Fatigue and Thermo Sensitivity Affect Physical Activity in Multiple Sclerosis

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ABSTRACT

Background

Thermo sensitivity (TS), characterized by worsening of neurological symptoms due to increased body temperature, is common in individuals with multiple sclerosis (MS). Fatigue is also a common complaint. Both TS and fatigue can lead to decreased participation in physical activity (PA) in this population.

Purpose

The primary purpose of this study was to determine through self-report if TS and fatigue have any effect of PA levels in individuals diagnosed with MS.

Methods

Seventy seven men and women between the ages of 22 and 69 with a diagnosis of Multiple Sclerosis according to McDonald criteria participated in this study ($\mu = 45.2 \pm 1.4$). Physical activity level was measured by Godin Leisure-Time Exercise Questionnaire, and fatigue by the Fatigue Severity Scale (FSS). TS was recorded by self-report.

Results

Eighty-three percent of the group reported TS (91.8% of females and 65.2% of males). Individuals that reported TS participated significantly less in physical activity than individuals who did not report TS ($p<.05$). There was a moderate negative correlation ($p<.01$) between physical activity and FSS. Significant gender differences were seen for FSS ($p<.05$), and PA ($p<.05$), with men reporting less fatigue and more participation in PA than women. Classification of MS did not influence participation in PA or FSS ($p>.05$).

Conclusion

Individuals with MS that scored higher on FSS and those that reported TS had lower participation in PA. As for gender differences, men reported less fatigue, more participation in PA, and less occurrence of TS than women ($p<.05$). According to our results, both TS and fatigue have a negative

effect on participation in PA in individuals diagnosed with MS.

INTRODUCTION

Multiple sclerosis (MS) is a chronic neuro-degenerative inflammatory disease of the central nervous system, and is the most common cause of neurological disability in young adults [1]. Historically, people with MS were encouraged not to exercise, as it was observed that symptoms such as fatigue worsened after exercise [2]. Although recommendations for physical activity in the healthy population have gained considerable attention, this is not the case for the disabled population [3]. Regular physical activity has been recognized as one of the most consistent positive interventions in patients with MS [4] resulting in improved cardiovascular function [5] , muscular strength [6], and delaying the early onset of fatigue [7]. Therefore, although there have been studies examining the role exercise could potentially play in the treatment and prevention of MS symptoms, the link between exercise and MS has yet to be fully explored.

Intolerance to heat resulting from physical activity or increased ambient temperature is very common in MS. As many as 60-80% of people with MS report clinical deterioration resulting from thermo sensitivity [8]. An increase of 0.5°C may slow or even block nerve impulse conduction in demyelinated fibers [8]. This phenomenon, also called Uhthoff's, manifests as a temporary worsening of neurological function with increased body temperature [9]. This worsening usually subsides within 30 minutes following cool down. Although there has been an interest in the role of heat-intolerance [10], the effect of heat-intolerance on exercise in MS still remains somewhat undetermined.

Excessive fatigue, described as the feeling of lassitude or lack of energy, is one of the most common complaint in individuals with MS,[11] often leading to a loss of motivation for physical exercise, which in turn results in greater muscle weakness[12] and decreased bone mineral density.[13]This in turn may further result in increased risk of injury through falls and fractures. Indeed, some MS patients feel they need to preserve their energy for essential activities of daily living. The way in which fatigue is both perceived and influences exercise in MS remains largely unexplored. There is a need to better understand the mechanisms responsible for fatigue in patients with MS.

This study sought to examine the effect fatigue and perceived thermo sensitivity has on participation in physical activity in patients with MS. We hypothesize that fatigue and perceived thermo sensitivity will result in decreased participation in physical activity.

METHODS

Participants

Participants in this study consisted of 77 men and women between 22 and 69 years of age with a diagnosis of Multiple Sclerosis according to the McDonald criteria [14]. All participants were volunteers from the MS Center of Oklahoma, Mercy NeuroScience Institute in Oklahoma City.

Research Design

This was a correlational study requiring participants to fill out self-report questionnaires in a single session lasting approximately 30 minutes. The study protocol was approved by the institutional review board at Mercy Health Center, and all participants in the study provided written informed consent before testing.

Assessments

Physical Activity level (PA)

Physical activity level was measured by the Godin Leisure-Time Exercise Questionnaire, which consisted of two main questions.15 . It determined the average number of times an individual participated in strenuous, moderate and mild exercise, for more than 15 minutes during their free time in a typical 7-day period.

Strenuous exercise is considered when the heart beats rapidly and includes activities such as running, jogging, vigorous swimming, and vigorous long distance bicycling. Moderate exercise is considered not ex-

hausting, and includes activities such as fast walking, baseball, tennis, easy bicycling, and easy swimming. Mild exercise is considered minimal effort such as yoga, archery, bowling, golf, and easy walking. It also determines how often during a typical 7-day period an individual engages in any regular activity long enough to work up a sweat. Each participant could answer: "1-often," "2-sometimes," or "3-rarely/never." Total weekly leisure activity is calculated by using the weekly frequencies of "strenuous," "moderate," and "light" activities multiplied by nine, five, and three METs, respectively.

Fatigue

Fatigue was measured by the Fatigue Severity Scale (FSS) [16]. The FSS is a method that evaluates fatigue in individuals diagnosed with MS and others that also have conditions such as chronic fatigue immune dysfunction syndrome and systemic lupus erythematosus. FSS is widely used in MS studies and shows high reliability, validity and internal consistency [16]. This scale is specifically designed to differentiate fatigue from clinical depression, since both may share common symptoms. A score of 4.5 is on average seen in people with depression alone, but people with fatigue-related MS, score an average of 6.5 [16]. The FSS is a 9-item questionnaire, each item rating from 1-7, and requires the subject to rate his or her own level of fatigue. Each participant was asked to answer the questions depending on how appropriate they felt the statement applied to them over the preceding week. A low value indicates low agreement with the statement whereas a high value indicates high agreement [16]. The score is calculated by adding all 9-items and dividing it by 9.

Thermo Sensitivity (TS)

Thermo sensitivity was recorded by self-report as to whether they experienced thermo sensitivity or not on a "yes-or-no" basis while participating in physical activity.

Demographic Data Questionnaire

A questionnaire recording demographic data such as age, height, weight, gender, type of MS, and duration since MS diagnosis was obtained from each participant.

Statistical Analysis

The results of all descriptive analyses were reported as mean ± standard error for the group. A univariate analysis of variance was used to determine thermo sensitivity group differences in physical activity (ie, Group 1 did experience thermo sensitivity; Group 2 did not experience thermo sensitivity). Chi-square analysis was used to examine gender differences in thermo sensitivity. Pearson product moment correlation coefficients

Table I. *Subject Characteristics (n = 77; 23 males/54 females)*

Age (yrs)	77	45.2 ± 1.4
Height (cm)	77	169.0 ± .01
Weight (kg)	77	79.7 ± 2.7
BMI (kg/m²)	77	26.9 ± .78
MS (yrs)	77	7.6 ± .82
Type of MS		
RR-MS (n)	61	
PP-MS (n)	3	
SP-MS (n)	12	
CIS (n)	1	

Mean ± Standard Error (SE), BMI; body mass index, MS; multiple sclerosis, RR-MS; relapsing remitting MS, PP-MS; primary progressive MS, SP-MS; secondary progressive MS, CIS; clinical isolated syndrome

were computed for physical activity and FSS measures. Finally, univariate analysis of variance was used to determine gender differences in PA, TS, and FSS, and whether differences in PA or FSS existed between individuals with different types of MS.

Univariate analysis of variance was also used when filtering FSS scores into "low" and "high" levels of fatigue. Everyone scoring 0- 4.4 got coded 0 (or not selected) and everyone scoring 4.5 and above got coded 1 (or selected) in the analysis. All statistical analysis was performed using SPSS, version 16.0 (SPSS Inc, Chicago, IL, USA). Statistical significance was defined as P-value < 0.05.

RESULTS

Clinical Characteristics

Participants consisted of 77 individuals (23 males/54 females), ranging in age from 22 to 69 years (μ=45.2), with an average disease duration of 7.6 years (range 1 month to 30 years). Subject demographic data are displayed in table I.

Thermo Sensitivity (TS)

Overall, 83.3% of the participants reported TS (91.8% of females and 65.2% of males). Individuals that reported "yes" to TS also reported higher FSS scores compared to individuals that reported "no" to TS (4.9 vs 3.3), indicating a trend that people with TS experience more fatigue compared to people that do not have TS. Individuals that reported TS had significantly lower rates of physical activity participation compared to individuals who did not report TS ($p<.05$), (Graph I).

Fatigue

There was a negative correlation ($p<.01$) between physical activity and FSS, indicating that as levels of fatigue increase, participation in physical activity decrease, (Graph II). Individuals that scored 4.5 or higher on FSS reported significantly less participation in PA ($p< .05$) compared to those who reported fatigue less than 4.5 on the FSS test.

Gender Differences and Type of MS

Significant gender differences were seen for FSS ($p< .05$) and PA ($p< .05$), with men reporting less fatigue and more participation in PA than women. There were gender differences with women reporting occurrence of TS significantly more often that men ($p<.05$). Type of MS did not influence participation in PA or FSS ($p>.05$).

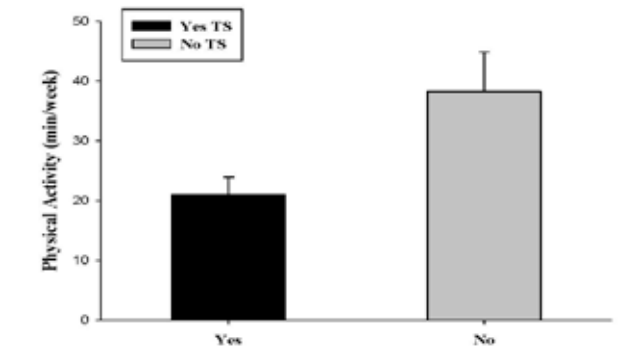
DISCUSSION

This study examined whether individuals diagnosed with MS participated less in physical activity if they reported being bothered with fatigue or thermo sensitivity.

Thermo Sensitivity

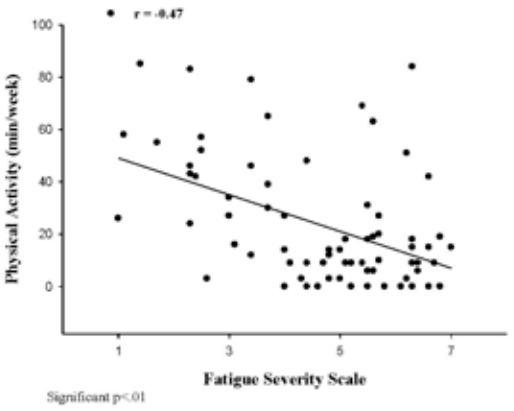
Participants who reported experiencing thermo sensitivity during physical activity showed markedly less participation in physical activity when compared to individuals who reported not experiencing it. An increase in body temperature, either passively or by exercise, even only by a few degrees, has shown to cause a reduction in CNS activation with core temperature reaching 39.5˚C and thereby slowing down the central motor drive to the working muscles [17]. There is evidence of decreased maximal motor unit firing rates [18] and inadequate motor unit re-

Graph I. *Physical Activity and Thermo sensitivity*



Significant p<.05

***Graph II**. Pearson correlation between Physical Activity and Fatigue severity scale*



cruitment [19] during maximal voluntary contractions in MS muscles compared to that of normal subjects. This suggests that the neural mechanisms are responsible for the deficit in muscular strength that is seen in MS [20]. Combining this with increased body temperature could possibly reduce physical functionality and thereby hasten fatigue, causing greater difficulties with engaging in physical activity.

In areas of demyelination, even a small increase (e.g. 0.5˚C) in core temperature could completely block action potentials and the affected axons can only transmit single or low frequency impulses [8, 21]. Individuals that have a greater fitness level, seem to acclimatize faster and are able to sweat more [22]. Studies involving MS response to sweating are scarce even though autonomic dysfunction has been reported [23], as well as lower sweat rate and sweat gland output following aerobic training along with patients with more disease severity compared to that of controls [24,25].

An added element is the potential for decreased sweat gland output, which can have a potentiated effect on thermo regulation. The hypothalamus is the temperature-regulating center, and hypothalamic lesions within the CNS could possibly play a role on how well the autonomic temperature regulation functions in an individual with MS.[24]

Fatigue

Fatigue is one of the most common complaint in individuals with MS [11], with sudden feeling of extreme fatigue for no specific reason, often occurring as the day progresses. The exact etiology of fatigue is unknown, but it might be multifactorial, affecting functioning on several levels and not only by muscular strength weakness[26]. The weakness, disability and fear of aggravating their clinical state, may lead these chronically ill patients, who already suffer from fatigue, to magnify this symptom. Both asthenia (fatigue at rest) and pathological fatigability (fatigue upon physical loading) may be translated into a sensation of increased effort to perform even the slightest activity[27]. Feelings like these may be a deterrent for patients to participate in any physical activity program.

The relationship between physical activity and fatigue however, have shown equivocal results, with some studies reporting no increase in fatigue with physical activity [28] and others reporting increased fatigue with physical activity participation [29]. A 24% reduction in self-reported fatigue was reported in a study by White et al. [30] following an eight week progressive resistance training program focusing on lower extremity. This was further supported in a study by Dodd et al. [31] whom also reported reduced fatigue following a progressive resistance exercise program twice weekly for 10 weeks in MS individuals.

Fatigue may affect participation in physical activity, which coincides with the results of our study that showed significantly less participation in physical activity with increased fatigue in individuals with MS. Induction of fatigue with increased body temperature was demonstrated by Baker[32] in a study in which MS patients exercising in a pre-heated pool experienced greater symptoms of exhaustion. Significant improvement in 25-ft walk performance and fatigue scores were demonstrated in a different

study following pre-cooling in a pool prior to exercise.[33] Although, with sudden onset of MS-related fatigue, any physical task may take considerable effort to execute, so reducing the thermal strain may help attenuate fatigue and also the reduction of participation in physical activity.

Gender Differences

In relation to gender differences and heat-related issues, reports have suggested, although with some controversy, that most women appear to be less heat tolerant than men, which coincides with the results of this study. A possible explanation is that women generally have higher percentage of body fat, which reduces heat loss.[34]

Type of MS

Type of MS did not influence PA or FSS in our study. However, a study by Cartlidge[25] found impaired sweat function in MS patients with more severe disease progression. In our study, we demonstrated that MS individuals that reported issues with thermo regulation also reported significantly less participation in PA.

CONCLUSION

These findings provide a framework for future studies of physical activity and the relationship to fatigue and thermo sensitivity in the MS population. With both thermo sensitivity and fatigue negatively affect participation of physical activity, future research should include ways to prevent thermo sensitivity in order to increase participation in physical activity in this population. Cooling equipment to minimize heat related problems, such as cooling vests or pre-cooling by water immersion, have shown beneficial results with balance and gait [35], improved visual field in individuals with acute optic neuritis [36], reduced spasticity [37], as well as improvement in fatigue [38]. Since it has been proven that cooler temperatures improves both neurologic function and fatigue, exercise programs should be monitored and performed in a cool controlled environment to be most beneficial. Another way to control for minimal increase in core temperature is with resistance training as the chosen type of physical activity, as it does not result in the same increases in core temperatures that is seen with endurance training [20]. Further, pharmaceuticals such as potassium channel blockers like 4-aminopyridine (4-AP) have shown to improve motor and visual function [39-41] and walking speed [42] in MS patients by increasing the conduction of action potentials in demyelinated fibers [43]. Another way to control for minimal increase in core temperature is with resistance training as the chosen type of physical activity, as it does not result in the same increases in core temperatures that is seen with endurance training.[20] Further, pharmaceuticals such as potassium channel blockers called 4-aminopyridine (4-AP) haveshown to improve motor and visual function[39-41] and walking speed[42] in MS patients by increasing the conduction of action potentials in demyelinated fibers.[43] This may be even more important to follow for female MS patients, as women may be less tolerant to heat compared to men, which also coincides with this study with more women reporting heat sensitivity than what men did.

Study Limitations and Future Studies

Paragraph Number 23

This study was based on results of self-report and can therefore not be generalized to the entire MS population and can have the bias of improper recollection. However, the sample size was large enough to draw general conclusions on what affects participation in physical activity in an MS population. Future studies should be done to include objective measures of heat sensitivity and fatigue by perhaps measuring force generation or maximal voluntary muscle contraction, in order to get a better understanding of more effective therapeutic strategies to treat MS symptoms, reduce the incidence of secondary diseases such as cardiovascular diseases and obesity and also improve functional independence.

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