL, despite greater physical disability as measured by expanded disability status scale (EDSS) [28-30], possibly due to the capacity to adjust to the effects of the disease and accept limitations over time. Participation in physical activity has shown to improve QOL in MS individuals [29, 30] with the most active individuals reporting higher levels of health related QOL (HRQOL) on both physical and mental components [31].

Purpose

The purpose of this study is to identify the relationship between physical activity level and self-efficacy with components of QOL. Our hypothesis is that individuals with low self-efficacy would also report decreased quality of life and have less participation in physical activities. Understanding this process can lead to interventions that will offer better results in the comprehensive management of MS by identifying barriers to patient's participation in their own care.

Material and Methods

Subjects

Patients were recruited from a single specialized MS center at the time of scheduled office visits and data was collected as part of routine clinical assessments. The sample was a convenience sample and consisted of a total of 109 subjects with diagnosis of MS following 2010 McDonald criteria [32], with mean age 45 years, height 168 cm, weight 80 kg and mean duration since diagnosis of 7.6 years. The sample was 75% females, 68% married, 44% employed, 40% with partial college education, and 38% being college graduates. Of the 109 individuals, 81% had relapsing remitting MS (RR-MS); 14% had secondary progressive MS (SP-MS); 5% had primary progressive (PP-MS). All of them were ambulatory without aids but ankle-foot orthosis and peroneal nerve electric stimulators to compensate for foot drop were allowed.

The study protocol was approved by the institutional review board, and all participants in the study provided written informed consent prior to data collection. All subjects had the cognitive ability to read and sign informed consent as determined by clinical assessment of the treating neurologist.

Protocol for acquisition

Each individual completed the following questionnaires: Multiple Sclerosis Self-Efficacy scale (MSSE) [33], a disease-specific 14-item questionnaire with a 6-point scale, ranging from 1 (strongly disagree) to 6 (strongly agree). The MSSE has been proven to be reliable and is a useful tool in assessment of psychological adjustments in both clinical

and research settings [33]. Total scores range from 14 to 84, where a higher score indicates an elevated level of self-efficacy.

The Multiple Sclerosis Impact Scale (MSIS-29), a disease-specific, self-administered questionnaire asking about the day to day impact that MS has had on life for the immediate previous two weeks. It includes physical (20 items) and psychological (9 items) subscales [34], and is proven to be a useful tool in the assessment of disease impact and quality of life in community [34], hospital setting [35] and in clinical research [36]. It is a 29-item questionnaire and is scored as follows: 1=not at all, 2=a little, 3=moderately, 4=quite a bit, 5=extremely, for evaluating the degree of an experienced problem the last two weeks. The score ranges from minimum of 29 to a maximum of 145, with higher scores indicating greater impact of the disease on the individual's QOL.

The Good in Leisure-Time Exercise Questionnaire (GLTEQ) [37], is a simple generic measure of physical activity that is widely used in clinical and epidemiological settings. It is a self-administered two-item questionnaire that measures an individual's physical activity level, with the first question determining the average number of times an individual participated in strenuous (e.g., jogging), moderate (e.g., fast pace walking) and mild exercise (e.g., easy pace walking), for more than 15 minutes during their free time in a typical 7-day period. These frequencies are then multiplied by nine, five, and three metabolic equivalents respectively and then summed to a total single measure of physical activity. In this particular study, we only included the first question in the analysis, as it provides more information of the amount of PA, as done in previous research [38]. The second question is ordinal in nature and has three options (1=often, 2=sometimes, 3=never/rarely) and measures how often the individual engages in any regular activity long enough to work up a sweat or rapid beating of the heart. Evidence has shown that GLTEQ gives a valid measure of physical activity in individuals diagnosed with MS [39].

Data analysis

Descriptive analyses are presented as mean \pm standard errors and were carried out for all variables in the group. The relationship among scores from the three measures was examined using Pearson product moment correlation coefficients. All statistical analysis was performed using SPSS, version 16.0 (SPSS Inc, Chicago, IL, USA). Statistical significance was set at $p \leq 0.05$. Demographic characteristics of the sample are displayed in Table 1.

Results

Self-efficacy (MSSE) and quality of life (MSIS-29) psychological and physical impact

A moderate negative correlation between MS self-efficacy (MSSE) and quality of life (MSIS-29) psychological impact of MS ($r=-0.63$, $p<0.01$) was demonstrated, indicating that as levels of self-efficacy increase, the psychological impact on QOL decreases (Figure 1). There was a moderate negative correlation between self-efficacy and physical impact of MS ($r=-0.65$, $p<0.01$), with greater self-efficacy being associated with a lesser impact of physical deficits on QOL (Figure 2).

Age (yrs)	45.05 \pm 1.13
Height (cm)	168.00 \pm 0.01
Weight (kg)	79.70 \pm 2.33
MS yrs	7.62 \pm 0.62

Mean \pm SE, MS; multiple sclerosis;

Table 1: Subject Characteristics (n=109).

Physical activity and MSIS-29 psychological and physical impact

A weak negative correlation was found between total time spent in leisure time physical activity and quality of life physical impact ($r=-0.21$, $p<0.05$), suggesting the less physical impact MS had on individuals, the more time they spent in physical activity, (Figure 3). No correlation of significance was found for time spent in physical activity and psychological impact of MS ($p>0.05$) (Figure 4).

Discussion and Conclusion

This study provided information of MS self-efficacy and the time spent in physical activity and its effect on quality of life, both physical and mental, in MS individuals. A moderate relationship was evident, with those individuals having increased levels of self-efficacy reporting a lesser mental and physical impact of their underlying disease on QOL. A weaker relationship was found between time spent participating in physical activity and the physical impact component of quality of life.

Participation in physical activity may help minimize some of the symptoms associated with MS, to include fatigue, ambulation and postural balance, due to increased muscle strength [40]. It may also help decrease the risk of developing secondary diseases that result from sedentary lifestyles and inactivity such as cardiovascular disease

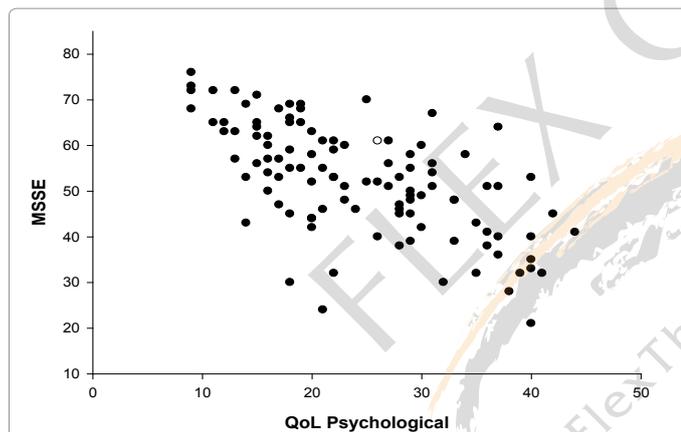


Figure 1: Self-efficacy (MSSE) and QoL (MSIS-29) psychological impact of MS.

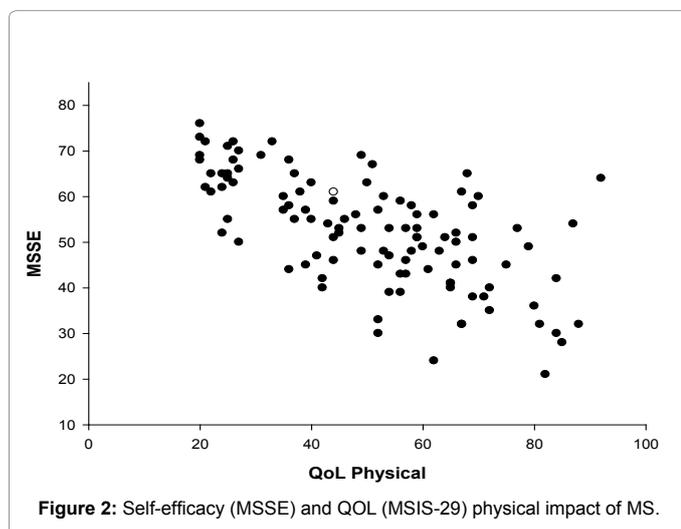


Figure 2: Self-efficacy (MSSE) and QoL (MSIS-29) physical impact of MS.

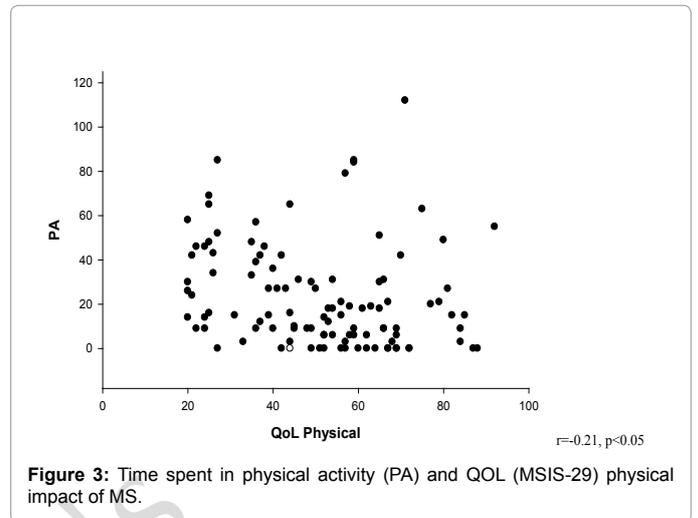


Figure 3: Time spent in physical activity (PA) and QoL (MSIS-29) physical impact of MS.

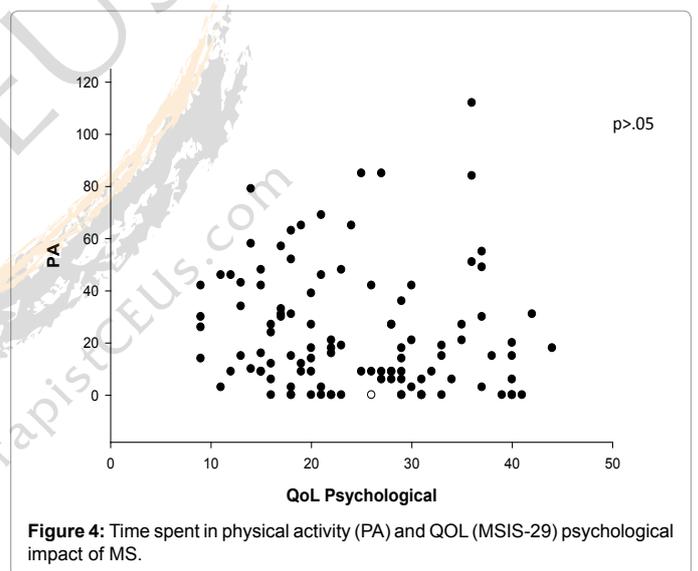


Figure 4: Time spent in physical activity (PA) and QoL (MSIS-29) psychological impact of MS.

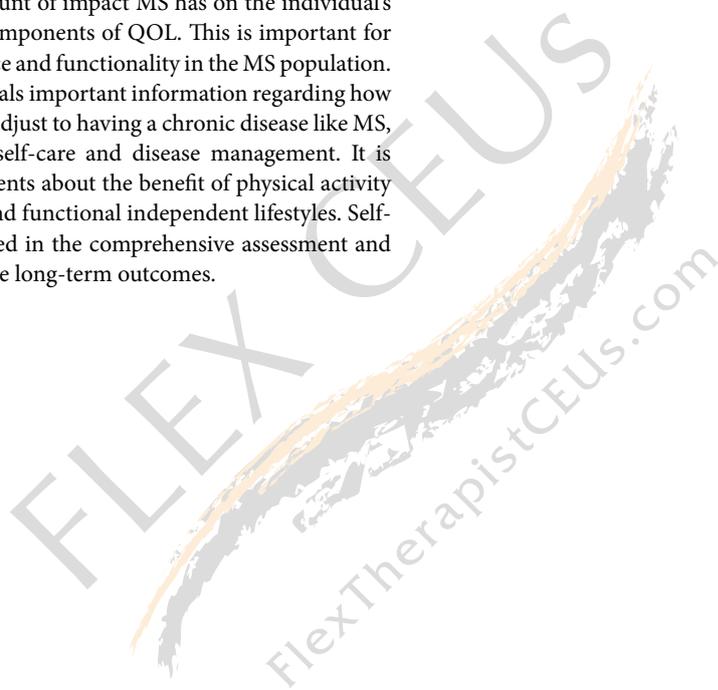
and osteoporosis. Many factors influence the ability and willingness to engage in regular physical activity in MS. An individualized program that adapts to the participant's limitations is recommended. Some modalities include aquatics and resistance training for MS individuals affected by thermo-sensitivity, as the core temperature will not increase as much with this type of exercise as it does with others such as running.

Quality of life is commonly compromised in MS individuals. Studies have established that QOL can be influenced by factors such as self-efficacy and physical activity, with an increase in quality of life often seen in individuals that report greater self-efficacy and more participation in physical activity [41]. A recent study showed that self-efficacy is a significant predictor of self-reported physical, cognitive and social function [42]. Those results coincide with some of the results of this study, where we demonstrated that individuals with greater self-efficacy reported less psychological and physical impact from MS in their QOL. In addition, this investigation found that individuals that spent more time participating in physical activity reported less physical impact of MS and thus increased physical independence. This positive effect was not found for time spent in physical activity and psychological impact.

There are many ways to obtain measures of physical activity levels in individuals with MS. In this study, amount of time spent exercising was measured by self-report questionnaires and not by objective measures often used by other researchers [43,44]. One previous study was able to detect differences in physical activity levels between MS individuals compared to a sedentary control group by the use of accelerometers but did not find any significant difference by self-report in the same study [44]. The use of both objective means and self-report as measures of physical activity has been previously validated [39].

The predominance of females (75%) in this study reflects the demographics of MS. Two of the 3 instruments used in this study are disease-specific, making the results not generalizable to other chronic entities.

In conclusion, this study showed that with greater self-efficacy there is a decrease in the amount of impact MS has on the individual's physical and psychological components of QOL. This is important for overall increased independence and functionality in the MS population. Determining self-efficacy reveals important information regarding how individuals handle, cope and adjust to having a chronic disease like MS, influencing participation in self-care and disease management. It is important to educate MS patients about the benefit of physical activity to promote better, healthier and functional independent lifestyles. Self-efficacy should be incorporated in the comprehensive assessment and management of MS to improve long-term outcomes.



The Importance of Physical Fitness in Multiple Sclerosis

Abstract

The present review paper provides an overview on the importance of physical fitness in persons with Multiple Sclerosis (MS). We first present a model describing a cyclical association among physical inactivity, physiological deconditioning, and worsening of MS over time. We then provide a comprehensive review of research indicating extensive physiological deconditioning in cardiorespiratory, muscular, motor, and morphological domains of physical fitness among those with MS compared with controls and as a function of disability status. There further is substantial evidence for associations between physiological deconditioning and a variety of consequences of MS (e.g. outcomes of brain structure and function, ambulation, cognition, and fatigue), emphasizing the importance of counteracting and maintaining all domains of physical fitness. Exercise training may be an effective approach for improving physical fitness and managing secondary consequences among persons with MS. To that end, researchers have recently developed evidence-based physical activity guidelines indicating that adults with MS should participate in 2 weekly sessions of 30 minutes of moderate intensity aerobic activity to improve aerobic capacity and 2 weekly sessions of resistance training to improve muscular fitness. We believe that these guidelines provide an important basis for the prescription of exercise training by clinicians as a therapeutic approach for managing many of the consequences of MS.

Keywords: Multiple sclerosis; Physiological deconditioning; Morphological domains

Multiple Sclerosis (MS) is a common and life-altering neurological disease among adults in the United States and worldwide. This disease has an estimated prevalence of 1 per 1,000 adults in the United States [1] with the majority of cases occurring in women of European descent. The MS pathophysiology initially involves episodic periods of immune-mediated demyelination and transection of axons within the Central Nervous System (CNS). This results in the disruption of saltatory conduction of action potentials along myelinated axonal pathways in the brain, spinal cord, and optic nerves. The MS pathophysiology later transitions into a neurodegenerative disease process, presumably associated with insufficient neurotrophic support, and results in the accumulation of irreversible neurologic disability. The degree and location of axonal and neuronal damage within the CNS result in the heterogeneous expression of symptomatic, functional, and participatory consequences among persons with MS [2]. Such manifestations might be initiated or worsened by physical inactivity and resulting physiological deconditioning.

We have previously described a model of physical inactivity, deconditioning, and worsening MS [3,4], and this was based on a similar framework for persons with chronic disease conditions [5] including MS [6]. The model is displayed in figure 1 and indicates that MS onset results in physical inactivity [7,8] that initiates physiological deconditioning (i.e., compromised or reduced physical fitness). This physiological deconditioning, in turn, results in worsening of MS, as indicated by loss of brain structure and function as well as symptomatic (e.g., fatigue) and functional (e.g., walking impairment) manifestations. The worsening of MS results in further physical inactivity and subsequent physiological deconditioning thereby yields a cycle of associations among physical inactivity, deconditioning, and worsening MS that develops over time. This model is important as it conceptualizes the importance of maintaining and improving physical fitness levels in persons with MS. Physical fitness might provide a form of “physiological reserve” that is protective of disease consequences and worsening of MS and this is consistent with other literatures such as cancer [9].

on physical fitness in persons with MS. We begin by defining physical fitness and its domains as well as differentiating it from physical activity. We then present research on physiological deconditioning (i.e., detraining that manifests as a reduction in domains of physical work capacity or fitness) in persons with MS as well as evidence on the association between markers of physical fitness and consequences of MS. We lastly review research regarding the effects of exercise training on physical fitness and consequences of MS, and conclude with recently developed exercise recommendations for improving physical fitness. Our goal is the provision of a paper that underscores the (a) importance of physical fitness and (b) role of exercise training for its improvement among persons with MS.

Overview of Physical Fitness and Its Components

Bouchard and Shephard [10] have provided clear definitions of physical fitness and physical activity that can be adopted to avoid confusion regarding these two related, but distinct terms. Physical fitness describes one’s capacity for performing work or, in other words, it represents the characteristics of a person that describe the capacity for engaging in physical activity and exercise behavior. Performance-related fitness involves components necessary for optimal work or sport outcomes; whereas health-related fitness reflects components that are influenced favorably or unfavorably by physical activity levels and reflects one’s health status and risks for morbidity and mortality. The latter is the type of fitness that is relevant within the current paper and its reduction over time is consistent with the idea of physiological deconditioning.

To that end, this paper provides a comprehensive review of research

Physical activity, by comparison, is a behavior described by the movement of one's body through the contraction of skeletal muscles that yields a substantial increase in energy expenditure over resting values. Physical activity can broadly involve active physical leisure-time pursuits, occupational work and household chores, transportation, sport, and exercise. Exercise is a subset of leisure-time physical activity that involves planned, structured, and repetitive bouts of physical activity over an extended period of time with the objective goal of improving aspects of health-related fitness.

Health-related fitness is a broad term and it has several components, much like physical activity. The important components of health-related fitness include cardiorespiratory, muscular, motor, and morphological components. The cardiorespiratory component reflects one's capacity for performing aerobic or endurance forms of physical activity (e.g., walking, bicycling, and jogging) and is often reflected by peak aerobic capacity (VO_{2peak}). VO_{2peak} is measured by analysis of expired respiratory gases during a symptom limited exercise test performed until exertional fatigue (i.e., maximal voluntary exertion). Based on the Fick equation, VO_{2peak} can be described based on the highest rates of delivery (i.e., cardiac output) and extraction (i.e., difference in arterial-venous oxygen content) of oxygenated blood during exercise and reflects one's capacity for engaging in endurance or aerobic physical activity. This domain of fitness has been identified as the most important from the perspective of preventing morbidity and premature mortality as well as maintaining health in the general population [11,12].

The muscular component of fitness reflects one's capacity for work that requires muscle strength and endurance. Muscle strength reflects the ability of a specific muscle or muscle group to exert or generate an external force, whereas muscle endurance reflects the ability of muscle to generate submaximal force across successive repetitions. Muscle strength is most often measured and is based on either maximal force using an isokinetic dynamometer (i.e., maximum voluntary contraction) or the greatest resistance that can be moved through the full range of motion (i.e., 1-repetition maximum). The motor component, particularly upright balance, reflects one's capacity for maintaining a standing posture and is often measured by posturography (i.e., whole body sway based on excursion of the center of pressure). The morphology component reflects fat, lean, and bone components of one's body based on a three-compartment model. This is typically measured with Dual-Energy X-Ray Absorptiometry (DXA), although fat mass can further be reflected by Body Mass Index (BMI) or percentage of one's body that is fat based on skin folds, bioelectrical impedance, or densitometry from hydrodensitometry (underwater) weighting or air displacement plethysmography. These domains of health-related fitness have further been identified as important from the perspective of preventing morbidity and premature mortality.

Evidence for Physiological Deconditioning in MS

One premise of this paper, and the model in figure 1, is that persons with MS experience physiological deconditioning compared with controls, and this worsens over time, for example, as disability progresses (e.g., mild vs. moderate and/or severe MS). To that end, researchers have sought to quantify differences in components of fitness, particularly aerobic capacity, muscular strength, balance, and body composition, between persons with MS and the general population and, in some cases, among persons with MS as a function of disability levels. The body of evidence generally indicates that significant physiological deconditioning occurs in persons with MS, particular as a function of disability progression.

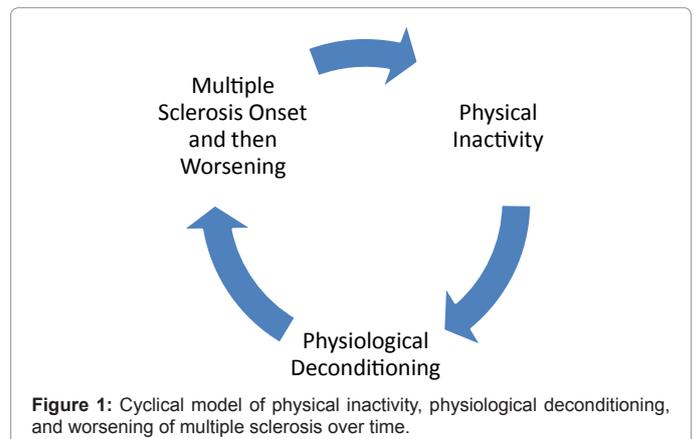


Figure 1: Cyclical model of physical inactivity, physiological deconditioning, and worsening of multiple sclerosis over time.

There is evidence that persons with MS have diminished VO_{2peak} compared to the general population [6,13]. For example, one study compared the VO_{2peak} recorded during a maximal, incremental exercise test on a cycle ergometer among 32 women with relapsing-remitting MS who had minimal disability with 16 sex, age, height, and weight-matched controls [14]. The researchers reported that the persons with MS demonstrated significantly and moderately reduced absolute ($d=0.56$) and relative ($d=0.53$) VO_{2peak} compared with the matched controls. There is further evidence that VO_{2peak} differs between persons with MS who have mild and moderate-to-severe disability [15, 16]. For example, one study compared VO_{2peak} recorded during a maximal, incremental exercise test performed in a semi-recumbent position on a cycle ergometer between 11 persons with mild disability and 8 persons with moderate-to-severe disability [15]. The researchers reported that persons with MS who had moderate-to-severe disability demonstrated significantly and moderately (27%) reduced absolute VO_{2peak} compared with those who had minimal disability.

There is additional evidence that persons with MS have worse musculoskeletal fitness (i.e., characteristics of muscular strength/fatigue) than the general population [6,13]. One study examined lower limb strength asymmetries (i.e., relative differences in the strength of a particular muscle group between strong and weak limbs) and muscle fatigue (i.e., endurance) in 52 persons with Clinically Isolated Syndrome (CIS) (i.e., the precursory diagnosis of MS) compared with 28 age and sex matched healthy controls [17]. Those with CIS demonstrated greater strength asymmetries in the ankle muscles as well as muscle fatigue compared with the controls, and this indicates that muscle weakness manifests even in the earliest stages of MS. Another study of 9 persons with MS and 11 healthy controls reported that persons with MS had a substantially smaller maximal voluntary contraction of ankle dorsiflexors, measured using a force transducer, compared with controls [18]. This difference in maximal voluntary contraction might be explained by persons with MS requiring greater central motor drive to achieve the same relative force during a maximal muscle contraction as healthy controls [19]. The weakness of lower extremity muscles seems to differ as a function of disability in those with MS. For example, one study compared the peak isometric and isokinetic torque in the knee extensors and flexors between 31 persons with MS who had mild disability and 21 persons with moderate disability [20]. The researchers reported that all muscle strength variables were significantly worse in the subgroup with moderate disability compared with those who had mild disability.

Persons with MS have worse balance, indexed by posturography,

than the general population. For example, one study of 12 women with MS and 12 age-matched controls examined differences in postural stability using a force plate (i.e., static posturography). Participants stood quietly on the force plate for 20 seconds with eyes open and directed forward gaze. Overall, the women with MS had greater Center-of-Pressure (COP) sway in the antero-posterior direction (mean=7.52 mm) than the age-matched controls (mean=4.33 mm) [21]. Another study of 16 persons with MS and 16 sex-matched controls used a similar static posturography protocol (i.e., participants stood quietly on a force plate with eyes open and directed forward for 30 seconds) [22]. This study reported that persons with MS had significantly greater COP sway area, sway velocity, and medio-lateral sway compared with controls [22]; those balance metrics were worse in participants with greater spasticity compared with persons with MS who had lesser spasticity and controls [22]. An additional study of 19 persons with mild MS disability (EDSS range=2.0-3.5) and 26 persons with moderate MS disability (EDSS range=4.0-6.5) examined the possibility that COP sway differed as a function of disability in persons with MS [23]. All participants stood quietly on a force plate for 30 seconds for measurement of COP sway. Persons with moderate disability had greater COP sway than the mildly disabled persons with MS, and, in the overall sample, COP sway was associated with disability ($r=0.36$), further suggesting that persons with worse MS disability had greater COP sway [23].

There is some emerging evidence that persons with MS have poor body composition based on BMI, body fat percentage, and waist circumference. Indeed, persons with MS have similar rates of overweight and obesity as the general population [24,25], and this is problematic given the rates in the general population of adults [26]. For example, one study reported an average BMI of 27.0 kg/m² in a large sample of persons with MS (n=8983); this average BMI value is comparable with the general population, but suggests that many persons with MS are overweight [25]. Another study of 123 women with MS reported that participants had higher BMI, waist circumference, and total body fat percentage than recommended by the World Health Organization [26]. As persons with MS have similar body composition characteristics as the general population [27], body composition metrics do not seem to vary as a function of

disability in persons with MS. For example, studies of small (n=17) [28] and large (n=68) [29] samples of persons with MS have reported no associations of body composition measures (e.g., fat percentage, lean mass percentage, and bone mineral density assessed by DXA) and EDSS score [28,29].

One limitation of previous research on deconditioning in persons with MS is that the studies measured single domains of physical fitness. One recent study examined differences in *multiple* domains of fitness between persons with MS and matched controls [30]. This study measured VO_{2peak}, muscle strength asymmetry of knee extensors and flexors, and upright balance based on posturography in 31 ambulatory persons with MS and 31 healthy controls matched by age, sex, height, and weight [30]. Persons with MS had substantially worse VO_{2peak} ($d=-0.72$) and balance ($d=0.91$) compared with healthy controls, and the differences between groups were moderate in magnitude for lower limb strength asymmetries of the knee extensors and flexors (d 's~0.50). This study provides evidence for comprehensive deconditioning in persons with MS, although it did not assess metrics of body composition.

Collectively, the published evidence generally supports the hypothesis that persons with MS exhibit physiological deconditioning (i.e., worse physical fitness) compared with the general population, particularly in aerobic, strength, and balance domains. There are not differences in body composition, although a large number of those with MS are overweight and obese. There is additional evidence that physiological deconditioning differs among persons with MS as a function of disability, such that persons with worse MS disability exhibit greater reductions in the physical fitness domains of aerobic capacity, muscle strength, and balance. The aforementioned evidence is consistent with our proposed model of physiological deconditioning developing in MS and progressing over time based on a comparison across disability levels [3,4].

Consequences of Physiological Deconditioning in MS

Another premise of this paper is that physiological deconditioning is associated with many of the consequences of MS. To that end, this section of this paper will describe evidence of associations among

Consequence/Outcome	n	Participant characteristics	Domain of deconditioning	Results
Brain Structure and Function				
Axonal and neuronal loss [34]	21	Age: 44.2 years (1.9 years) EDSS: 2.2 (range 0-6) Course: RRMS Duration: 7.3 years (0.1 years)	CRF	Worse CRF associated with reduced WM integrity, reduced GM volume, and higher lesion load
Mobility				
Walking and gait outcomes [41]	31	Age: 43.4 years (7.7 years) EDSS: not reported (PDDS: 2 (range 0-5)) Course: RRMS Duration: 8.6 years (6.3 years)	CRF Muscular Strength Balance	Worse CRF and worse lower limb strength asymmetries associated with slower T25FW performance, shorter 6MW distance, slower gait velocity, shorter step length, more time in double support
Cognition				
Cognitive processing speed [30]	31	Age: 43.4 years (7.7 years) EDSS: not reported (PDDS: 2 (range 0-5)) Course: RRMS Duration: 8.6 years (6.3 years)	CRF Muscular Strength Balance	Worse CRF, worse balance, and worse muscular strength asymmetries associated with slower CPS (PASAT, SDMT)
Fatigue				
Self-report fatigue [42]	25	Age: 36.9 years (9.5 years) EDSS: 4.4 (2.6) Course: Not reported Duration: 6.0 years (4.5 years)	CRF	Worse CRF associated with greater fatigue (Fatigue Severity Scale)

*Note: EDSS=Expanded Disability Status Scale; RRMS=Relapsing-remitting multiple sclerosis; CRF=Cardiorespiratory fitness; WM=white matter; GM=gray matter; PDDS=Patient-Determined Disease Steps; T25FW=Timed 25-Foot Walk; 6MW=Six-Minute Walk; CPS=Cognitive Processing Speed; PASAT=Paced Auditory Serial Addition Test; SDMT=Symbol Digit Modalities Test

Table 1: Summary of exemplar studies for consequences of physiological deconditioning in persons with multiple sclerosis.

aerobic capacity, muscle strength, balance, and body composition/morphology with brain structure/function, walking, cognitive, and fatigue outcomes in persons with MS. We selected these outcomes as there is existing research and because each represents a major and life-altering feature of MS. We have provided examples of exemplar studies on consequences of deconditioning in table 1.

Brain Structure and Function and Fitness Outcomes

Researchers have examined physical fitness variables and the association with brain structure and function based on Magnetic Resonance Imaging (MRI) in persons with MS, and this line of research was largely undertaken based on examinations of physical fitness and brain structure/function in the gerontology literature [31-33]. One study examined the associations between aerobic fitness levels (VO_{2peak}) and brain gray matter volume, white matter integrity, and lesion load in 21 persons with relapsing-remitting MS and minimal disability. The researchers reported that low aerobic fitness was associated with reduced structural integrity of white matter tracts in the left posterior thalamic radiation ($pr=0.40$) and the right anterior corona radiata ($pr=0.44$); reduced grey matter volume in the right post-central gyrus ($pr=0.45$) and midline cortical structures ($pr=0.45$); and higher lesion load volume ($pr=-0.44$) [34]. There is additional evidence that lower aerobic fitness levels (VO_{2peak}) were associated with less activation in the right inferior and middle frontal gyri ($pr=0.46$) and increased activation in the anterior cingulate cortex ($pr=-.44$) during performance of the Paced Visual Serial Addition Task (PVSAT) in 24 persons with relapsing-remitting MS who had minimal disability [35]. Other researchers have reported that muscle strength of the ankle dorsiflexors and hip flexors, assessed using a hand-held dynamometer, has been associated with brain imaging abnormalities along the intracranial corticospinal tract in 47 persons with moderate MS-related disability [36]. One study reported that larger postural sway amplitude (i.e., worse balance) was associated with reduced structural spinal cord integrity (i.e., cerebrospinal-fluid-normalized magnetization-transfer imaging) in 42 persons with MS who had moderate disability (mean EDSS=3.7) [37]. To date, there are no published studies examining the relationship between outcomes of morphological fitness and brain structure or function in persons with MS. Collectively, the existing research suggests that lower levels of aerobic fitness, muscle strength, and balance are associated with changes in brain structure and/or function in persons with MS.

Walking outcomes

Researchers have examined multiple domains of physical fitness as correlates of walking outcomes in persons with MS. For example, one study of 24 persons with mild MS examined the association between O_2 cost of walking (i.e., a physiological marker that reflects submaximal aerobic efficiency) and self-reported walking impairment based on Multiple Sclerosis Walking Scale-12 (MSWS-12) scores [38]. O_2 cost of walking under comfortable, fast, and slow walking speeds demonstrated moderate-to-large correlations with MSWS-12 scores (r^2 's=0.62-0.64) such that greater O_2 cost of walking was associated with worse perceived walking performance and quality [38]. Another study reported that persons with mild MS-related disability who had a higher O_2 cost of walking took slower ($r=-0.25$) and shorter ($r=-0.32$) steps, while spending a greater percentage of time in double support ($r=0.27$), based on measurements from a GaitRite electronic walkway during comfortable walking pace [39]. Other studies have reported that lesser peak isometric torque and greater torque asymmetries were associated with worse timed 25-foot walking (T25FW) performance in MS [20,21]. One study examined the association of peak torque in

knee flexors and extensors with 2-minute walk test (2MWT) distance in 52 persons with mild and moderate MS disability. Peak torque was measured with a Biodex isokinetic dynamometer, and peak torque of both knee extensors and flexors was moderately associated with 2MWT distance in the mild disability group (r^2 's=0.43-0.50), whereas only peak torque of knee flexors was associated with 2MWT distance in the moderate disability group (r^2 's=0.59-0.70). There is some evidence that balance, measured by static posturography, is associated with walking performance in persons with MS, as one study of 12 women with MS reported that greater antero-posterior COP sway (i.e., worse static balance) was moderately associated with slower walking speed (r^2 's=0.47-0.55) [21]. There is evidence that body composition is associated with walking performance in MS. One study classified 168 ambulatory persons with MS as normal, overweight, or obese, based on BMI, and compared the groups on multiple walking outcomes. Obese persons with MS had slower T25FW performance, shorter six-minute walk (6MW) distance, and took fewer steps per day under free-living conditions with these effects being small in magnitude (d 's=0.27-0.29) [40].

One recent study involved a comprehensive examination of the associations among aerobic capacity, balance, and lower limb strength asymmetries with walking performance (i.e., T25FW performance and 6MW distance) and spatiotemporal parameters of gait (i.e., velocity, cadence, step length, base of support, and time spent in double support) in 31 persons with MS and 31 controls matched by age, sex, height, and weight [41]. Regression analyses indicated that worse aerobic capacity and greater lower limb strength asymmetries independently explained variance in worse T25FW performance ($R^2=0.44$), shorter 6MW distance ($R^2=0.58$), slower gait velocity ($R^2=0.32$), shorter step length ($R^2=0.41$), and more time spent in double support ($R^2=0.32$) in persons with MS [41]. Interestingly, balance did not explain significant variance in any mobility outcome, however, in this study, worse balance was correlated with slower T25FW performance ($r=0.35$) and shorter 6MW distance ($r=0.32$), though these correlation coefficients were small in magnitude. Collectively, such evidence suggests that reduced aerobic fitness, muscular strength, worse balance, and poor body composition are associated with worse walking performance, across a variety of outcomes.

Cognitive outcomes

There are a limited number of studies examining associations among domains of physical fitness and cognitive outcomes in MS, with the majority of studies focusing on cardiorespiratory fitness and Cognitive Processing Speed (CPS). For example, one study included 24 persons with relapsing-remitting MS and reported that worse cardiorespiratory fitness was associated with worse performance on the Paced Serial Auditory Addition Test (PASAT) [35]. However, worse cardiorespiratory fitness was not significantly associated with performance on the selective reminding task ($pr=-0.22$) or the spatial reminding task ($pr=-0.12$), measures of verbal and visuospatial learning, respectively [35]. Another study reported that worse cardiorespiratory fitness was associated with worse scores on a composite measure of CPS in persons with MS and healthy controls [34]. One study recently examined the relationships among multiple domains of physical fitness (e.g., cardiorespiratory fitness, muscle strength asymmetry, and balance) and CPS in 31 persons with MS and 31 controls matched by age, sex, height, and weight [30]. In the MS subsample, worse aerobic capacity ($r=0.44$), worse balance ($r=-0.52$), and greater knee extensor asymmetry ($r=-0.39$) were significantly associated with slowed CPS, accounted for differences in CPS between persons with MS and controls, and explained a statistically significant

amount of variance in CPS ($R^2=0.39$) in the MS subsample [30]. We are unaware of research that has directly examined associations among domains of physical deconditioning with other domains of cognition that are impaired in MS (e.g., executive control). We are further not aware of published studies on the associations of measures of body composition and cognitive performance in this population.

Fatigue

There is some evidence to suggest a relationship between physiological deconditioning and symptomatic fatigue in persons with MS; very little is known about fitness levels and other symptoms of MS. In a sample of 25 persons with MS (mean EDSS=4.38), aerobic capacity (VO_{2peak}) determined on an arm-crank ergometer was significantly, strongly, and negatively correlated with fatigue assessed using the Fatigue Severity Scale (FSS; $r=-0.70$) [42]. Submaximal aerobic efficiency, or the O_2 cost of walking, was significantly correlated with scores on the FSS ($r=0.31$) in a sample of 44 persons with MS with minimal disability (median PDDS score=1) [39], suggesting that increased energetic demands of movement are associated with worse symptomatic fatigue. With respect to muscular strength, knee extensor power asymmetry (i.e., the relative difference in strength between muscles on opposite sides of the body) measured on a seated dynamometer has correlated significantly with symptomatic fatigue assessed using the FSS ($r=0.50$) and the Visual Analog Fatigue Scale ($r=0.67$) in 12 women with moderate MS (mean EDSS=4.0) [21]. Balance impairment assessed using dynamic posturography was significantly associated with symptoms of fatigue assessed using the Modified Fatigue Impact Scale ($r=-0.78$) in a sample of 17 ambulatory individuals with MS [43]. Individuals in this study with cerebellar and brainstem involvement, determined by a clinical neurological exam, presented with greater concurrent balance impairment and symptomatic fatigue compared to those who did not present with involvement of these systems. This suggests impaired balance is associated with symptomatic fatigue in MS, and this association may differ depending on neurological system involvement. There is evidence for an association between morphological fitness, assessed as BMI, and symptomatic fatigue in MS. In a sample of 53 participants with moderate MS (mean EDSS=3.4), a higher BMI was associated with higher scores on the Multidimensional Fatigue Symptom Inventory physical fatigue subscale ($r=0.36$) [44]. Collectively, the existing research suggests physiological deconditioning in multiple domains might be related with more frequent and severe symptoms of fatigue in persons with MS.

Exercise Training and Its Influence on Physical Fitness in MS

We have documented that persons with MS demonstrate significant deconditioning that worsens with disability accumulation over time, and this deconditioning is associated with a variety of outcomes ranging from brain structure/function through symptomatic expression of fatigue. Such results highlight the consideration of approaches for prevention of deconditioning as a way of forestalling other consequences and breaking the cycle in figure 1. The third premise of this paper, therefore, is that it conceptualizes the importance of maintaining and improving physical fitness levels for persons with MS. To that end, exercise training may be a way of addressing physiological deconditioning in persons with MS, and improvements in physical fitness may, in turn, result in secondary benefits.

There are over 60 studies that have examined the effect of exercise training in persons with MS [45], and there is evidence for

concurrent improvements in physical fitness along with functional and symptomatic outcomes in many of those studies. Aerobic and combined aerobic and resistance training interventions have improved cardiorespiratory fitness along with beneficial changes in walking performance [46,47], spatiotemporal gait parameters [48], and symptomatic fatigue [46,47,49-51] in persons with MS. For example, 8 weeks (3x/week) of moderate intensity leg cycling resulted in a significant increase in VO_{2peak} measured on a leg cycle ergometer, 6MW distance, and self-reported energy levels in 11 persons with MS who had moderate disability (mean EDSS=3.5) [46]. Exercise training interventions that primarily involved resistance training have improved muscular fitness, as well as walking performance [52-56], and symptomatic fatigue [49,51,55,57] in persons with MS. For example, significant improvements in knee flexor peak torque measured on a seated dynamometer, and T25FW and 500 MW performance were observed following 26 weeks of resistance (4x/week) and aerobic training (1x/week) in 91 persons with MS who had a range of disability (EDSS range=1-5.5) [16]. There are some data suggesting that exercise training influences balance and body fatness as indicators of motor and morphological domains of fitness, and such changes have occurred along with improvements in walking and fatigue outcomes [49,58-60]. Collectively, such research is suggestive that exercise training can improve components of physical fitness in MS and that such improvements often correspond with changes in walking and fatigue outcomes.

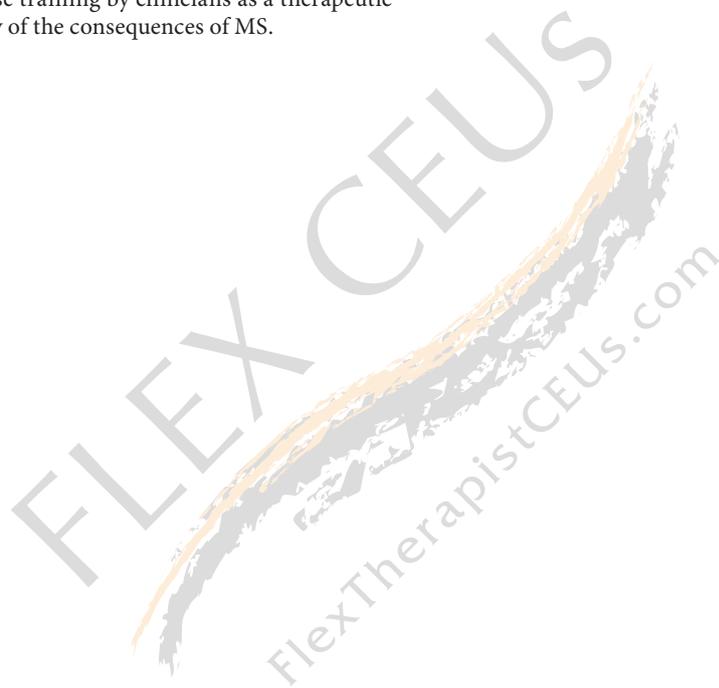
To date, no studies have directly examined improvements in physical fitness as direct mediators (i.e., variables that complete the causal link between variables) of the effect of exercise training on changes in secondary outcomes. This limits the ability to draw causal conclusions regarding the importance of counteracting physiological deconditioning in persons with MS. We are aware of two studies that reported associations between improvements in physical fitness and secondary outcomes following exercise training. For example, 15 weeks of aerobic exercise training based on arm and leg cycling training (3x/week) resulted in a 21% improvement in VO_{2peak} , and the improvement in cardiorespiratory fitness was significantly correlated with a reduction in symptomatic fatigue ($r=-0.68$) in 46 persons with moderate MS (mean EDSS=3.8) [49]. Another study reported that improvements in maximal voluntary contraction of the knee extensors measured on a seated dynamometer were significantly correlated ($r=0.26-0.43$) with improvements in lower extremity function including 6 MW and 10 MW performance following 12 weeks (2x/week) of progressive lower extremity resistance training in 31 people with MS [52]. Such evidence provides an important first step in establishing the relationship between changes in fitness outcomes with exercise training and the consequences of improving physical fitness in MS. The next step will be to establish a causal role for physical fitness in improving secondary outcomes that are important in persons with MS as is currently underway [61].

Conclusion

We provide a framework for the importance of maintaining and improving physical fitness in persons with MS as well as a comprehensive review of research on physiological deconditioning in cardiorespiratory, muscular, motor, and morphological domains among those with MS. There further is substantial evidence for associations between physiological deconditioning and a variety of consequences of MS, emphasizing the importance of counteracting and maintaining all domains of physical fitness. Exercise training may be an effective approach for improving physical fitness and managing secondary consequences among persons with MS. Importantly, the

evidence we present herein did not follow the guidelines of a systematic literature review, and we might have missed important articles on the topic of deconditioning and its consequences in MS.

Importantly, researchers have recently undertaken a systematic review of the effects of exercise training in MS [62] to develop evidence-based physical activity guidelines [63]. Based on the review, adults with MS should participate in 2 weekly sessions of 30 minutes of aerobic activity and 2 weekly session of strength training to improve aerobic capacity and muscular fitness, respectively. The amount of literature did not make it possible to identify the prescription necessary for improving other physical fitness outcomes, including balance and body composition. We believe that future research should examine the veracity of these prescriptive guidelines for improving physical fitness along with secondary outcomes in those with MS. We further believe that these guidelines provide an important basis for the prescription of exercise training by clinicians as a therapeutic approach for managing many of the consequences of MS.



Evidence Based Therapeutic Exercise Recommendations for Patients with Multiple Sclerosis: A Physical Therapy Approach

Abstract

Multiple Sclerosis (MS) is a chronic demyelinating disease of the central nervous system affecting over a million people worldwide. The demyelinating process begins when inflammatory T cells of the immune system attack the oligodendrocytes after infiltrating the blood-brain barrier, creating a cascade effect of neurological symptoms. MS presents itself through physical symptoms including fatigue, depressed mood and motor deficits. Current research has shown promise in using exercise intervention to curb the symptoms of this autoimmune disease.

This brief review evaluated studies that utilized exercise to decrease fatigue, improve quality of life (QoL), and improve ability to perform activities of daily living. Assessments utilized to examine efficacy of exercise include the Fatigue Severity Scale, Multidimensional Fatigue Inventory-20, and the Major Depression Inventory. These tests provide both an objective and subjective view of the MS disease process.

The purpose of this review is to provide information related to resistance exercise recommendations for physical therapists to use as a guide when prescribing exercise interventions to patients with MS. The training program aims to reduce mobility related impairments, decrease fatigue and improve QoL in individuals with MS. After review of this article the reader should ascertain a newfound comfort and knowledge for delivering progressive resistance training to persons with MS. This guide provides both novice and intermediate-advanced recommendations for exercise.

The exercise recommendations are indicated for patients with less than or equal to a 6.0 on the Expanded Disability Status Scale. MS patients should consult a physician before actively engaging in any exercise program.

Keywords: Multiple sclerosis; Patients

Introduction

Multiple Sclerosis (MS) is a neurological disease that presently affects over one million people in the world making it among the most common neurological diseases. Perhaps more concerning is that the incidence is growing [1,2]. MS is a degenerative autoimmune disease in which damage to the myelin sheath in the central nervous system (CNS) leads to a cascade of neurological effects [1,3-6].

Patients with MS either experience progressively worsening symptoms or they experience relapses [7]. Relapses are points in time when patient's symptoms become worse. A remission or recovery period follows the relapse and is characterized by symptom withdrawal and/or complete recovery. However, with any type of MS, as the patient ages the symptoms become harder to manage and the exacerbations become more severe [8]. Currently there is no cure for the disease.

Multiple Sclerosis presents with symptoms including, but not limited to: pain, fatigue, weakness, and altered coordination [9,10]. Symptoms related to mobility have been found to be severely debilitating. Symptoms are often managed with various pharmacological interventions [10,11]. Past recommendations suggest that any exercise could elicit symptoms of a relapse. However, patients with MS who have added aerobic and anaerobic routines have had positive outcomes in quality of life [2]. Considering that patients with MS typically are less active due to their fatigue, their subjective ratings of fatigue tend to be higher, in adjunct with lower QOL and IADL scores.

Currently, there is need for resistive exercise training recommendations for patients with relapsing remitting MS due to the dearth of literature. It is well known that exercise not only improves the psychosocial well-being of the healthy patient, but their overall muscular fitness [12]. It is also shown that exercise can have the same beneficial effects for the MS population including an overall reduction of fatigue, psychosocial benefits, and improved cardiovascular and muscular fitness pertaining to strength and endurance [5,7,12-15].

Our knowledge of cost dictates that it is cheaper to treat a patient on an outpatient basis than during an inpatient acute relapse [16]. Durable medical equipment, pharmacological interventions and in-hospital related cost can potentially be decreased with an exercise prescription that decreases fatigue, increases strength and improves QOL.

Pathophysiology

Multiple Sclerosis (MS) is a degenerative neurological disease affecting the central nervous system. The etiology of MS is believed to be both environmental and genetic [3]. A person with a family history of MS is more likely to develop the disease than someone without a family history. This disease specifically affects white matter in the central nervous system leading to degradation of the myelin surrounding nerves, especially the oligodendrocytes [3].

Patients with relapsing-remitting MS go through periods of exacerbations when their neurological symptoms worsen from days to several weeks due to inflammation and demyelination followed by time during which some of the myelin is replaced [3]. However, the myelin that is replaced is not as thick and there are more nodes of Ranvier [4]. It is known that lymphocytes in the periphery are activated which then penetrate the blood brain barrier and attack the body's own myelin sheath [2].

It is believed that auto-reactive T cells are the cause of the inflammation and demyelination. Studies show that patients with MS and healthy patients have the same number of T cells (CD4+ and CD8+), however the cells differ in activity. The T cells in patients with MS have an active phenotype and the T cells in the healthy population have a phenotype with no memory. In patients with MS the myelin specific T cells produce cytokines such as interferon- γ which are suggested to cause inflammation. Cytokines cause many T cells to evolve into inflammatory Th1 (type 1 helper T cells) lymphocytes rather than the Th2 anti-inflammatory lymphocytes which are seen in the healthy population. The inflammatory Th1 lymphocytes attack the body's myelin sheath in the central nervous system [1]. This process draws macrophages and granulocytes to the area to further mediate the inflammatory process [2].

The purpose of the myelin sheath is to increase conduction velocity along the white matter tracts, called axons, as well as to increase the capacity for action potentials. Nodes of Ranvier exist between sections of myelinated axon to increase the speed of the action potential, however the node can only be so wide before the action potential is unable to cross the node. Demyelination begins at the Node of Ranvier making these gaps wider. This decreases the current that is available for the nerve to depolarize, thus affecting muscular action. This process causes slow conduction speeds and conduction block [2]. As the myelin deteriorates some re-myelination occurs. However, much of the myelin it is replaced by scar tissue, referred to as plaque, which further interrupts the conduction of the nerve.

In patients with multiple sclerosis the slowed conduction speed presents as awkward or uncoordinated movements [1]. Due to the demyelination of patients with MS, a lower tetanic and twitch tension are realized along with greater fatigue during stimulated contractions [17]. To produce the same amount of force as a healthy person, patients with MS need to recruit more motor units per contraction. This could lead to the peripheral fatigue in patients with MS due to increased work [2]. Weakness and atrophy contribute to a decline in mitochondria concentration in contractile units [17]. This explains the importance of incorporating a strengthening program into the MS patient's multidisciplinary treatment plans. Strengthening muscles that still have strong innervation will help compensate for the weaker or denervated muscle groups. This will improve baseline strength and function, and expedite recovery after exacerbations. Treatment should focus on coordination, balance, strength and functional rehabilitation.

Another factor that can increase the symptoms of MS is core temperature. MS patients have difficulty regulating their autonomic nervous system; therefore they have difficulty regulating their core temperature. An increase of at least 0.5 degrees Celsius will slow and ultimately block nerve impulse conduction in demyelinated fibers. This results in a temporary increase in neurological symptoms that can worsen fatigue and prevent the patients from being able to perform their ADLs [2]. When treating patients with MS it is important to incorporate a work to rest ratio that is patient specific to avoid overheating. One suggestion to incorporate this into a training program is to break up aerobic exercise. For example: if the patient wishes to do 20 to 30 minutes of aerobic exercise, they can do 2 periods of 10-15 minutes with a rest period of 10 to 15 minutes. Patients can be monitored with the RPE scale and should not exceed a moderate intensity for aerobic exercise, corresponding to 11-14 on the Borg Scale of Perceived Exertion [18]. When performing resistance training it is important to take breaks between each set and allow the patient to fully recover before moving on. This will significantly lengthen treatment times and there may not be time to do as many exercises per treatment. Therapists should plan

their treatments prior to patient contact, choosing resistance exercises that will yield the best results. Therapists need to account for work to rest ratios and any necessary reassessment before progressing exercise.

There are still many unanswered questions regarding the pathology of multiple sclerosis. However, it is clear that the neuronal damage significantly effects patient's strength, energy level and motor control. High intensity resistance training may play a pivotal role in maintaining functional capacity and improved quality of life.

Epidemiology

Over 350,000 people in the United States have been diagnosed with multiple sclerosis and it is estimated that 1,080,000 people worldwide have the disease [2]. Petajan and White reported that in 1999 approximately 8,000 new cases of MS were diagnosed per year in the United States. An article by Rumrill in 2009 indicates approximately 10,000 new cases of MS are diagnosed each year [1,2]. This shows an increased incidence of MS within the past decade, leading to higher health care cost associated with this disease. The incidence of this disease is much greater in temperate zones, and in areas of higher latitude. Areas closer to the equator have very little incidence of MS [2].

MS is typically diagnosed between the ages of 20 and 40, but most often before the age of 30. MS is occasionally diagnosed in children and the elderly. MS is three times more prevalent in women than in men [1,3,19]. MS is uncommon among African Americans and rarely seen in the Asian population. Those of German, Anglo Saxon, and Scandinavian decent have an increased prevalence of MS [1].

80% of people that are diagnosed with MS have a subtype called relapsing-remitting multiple sclerosis. This subtype is defined by periods of exacerbations of worsening neurological symptoms which can last for up to two months. Symptoms then fade or are completely relieved [20].

Cost

Cost associated with the treatment of MS is an important factor in the treatment regime of the health care team. It is imperative to have rationale for treatment when billing payers. Cost can be considered either direct or indirect, while direct cost refers to resources consumed by MS interventions, and indirect cost correlates to productivity and functional loss. Also, with an estimated 1,080,000 people in the United States that have MS, much of our health care spending is devoted to these patients [2]. Cost associated with an inpatient hospital stay due to a relapse is six times greater than treatment on an outpatient basis [16]. Patients with MS require multiple medical services and as of 2007 the greatest amount has been spent on drugs, hospitalization and other direct costs such as equipment for their disability and nursing services [1]. It costs nearly 50,000 dollars per patient with multiple sclerosis to be treated annually. On average over 3 million dollars are spent on each patient throughout their lifetime [6].

By improving physical therapy services and inevitably improving their quality of life through exercise, we can potentially decrease some of the cost for drugs, hospitalization and equipment. For example, if we can improve or maintain strength, the person is less likely to need a wheelchair and can better perform their work.

Anti-depression and anti-anxiety medications are widely used by patients with MS. If the health care team can make these patients more mobile and able to complete their activities of daily living, they will be less likely to suffer from anxiety or depression. Exercise and functional training should eradicate the need for these medications. Improving the

quality of physical therapy services for MS patients can reduce health care spending for patients with MS.

History of exercise training for patients with multiple sclerosis

Resistance training has often been avoided in patients with multiple sclerosis because it often initiates an immediate increase in neurological symptoms. However, this increase in symptoms, which appears in approximately 40% of patients, is shown to last only half an hour post-training [21]. There remains a necessity to educate the patients and the health care team about this ephemeral increase in symptoms due to exercise, and that there are no lasting consequences related to relapse. The long term benefits of a comprehensive treatment program outweigh the short term fatigue and increase in symptoms. Resistance training however, is not for patients who have recently experienced an acute exacerbation (see Appendix-B).

Most successful studies have involved subjects that have been in remission for at least 8 weeks [22]. Most studies with successful outcomes used a 2-4 minute rest period between sets of resistive exercise to avoid adverse effects [21]. For many years it was idealized that an increase in core body temperature caused symptom instability in the MS population, thus physical activity beyond ADLs was not advised. Also, by foregoing exercise, these patients were thought to conserve energy for ADLs [23]. To help prevent an exacerbation of symptoms due to an increase in core temperature, room temperature should be set lower than usual, careful attention should be paid to the work: rest ratio, cool garments should be worn when possible- and patients should be well hydrated throughout exercise [2]. It can help if patients take a cool bath or shower prior to exercise [24].

The benefits of resistance exercise include muscle hypertrophy, improved cardiovascular and respiratory fitness, increased arousal, improved mood and reduced fatigue [25]. Past exercise routines have included a "muscular fitness pyramid" moving up from the base of passive range of motion to active flexibility, then resistive exercise, and lastly a specific muscle strengthening and integrated strength grading program. Tai Chi and yoga have been found useful in flexibility- and body weight exercises have been shown to strengthen patients who are physically able.

Aquatic programs, endurance training and resistance exercise using high reps and low to moderate exertion have been a traditional therapeutic exercise approach to care for MS patients [2]. There is limited access to exercise recommendations involving progressive resistance training for MS. It has been shown in a study by Kraft et al. that progressive resistance training improves patient's ability to perform activities of daily living and improves their overall mood and health [26]. In addition former exercise programs focused on lower extremity training [27]. Rather than challenging the potential of MS patients, rehab specialists have stopped progressing MS patients before they have reached their maximal exertion.

Effects of Resistance Training on Type II Muscle Training vs. Type I Muscle Training

Muscles are made up of different percentages of fiber types. Type I or slow twitch fibers and are highly oxidative with the greatest amounts of mitochondria. They are highly resistant to fatigue and have a slow velocity of shortening. Type II fibers are divided into subtypes. Type IIa muscle fibers are less oxidative than type I fibers, and are considered highly anaerobic. They fatigue more quickly than type I fibers and have a higher velocity of shortening. Type IIb fibers are the fastest to fatigue but

can produce the greatest force and velocity of shortening. Type IIx is found to be an intermediate fiber type between type IIa and type IIb [28].

Type I and type II muscle fiber diameter and mass is decreased in patients with multiple sclerosis. In a study by Kent-Braun JA et al., it has been shown that there is greater atrophy in type II fibers vs. type I fibers in patients with MS [17]. The combination of decreased strenuous activity and past suggestions to only participate in low intensity activity propagate muscle atrophy in the MS population. This phenomenon combined with decreased strenuous activity is likely to be reason for muscle atrophy in patients with MS. Allowing type II fibers to atrophy can lead to difficulty performing activities of daily living, reinforcing the necessity of a resistance strengthening program [29].

Adequate intensity should be considered when prescribing a resistance training program for patients with MS. Intensity can be described in terms of a percentage of age predicted maximal heart rate (APMHR) [22]. It is important to understand that people with MS may have a decreased average maximal heart rate compared to a healthy person. One study showed that with cycle ergometry peak heart rate was 10 less beats per minute than the age predicted estimate [30]. To measure intensity objectively, the health care professional can use a HR monitor to track the patient's performance over time. The patient can also report their perceived intensity subjectively using the Borg scale of rate of perceived exertion (RPE). A score of 11-14 on the Borg Scale of Perceived Exertion is considered moderate intensity training [27].

"Henneman's size principal" indicates that larger motor neurons innervate type II muscle fibers and are activated with moderate to high intensity exercise. In MS patients the larger motor neurons are not triggered as often since they do not typically engage in moderate to high intensity exercise or activity. In one study by Dugas et al., it was shown that resistance training increased type II muscle fiber cross sectional area. Isokinetic muscle strength was improved especially in fast muscle contractions. For example, there was a significant increase in the knee extensor group with fast contractions at 180 degrees per second, and in the knee flexor group with fast and slow contractions at 180 and 90 degrees per second, respectively [31].

In a study by Bacou et al., who denervated fast and slow twitch muscles in rabbits, it was found that type IIb muscle fibers were the most affected by neural influence. After 5 months of denervation, muscles with 70% type IIb fibers and 22% type IIx/d converted to 2% type IIb fibers and 98% type IIx/d fibers. Muscles consisting of type I fibers only, were hardly affected by denervation with respect to fiber numbers and size [Bacou]. Therefore it is important to train type II muscle fibers in patients with neurological disorders considering anaerobic fibers are most affected by neural degeneration. If the integrity of these fibers is maintained or even improved, MS patients should experience less fatigue with activity.

Additionally, women have a smaller cross sectional area of all fiber types, especially type II. This is true for both the healthy population and people with multiple sclerosis. Since MS primarily affects women, type II fibers need to be targeted during exercise to maintain strength. Another factor affecting type II muscle fibers is age. It has been shown that type II muscle fibers are more affected by aging than type I fibers [32,33]. Skeletal muscle high in type II muscle fibers showed a decrease in size and number of type II muscle fibers with aging [29]. This study shows that age further deteriorates the MS patient's ability to perform quick muscle contractions which are needed daily to perform activities required for their role in society.

Age is an additional factor leading to decreased strength. A review

by Faulkner et al., shows that muscle mass, and resultant strength and power, gradually decline starting as early as age 40. This is known widely as sarcopenia- and is caused by the cross sectional area of type II muscle fibers decreasing with age. Type I fibers tend to maintain their cross sectional area [34]. The normal decline in power with age, in combination with the neurological effects of MS accentuates the severe motor deficits seen in the MS population. Resistance training can help reduce the functional deficits resultant from weakness from the aging and disease process.

Resistance Training in Patients with Multiple Sclerosis

Since type II muscle fibers are more affected by multiple sclerosis and aging, it is important to perform resistance training to hypertrophy the tissue. These muscles need to be able to produce the adequate fast contractions that MS patients need in order to independently perform activities of daily living.

The goals of resistance training are: to increase cardiorespiratory fitness, strength and endurance, reduce fatigue, improve ability to perform ADLs, improve mood and better the quality of life. Resistance training reduces the risk of obesity, vascular disease, heart disease and individual propensity to osteopenia. Failure to perform resistance exercise leads to decreased bone strength, an increase risk of fracture, decreased breathing efficacy and a greater amount of fatigue [25].

Although there are barriers to resistance training such as spasticity, tone, fatigue and ataxia, it is important to perform resistance training specifically to meet the needs of each patient [35]. Exercise should be planned to avoid overheating for MS patients. Some things that the therapist can do include turning down the temperature in the room and giving the patient frequent breaks. Research suggests 2-3 min rest between sets during resistance bouts [12,15,31].

To cool core body temperature before resistance exercise patients can take a cold bath for half an hour. This will allow for approximately 40 minutes of sustained exercise without significant increase in core temperature [24]. Patients can also use cryotherapy during a session of resistance training on body parts that are not being exercised [2]. In addition to resistance training, therapists should include stretching and tone reduction techniques in their treatments such as rhythmic rotation and sustained deep pressure.

One study by Dalgas U, et al. showed that biweekly progressive resistance training in MS patients leads to an increase in type II fiber cross sectional area without any deviation from the original fiber proportions in respect to fiber number [21,31]. This shows that the individual type II muscle fibers increased in diameter. Other populations with weakness have showed improvements with a resistive training regime. These populations include arthritis patients, nursing home residents and life care community residents [2]. After several months of training it is possible for all patients to reach a plateau [2]. The resistance training program should be progressed to provide a continuous overload by adding new exercises to target neglected muscle groups.

Not only has resistance training been shown to increase muscle volume and strength in patients with MS, but studies show that it improves the quality of functional activities such as gait. A study by Gutierrez GM, et al. showed that after 2 months of resistance training in patients with MS their gait was improved. Specifically, patients demonstrated a longer swing phase (less time spent in double limb support), longer step and stride length and better toe clearance. Also, a decrease in the amount of fatigue was reported by the patients in this study [13]. In addition, one study showed that knee extensor and flexor

strength is an important indicator for ambulation. It shows that people with improved knee extensor and flexor strength have more advanced gait. This implies the necessity for strength training of the quadriceps and hamstrings [36,37].

In a study by Gehlsen GM, et al. patients performed an aquatic exercise program working up to 75% of their maximal heart rate. Results from the study showed that these patients had improved muscle strength and endurance in the upper and lower extremities. Specifically, upper extremity arm power was increased and fatigue was reduced after performance of lower extremity exercise [14]. Decreased fatigue with daily activities will lead to improved mood and greater ability to be a part of larger social groups.

A study by Kraft GH, et al. found that after progressive resistance exercise three times a week for twelve weeks comparing mild to severely impaired MS patients that walking, climbing, and chair mobility all improved as a measure of function in both groups. Improved ability to perform these activities results in increased participation in society and improved quality of life. Studies also reported that there were no sustained increases in neurological symptoms during progressive resistance training trial periods [34].

Psychosocial Benefits of Exercise

Among psychosocial aspects of this disease condition, fatigue is considered the most limiting to a patient's daily activities. The Social Security Administration recognizes fatigue as a criterion for MS disability. 67% of MS patients reported fatigue as limiting their social and occupational responsibilities; healthy adults had null reports in comparison [38]. Fatigue and depression have a high correlation of coexistence in the MS population [39]. MS patients have less of a tolerance for exercise, ADLs, social activities etc. all contributing to a decreased quality of life. As their motivation to exercise declines, their strength decreases contributing to a deconditioned state that continues its morbid cycle over time.

Patients with MS were previously discouraged to exercise, leading to a decrease in baseline ability and social capacity, further implicating depression.

Physical therapy exercise recommendations for individuals with multiple sclerosis

When treating patients with multiple sclerosis a thorough assessment should be performed prior to intervention. This assessment should be inclusive of the Expanded Disability Severity Scale (EDSS) and the Fatigue Severity Scale (FSS). The design of this protocol is targeted for MS patients who are still ambulatory, and score equal to or less than a 6.0 on the EDSS. Each patient presents differently with the disease and it is important to know what the patient is capable of doing and where they need strengthening. A baseline assessment and a reassessment after every four to five treatments are crucial to goal setting and objective outcome measurements. Exercises should be targeted to improve the patient's ability to proficiently perform ADLs and social responsibilities.

The prescribed exercises aim to strengthen and decrease fatigue so that the patients can participate in recreational activities and enhance their quality of life. Fatigue and depression decrease the patient's activity levels, leading to deconditioning over time. As clinicians it is important to consider psychosocial factors such as depression, difficulty with sleeping, and decreased motivation when prescribing an exercise regimen [39]. Patient education is crucial, along with reassurance of the benefits of exercise. Guidance should be provided by

the rehab team to resolve psychosocial matters. In addition, clinicians need to be sure to recognize any contraindications and precautions to treatment, which defines common precautions or contraindications to the MS population. This chart is not all inclusive; be aware of any other contraindications or precautions to exercise pertaining to your specific patient.

The American College of Sports Medicine recommends that resistance exercises should be done two to three times per week [11]. The first to occur are physiological in nature and are the result of neurological adaptation. More rapid changes may be seen initially, with a decrease in the speed of results as they progress with the program.

To determine the amount of weight for each exercise a one repetition maximum (1RM) needs to be calculated. This is calculated using the following formula:

$1RM = (0.03 \times \text{repetitions} \times \text{weight (lbs)}) + \text{weight (lbs)}$. Prior to finding the 1RM, manual muscle tests should be performed to obtain a baseline strength measurement. To further evaluate their capacity a thorough history of functional and recreational activity should be taken into account when choosing a starting weight.

Repetitions represent the frequency of the exercise and the number of sets represents the duration of the exercise. Once a full evaluation and 1RM are assessed, the patient is ready to begin exercise training. Exercise should begin the second session. During the next session, when exercise training begins, the weight for each exercise should be set at 60-70% of the patient's 1RM for the muscle groups being trained. At this weight the patient should be able to perform approximately 10-12 repetitions. Once the patient can perform 15 repetitions with correct posture at this weight, the weight should be increased to by 2-5% of what they were previously lifting. If the patient can perform up to 15 repetitions with correct posture at the new weight, this patient needs to be reevaluated for their 1RM. Prior studies that have used a 2-3 minute rest period between sets have had successful outcomes with no adverse effects from exercise [12,15,31].

Task Specific Strength Training

Task specific training is exercise designed to directly improve a specific task that a patient has difficulty performing. Research shows that doing parts of the task in isolation to strengthen movements that are weak or uncoordinated, followed by practicing the complete sequence of movements involved in the task is more beneficial than strengthening alone. When muscles are trained in the correct position and sequence of the task that needs improvement, patients have more successful goal related outcomes [34,40,41]. An example of training in the correct position with the correct sequence would be squats to improve sit to stand.

Prior to focusing on task specific training it is important to determine where to focus interventions. Functional assessments such as the Dynamic Gait Index, Functional Independence Measure, Timed up and Go, 6 minute walk, and Berg Balance Test will objectively measure functional activity. These tests can also be used to document functional outcomes. Once deciding what area of function is most important to focus on, the physical therapist should incorporate task specific training. When prescribing exercise to patients with multiple sclerosis, strengthening should be followed by an activity that targets patient-specific goals [42].

When doing task specific training, movements should be practiced repeatedly and positive reinforcement from the therapist should be used. Tasks can be progressed from blocked practice, doing the task

the same way multiple times, to performing the task in a randomized fashion in varying conditions [34]. To avoid fatigue, strength training should last no longer than 45 minutes to an hour with periods of rest incorporated. Resistance training should be followed by 10 minutes of task specific strength training. This functional training can include tasks such as gait training on uneven surfaces, stair climbing, swimming, or other tasks that are important to the patient.

Conclusion

It is important for clinicians to realize that Appendix A is a suggested protocol for exercise and that this study is a review of literature, not a randomized controlled trial. Therefore, it is important to realize any contraindications and precautions to exercise especially in this population. Recent research shows statistically significant gains in functional ability when exercising patients with MS whose EDSS score is less than 6.0. Those patients whose EDSS score is more than 6.0 should be carefully monitored when performing any resistance exercise. This study shows no conclusions pertaining to the benefits of exercise for the severely disabled- due to the inability exercise these patients at a moderate intensity.

Clinicians are reminded to prioritize the safety of their patients, as well as to closely monitor their symptoms before and after exercise. Physical therapists should establish short and long term exercise goals with their patients, and ensure patient adherence through verbal contract. The patient is more likely to experience psychosocial gain if they can achieve mini-milestones during rehabilitation. It is necessary for the clinician to educate patients of the benefit of resistance training and its positive effect on fatigue. It is important for the patient to draw correlate to an improvement in all aspects of fatigue and a better quality of life.

In order for health care providers to decrease cost, a thorough assessment of the literature is always recommended when working with special populations. In particular, keeping the cost of inpatient relapse stays down can reduce the total expenditure per capita in this population. This review provides exercise guidelines to follow in order to improve baseline function of the individual in order to decrease the demand for further specialty care.

People with Multiple Sclerosis (MS) Improve in Measures of Health and Function after Participation in a Community-based Exercise Program

Abstract

Objective: Exercise is safe for people with Multiple Sclerosis (MS) and is necessary to combat the secondary deconditioning resulting from MS-related weakness and fatigue. People with MS often encounter barriers to exercise, such as inaccessible facilities/equipment, lack of proper guidance, and limited finances. This study examined outcomes in nine people with MS who participated in an outpatient exercise program designed specifically for people with MS.

Design: The program was designed in part based on input from a focus group of participants with MS. Group exercise and education classes were coordinated by a physical therapist and an exercise specialist. Specific exercises were chosen for each individual based on their impairments and ability. Outcome measures collected before, and 3 and 6 months after, program initiation assessed cardiorespiratory function, weight and body mass index, metabolic function, functional strength and quality of life.

Results: Participants demonstrated improvements to varying degrees in all outcomes.

Conclusions: A semi-individualized, group exercise program may provide people with MS an alternative feasible and viable method for exercising in an outpatient setting. Further research is necessary to determine the combination of exercise and educational variables that will lead to the most efficacious outcomes for any given individual with MS.

Keywords: Exercise; Fitness; Multiple sclerosis; Wellness

Introduction

The phrase “exercise is medicine” has recently come to the forefront of the exercise physiology field, in recognition of the fact that exercise can ameliorate or reverse many of the most common causes of disease and disability [1,2]. Although current evidence suggests that regular exercise for people with Multiple Sclerosis (MS) is safe, [3-8] there remain several barriers to exercise participation. Symptoms of MS, as well as external barriers, such as inaccessible gyms or equipment, lack of knowledge about how to safely exercise with MS, lack of understanding about the types of exercise that would be beneficial, and financial concerns may all negatively impact their ability or desire to participate in exercise [9-13]. In order to promote exercise and activity in people with MS, these disease-specific barriers must be broken down.

Many studies have quantified the positive effects of exercise, but people with MS tend to engage in physical activity at a level well below that of the general population [14-16]. The concern that exercise aggravates MS symptoms has been diminished in part by studies that demonstrate that exercise can decrease fatigue [17-20], pain [21],

spasticity [22] and even cognitive deficits [18,23] and depression [24]. Yet people with MS continue to report barriers to participation in exercise [10]. The working hypothesis for this study is that by eliminating, or at least decreasing, these barriers, people with MS will exercise, and will receive health and functional benefits from this exercise.

The purpose of this paper is to present the perception of barriers and facilitators to exercise in members of an MS community, and to describe a program and related outcomes based on the information gained from this group.

Methods

Overview

A team comprised of two researchers, a physical therapy manager, and an exercise physiologist hosted a focus group to discuss the exercise and wellness needs of people with MS in the local community, and the barriers they perceived to their participation in exercise. The focus group was conducted as an in-person, directive and structured discussion session led by a researcher trained in focus group moderation and a researcher with expertise in MS. Interview questions

were defined prior to the meeting, and were reviewed and edited by the MS researcher, the moderator researcher, and the MS clinical manager and exercise physiologist in the MS clinical program. Questions focused on identifying specific barriers to exercise that had tangible solutions, as well as addressing subjective reasons for engaging in or avoiding exercise. Participants for the focus group were identified by the clinical team based on their availability to participate. The focus group was convened and the researchers posed the questions to the group and led the discussion.

A physical therapist and exercise physiologist then designed a program tailored to respond to the needs identified by the focus group participants. The program was specifically designed to ameliorate barriers to exercise, and combined theories of physical therapy, exercise science, and nutrition. The resulting health and wellness program was based in an outpatient department in a private, non-profit rehabilitation facility, and was open to the MS community.

Intervention

All classes for the health and wellness program were offered in a group setting. The exercise classes addressed core and lower extremity strengthening, and cardiovascular conditioning. Clients could elect to take one, two or three of the classes each week. Designed to isolate certain muscle groups, each class allowed clients to receive a personally tailored workout. All exercise classes were 60 minutes in duration and were instructed by an exercise physiologist with knowledge and experience in MS. One therapy technician provided assistance as necessary to guide exercise or provide support. Each class consisted of people with different MS subtypes.

The Core Strengthening class focused on strengthening the major muscle groups of the core, e.g., rectus abdominis, external obliques, and the paraspinal muscles. Examples of exercises for the core class include abdominal crunches, planks, side crunches, and lumbar rotations using a large Swiss exercise ball. The core class used an instructor to client ratio of 1:7.

The Cardiovascular class was intended to provide the client with a beneficial and safe cardiovascular workout. This was accomplished by increasing the client's heart rate to their target heart rate range, or as close to it as possible, under the guidelines of the American College of Sports Medicine [25]. A circuit-rotation structure was used to move clients around to each "station" which included: boxing, Nintendo Wii, tubing, cycling, and ropes. This class had an instructor-to-client ratio of 1:5. Traditional and non-traditional exercise methods were used. Upper and lower extremity cycling are examples of traditional exercises used in the class while boxing, and fitness training ropes are examples of non-traditional cardio exercises.

The Lower Extremity Strengthening class focused on strengthening and conditioning of the major leg muscles. Squats, leg extensions, and bridging were used to strengthen the rectus femoris and gluteus maximus muscles. Other exercises used for strengthening included side-lying hip abduction for the gluteus medius, hip hiking for hip flexors, and calf raises in standing targeting the gastrocnemius and soleus. The lower extremity class had a ratio of 1:7 to allow for attention to quality of the exercises performed.

In addition to the exercise classes, clients could participate in education classes addressing other areas of wellness for people with MS (Table 1). A meditation class was offered once a week. Led by a psychologist certified in stress management, the clients were guided through a number of stretching, breathing, and relaxation exercises.

The maximum number of participants for this class was ten. The skills-based social group was designed to offer clients a place to socialize and fellowship. One area of focus involved sharpening fine-motor function and hand-eye coordination by playing board games. Clients also played card games to practice cognitive functioning and task performance. There was no limit on group size for this class.

Lecture Topic	Profession of Speaker
Energy Conservation/Managing Fatigue	Occupational Practitioner Therapist/Nurse
Managing Your Healthcare Team	Case Manager
Trustworthy Resources	Librarian
Therapeutic Recreation	Recreation Therapist
"Can I work again?" - Vocational Rehab	Vocational Rehab Specialist
MS and Nutrition	Registered Dietician
Stress Management	Psychologist
"On The Horizon" - New Therapies	Doctor
Adapted Yoga	Certified Yoga Instructor
Medication Management	Nurse Practitioner
MS Research Update	Research Director
Bowel and Bladder	Nurse Practitioner
Pain and Spasticity	Physician's Assistant
Cognitive Dysfunction	Nurse Practitioner
MS Relapses	Physician's Assistant
Massage	Licensed Massage Therapist
Aquatics	Aquatics Specialist
Acupuncture for MS	Licensed Acupuncturist
Exercise Benefits For MS	Exercise Physiologist
Financial Wellness	National Disability Institute - Webinar
Sleep Disorders and MS	Psychologist
"Getting Organized"	Speech Ttherapist
Pilates	Certified Pilates Instructor

Table 1: Lecture series topics and speakers.

Program funding was supported by membership fees paid by program members or by subsidized membership through the local chapter of the National Multiple Sclerosis Society. Existing equipment and space in the rehabilitation gym was used for classes with the exception of a Theraband station (cost of \$45). Membership fees covered 85% and donated funds covered 15% of the exercise physiologist salary.

Data Collection

Focus group

Data for the focus group was collected via notes taken by the researchers at the time of the focus group session, and was also collected offline after completion of the focus group session. The session was recorded, and transcribed, then vetted by the principal investigator and one other clinical investigator to identify major themes in the responses to the questions.

Health and Wellness program

Approval for the collection of outcome measures to obtain pilot data related to the health and wellness program was granted through the Research Review Committee at the institution.

Clinical measures were collected before initiation of the program and 6 months later. Measures included cardiac function (heart rate, blood pressure), body mass weight and index, respiratory and metabolic function (metabolic cart), functional strength (pull ups and pushups), walking, and quality of life (MS Quality of Life Inventory; MS-QLI) [26]. All outcome measures were collected by a trained exercise specialist, except for the MSQLI, which was completed by the participant and returned to the exercise specialist upon completion.

Heart rate and blood pressure were measured primarily using the Dynamap V100 automatic pressure cuff (GE Medical, Freiburg, Germany). For ambulatory participants, body weight was measured using a standard "step-on" digital scale (Omron Healthcare, Inc., HBF-514, Bannockburn, IL). Body weight for non-ambulatory participants was measured using a large "roll-on" digital scale (Health Weigh by Rice Lake Weighing Systems, H340-10-3, Israel), subtracting the weight of the wheelchair from the total weight.

Percent body fat was measured using the US Navy standard algorithm in which circumferences were measured at the hips (for females), waist and neck. Those values were then input into the following equations:

Formula for men:

$$495 / (1.0324 - 0.19077(\text{LOG}(\text{waist-neck})) + 0.15456(\text{LOG}(\text{height}))) - 450$$

Formula for women:

$$495 / (1.29579 - 0.35004(\text{LOG}(\text{waist+hip-neck})) + 0.22100(\text{LOG}(\text{height}))) - 450$$

Resting respiratory and metabolic function was assessed using an Oxycon Mobile metabolic cart (CareFusion, San Diego, CA). Participants were placed in a supine position on a mat table and asked to completely relax but remain awake. Participants donned a face mask for 30 mins while resting metabolic rate and oxygen uptake (VO_2) were collected.

Hand strength was assessed bilaterally using a JAMAR Hydraulic Hand Dynamometer (Sammons Preston Rolyan, Bolingbrook, IL) [27,28]. While seated in a supported position, the participant was asked to hold the dynamometer, with the shoulder by their side, the elbow bent to 90 degrees, and squeeze at their maximal ability one time. Each hand was measured three times with a 30 second break in between each assessment and the three outcomes were averaged.

Abdominal strength was measured using an abdominal crunch test. Participants were supine on a mat table, and asked to complete as many abdominal crunches as they could in one minute. In order for an abdominal crunch to be counted, participants were instructed to crunch up until the shoulder blades made it completely off the mat. Once a participant was unable to move the shoulder blades off the mat, the test was stopped and the number completed to that point was recorded.

A modified pull-up test was used to measure upper extremity strength and endurance. Participants started in a supine position and reached up to grab a bar and pulled themselves up until their arms reached 90 degrees of elbow flexion. They performed as many as they could until they reached exhaustion. In this test, exhaustion was defined either to be the participant's inability to complete the full motion, or by the participant themselves stating they needed to stop the activity.

Leg strength was measured using a one-repetition maximum (1RM) leg press test. Participants were tested to determine the maximum weight they were able to push just one time using a seated leg press machine (Leg Press, Cybex, Owatonna, MN). The weight on the leg press was started at 250 lbs, and then adjusted lower or higher until the participant is able to complete the 1RM.

Gait assessments included the 6 minute walk test [29,30] and the 10 meter walk [31]. Agility and balance during walking were assessed using the Timed Up and Go test [32]. Participants completed these tests wearing a gait belt around the waist for added safety and were monitored by only one clinician. The clinician's responsibility was to guard the participant and record the time to completion of each test.

The participant's perception of their quality of life was measured using the MS-QLI.26 This a MS-specific health-related quality of life instrument consists of the Health Status Questionnaire (SF-36), supplemented by nine symptom-specific to measures of fatigue, pain, bladder function, bowel function, emotional status, perceived cognitive function, visual function, sexual satisfaction, and social relationships, was completed by the participant. Upon completion the questionnaire was returned to the exercise specialist.

Data Analysis

Focus group

Data obtained from the focus group data was organized based on identifying the barriers to exercise for people with MS. The analysis was qualitative. The MS researcher organized and subdivided the transcribed notes based on themes related to exercise barriers, and searched for patterns within the subdivisions. A clinical investigator reviewed the data to ensure that all themes were identified.

Health and Wellness program

All data related to the outcomes measures for the health and wellness program were entered into a database, and analysis was carried out using means and ranges to describe the outcomes. T-tests of pre- and post-measures were performed to determine statistical significance for each outcome measure.

Effect size indicates the standardized difference between two dependent means and expresses this relationship in standard deviation units. Effect size was determined utilizing Cohen's d formula for dependent, single group, pre-post change. The formula takes the

difference between pre and post means for the group, and then divides the difference by the baseline variance. Baseline variance is the standard deviation for the first time period (pre) of measurement [32]. Effect size (Cohen's d) for dependent means differences (matched pairs t-tests) is calculated by the equation:

$$\text{Cohen's } d = \frac{\text{Paired Differences Mean}}{\text{Baseline Standard Deviation}}$$

Results

Focus group results

Nine individuals with MS (6 female, 3 male), mean age 51 (38-69) participated in the focus group session. Focus group participant demographics are presented in Table 2.

Participant #	Sex	Year of Dx	Age at Dx	Current Age	Type of MS
F1	F	1998	43	59	RR
F2	F	2011	61	64	RR
F3	M	1993	36	55	PP
F4	F	2011	57	60	SP
F5	M	2008	37	43	PP
F6	M	1995	43	62	PP
F7	F	2006	24	32	RR
F8	F	2009	61	66	RR
F9	F	2000	39	55	RR

RR: Relapse remitting; PP: primary progressive; F: indicates participant in focus group, which may not correspond with Wellness study participants (i.e. Tables 5-7); Dx: Diagnosis

Table 2: Focus group participant demographics.

Barriers	No. of participants indicating barrier (n=9)	Facilitators	No. of participants identifying facilitator (n=9)
Fatigue	7	Knowledgeable coordinator	7
Cost	5	Encouragement	5
Transportation	4	If exercise alleviates symptoms	5
Effort (starting or continuing)	3	Seeing tangible results	4
Availability of preferred exercise machines in gym	3	Weight loss	1
Don't like to exercise	2	Increased flexibility	1
Time	2	Feeling better	4
Need for assistance	2	Community working out with	4
Distance to travel to facility	2	If it's fulfilling	3
Distance to from parking to location for exercise	2	Knowledge of benefits	3
Exercise is boring	1	Wanting to fight MS	3
Pain	1	Making/having an appointment	1
Too repetitive	1	Not feeling disabled	1
Uncertainty regarding what to do	1	Scheduling transportation	1
Uncertainty about potential results	1		

Table 3: Barriers to exercise participation identified by focus group participants.

Table 4: Facilitators to exercise identified by focus group participants.

Participants identified a number of barriers that prevented them from participating in regular exercise (Table 3), and the facilitators that would help them participate (Table 4). Although some participants indicated they would prefer to exercise at home, the majority identified

the need for guided exercise groups with leaders educated in MS, as well as educational classes in symptom management, stress management and complementary/alternative options for treatment. Several participants (n=5) requested Saturday morning exercise classes. One person requested cognitive exercises. Three participants indicated they would like to be informed of reaching milestones or receive rewards for reaching those milestones.

Wellness study results

There were 88 clients enrolled in the health and wellness program, and specifically 48 were enrolled in the exercise classes. Data for the first 9 clients in the health and wellness program was analyzed. These

clients agreed to participate in the collection of additional clinical outcome measures. Participant characteristics are presented in Table 5. The majority of participants were female (n=6), the mean age was 51.22 (range 38-69), and the mean time since diagnosis was 15.78 (range 3-30). All but one participant had a diagnosis of relapse-remitting MS, and this participant had a diagnosis of primary progressive MS. The average attendance rate across the group was 71% (range 62-84%). Typical reasons for missing were transportation difficulties, fatigue pertaining to MS (lassitude), lack of confidence, failure to remember appointments (cognitive dysfunction), and report of lack of motivation.

Participant #	Sex	Approx time since Dx (years)	Current Age (years)	Type of MS	Classes	Attendance Rate (%)
1	F	11	41	RR	Cardio Core	84
2	F	18	54	RR	Cardio Core LE Meditation	69
3	F	7	57	RR	Cardio Core	70
4	F	14	38	RR	Core LE	62
5	M	30	69	PP	Cardio Core LE	73
6	M	21	50	RR	Core Balance	69
7	F	12	42	RR	Balance Core	62
8	F	3	52	RR	LE Balance	66
9	M	26	58	RR	Core	84
Mean (range)		15.78 (3-30)	51.22 (38-69)			71 (62-84)
SD		8.80	9.81			8

Dx: Diagnosis; RR: Relapse Remitting; PP: Primary Progressive; SD: Standard deviation; LE: lower extremity

Table 5: Wellness study participant demographics.

Table 6 presents health-related outcomes. Although there was not a significant decrease in body weight or total body fat, there was a statistically significant decrease in the average percent body fat at the hip and neck (p=0.02 and 0.04, respectively), with a small effect size for

both (Cohen's d=-0.30 and -0.23, respectively). Metabolic rate, VO₂ max and resting heart rate did not change (p=0.32, 0.33, 0.87, respectively), in the group.

Outcome	Pre Ave (SD)	Post Ave (SD)	% Change	Ave% change	P value	Cohen's d
Weight (lbs)	162.00 (28.22)	162.96 (27.62)	0.59	0.67	0.61	0.03

Total %BF	33.35 (14.64)	31.40 (12.28)	-5.86	-1.04	0.12	-0.13
%BF waist	35.39 (4.44)	34.53 (3.12)	-2.43	-2.08	0.15	-0.19
%BF hips	41.56 (3.76)	40.44 (3.66)	-2.67	-2.65	0.02	-0.30
%BF naval	38.67 (6.81)	35.92 (4.40)	-7.11	-6.20	0.06	-0.40
%BF neck	14.06 (1.42)	13.72 (1.16)	-2.37	-2.37	0.04	-0.23
Metabolic rate	1511.78 (230.22)	1600.89 (301.16)	5.89	6.43	0.32	0.39
VO ₂ max	2.87 (0.39)	3.02 (0.58)	5.19	5.36	0.33	0.38
Resting HR	77.56 (12.80)	78.44 (10.67)	1.15	3.09	0.87	0.07

BF: Body fat; BMI: Body Mass Index; SD: Standard deviation; % Change represents the change in group averages pre and post; Ave % Change represents the average change for each individual from pre- to post-test.

Table 6: Health-related Outcomes (N=9).

Functional data are presented in Table 7. There was a significant increase ($p=0.03$) of a moderate magnitude (Cohen's $d=0.56$) in the number of abdominal crunches performed, as well as a significant increase in distance walked during the 6 minute walk test ($p=0.04$).

The effect size for this change in distance was small (Cohen's $d=0.27$). Although there were minimal improvements in the other measures, these were not statistically significant.

Outcome	Pre Ave (SD)	Post Ave (SD)	% Change	Ave% change	P value	Cohen's d
Left Hand Strength (Dynamometer)	55.67 (18.40)	59.74 (10.67)	7.33	19.70	0.34	0.22
Right Hand Strength (Dynamometer)	57.67 (15.88)	60.59 (10.35)	5.07	13.98	0.44	0.18
Abdominal Crunch (#)	26.56 (15.78)	35.44 (19.96)	33.47	53.67	0.03	0.56
Pull Up Test (#)	15.33 (8.34)	16.67 (7.92)	8.70	32.10	0.55	0.16
1RM Leg Press (lbs)	123.33 (44.44)	132.22 (47.90)	7.21	8.03	0.12	0.20
6 Min Walk Test (feet)	11501.71 (5858.74)	13111.29 (6308.87)	13.39	16.83	0.04	0.27
10 m Test (secs)	15.63 (12.88)	11.74 (5.56)	-24.89	-12.54	0.23	-0.30
TUG (secs)	16.55 (7.71)	18.69 (13.00)	-12.91	-5.72	0.38	0.28

SD: Standard deviation; % Change represents the change in group averages pre and post; Ave % Change represents the average change for each individual from pre- to post-test.

Table 7: Strength/Functional Outcomes (N=9, except 6 Min Walk Test N=7).

Discussion

There is a growing body of evidence suggesting that exercise is not only safe for people with MS but necessary to combat some of the consequences of MS. Yet people with MS remain relatively inactive [14,16]. Several barriers to exercise likely contribute to the sedentary lifestyle of people with MS. The findings from the focus group were in accordance with those reported by Asano et al. [9] who found that the top barrier to exercise is fatigue. Other barriers identified in their study were the same as those identified by the focus group participants for this study, albeit in a different order of importance. Based on this information, a combined exercise and education program was developed, and instituted in an accessible fashion for people with any type (relapsing-remitting or progressive) of MS, at any level of disability. The number of enrolled clients and the relatively high adherence rate (71%) demonstrate the benefit of incorporating insights from people with MS about their exercise and wellness needs.

Outcomes collected from this program indicate a positive effect of exercise on health and wellness. Study findings demonstrate that people with MS can achieve health-related and functional improvements after exercising regularly in a guided group exercise program. In many exercise studies to date, the participant is encouraged to work to a level that is "somewhat hard", [34-36] or to 50-70% of their max VO₂ [34]. No attempt was made to monitor exercise intensity, and for some participants, the intensity was somewhat less than what is reported in other studies. Yet, participants achieved meaningful outcomes even with this lower intensity of exercise. They also demonstrated good attendance and low drop out, suggesting that this level of exercise may be achievable in individuals with chronic disability due to MS.

There was a significant change in percent body fat at the neck and hips, and a trend toward a decrease at the naval, but the waist to hip ratio was not decreased in the participants in this study. Amount and

location of body fat are important variables when considering ones risk of co-morbidity, such as cardiovascular disease [37]. People with MS are already at risk for obesity due to their immobility, as well as their disease modifying agents, and thus a decrease in these variables would be meaningful. That only percent of fat at the neck and hip decreased significantly has questionable significance related to the risk of cardiovascular disease. However, any decrease in body fat would be useful if it leads to increase ease of functional activities. This needs to be evaluated further.

The significant functional changes in walking endurance, as measured with the 6 minute walk test, are also of interest. Similar improvements have been noted previously after exercise in people with MS [34-36,38,39]. Performance on the 6 minute walk test has been shown to correlate strongly with both the EDSS and the MS Walking Scale 12, [38,39] and therefore these increases in endurance may positively impact daily activities, and potentially participation. This should be studied further with programs providing this level of exercise on an ongoing basis.

Limitations

Several limitations preclude the generalizability of these findings to the MS population as a whole. First, this was not a controlled trial, but represents analysis of data collected to measure outcomes in a clinically-oriented program. Therefore, there are many variables that may have impacted the findings. For instance, there was no control group, either of people who did not participate in the exercise program or who received a different intervention. There was no control over the number of exercise or educational sessions attended. The program was completely voluntary and clients could attend any or all classes they chose. Although attendance was taken, and the participants attended sessions fairly regularly (62%-84%), determining a dose-response from the current data is not feasible. Furthermore, perceived exertion was not collected from each individual, so it is difficult to know the participant's perception of how hard they were working. There were also no other measures of intensity, so it is difficult to compare the findings from this study to others, or to draw any conclusions about the efficacy of any of the interventions included in this program. Finally, the sample of participants for this study included only one person with primary progressive MS, and the remainder had relapse-remitting MS. Future studies should explore the benefits of a similar program for a larger population, and specifically in people with progressive MS. Information was not collected related to the education classes that participants in the wellness program attended. Future studies should consider standardizing the classes in order to better understand the relative contributions of different types and dosing of exercises for health and functional gains.

Conclusion

An outpatient MS exercise program may provide people with MS an alternative method for exercising that is feasible. Initial outcome measures show a positive effect in a subgroup of participants involved in classes guided by an instructor educated in MS. Assessment of outcomes related to real life interventions, however, may be a meaningful approach to explore more fully in order to gain greater insight into what approaches will lead to the greatest function, health and wellness for people with MS.

Further research is warranted and necessary. A controlled study focused on evaluating the efficacy of the various components of this

program is necessary in order to determine the combination of exercise and educational variables that will lead to the most efficacious outcomes for any given individual with MS.

Benefits of Static Stretching, Pilates® and Elastic Bands Resistance Training on Patients with Relapsing-Remitting Multiple Sclerosis: A Longitudinal Study

Abstract

Objective: To compare the effects of Pilates®, a 30 s static stretching protocol and elastic bands resistance training on lower and hand-grip strength, rachis morphology, flexibility and body balance among RRMS patients.

Methods: Twenty-two subjects affected by relapsing-remitting multiple sclerosis (RRMS, EDSS \leq 6) were randomly divided into 3 groups whose members each performed 16 weeks of training. Stabilometry, rachis morphology, sit and reach, handgrip and sit to stand tests were performed three times: T0, after a month of learning training protocols; T1, after eight weeks of training; and T2, after sixteen weeks of training.

Results: Static stretching group. Spinal Mouse (inclination line between ThSp1 and S1 from a standing position): T0 vs. T2, -55%; Sit and Reach test: T0 vs. T2, +15%. Pilates group. Sit and Reach test: T0 vs. T2, +15%; Sit to Stand test: T0 vs. T2, +31%. Elastic group. Stabilometry with eyes open: T0 vs. T1, -51%; stabilometry with eyes closed: T0 vs. T1, -52%; sit to stand test: T0 vs. T2, +39%.

Conclusion: Static stretching, Pilates and resistance training are useful to increase the autonomy in the daily life of people with MS thanks to the adoption of these three different training methods.

Keywords: Multiple sclerosis; Physical exercise; Quality of life; Body balance; Muscle strength; Flexibility

Abbreviations A: Area defined by the orthostatic center of pressure (mm^2); APS: Average anterior-Posterior Speed of the center of the body ($\text{mm} \times \text{s}^{-1}$); CoP: Center of Pressure; ES: Effect Size; EDSS: Expanded Disability Status Scale; EG: Elastic bands Group; Incl: Inclination Corresponding to the Inclination Line between ThSp1 and S1; IPS: Information Processing Speed; LSp: Lumbar Segment between the last thoracic (ThSp12) and the first sacral (S1) vertebrae; MLS: Average Medial-Lateral Speed of the center of the body ($\text{mm} \times \text{s}^{-1}$); MS: Multiple Sclerosis; P: Perimeter P described by the orthostatic center of pressure (mm); PG: Pilates Group; PP: Primary-Progressive; PR: Progressive-Relapsing; RR: Relapsing-Remitting; SP: Secondary-Progressive; SS: Static Stretching; SSG: Static Stretching Group; ThSp: Thoracic Segment between the first (ThSp1) and the last (ThSp12) thoracic vertebra; ThSp1: the first Thoracic Vertebra; ThSp12: the last Thoracic Vertebra; S1: the first Sacral Vertebra

Introduction

Multiple sclerosis (MS) is a chronic-degenerative and auto-immune disease, which affects the central nervous system and brings about a progressive loss of myelin, an essential component of nerve cells that allows them to conduct electric stimuli along the nerve fibers. In MS, four disease types have been defined [1] relapsing-remitting MS (RRMS), which is characterized by clearly defined acute relapses or

exacerbations, followed by either complete or partial remission of symptoms, with no symptoms worsening between the said attacks; primary-progressive MS (PPMS), characterized by slowly worsening symptoms from onset and the absence of any acute relapses; secondary-progressive MS (SPMS), which begins as relapsing-remitting MS but then transitions to include a slow worsening of symptoms without improvements or remissions; progressive-relapsing MS (PRMS), which involves a progression from onset with occasional acute relapses along the way. A cure has not yet been discovered, even though the effects of the disease can be restricted. MS patients can suffer from somatosensory, cognitive or organic-muscular damage and the clinical course is extremely variable and the life expectancy is reduced [2]. Indeed, physiotherapy may be an effective form of rehabilitation, especially in the presence of progressive MS [3]. Environmental factors, such as exposure to cigarette smoke or vitamin D deficits seem to be associated with both pediatric and adult onset of MS [4]. One of the most debilitating consequences of MS is muscle spasticity, which is a disorder in neuromuscular reciprocal inhibition with a greater excitation of the muscle-tendon strain reflex that accounts for arrhythmic movements of the musculoskeletal system by affecting ambulation, decreasing muscle strength and increasing the risk of falls [5]. Skjerbæk et al. [6] have investigated the negative influence of fatigue and pain-related symptoms on MS patients' performance in the "six minute walk test". Fatigue should be adequately controlled by means of pharmacological therapies and physical activity [7] as well as different coping strategies [8]. Regular fitness training correlates with improvements in the quality of life and a reduction in

fatigue perception among MS patients [9,10], and resistance training in particular is very useful for this aim [11]. The effects of on MS patients have been studied [12] and incremental improvements in body balance, joint mobility and upper body muscle strength have been observed. Marandi et al. [13] compared the Pilates method with microgravity exercises among MS patients and the outcomes revealed positive benefits on dynamic body balance, in keeping with Freeman et al. [14], who demonstrated that Pilates also positively influences ambulation. Moreover, 10 weeks of proprioceptive training prove to be efficacy in the improvement of the stability and in the reduction of the energy required to maintain it [15]. On the other hand, static stretching (SS) is believed to be a valid technique in the presence of chronic-degenerative diseases in reducing spasticity and normalizing muscle tone, along with the maintenance or the increase in the extensibility of slack tissues [16]. The role of physical exercise, especially cardiorespiratory fitness, muscle strength, endurance and muscle-tendon flexibility, is fundamental in order to preserve and improve residual motor abilities of people with MS [17]. Furthermore, a positive correlation between the independence in the daily life activity and the healthcare quality has been demonstrated [18]. Hence, the purpose of this study was to compare the following training methods: Pilates, a 30 s static stretching protocol and resistance training with elastic bands, with the ultimate goal to highlight the most effective treatment to modify significantly lower body strength, rachis morphology and body balance among MS patients.

Methods

Participants

Twenty-two subjects affected by relapsing-remitting multiple sclerosis (RRMS) were enrolled in this study. They provided their formal approval for the participation in this study by signing a specific written informed consent form. Furthermore, the authors certify that all applicable institutional and governmental regulations concerning the ethical use of human participants were followed during the course of this research. The exclusion criteria required that none of the patients had practiced the same physical activity used in this study in at least the preceding 12 months and that all of them were in possession of a certificate of good health and eligibility for non-competitive physical activity released by their physician. Furthermore, no pharmacological treatments were used and no changes in diet were required during both the test and intervention periods. Moreover, the subjects had to have been relapse-free during the previous 6 months to take part in the study. In addition, no patients were hospitalized and all were affiliated to the Italian Multiple Sclerosis Association (AISM). Afterwards, they were randomly divided into 3 groups: the first group (SSG), which included 8 people (age 50 ± 18 years, weight 64 ± 13 kg, height 167 ± 10 cm, expanded disability status scale (EDSS) 4 ± 2), that performed 30 s static stretching protocols; the second group (EG), which included 7 subjects (age 52 ± 10 years, weight 56 ± 5 kg, height 160 ± 6 cm, Expanded Disability Status Scale (EDSS) 3 ± 2), who performed resistance training by means of elastic bands; and the last group (PG), which included 7 participants (age 45 ± 6 years, weight 63 ± 15 kg, height 164 ± 6 cm, Expanded Disability Status Scale (EDSS) 2 ± 2), who underwent the Pilates protocol. The study flow chart is presented in Figure 1.

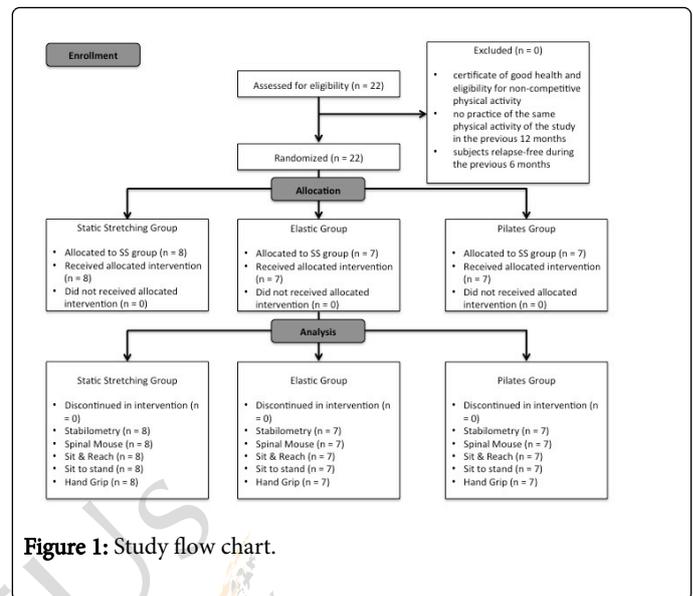


Figure 1: Study flow chart.

Functional assessments

The evaluations were performed in order from the metabolically least demanding to the most, in other words: stabilometry, rachis morphology, sit and reach, hand grip and sit to stand. The three groups were tested three times: T0, after a month of learning training protocols, to identify the baseline performance; T1, two months after T0, to evaluate the effects brought about by the first eight weeks of training; and T2, two months after T1, to evaluate the effects brought about by sixteen weeks of training. The functional evaluation took place in the Adapted Training and Performance Laboratory at the University of Turin.

Stabilometry

The assessment of bipodalic body balance was executed by means of a stabilometric platform (TecnoBody Prokin PK 214 P, Bergamo, Italy), once with eyes open and once with them closed. Both the trials had duration of 60 s with 60 s of passive recovery between them. The following variables related to the center of pressure (CoP) were taken into consideration: average anterior-posterior speed (APS) of the center of the body ($\text{mm} \times \text{s}^{-1}$), average medial-lateral speed (MLS) of the center of the body ($\text{mm} \times \text{s}^{-1}$), area (A) defined by the orthostatic center of pressure (mm^2), perimeter (P) described by the orthostatic center of pressure (mm).

Sit and reach

To assess the improvement of the flexibility of the posterior kinetic chain, the Sit and Reach test was used. It took place by means of a metal and wood parallelepiped (height 30 cm, width 50 cm, depth 51 cm) on which a 80 cm-long metal binary was applied along center line. On this, a movable carriage, supporting a digital distance measurement device (Bosch GLM 150 Professional, Bosch GmbH, Stuttgart, Germany; accuracy ± 1 mm, measurement time between 0.5 and 4 s, laser class 2) was installed. The foothold was located 30 cm from the origin of the binary, where a metal plate was set, with the aim of standardizing the assessments. On the vertical side of the foothold, a wood triangle, with its base oriented upwards and its vertex oriented downwards, thereby forming a 36° angle named Piok's angle, was

positioned in order to identify the correct positioning of the feet on its oblique sides. The participant starts from a sitting position with their legs extended and without shoes. The operator, after having verified that the feet were in full contact with the triangle to avoid their pronation and supination, supervised the starting position, with hands superimposed on the movable carriage. The participant then chose which hand to place on top, and this was kept constant during the subsequent experimental sessions in order to guarantee the reliability of the test. Then, participants were required to bend their trunk progressively forward as much as they could until they felt pain. This procedure was repeated only once to avoid it became a stretching training technique.

Spinal mouse

To monitor rachis morphology, a lateral inclinometer (Spinal Mouse, Idiag, Volketswil, Switzerland) allowing reliable measurement [19] on the sagittal plane was used. The spinous processes were identified via palpation and labeled with a demographic pencil. The data were detected with the sliding of the instrument along the rachis from C7 to S1 with a sampling frequency of 150Hz. The final outcome was the accurate description of all the vertebral corps and the following variables: thoracic segment (ThSp), between the first (ThSp1) and the last (ThSp12) thoracic vertebrae, lumbar segment (LSp), between the last thoracic (ThSp12) and the first sacral (S1) vertebrae, inclination (Incl), corresponding to the inclination line between ThSp1 and S1. All the measurements were performed once and the protocol of data acquisition included: a test from the standing position, in which the participants looked forward, with the feet in line with the shoulders, knees extended and arms along the sides; a test of the maximum flexion of the trunk in which, from a stationary position, the trunk was bent as much as possible while keeping the knees extended; and a test of the maximum extension of the trunk, in which the arms are crossed on the thorax and the maximum backward trunk extension was performed.

Hand grip

The hand-grip test was performed by means of a hydraulic hand-held dynamometer (Baseline, Fabrication Enterprises, White Plains, NY, USA). The subject was seated on a chair with the arm completely extended towards the ground and performed the maximum voluntary hand-grip contraction for 3 ± 1 s. They performed 3 trials for each hand and the best was recorded.

Sit to stand

To perform the sit to stand test, a specific wood and iron bench with a height of 43 cm [20] was utilized. A 1 cm-rigid rubber cushion was positioned to soften the impact of the hip on the seat. The width (70 cm) and depth (100 cm) were chosen to allow the positioning of the Optojump (Microgate srl, Bolzano, Italy) on the sides of the bench, where, to guarantee the safety of the participant during the execution of the tests, a seat-back (height 33 cm) and two lateral bars (height of 1 m from the ground, and a length of 1.30 m) were located 40 cm from the anterior part of the seat and to its sides respectively. Another 1 m-high security bar, which could be opened and closed to allow the participants to enter and leave the test area, was located 1 m in front of the seat-back. The whole structure was fixed to the ground to avoid any movements of the bench during tests, which consisted of counting of the total number of occasions the subject managed to sit down and stand up from the bench in 30 s [21]. The start occurred when the

participant was in the upright position with the legs at the same distance apart as the shoulders and an operator checked the correctness of the movements.

Intervention

Each training session began with a warm-up including joint mobility and muscle flexibility exercises aiming to increase body temperature and muscle-tendon elongation. In the static stretching group (SSG), a development phase with 3 sets of 30 s of static stretching exercise was adopted. The recovery time between sets was 30 s and all the exercises utilized are reported in Table 1. The subjects performed the SS protocols twice a week.

Exercise	Muscle groups
Hand extension	Arm and forearm
Side-bending of the trunk	Lateral region of the abdomen
Dorsal bending of the foot	Gastrocnemius and soleus
Anterior bending of the trunk	Lastissimus dorsi
Lunges with the anterior leg resting on a step	Ileo-psoas, quadriceps
Upper limbs extension	Arm and forearm
Bending of the lower limb on the hip	Hamstrings
Bending of the leg on the gluteus	Quadriceps
Lower limbs abduction from a sitting position and feet against each other	Adductors
Anterior bending of the trunk from a sitting position with legs extended	Hamstrings, lumbar
Bending of the lower limb on the hip with internal rotation	Gluteus, lumbar

Table 1: Exercises utilized by static stretching group (SS) in the static stretching protocols with the related muscle groups elongated.

The elastic band group (EG) performed two muscle strength training sessions each week by means of elastic bands. The protocol involved 3 sets of 10 repetitions, with 30 s of recovery between sets (Table 2).

Exercise	Muscle groups
Internal and external rotation of the arm*	Rotator cuff
Bench press sitting on a chair*	Pectoral major
Forearm bending (Curl)*	Biceps brachii
Side raises*	Lateral delt
Arm extension behind the head*	Triceps brachii
Lower limbs abduction*	Tensor fasciae latae
Lower limbs adduction with elastic ball*	Adductors
Lower limbs extension forward starting from a bent position*	Quadriceps

Squat (starting and touching a chair in the return phase)*	Quadriceps, hamstrings
Crunch	Rectus abdominis

Table 2: Exercises utilized by the elastic band group (EG) in the resistance training protocols with the related muscle groups trained. * = exercise performed sitting on a chair.

Exercise	Muscle groups
Hip retroversion	Rectus abdominis
Half curl and Criss Cross	Rectus abdominis and obliquous abs
Roll down and Roll up facilitated	Rectus abdominis
Side leg lift	Tensor fasciae latae
Saw	Lumbers, lastissimus dorsi, hamstrings
Spine stretch	Lumbers, lastissimus dorsi, hamstrings
Cat stretch	Lumbers, lastissimus dorsi
Mermaid	Rectus abdominis and obliquous abs
Bridge	Hamstrings, lumbers
Plank with leg lift	Lumbers, hamstrings
Single leg circles	Rectus abdominis, quadriceps, hamstrings
Side kick	Hamstrings, quadriceps

Table 3: Exercises utilized by pilates group (PG) in the static stretching protocols with the related muscle groups elongated or strengthened.

The Pilates group (PG) was assigned a Pilates protocol to be repeated twice a week. It included 2 sets of 8 repetitions of each exercise with a resting time of 30 s between sets (Table 3).

Statistical methods

Data are presented as mean and standard deviation (\pm SD). Friedman's ANOVA and Dunn's post hoc were used to investigate differences between test sessions. The significance level was set at $p < 0.05$ and the percentage differences were calculated with the following formula: $\% \text{ difference} = ((FV - IV) / IV) * 100$, where IV: Initial Value; FV: Final Value. For interpretation of the relevance of differences, effect sizes (ES) were calculated and interpreted as follows: 0.2 to < 0.6 , small; 0.6 to < 1.2 , medium; 1.2 to < 2.0 , large; 2.0 to < 4.0 , very large; and ≥ 4.0 , extremely large [22].

Results

No significant variations concerning unlisted parameters emerged from this research. In the static stretching group, the Spinal Mouse showed a significant difference in the test concerning the inclination line between ThSp1 and S1, performed from a standing position between T0 and T2 ($p < 0.05$, -55%, ES=0.67). Moreover, the Sit and Reach test highlighted a significant improvement between T0 and T2 ($p < 0.05$, +15%, ES=0.36). In the Pilates group, The Sit and Reach test revealed a significant variation between T0 and T2 ($p < 0.05$, +15%, ES=0.4), while the Sit to Stand test pointed out significant differences between T0 and T2 (ANOVA: $p < 0.05$; post hoc: $p < 0.01$, +31%,

ES=1.21). Taking into consideration the elastic group, the stabilometry showed a significant differences concerning the ellipsis area when performed with eyes open (T0 vs. T1, $p < 0.05$, -51%, ES=0.52) and closed (T0 vs. T1, $p < 0.01$, -52%, ES=1.69). Meanwhile, the sit to stand test showed significant improvements between T0 and T2 ($p < 0.05$, +39%, ES=1.83).

Discussion

The main goal of this study was to evaluate the effects of training protocols by means of Pilates, elastic bands and static stretching on muscle strength, muscle-tendon flexibility and body balance among patients affected by multiple sclerosis. Although, in the past, physical training was not recommended for MS patients as it was thought that it would accelerate deterioration, now it is often part of therapy in conjunction medication. However, since MS is incurable, rehabilitation mainly focuses on improving residual abilities and mobility rather than aiming for full recuperation [23]. Individuals with a high self-efficacy or those that spend more time in participating in physical activity report less physical impact of MS on their quality of life and thus an increased physical independence [24]. Moreover, 70% of patients reported impairments on complex attention tasks [25] and physical activity also seems to be associated with information processing speed (IPS) [26]. Additionally, although moving a spastic muscle to a new position may increase symptomatology, daily stretching of muscles to their full length helps to manage the tightness of spasticity, one of the most common symptoms of MS, thereby allowing for optimal movements [27]. In this study, the Sit and Reach test highlighted a significant improvement between T0 and T2 (+15%) following both the static stretching and the Pilates protocols, in accordance with Oliveira et al. [28], who demonstrated the efficacy of these two kinds of training methods on muscle-tendon flexibility among older women. Furthermore, 6 weeks with 2 training sessions of stretching and yoga are the minimum time required to show significant reductions in fatigue-related symptoms among MS patients [29]. In addition, stretches in weight bearing positions let patients achieve higher ankle torques, probably as a result of the use of the body to apply a constant force [30]. These results corroborate and justify the minor frontal inclination of the rachis which emerged from the test with Spinal Mouse, which showed a significant difference (-55%) after sixteen weeks of training. This demonstrates the greater body and postural control acquired by participants after training. Lim et al. [31] studied the effect of a Pilates protocol on nineteen individuals affected by unilateral chronic hemi-paretic strokes, and they highlighted significant improvements in both static and dynamic body balance. However, among the MS patients involved in this study, this technique was useful in improving performance in the Sit and Reach and the Sit to Stand test after 16 weeks of training, with no effects on body balance, confirming the greater utility of other training methods to this end, such as core stability [14]. Our outcomes seem to be consistent with a previous study [32] which revealed the great importance of Pilates in the improvement of performance in the sit to stand test after 8 weeks of training. In the research presented herein, 16 weeks of training were necessary to observe significant variations: this could be a consequence of the different protocols utilized. Küçük et al. [32] adopted two different versions of the sit to stand test: in the first, patients were asked to sit on a bed set at a standard height from the floor and stand up once, while, in the repeated sit to stand on/from a chair, they were asked to sit on a chair set at a standard height and stand up 3 times. On the other hand, in this study, the indications provided by Milanović et al. [21], according to which the total number

of times the subject manages to sit down and stand up from the bench in 30 s were counted, were followed. In addition, Pilates is believed to be effective in improving sitting posture while reducing shoulder and back pain as well as the value in the Multiple Sclerosis Impact Scale among MS patients relying on a wheel chair [33]. In any case, the importance of Pilates to improve the quality of life has been confirmed, as well as that of exercise therapy, which can help to reduce fatigue in MS patients [34]. However, resistance training should be preferred, because it is not usually accompanied by an increase in core temperature, as seen during endurance training. Therefore, unpleasant feelings caused by the exacerbation of symptoms, as brought about by endurance training, are more rarely experienced [35]. In addition, resistance training should focus on hamstrings and quadriceps muscles which are positively correlated with gait characteristics [36]. Nevertheless, moderate-intensity cycling proved to be beneficial in reducing fatigue and may help in its chronic management among MS patients [37]. Besides this, visual cognition impairments are present in 14% of MS patients [38]: however, in the present study, after 8 weeks of training, the protocol with elastic bands proved to be efficacious to improve stabilometry, performed with eyes both open and closed, as well as the sit to stand test, which showed significant improvements after sixteen weeks of training. This means that, after this kind of training, patients become stronger and more powerful on the one hand and more able to manage their balance on the other. These outcomes corroborate those of a previous study [39], which showed that a very short circuit training program with elastic bands designed for MS patients generates modest improvements in power, an increase in functional capacity and a reduction of their perception of fatigue. Additionally, 6 weeks of isokinetic strength training are sufficient to increase maximum strength and reduce the levels of fatigue in the ankle dorsiflexors of MS patients [40], which showed that a very short circuit training program with elastic bands designed for MS patients generates modest improvements in power, an increase in functional capacity and a reduction of their perception of fatigue. Similarly, the same training period performed three times per week by means of seated rowing, chest press, leg extension and leg press exercises significantly improved performance in the 10 m timed walk test, the 3 min step test and the timed up and go test, with no significant effects on balance [41]. The discrepancies between the previous two studies and this one, concerning the effects of strength training on body balance, can be attributed on the one hand to the different instruments utilized for assessment, and on the other hand to the different type of contraction performed: in this research, the use of elastic bands instead of gym machines or calisthenics exercises can account for a continuous and greater stimulus of neuro-muscular coordination, which reflects positively on body balance. Nevertheless, in keeping with Backus et al. [42], which proposed different training programs though non-specific for the hand-grip strength, this parameter did not showed significant improvement in the present study as well. Additionally, short-term progressive strength training can be considered a valid means to improve the quality of life of people living with relapsing-remitting MS and mild to moderate walking difficulties, since it reduces physical fatigue and increases both muscle strength and endurance. However, the benefits do not persist after complete interruption of the training [43]. Besides this, the present study has some limitations. The first aspect to consider is the limited number of participants. On the one hand, the use of parametric statistical calculations should have been possible due to a larger sample, also bringing about higher effect sizes values. On the other hand, a larger number of subjects could have allowed the creation of a control group to compare their functional evaluations with those of the three treatment groups of this study. In

addition, considering the difficulty to find many subjects with the same type of MS and who respect the inclusion criteria, the option to lead multi-centered studies must be considered in the future. Besides this, the intervention of this research could have ameliorated also the pathological condition of the participants, in addition to their physical abilities. Consequently, it can be interesting to verify if physical training is able to stabilize the progression of multiple sclerosis; hence future researches could perform a magnetic resonance, to monitor the progression of the inflammation process and the volume of MS plaques, as well as a bone densitometry, to study the effects of physical training on bone mineral density among people affected by multiple sclerosis.

Conclusion

This study provides useful indications with regard to the rehabilitation and the improvement in the quality of life of people affected by relapsing-remitting multiple sclerosis. In particular, static stretching is useful in increasing the motor control of the rachis and flexibility, as well as the Pilates protocol, which also improved performance in the Sit to Stand test. Moreover, the latter is affected by resistance training by means of elastic bands, which in turn helps the management of body balance. The practical implications which emerged from this study allow us to hypothesize an increment in autonomy in the daily life of MS sufferers thanks to the adoption of these three different training methods.



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