

AN ABSTRACT OF THE THESIS OF

Louisa Summers for the degree of Doctor of Philosophy in Human Performance
presented on November 2, 1999. Title: The Effects of Resistance Exercise on
Lower Extremity Power in Women with Multiple Sclerosis.

Abstract approved:

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A common perspective promoted by health care professionals is that exercise may help reduce symptoms and improve activities of daily living among persons with multiple sclerosis (MS). Yet, the effects of resistance exercise on power, functional mobility, and fatigue are largely unknown. The purpose of this study was to examine the effects of an eight-week resistance training program on lower extremity power, functional mobility, and daily levels of fatigue in women with MS. Twenty-nine women ($\bar{M} = 50.5 \text{ years} \pm 8.5 \text{ SD}$) with an average Expanded Disability Status Scale score of 3.6 were stratified by disability level and age, and then randomized ($n = 24$) into the exercise ($n = 16$) and control group ($n = 13$). The exercise group participated in six exercise instructional sessions prior to the implementation of the eight-week home based exercise program. The lower extremity resistance training intervention was three times per week (for an hour) and consisted of functional exercises with weighted vests. Power was examined in

both legs using the Lower Extremity Power Rig (Bio-Med International), and functional mobility was examined with the Up and Go test. Fatigue was recorded every morning (10 a.m.) and evening (7 p.m.), using a visual analog scale. All participants completed a familiarization session prior to testing. Following the intervention, data analysis indicated significant differences in lower extremity power. Functional mobility tests scores improved in the exercise group by 11.7%, but the improvements were not statistically significant. Fatigue data were summarized by regressing the average daily fatigue values over time, yet, there were no significant differences in fatigue slope between groups. The home-based exercise program offered a practical means for ambulatory adults with MS to improve lower extremity power by over 30% in a short period of time. While functional mobility results were not significant, anecdotal evidence demonstrated that four participants in the exercise group stopped using their canes for ambulation. This type of progressive resistance exercise may be a feasible way for adults with MS to improve lower extremity power and overall physical activity using a program accessible to all.

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November 2, 1999

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The Effects of Resistance Exercise on Lower Extremity Power in Women with Multiple Sclerosis

by

Louisa Summers

A THESIS

submitted to

Oregon State University

**in partial fulfillment of
the requirements for the
degree of**

Doctor of Philosophy

**Presented November 2, 1999
Commencement June, 2000**

Doctor of Philosophy thesis of Louisa Summers presented on November 2, 1999

APPROVED:

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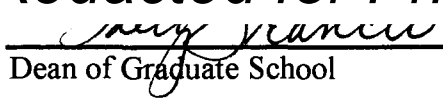
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Louisa Summers, Author

ACKNOWLEDGEMENTS

I would to thank many people who have helped me accomplish this and many other projects that I have been involved with while at Oregon State University. First, I would like to sincerely thank my major advisor, Jeff McCubbin. Thank you for helping me pursue and accomplish my goals as a doctoral student. I appreciate all of time you have spent training and mentoring me. Thank you for your patience and opportunities you have given me during my doctoral training. Thank you for your financial support and working so hard to maintain the U.S Department of Education Doctoral Training grant. I can't thank you enough for the experience that I have had here at Oregon State University.

I would like to thank my other committee members who, each in their own special way have helped and guided me along this path. I would like to thank Dr. Doug Collier for his guidance during my comprehensive exams. I would like to thank Dr. Dan Williams for his teaching and training in exercise physiology and statistics. I would like to thank Dr. Christine Snow for allowing me to work in the OSU Bone Research laboratory. The experience and interaction with other lab members was awesome. I would like to thank Dr. Becky Donatelle for her guidance and expertise in public health. I thoroughly enjoyed my public health classes, and have enjoyed applying health principles and techniques to adapted physical activity. I would also like to thank you Graduate Council Representatives, Dr. Thomas Maresh, and Dr. Jack Higginbotham, for their time and energy spent at committee meetings.

I would like to recognize the John C. Erkkila Foundation and the National Multiple Sclerosis Society for financial support of this project. Without this assistance, it would have been very difficult to complete a project of this magnitude.

Conducting a project of this nature was a huge, but rewarding task, and I would like to recognize members of the research staff. I would like to thank Trish Manns, for performing all of the pre and post neurological evaluations. Your expertise was invaluable. I would like to thank Kendra Bennett, Justin Carson, Andrea Juhl, Marvin Smith, and Daniel Barnet for their exceptional work. They were extremely helpful during data collection. Their attention to detail, and care they gave while maintaining phone contact and during home visits is very much appreciated.

Most importantly, I would like to thank my family and friends for their never-ending support during my entire college career and doctoral program. James, you added a spark to my life and helped me become the person I am. Thank you for the support and love you have given me. I can't thank you enough. Thanks Mom, Dad, Marv, Dee, and my big sister Kim. You have been with me the whole way, and I wish I could give you all a doctoral degree in family support.

CONTRIBUTION OF AUTHORS

Dr. Jeffrey McCubbin was involved in the design, analysis, and writing of the manuscript. The data collection was performed in the Bone Research Laboratory at Oregon State University, under the direction and guidance of Dr. Christine Snow. Dr. Dan Williams assisted in the statistical analysis of the data. Dr. Becky Donatelle assisted with contributions relating to study design, and addressed the potential for confounding variables. This project was supported by grants from the John C. Erkkila Endowment for Health and Human Performance, and the National Multiple Sclerosis Society Pilot Research Program.

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THE EFFECTS OF RESISTANCE EXERCISE ON LOWER EXTREMITY POWER IN WOMEN WITH MULTIPLE SCLEROSIS

BACKGROUND AND SIGNIFICANCE

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system, which is the most frequent form of neurologic disorder among adults. In the United States, approximately 300,000-350,000 persons have MS, with as many as 10,400 being diagnosed each year (National Multiple Sclerosis Society, 1998). MS affects Caucasians more frequently than individuals of Asian or African-American descent. MS is more frequently found in a temperate climate and in industrialized areas of the world. Women are 1.5 – 2.0 times more likely to develop MS than men, and the average age of onset is 25 for women and 28 for men (Carroll & Dorman, 1993).

MS is an autoimmune disease that may have a viral origin. The initiation and progression of the disease involves an attack of the myelin sheath of the brain and spinal cord. After the myelin sheath is damaged, scar tissue or plaques called scleroses, are formed. The scleroses inhibit neural impulses from the brain by interrupting the messages sent to the brain, or slowing down the transmission rate (Carroll & Dorman, 1993). The demyelination of the nerve tissue causes a variety of symptoms. These symptoms may express themselves as paralysis or partial paralysis of the lower or upper extremities, bowel and bladder dysfunction, vision

impairment, heat intolerance, and cognitive impairment. Other symptoms which affect physical activity include: excessive muscle fatigue (Sharma, Kent-Braun, Mynhier, Weiner, & Miller, 1995), muscular weakness (Ponichtera, Rodgers, Glaser, Mathews, & Camaione, 1992), spasticity, impaired balance, impaired autonomic cardiovascular control (Serman, Coyle, Panasci, & Grimson, 1985; Pepin, Hicks, Spencer, Tran, & Jackson, 1996). These symptoms may lead to an abnormal gait or immobility, and are frustrating for persons with MS due to their effects on daily activities. In addition, these symptoms often limit a person's ability to be physically active.

Different Types of MS

Similar to the different symptoms of MS, are the different forms or types of MS. Many authors agree that there are three to four main patterns of MS (Carroll & Dorman, 1993; Holland, 1998), but disagree over the name or classification of each. Each type of MS affects the progression of the disease in a different manner. The *primary progressive* form of MS, is one in which there may be a slow and steady progression of symptoms, leading to greater deterioration, and increasing disability. Progression may or may not be due to exacerbations, and as many as 10% of adults with MS may have this form (Carroll & Dorman, 1993).

The second type of MS is called *relapsing-remitting*. This form of MS is characterized by a series of clearly defined exacerbations, followed by complete, or almost complete recovery. After, an exacerbation an individual with relapsing-

remitting MS goes into a stage of remission; which is a time when the disease is not progressing (Holland, 1998). Exacerbations may not occur for many years or decades (Carroll & Dorman, 1993). Up to 30% of the total MS population may have relapsing-remitting MS, with little or no residual disability.

In contrast to relapsing-remitting MS, some adults with MS (20%) begin with the relapsing-remitting form and, as a person ages, the disease turns more progressive. This type of MS, has been classified as *secondary-progressive* (Holland, 1998). As one ages, the number of relapses may decrease and there may be periods of minor remissions and plateaus (Holland, 1998), but there is increasing disability. The increased disability may or may not be caused by exacerbations.

A similar type of MS has been termed *progressive-relapsing* MS. This form of the disease is characterized by its progressive nature from the onset. Persons with this type of MS experience clear, acute relapses, which may or may not lead to a full recovery. Unlike relapsing-remitting, in between relapses, the disease continues to progress. Some authors suggest that up to 40% of adults have progressive-relapsing form of the disease (Carroll & Dorman, 1993).

There is no known cure for any of the different types of MS, but the life expectancy has been described as equal to that of the general population (Ponichtera-Mulcare, 1993). With a life expectancy similar to that of the normal population, adults with MS were found to have similar rates of death for coronary heart disease, cancer, and stroke (Sadovnick, Eisen, Ebers, & Patton, 1991).

Although most adults with MS have the ability to ambulate 25 years after diagnosis

(Ponichtera-Mulcare, 1993), many reduce their physical activity levels to below that of sedentary adults (Ng & Kent-Braun, 1998). A combination of reduced physical activity levels, and intermittent corticosteroid treatments (Troiano, et al., 1992) may put this group at an even greater risk for hip fractures and/or osteoporosis. Research has shown that male and female adults with MS had significantly less bone mineral density at the femoral neck (Nieves, Cosman, Herbert, Shen, & Lindsay, 1994; Schwid, Goodman, Puzas, McDermott, & Mattson, 1996), and spine (Nieves, et al., 1994) than others of the same age. Other research has identified that adults with MS frequently fall (due to vision and balance impairments), and therefore increase fracture risk and the rate of fractures in this population (Troiano, et al., 1992). The combination of falls, low bone mass (Hayes et al., 1993), and decreased muscular strength (Lord, Ward, Williams, Anstey, 1994; Rosenburg, 1998) have been shown to be primary contributors for fracture risk. Therefore, maintaining an active lifestyle may be important for adults with MS to decrease the risk for hip fracture, chronic disease (Pate et al., 1995), and osteoporosis.

In the past, exercise was not prescribed or recommended by physicians due to the fear of initiating fatigue and increasing symptoms of heat intolerance (Ponichtera-Mulcare, 1993). Recently, various professionals have begun to recognize the important contribution of exercise in maintaining physical and psychological health for persons with MS (Krupp et al., 1988, Ng & Kent-Braun, 1998; Petajan et al., 1996). Yet, the role of exercise and its benefits are not well

understood. Unfortunately, daily fatigue may lead to the lower levels of physical activity and ultimately a reduction in muscular strength reported in adults with MS as compared to sedentary adults (Ng & Kent-Braun, 1998; Ponichtera et al., 1992). Physical inactivity may then perpetuate the cycle of fatigue, inactivity, and deconditioning, resulting in decreased functional ability. Exercise may play a key role in breaking the cycle of inactivity and deconditioning, whereby maintaining functional ability and independence over time.

Exercise and MS - Aerobic Training

Aerobic exercise training has been researched more frequently than resistance training in adults with MS. Many studies were conducted early-on to determine that maximal aerobic capacity testing (VO_{2max}) was safe for adults with MS (Kosich, Molk, Feeney, & Petajan, 1987; Lohman, Smith, La Rocca, & Abrahams, 1992; Ponichtera-Mulcare, Glaser, Mathews, & Camaione, 1993; Ponichtera-Mulcare, Mathew, Glaser, & Gupta, 1995). These studies used stationary bike ergometers, recumbant bikes, arm ergometers, and combination arm/leg bicycle ergometers. All of the studies were conducted with ambulatory adults with mild disability, and the samples ranged from 4 to 39 adults with MS. These studies concluded that it was safe for adults with MS to complete a maximum aerobic capacity test using different modes of ergometry. There were no adverse effects from the assessments, nor did the tests induce MS symptoms, nor exacerbations.

After the initial safety of maximum testing was determined, researchers moved into the area of aerobic training. Early on, Schapiro et al., (1988) examined 16 weeks of unsupervised home exercise using in 50 adults with MS. Twenty-five adults with MS exercised 15-30 minutes, four to five times a week. They were compared to 25 non-exercising adults with MS on graded exercise time, and highest workload achieved using an arm/leg cycle ergometer. Overall, the exercise group had a modest 10% improvement in workload. The participants with a lower level of disability had greater improvements in exercise time and workload achieved, as compared to participants with a higher level of disability. The authors concluded that it was safe for adults with MS to engage in an aerobic exercise program, and that neurological impairment may have effected the intensity at which participants trained.

Ponichtera-Mulcare, Mathews, Glaser, and Gupta (1994) examined aerobic capacity (VO_{2max}), power output, and maximal heart rate, before and after three months of aerobic training in 19 adults with MS. The fully ambulatory adults improved VO_{2max} by 10%, increased their age predicted max HR from 88% to 95% (post-test), and power output by 9%. The semi-ambulatory group also had improvements in VO_{2max} (7%), power output (4%), and maximal heart rate (11%). Although the study did not have a control group, and post-test results were not statistically significant (compared to pre-test), the results are still meaningful with respect to the compliance and improvements made by the adults.

More recently, Petajan et al., (1996), studied the results of a 15 week aerobic exercise training program with 54 adults with MS. This study measured many different items including: a host of psychological parameters (Fatigue Severity Scale, Sickness Impact Profile, Profile of Mood States), blood lipids, body composition, isometric strength, and VO_{2max} . This study examined scores prior to exercise, and after 5, 10, and 15 weeks of exercise. Following a warm-up, the exercise group trained at 60% VO_{2max} for 30 minutes on arm/leg bicycle ergometers, three times a week. The results for the psychological parameters were very positive. There were significant changes between baseline and 10 weeks of exercise in the total Sickness Impact Profile (SIP) score, and the physical dimension (ambulating, mobility, body care and movement), social interaction, emotional behavior, and home management subsections for the exercise group. Mobility improvements were seen after 5 and 15 weeks of exercise as well. After 10 weeks of exercise, the exercise group improved fatigue, depression, and anger scores on the Profile of Mood States.

After 15 weeks of aerobic exercise, many improvements were made in different areas of health related variables, such as, muscular strength, body composition, aerobic capacity, and blood lipids. Although this study was not designed to increase strength, both the upper and lower extremity isometric strength scores improved over time for the exercise group as compared to the control group. After 15 weeks of exercise serum triglyceride levels were significantly less (17%), and skinfold thicknesses were significantly different from

baseline for the exercise group. Aerobic capacity improved by 22% in the exercise group (1% in the control group), and maximal power output improved by 48% in the exercise group (12% non-exercise group). Relationships between EDSS score and improvements in VO_{2max} were not statistically significant, implying that improvements were made regardless of neurological impairment. This is the first study, which showed that adults with MS with a more severe level of disability improved at a similar rate, as adults with less disability.

Other research has examined the energy cost of walking in adults with MS (Olgiati, Burgunder, & Munmenthaler, 1988). The level of spasticity was shown to be a major factor in the amount of energy expended during ambulation in 33 adults with varying levels of disability as compared to other 12 controls. This study examined the aerobic capacity (VO_2) during rest, and walking on a treadmill for 3 minutes at speeds of 1.5 km/hr and 2 km/hr. The authors concluded that for the adults with MS, the cost of walking was related to spasticity of the legs, and not leg or trunk weakness (Olgiati, Burgunder, & Munmenthaler, 1988).

Exercise and MS - Strength Training

Research involving strength training in adults with MS has followed a similar pattern as the research involving VO_{2max} . One of the first studies using isokinetic dynamometry was completed to ensure that testing was reliable, and would not harm the participants, or induce MS symptoms (Armstrong et al., 1983). After it was determined safe, research then used isokinetic dynamometry to

examine the rate at which muscle tension developed in adults with MS ($n=15$), as compared to 17 controls (Chen, Pierson, & Burnett, 1987). The authors concluded that adults with MS had significantly decreased rate of muscle tension development, and a significantly decreased muscle tension-maintaining capacity. Later, strength studies using isokinetic dynamometry, determined that nine adults with MS had less concentric peak torque in the quadriceps and hamstrings than nine matched adults without MS (Ponichtera et al., 1992).

After the safety of isokinetic dynamometry was determined, researchers implemented an endurance training program of the knee flexors in five adults with MS (Swensson, Gerdle, & Elert, 1994). Five participants used weight cuffs, a pulley apparatus, or an isokinetic dynamometer two or three days per week, for four to eight weeks. The training program took place at either a rehabilitation clinic, or physical therapy clinic. Pre and post-testing consisted of: 50 repeated maximal repetitions of the knee flexors, measurements of peripheral muscle fatigue using a Borg 10 point scale, and five aspects of general well-being measured with visual analog scales. After training, three of the five participants increased the peak torque of the knee flexors and decreased perceptions of fatigue. Aspects of general well being (fatigue, health, physical fitness, somatic health, and mood) also improved. The authors concluded that training improved aspects of well-being, and that more comprehensive studies of exercise prescription in adults with MS were needed.

Another study, used isokinetic dynamometry to assess the effects of a 10 week aquatic fitness program on upper and lower extremity muscular force, torque, fatigue and work (Gehlsen, Grigsby, & Winant, 1984). As compared to baseline measures, peak torque during knee extension was significantly greater for all velocities (60, 120, 180, 240, 300 degrees per second) after 5 weeks of the program (non-significant difference for knee flexion). Following the exercise program, ten adults with MS had an 82% improvement in total work for the upper extremities, and a 33% improvement for both of the lower extremities (Gehlsen, Grigsby, & Winant, 1984).

A similar study examined the effects of progressive resistance exercise on muscular strength in nine adults with MS. The 10-week community based exercise program utilized machine-based resistance and free weights, two days per week. Assessments of peak force were made prior to and following the exercise program, with an isokinetic dynamometer set at 60 and 120 degrees per second. The results of the study indicated that the participants improved their knee flexors/extensors by 16 - 57%, elbow flexors/extensors by 6 - 29%, and shoulder abductors/adductors by 3 - 11%. The authors concluded that although some participants did not improve, the results indicate that overall, the majority of the participants improved their muscular strength (Kasser & McCubbin, 1996).

Exercise studies that emphasize muscular strength and endurance training have been performed with adults with MS in very limited samples (Svensson, Gerdle, Elert, 1994) without control groups, and lack results with regard to

mobility. Although these studies have determined the safety of resistance training, little work has been done to evaluation the efficacy and functional benefits for adults with MS.

Exercise and MS - Intramuscular Fatigue

Kent-Braun, Sharma, Miller, & Weiner (1994) have completed a series of studies examine that metabolic muscle changes related to fatigue and exercise and adults with MS as compared to controls. These studies used phosphorus magnetic resonance spectroscopy (MRS) to monitor rates of intramuscular metabolites (phosphocreatine, inorganic phosphate, & ph), electromyography, and electrical stimulation to assess the change in amplitude of the evoked maximum compound muscle action potential (CMAP). One study determined that 13 adults with MS had slower phosphocreatine resynthesis following intermittent isometric tetanic contractions as compared to 8 controls. The authors concluded that the intramuscular metabolic changes might be partially due to deconditioning of the muscles (Kent-Braun, Sharma, Miller, & Weiner, 1994).

This research group had similar results for two studies examining muscle fatigue, intramuscular metabolic changes, and neurophysiological changes in adults with MS as compared to controls. Both studies used the same type of procedures (metabolic changes, and CMAP) described above. The first study examined the metabolic factors of muscle fatigue during voluntary isometric exercise in 6 adults with MS, as compared to 8 controls (Kent-Braun, Sharma, Weiner, & Miller, 1994). The second study, (Sharma, et al., 1995) used intermittent electrical

stimulation to examine intramuscular muscle fatigue and its relation to disability status, and perceived fatigue in 28 adults with MS and 14 controls. The disability level of participants (EDSS score) was related to the level of muscular fatigue, but not perceived fatigue (Fatigue Severity Scale & Visual Analog Scale). In both studies, the authors concluded that there was no impairment at the neuromuscular junction, and that muscle fatigue in MS may be due to impairments in excitation-contraction coupling and intramuscular metabolism (Sharma, et al., 1995). Throughout the papers, the authors suggest how deconditioning or immobilization may play a role in the muscle fatigue of MS, and may be somewhat reversible with exercise.

Later, Kent-Braun, Sharma, Miller, & Weiner (1996) attempted to reduce muscle fatigue in adults with MS. Specifically, the research was designed to improve the intramuscular metabolic response (tetanic force, pH, and ratio of inorganic phosphate/phosphocreatine) of the dorsiflexors. The dorsiflexors in six adults with MS were trained, 60 minutes a day, six days a week. After eight weeks, four adults has shown improvements in muscle fatigue ability, and in muscle metabolites (decreased pH). Unfortunately, two participants did not have these improvements in muscle metabolism. The authors concluded that training using electrical stimulation may be useful for some adults with MS, but cautioned that electrical stimulation protocols which are used for other adults may not be suitable for adults with MS.

In summary, research has shown that adults with MS have lower levels of physical activity than sedentary adults, lower levels of strength, and that metabolic cost of walking and exercise are greater for this group. The research has shown that it is safe for adults with MS to perform VO_{2max} tests, moderate intensity (60%) aerobic exercise, and isokinetic strength testing. Aquatic exercise training for 10 weeks and 15 weeks of arm/leg cycle ergometry has been shown to improve upper and lower body isometric (Petajan et al., 1996) and concentric strength of various muscle groups (Gehlsen, Grigsby, Winant, 1984). Many health related fitness items (triglyceride levels, skinfold thicknesses) and psychological parameters (anger, depression, and fatigue) were also improved following 15 weeks of aerobic exercise. Others have found that intramuscular metabolism may be impaired in adults with MS as a result of physical inactivity, but may be reversible with exercise.

Exercise and MS - Needed Research

Research involving exercise and MS has had a good beginning, but what has not been examined are related issues involving strength training, and their effects on mobility, and fatigue. Many studies have stated that adults with MS have decreased levels of concentric strength in the quadriceps and hamstrings (Ponichtera et al., 1992), and greater levels of intramuscular fatigue in dorsiflexors (Kent-Braun et al., 1994; 1995). This combination of less leg strength and spasticity may increase the energy used during walking (Olgiati, Burgunder, &

Mumenthaler, 1988). Yet, unfortunately, adults with MS feel like they have less energy to perform physical tasks (Krupp, LaRocca, Muir-Nash, & Steinberg (1989) or activities of daily living (Vercoulen et al., 1996) due to their fatigue. Thus, the benefits of resistance training on lower extremity power and mobility, and their effects on daily fatigue need to be more closely evaluated.

Although many adults with MS are interested in exercise, often it is difficult to find community-based programs that are at a nominal cost with the adequate knowledge and supervision needed. Transportation may be difficult for those adults with vision impairments or paralysis due to the disease. On the other hand, those adults who are still working part-time and/or raising children may find that committing to an exercise program in the community is also difficult. Thus, home-based exercise may be an appropriate tool for many adults with MS. Schapiro and colleagues (1988) determined that 12 weeks of home-based arm/leg cycle ergometry improved aerobic exercise by 10% in 25 adults with MS exercising (as compared to 25 adults with MS who were not exercising). Participants also had a high compliance rate when training at home with electrical stimulation (to improve muscle fatigue ability of the dorsiflexors) (Kent-Braun et al., 1996). Therefore, this study will examine the efficacy of a home-based resistance training program in adults with MS.

Rationale

Physicians and therapists tell many people with MS that exercise may help, and there is less questioning of its benefits than in the past, yet the specific effects of exercise on lower extremity power, functional mobility, and fatigue are not known. It is known that adults with MS are less physically active, and weaker than other adults. It has been suggested that adults with MS can improve strength with progressive resistance exercise (Kasser & McCubbin, 1996). Very little is known about the effects of strength training on everyday function. It is also not known if adults with MS can train at levels which will improve lower leg strength without increasing daily fatigue. Lastly, due to a variety of MS symptoms, transportation is a difficult problem to overcome for many adults with MS. An effort to create a feasible exercise program that may be easily replicated is essential.

Goals of the Project

The goals of this project are to improve lower extremity muscular strength and power in persons with MS. The primary objectives of this study are to determine if, after a two week learning phase, an eight-week home based resistance training program will improve lower extremity power in females with MS. The secondary objectives will examine the effects of this exercise program on functional mobility, and daily fatigue. The exercise intervention will focus on functional activities, which are designed to increase strength and power of the lower extremities.

Research Questions

The following research questions will be examined: 1) Will an eight-week home based muscular strength and endurance program increase the lower extremity power in women with MS? 2) Will an eight-week home based muscular strength and endurance program improve functional mobility? 3) Will an eight-week home based muscular strength and endurance program increase levels of daily fatigue?

METHODS

This section describes the methods and procedures used in this study. A description of participants, instruments, apparatus, procedures, and analysis follows.

Participants

The participants included 32 female volunteers with MS, aged 25-69 years ($M = 50.5$, $SD \pm 8.5$). Men were excluded from this study due to the high frequency of MS in women as compared to men (66% and 33% respectively), and the unequal prevalence between genders (Carroll & Dorman, 1993). Inclusion criteria for this study included: a) healthy females with MS; b) the ability to walk (with or without assistive devices) at least 20 meters (21.8 yards) without rest; and c) participants could not have participated in a community based resistance training program for at least two months prior to the study. Subjects were recruited through local chapters of the National Multiple Sclerosis Society's support group meetings from the mid-Willamette Valley in Oregon. In an effort to assist in the recruitment of subjects from surrounding communities, participants were transported for testing, or reimbursed for testing and/or training sessions. Volunteers signed informed consent that was approved by the Oregon State University Institutional Review Board (Appendix A).

Study Design and Assessment

This study used a quasi-experimental group design. Following the intervention, an analysis of covariance (ANCOVA), with pretest scores as the covariate, was used to determine differences between groups. For both groups, neurological score, lower extremity power, and functional mobility tests were determined prior to and following the eight-week intervention. To counter the potential effects of learning on the dependent measures, each participant during pre and post-testing were assessed over two days (at least 48 hours apart). The first testing session was used as a familiarization period, and the top scores for lower extremity power and functional mobility on the second test day were used for the final analysis.

Neurological Evaluation

For all participants, level of disability was determined by using the Kurtzke Functional System Scales and the Expanded Disability Status Scale (Kurtzke, 1983). This tool has been determined to be reliable and valid (Kurtzke, 1983), and is the primary tool for evaluating neurological impairment for research involving adults with MS (Ponichtera-Mulcare, 1993). The scale uses 0.5 increments to rate the level of neurological impairment due to MS lesions in the eight functional systems and ambulation (Appendix B). The final score ranges from 0 (normal) to 10 (death due to MS) (Kurtzke, 1983). A trained physical therapist evaluated participants at baseline and at the conclusion of the intervention. For this study,

seven functional systems were evaluated. Each functional system is mutually exclusive in its category, and the higher the numerical rating the higher the dysfunction. In the original Expanded Disability Status Scale (EDSS) evaluation, the visual system is examined by performing an eye exam and grading eyesight (e.g. 20/20, 20/10). The visual system was excluded from this study because the researcher did not have the capability to perform this test. The validity or reliability of the EDSS excluding one functional system has not been examined. Although one functional system was eliminated, because each functional system is mutually exclusive, the capacity for this tool to rate level of disability in all of the other areas, should remain intact.

Participants EDSS scores ranged between 1.0 and 6.5 (Kurtzke, 1983), and ambulatory ability ranged from the ability to walk 500 meters without rest, to the ability to walk 90 meters without rest (with an assistive device). Over half of the participants had the ability to walk greater than 500 meters without rest, and only two participants walked less than 100 meters without rest (with an assistive device). Thus, this study included participants of all levels of ambulatory ability and disability level (Table 1).

Table 1. Demographic Characteristics and Disability Level for Exercise Group

Group	Age	Status	ERT	MS	Years	EDSS	Height	Weight
EX or CON	(yrs)	PRE or POST	Yes, No, or N/A	type	since diag.		(m)	(kg)
Ex	46	PRE	N/A	RR	7	2.5	1.61	65.3
Ex	59	POST	Yes	SP	38	1.0	1.59	57.40
Ex	47	PRE	N/A	SP	17	6.0	1.66	97.10
Ex	56	POST	Yes	SP	10	2.0	1.72	80.10
Ex	58	POST	Yes	RR	12	2.0	1.71	87.70
Ex	48	POST	Yes	RR	7	4.5	1.73	88.60
Ex	39	PRE	N/A	RR	10	4.5	1.30	62.75
Ex	52	POST	Yes	RR	8	1.5	1.56	53.60
Ex	50	POST	Yes	RR	13	3.0	1.67	49.00
Ex	42	PRE	N/A	RR	1	1.5	1.64	54.00
Ex	47	PRE	N/A	RR	21	6.0	1.64	76.70
Ex	61	POST	Yes	RR	6	4.5	1.69	101.90
Ex	67	POST	Yes	RR	30	5.0	1.59	63.00
Ex	40	PRE	N/A	RP	5	6.0	1.67	79.60
Ex	51	POST	Yes	SP	11	4.0	1.59	83.30
Ex	57	POST	Yes	SP	7	5.0	1.57	72.10
Ex	41	PRE	N/A	SP	5	6.0	1.59	69.70

Note. RR = Relapsing-Remitting; SP = Secondary Progressive; RP = Relapsing Progressive; PRE = premenopausal; POST = postmenopausal; ERT= estrogen replacement therapy; years since diag. = years since diagnosis.

Table 2. Demographic Characteristics and Disability Level for Controls

Group EX or CON	Age (yrs)	Status PRE or POST	ERT Yes, No, or N/A	MS type	Years since diag.	EDSS	Height (m)	Weight (kg)
Con	43	PRE	N/A	RR	3	2.0	1.68	59.3
Con	52	POST	Yes	RP	14	3.0	1.73	78.50
Con	62	POST	Yes	RP	33	2.0	1.56	62.80
Con	48	PRE	N/A	RR	18	1.5	1.70	68.00
Con	54	POST	Yes	SP	29	3.5	1.67	62.90
Con	49	POST	Yes	RR	11	4.0	1.61	55.10
Con	40	PRE	N/A	RR	14	4.0	1.71	64.80
Con	48	PRE	N/A	RR	4	2.5	1.58	48.60
Con	57	POST	Yes	SP	1	4.5	1.56	73.00
Con	43	PRE	N/A	RR	3	1.5	1.79	87.30
Con	33	PRE	N/A	RP	8	5.0	1.66	107.8
Con	69	POST	No	RR	35	6.0	1.63	73.30
Con	25	PRE	N/A	RR	1	2.0	2.03	87.78
Con	44	PRE	N/A	SP	21	4.5	1.70	79.80

Note. RR = Relapsing-Remitting; SP = Secondary Progressive; RP = Relapsing Progressive; PRE = premenopausal; POST = postmenopausal; ERT= estrogen replacement therapy; N/A = not applicable; years since diag. = years since diagnosis.

Instruments

Health and History Questionnaire

A health and history questionnaire was used to collect information regarding type of MS, year of diagnosis, current health status, level of physical activity, and demographic information (Appendix C). This questionnaire was also used to determine if other serious co-morbidities (e.g., cancer, coronary heart disease) existed. If other conditions existed, physician approval was needed to participate in the study. No study participants required physician approval.

Center for Epidemiological Studies Depression Scale (CES-D)

The Center for Epidemiological Studies Depression Scale (CES-D) survey was used to evaluate symptoms of depression and their relationship to levels of daily fatigue (Appendix D). The CES-D is a short 20 item self-report questionnaire designed to measure symptoms of depression in the general population (Radloff, 1977). Participants were instructed to answer the 20 questions based on how frequently they may have felt during the past week". Statements such as, "I was bothered by things that usually don't bother me", were followed by four responses: 1) rarely or none of the time (less than 1 day), 2) some or little of the time (1-2 days), 3) occasionally or a moderate amount of time (3-4 days), 4) most or all of the time (5-7 days). Each response was assigned a point value based on the frequency of the symptom: 0 = rarely or none of the time, 1 = some or little of the

time, 2 = occasionally or a moderate amount of time, 3 = most or all of the time.

The 20 items are then summed, and a higher score relates to a greater frequency of depression symptoms, whereas a lower score relates to a lower amount of depression related symptoms. Scores range between 0 and 60, and a score of 16 or greater corresponds to clinical depression (Krupp, Alvarez, LaRocca, Scheinberg, 1988). The reliability and validity of this epidemiological survey has been established with the use of household interviews, clinical ratings of depression, and in psychiatric settings. This survey was given once during pre-testing and once during post-testing.

Modified Ashworth Scale

The Modified Ashworth Scale was used to determine the levels of spasticity in participants (Appendix E). The Modified Ashworth Scale (MAS) is a five-point ordinal scale designed to grade the level of resistance encountered during manual passive muscle stretching (Bohannon & Smith, 1987). The MAS grades level of spastically as follows: 0 = normal muscle tone; 1 = a slight increase in muscle tone, manifested by a catch and release, or minimal resistance at the end of the range of motion; 1+ = a slight increase in muscle tone, manifested by a catch followed by resistance throughout the remainder of the range of motion; 2 = more marked increase in muscle tone, but limb easily flexed; 3 = considerable increase in muscle tone, passive movement difficult, 4 = affected part(s), rigid in flexion or extension (Bohannon & Smith, 1987). This scale is the most widely used scale to grade the

degree of spasticity, and has a high rate of interrater reliability. Its' validity has been determined with the use of electromyographic recordings of muscle activity in patients with spinal cord injury (Skold, C., Harms-Ringdahl, K., Hultling, C., Levi, R., Seiger, A., 1998).

Fatigue

Due to the nature of MS and the potential impact of home-based exercise, the participants were asked to rate their fatigue twice daily, in the morning and evening. Daily fatigue was measured to help the researcher regulate the intensity of the exercise program, and to determine if exercise negatively affected perception of fatigue.

Daily fatigue was measured with a visual analog scale widely used with adults with MS (Krupp, 1988). Reliability and validity had determined in patients with sleep disorders (Lee, Hicks, Nino-Murcia, 1991). The original scale was a 10 cm line in which patients indicate their level of daily fatigue by marking a line between 0 (which indicates no fatigue) and 10 cm (which indicates severe fatigue). For this study, the participants were asked to rate their daily fatigue the same scale 0 to 10. Both the exercise and control group were asked to record fatigue levels every day at 10:00 a.m. and 7:00 p.m. A postcard, with separate boxes for each day (Monday – Friday) and time (10:00 a.m. and 7:00 p.m.) with a picture of a 10-cm line at the top, was used to record level of daily fatigue (Appendix F). At the bottom of the postcard, there was a box for participants to record their daily

physical activity. The physical activity box was included to monitor physical activities for both groups during the study. Participants were asked to document (in minutes) activities such as walking, swimming, biking, or others that may affect lower extremity strength. Aerobic type activities such as, biking, swimming, and snowshoeing were the types of activities that were included in the analysis. Activities such as, gardening or housework were not included. The time needed to complete the exercise intervention was not included in the assessment of physical activity. To promote compliance, a magnet was included (to put on refrigerator) with the self-addressed, pre-stamped postcards. Each Monday, participants were asked to mail the postcard back to the researcher. During the study, 86% of all postcards were returned and used in the final analysis.

Lower Extremity Power

Lower extremity power was measured using the Lower Extremity Power Rig (Bio-Med International, W. Yorkshire, England). The power rig was designed to provide a measurement for leg extensor power in older adults with poor mobility, as well as adults of all ages. This device measured the power delivered by a seated subject during a single leg extension. This device was determined to be safe, reliable and valid for all age groups (20-86 years) and levels of physical capability (Bassey & Short, 1990). During assessment, participants alternated legs and performed 8-9 trials per leg, or until power values plateaued. When examining lower extremity power, some authors have found it important to normalize the

power scores by body weight (Bassey & Short, 1990; Bassey, et al., 1991). For this study the primary outcome measure was obtained by summing, the maximum power output of the dominant leg, and the maximum power output of the non-dominant leg, and then dividing by body mass (Watts/kg).

The precision error of this tool when used with adults with MS has not been previously evaluated. The precision error was evaluated by comparing the highest score obtained during the familiarization session, and the highest score during the pre-test session. To compute precision error, the standard deviation (day one and day two) was divided by the average score (day one and day two). For this study, the precision error was 9.5% ($n = 30$). Others have found a coefficient of variation of 10.4% with 18 members of a hospital staff, with an average age of 27 years (SD ± 7.5 years).

Functional Mobility

The “Up and Go” test was used to evaluate functional mobility. This test measures, in seconds, the time taken by an individual to stand up from standard arm chair, walk a distance of 3 meters, turn, walk back to the chair, and sit down again (Podsiadlo & Richardson, 1991). This test has been widely used with adults and determined to be reliable and valid (Podsiadlo & Richardson, 1991). Participants may have used assistive devices (if needed). If assistive devices were used, they were the same for each testing period, and the device used for daily

ambulation (outside the home). This test was given two times a testing session and the best (or lowest score) for each testing session, was used in the analysis.

Although this test has been used with older adults, the precision error has not been examined in adults with MS. For this study, the precision error for the Up and Go test, was 5.6% ($n = 31$). The precision error was calculated using the same technique as with lower extremity power. The lowest time of two trials from the familiarization session and pre-test session were used in the analysis (SD [familiarization & pre-test] / average [familiarization & pre-test]).

Procedures

Group Assignment

Prior to assignment, all participants underwent baseline testing on all measures. At the beginning of the study, there were a total of 33 participants. Due to their work schedules, four participants agreed to be in the study, only if, they were assigned to the control group. Based upon the number of qualified participants, it was deemed necessary to include them in the study. All participants were then matched by disability level and age. Four participants were then matched by disability level and age, to the four whom asked to be in the control group.

The remaining 12 pairs of participants underwent stratified randomization. Each stratum was based on disability level (EDSS) and age, and then a coin toss

determined group assignment. There was one remaining participant without a match, and she was assigned to the exercise group (due to potential loss of participants from disease related issues). Thus, after assignment there were a total of 17 exercisers, and 16 controls.

Instructional Sessions

After group assignment and prior to the home-based experimental treatment, the exercise group participated in six exercise instructional sessions. The instructional sessions took place at three different sites (cities). The sessions were designed to teach participants the correct form for each exercise and proper data recording. The exercise sessions included instruction on the: warm-up stretches, resistance training exercises, and cool-down activities. The sessions occurred three times per week, on alternating days, for two weeks. The vests were worn without weight during the last session of the instructional phase of the program. After the two week instructional phase, the exercise group received all of the equipment (vest, ankle weights, step, and data recording sheets) needed to perform the exercises at home.

During the instructional phase of the program, an exercise video was produced that was specific for this study. For each exercise, a sign that depicted the name of the exercise was displayed above two people demonstrating the exercise. The video was filmed with both the front and side views of the exercise. Instructions and cues were given to remind participants of the correct positioning

and form during the exercise. The video was approximately six minutes in length, and was mass-produced and given to each participant. Participants were asked to watch the video prior to each exercise session.

Intervention

The eight-week resistance training intervention began after the instructional phase. The exercises focused on activities that were designed to be functional in nature and had been shown in previous work (Shaw & Snow, 1998; Winters, Shaw, Voegeli, & Snow, 1998) to increase the strength and power in the lower extremities. Three times per week, each participant performed 5-10 minutes of warm-up activities (walking) and stretches, 25-30 minutes of strengthening exercises, and 5-10 minutes of whole body stretching.

The length of the eight-week home-based exercise program was based on strength training periodization models (Stone, O'Bryant, & Garhammer, 1997). Specifically, the periodization model used for this study included the two-weeks of instruction sessions and eight-weeks of home-based exercise. For this study, a four-week hypertrophy phase, four-week strength phase, and two-week power phase was used. These periodization techniques have been used with athletes as well as untrained individuals (Fleck & Kraemer, 1997).

The exercise intervention was designed to increase the strength and power in the lower body without having detrimental affects on the participants. Due to the variability in ability levels, the exercise programs were individualized so that each

participant would be able to perform the exercises safely and effectively. For some exercises, some participants had to perform modified versions of the exercise in order to complete the required number of repetitions (Appendix G).

The strengthening program included a sequence of five exercises that were originally based on an exercise program designed to decrease risk for osteoporosis (Shaw & Snow, 1998). During all of the strengthening exercises, a wall, chair, or stable structure was located to the left or right of subjects so that one could grasp it if balance was compromised. Chair raises were performed with feet slightly farther than shoulder width apart, in a toe-out position. One repetition consisted of standing up and sitting down. Forward lunges were performed by asking participants to step forward until the stepping leg reached a 90-degree angle, and then return to the original position. Step-ups were performed on a 4, 6, or 8-inch step (specific to the individual). One repetition consisted of the sequence up, up, down, down. The starting legs were alternated so that one leg did not continuously perform the up motion. Toe-raises were performed by rising up on the toes, and rocking back on the heels. Hamstring curls were performed with the use of adjustable ankle weights attached to their ankle. Participants were asked to stand and lift their lower leg up towards their buttocks. During the intervention nine participants performed this exercise standing up, and eight participants performed this exercise lying prone.

Participants were allowed to perform mini-squats in place of forward lunges if they had previous knee problems, which were aggravated by forward lunges, or

developed knee soreness during the intervention. If participants developed knee soreness during the intervention, they were instructed to perform mini-squats for one week, and then return to the forward lunges. Mini-squats were performed with feet slightly farther than shoulder width apart, and in a toe-out position.

Participants were instructed to squat down until their thighs were near a 90-degree angle. Participants who were unable to perform a full squat performed a half squat, but were encouraged to squat down as far as possible. One participant performed mini-squats during the entire intervention due to prior knee surgeries. During the intervention, three participants performed mini-squats for one week (during weeks 4-6) due to knee soreness, and then returned to performing forward lunges without any further complications.

This program utilized weighted vests to increase the intensity of the training (Table 2). Although the intensity of the training varied with each individual, and the volume of exercise was also specific to the individual, the progression of the study was designed as follows: 1) the initial vest resistance was set at 0.5% of body weight, and increased by percentages of body weight (.05 – 1.5%) every one to two weeks; 2) during the first four weeks of the study, participants were instructed to perform 2-3 sets of 8-12 repetitions for each exercise; 3) during the second four weeks, participants decreased the number of exercises to, 1-2 sets of 8-10 repetitions (for each exercise). The initial weight and progression were based on an 11-week pilot study (Summers & McCubbin, 1998).

Table 3. Exercise Intensity During the Eight-Week Home Based Intervention

	Week	Week	Week	Week	Week	Week	Week	Week
	1	2	3	4	5	6	7	8
<u>M</u> %								
body	0.60	1.07	1.62	2.00	2.54	2.98	3.60	3.92
weight								
Sets/	2.5 /	2.5 /	2 / 10	2 / 10	2 / 10	2 / 10	2 / 10	2 / 10
Reps	10	10						

Bi-monthly home visits and weekly phone contact was made for both groups. During contact, the researcher discussed participants' fatigue level, and asked about changes in physical activity, medical status, medications, or home or work related stress. Prior to the home visits to the exercise group, the researcher discussed each participants' exercise intensity and fatigue levels with other research staff who had made contact with the participants. The researcher then adjusted the intensity of the individual exercise programs. At the end of the intervention both groups returned for post-testing.

Analysis

The statistical analyses were carried out using SPSS version 8.0 (SPSS, 1994). Characteristics of the participants at baseline were compared between the exercise and control group by Mann Whitney U tests for the EDSS and the

Modified Ashworth Scale (ordinal variables), and Chi square (χ^2) for type of MS (categorical variable). Mean scores (\pm standard deviation) are presented for pre and post-testing sessions. A t -test was used to determine if differences between groups existed at baseline for physical activity levels, lower extremity power, and functional mobility measures.

To determine whether significant differences between groups existed from pre to post-testing, an analysis of covariance (ANCOVA) was used, with pre-test scores used as a covariate. Separate ANCOVA's were used for the primary outcome measures, lower extremity power, and functional mobility.

To assess the effects of the intervention on daily fatigue, the overall fatigue slope for each individual was determined by regressing the average weekly fatigue values (a.m. and p.m.) on time. Specifically, the independent variable was week (1-14) and the dependent variable was the average a.m. (or p.m.) fatigue value for that particular week. Therefore, for each individual, a separate slope was calculated for a.m. and p.m. values for each week. This technique was used due to the variation in number of participants returning the fatigue data cards. This technique has been used elsewhere to determine the effects of weight variability on cardiovascular risk factors over a 10-year period (Taylor, Jatulis, Fortmann, & Kraemer, 1995). To ensure that the levels of daily fatigue were not confounded by symptoms of depression, the CES-D difference score was used as a covariate in the repeated measures ANOVA to test for differences between slopes.

Prior to the study, power analysis indicated with an expected effect size of 0.5 (Bassey et al., 1992), and the number of dependent measures, changes in lower extremity power would be detected with 80% power by evaluating 25 subjects per group (Thomas & Nelson, 1996). Although prior to the study, the sample size was not sufficient enough to detect changes with 80% power, the sample size was sufficient enough to detect changes with 60% power; thus a decision was made to continue.

Control group training

At the conclusion of post-testing, the control group had an opportunity to learn the home based exercises. The two-week instructional phase for the control group was held at the same locations, three times per week for about an hour. All participants in the control group were given the home exercise video either at post-testing or at the beginning of this training.

RESULTS

After data collection, all variables were entered for analysis and screened to determine if statistical assumptions were met. This screening included examinations for distribution linearity and outliers. All statistical assumptions were met for the primary outcome measure, lower extremity power. Two outliers from the exercise group and one outlier from the control group were excluded from the functional mobility analysis due to extreme scores (greater than two SD from the mean).

Participants

During the study, two participants (one in the exercise group, one control) were excluded due to MS exacerbations, and two participants who initially asked to be in the control group, dropped out of the study due to conflicting schedules (drive time to university or work). Therefore, for the final analysis there were 16 in the exercise group, and 13 in the control group.

All participants completed two days of baseline testing, and the best scores (maximum score for power, fastest time for mobility tests) from the second testing day were used for the analysis. Prior to the intervention, as determined by a t-test, no statistically significant differences between groups existed for demographic characteristics or disease characteristics (Table 3). No significant differences existed for the primary outcome measures of lower extremity power or functional mobility. There was a significant difference between groups for minutes of

physical activity per week. Prior to and following the intervention, the control group participated in a greater amount of physical activity per week.

Table 4. Demographic and Pre-test Measures for Groups (M \pm SD).

Variable	Exercise group (n = 16)	Control group (n = 13)
Age (yr.)	51.4 \pm 7.7	49.5 \pm 9.5
Postmenopausal women	n = 10	n = 6
Number on ERT	n = 10	n = 5
Years since diagnosis	12.3 \pm 10.2	14.9 \pm 11.7
EDSS	3.7 \pm 4.2	3.4 \pm 3.5
Modified Ashworth Scale	0.21 \pm 0.58	0.0 \pm 0.0
Height (m)	1.64 \pm 0.5	1.66 \pm 0.7
Weight (kg)	73.70 \pm 15.9	70.86 \pm 15.37
Physical activity (minutes per week)	46.5 \pm 61.0	129.0 \pm 83.2*
CES-D scale	12.5 \pm 9.9	9.46 \pm 5.4

Note: EDSS = Expanded Disability Status Scale; CES-D = Center for Epidemiological Studies Depression Scale; ERT= estrogen replacement therapy.

* p < .05 exercise group was significantly different from control group.

Training Intensity and Adherence

The adherence to the home-based program was perceived as successful, with 95% of the 24 exercise sessions completed (\underline{M} = 22.9, \underline{SD} \pm .43). All participants were visited a total of four times during the study period, with the

exception of one participant from the exercise group (out of town for three weeks, who continued the exercise program), and one from the control group (doctor's appointment).

Neurological Evaluation

Prior to the intervention, although there were no significant differences between groups, slight differences existed in the walking distance component of the neurological score. The exercise group had an average EDSS score of 3.80 and the control group had an average EDSS score of 3.38, thus the exercise group had a non-significant average level of disability (0.5) that was slightly higher than the control group ($\chi^2 [8, N = 29] = 4.25, p = .835$). The average walking distance for the exercise group was 364.1 meters, and the control group walked an average of 427.3 meters during baseline testing (Table 3). Following the intervention, the exercise group increased their average distance walked by 54 meters ($\underline{M} = 418.6, \underline{SD} \pm 147.0$), and decreased their average EDSS score by 0.6 ($\underline{M} = 3.1, \underline{SD} \pm 1.9$). Whereas, the control groups average distance walked decreased by 6 meters ($\underline{M} = 421.7, \underline{SD} \pm 155.0$), and average EDSS score decreased by 0.1 ($\underline{M} = 3.3, \underline{SD} \pm 1.6$). Although these changes were non-significant, they better describe the samples walking distances and disability levels.

Modified Ashworth Scale (MAS)

Prior to, and following the intervention, there were no significant differences in MAS between groups (Table 4). In the exercise group, three participants displayed spasticity prior to the intervention, and in the control group, zero of the participants exhibited any level of spasticity ($U = 78.0$, $z = -1.673$, $p = .094$). Following the intervention, two participants in the exercise group displayed spasticity, while zero of the participants in the control group displayed spasticity ($U = 72.0$, $z = -1.609$, $p = .108$).

Table 5. EDSS, Modified Ashworth Score, and Physical Activity Pre and Post Intervention or Control Period (M \pm SD).

Variable	EDSS	Modified Ashworth Scale	P. A. (minutes/ week)*
EX Pre	3.70 \pm 4.2	3 / 16	46.50 \pm 61.0 ^b
EX Post	3.09 \pm 2.5	2 / 16	28.18 \pm 56.4 ^b
CON Pre	3.40 \pm 3.5	0 / 13	129.00 \pm 83.0 ^c
CON Post	3.34 \pm 1.6	0 / 13	108.50 \pm 92.3 ^c

Note: EDSS = Expanded Disability Status Scale; CES-D = Center for Epidemiological Studies Depression Scale; EX = exercise group; CON = control group.

^b $n = 11$; ^c $n = 10$.

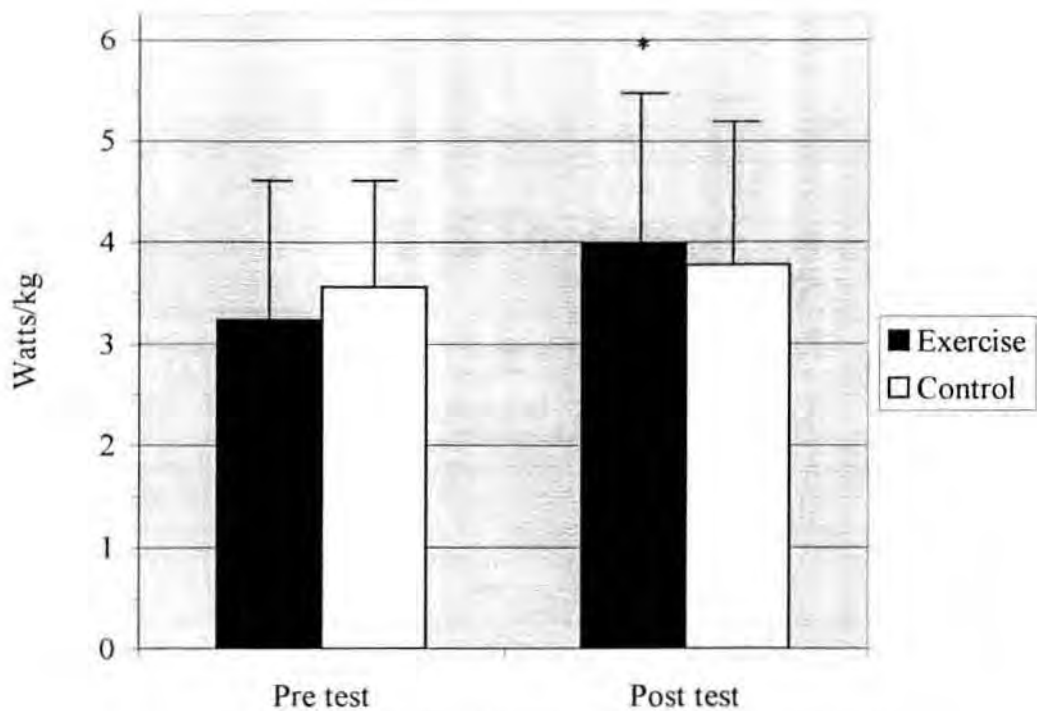
* $p < .05$, control group was significantly different than exercise group at pre and post testing

Lower Extremity Power

Due to its strong relationship with body weight, leg power was adjusted for weight in the analyses. Following the intervention, an ANCOVA revealed a significant difference in lower extremity power between groups (Figure 1). The exercisers (pre-test $\underline{M} = 3.23$ Watts/kg ± 1.37 ; post-test $\underline{M} = 3.99$ Watts/kg ± 1.15) improved their adjusted power in both legs an average of 30.7% more than the control group (pre-test $\underline{M} = 3.56$ Watts/kg ± 1.21 ; post-test $\underline{M} = 3.77$ Watts/kg ± 1.29). Although the exercise group had a slightly less lower extremity power than the exercise group at baseline, this difference was not significant. The difference in baseline lower extremity power may have provided the exercise group with a greater potential for improvement.

Although prior to the study the number of participants in each group was less than the expected 25 per group, the observed power for this analysis was .581 ($F(1, 27) = 5.534, p = .026$). Thus, although the exercise group improved their lower extremity power more than controls the lower statistical power should be taken into consideration when examining these results.

Figure 1. Lower Extremity Power in Both Groups



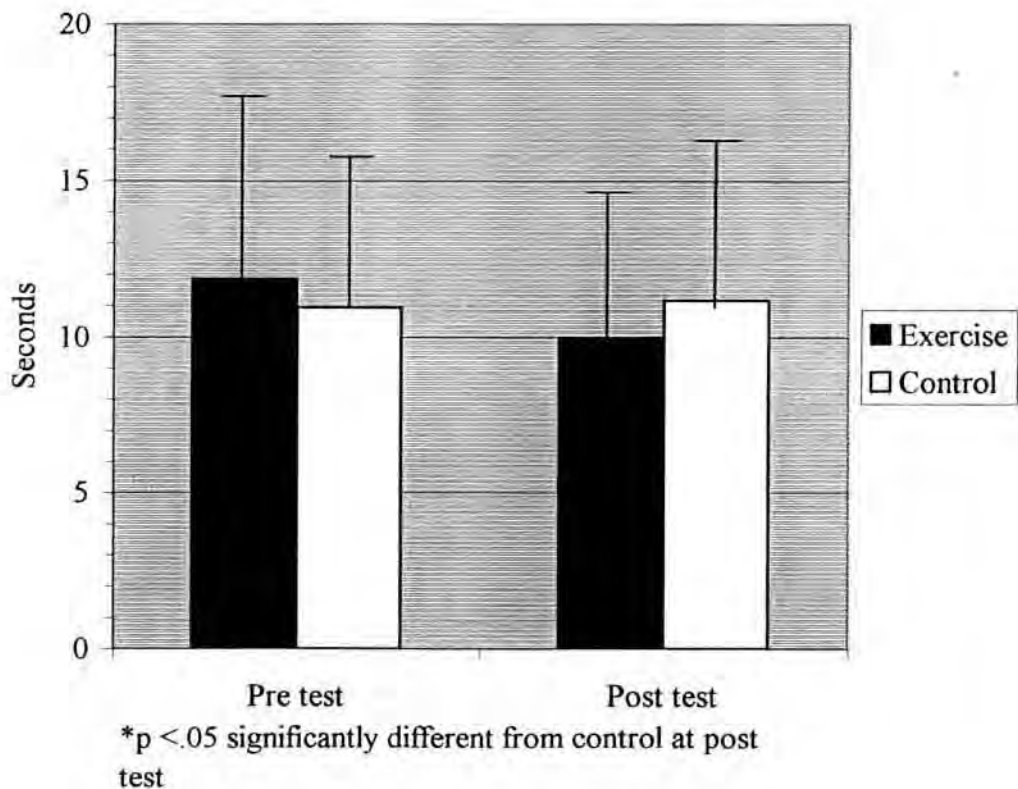
* $p < .05$ significantly different from control at post test

Functional Mobility

During the Up and Go analysis, there were three outliers (two exercise group, one control) removed due to extreme scores (greater than two SD above the mean). Following the intervention, the ANCOVA revealed that there were no statistically significant group differences ($p > .05$) in functional mobility measures. The final results for the Up and Go test indicated that the 15 adults in the exercise group improved their time by 11.7% ($\underline{M} = 11.85 \pm 5.90$ vs. $\underline{M} = 9.96 \pm 4.92$) and the control group showed no improvement ($\underline{M} = 10.94 \pm 4.92$ vs. $\underline{M} = 11.16 \pm 5.00$) in functional mobility (Figure 2).

The loss of participants due to their extreme scores affected the observed power of this statistical analysis. Due to small sample size the observed power was 0.200. Therefore, the non significant results of for this measure may have been due to the small sample size and lack of statisitcal power.

Figure 2. Functional Mobility in Both Groups



Fatigue

One of the secondary objectives of the study addressed the effects of exercise on levels of daily fatigue. For this study, the researcher was concerned about increasing daily fatigue during the home-based exercise intervention. Thus, a

One of the secondary objectives of the study addressed the effects of exercise on levels of daily fatigue. For this study, the researcher was concerned about increasing daily fatigue during the home-based exercise intervention. Thus, a system was set in place whereby the participants rated fatigue on a visual analog scale, and mailed in weekly fatigue cards so that the researcher would improve the ability to regulate the intensity of the exercise program.

The fatigue slope was determined by regressing the average fatigue values (a.m. and p.m.) on week (1-14). This technique was used due to the variation in number of participants returning the fatigue data cards. Although most participants returned the cards to the university weekly, the return rate was not 100% every week. The return rate for both groups during the fourteen-week period was 86%. For the exercise group, the a.m. fatigue slope was 0.01, and the p.m. slope was -0.04 (fatigue units). Thus, for this group, there was a slightly greater decrease in fatigue in the evening (7 p.m.), and a slight increase in the morning (10 a.m.). For the control group, the a.m. fatigue slope was -0.07 , and the p.m. slope was -0.05 . In contrast to the exercise group, this group had a greater decrease in fatigue in the morning than in the evening (Figures 3, 4). The repeated measures ANCOVA, with CES-D difference as a covariate, revealed that although there were changes in CES-D scores for both groups, they did not confound the fatigue slopes (Table 6).

Figure 3. Scatterplot of Predicted A.M. Fatigue Values in Both Groups

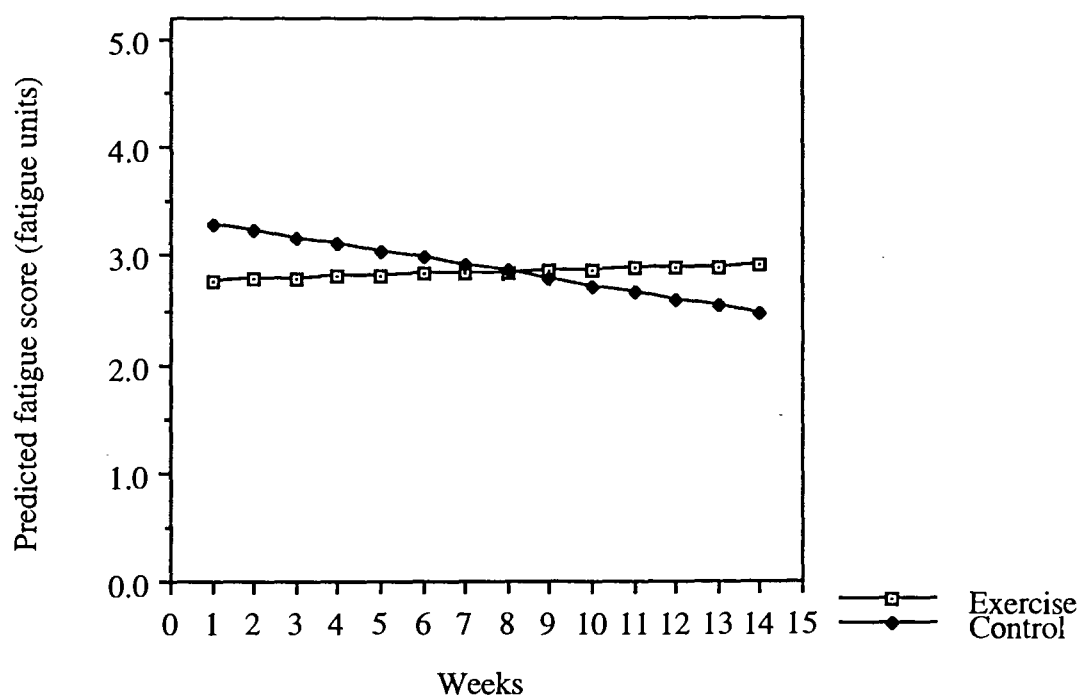


Figure 4. Scatterplot of Predicted P. M. Fatigue Values in Both Groups

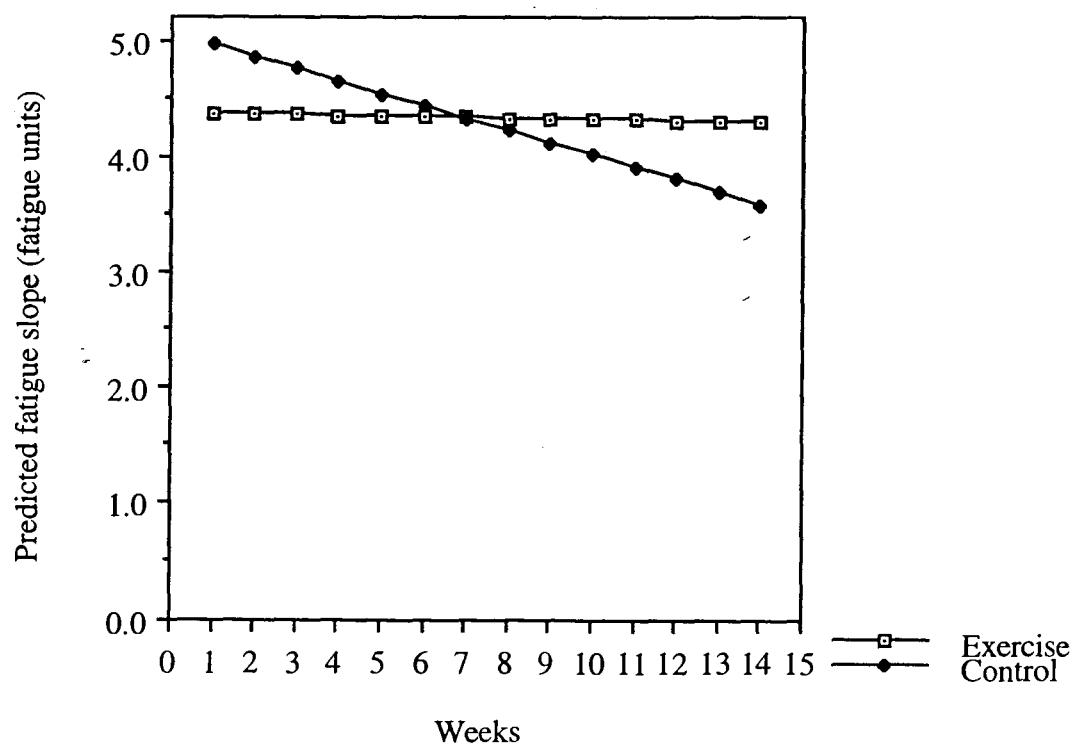


Table 6. Average Fatigue Slope and CES-D Scores in the Exercise Group and Control Group (M \pm SD).

Variable	Exercise group (n =14)	Control group (n =10)
CES-D pre test	12.5 \pm 9.9	7.25 \pm 5.6
CES-D post test	7.25 \pm 5.6	7.09 \pm 5.3
CES-D difference (post-pre)	- 4.71 \pm 5.7	- 1.1 \pm 4.5
Fatigue slope a.m.	0.01 \pm 0.09	- 0.07 \pm 0.06
	(fatigue units/week)	(fatigue units/week)
Fatigue slope p.m.	- 0.04 \pm 0.11	- 0.05 \pm 0.16
	(fatigue units/week)	(fatigue units/week)

Note: CES-D = Center for Epidemiologic Studies Depression scale.

Physical Activity

The week prior to and following the intervention, controls participated in a significantly greater amount of physical activity per week than the exercise group (Table 4) as determined by a Student's *t*-test (pre-test, $t(22) = -2.810$, $p = .010$; post-test $t(19) = -2.433$, $p = .025$). For this group, the primary activity was walking and swimming, with some participants walking as much 20 - 45 minutes per day. The control group had six participants that, throughout the study, performed at least 150 minutes of physical activity per week, with only one reporting zero physical activity. In contrast, the exercise group had three participants who participated in over 100 minutes of physical activity per week (outside the intervention), and seven who reported zero physical activity (outside

the intervention). This increased amount of physical activity was maintained throughout the study, and represents a potential confounding variable.

Although the control group was participating in a greater amount of physical activity prior to and following the intervention, the amount of time needed for the intervention was not included in the exercise group's weekly physical activity. Thus, if the time needed for the intervention (180 minutes) was included as weekly physical activity, the differences between groups would not have been significant at post-test. In addition, many of the participants in the exercise group replaced their previous activity at baseline with the intervention.

DISCUSSION

This eight-week home-based resistance exercise program significantly improved lower extremity power (adjusted for body weight) in women with MS. The strength training exercises did not negatively affect daily levels of fatigue, and there were no injuries or increases in MS symptoms due to the intervention. The home-based exercise program offered a practical means for ambulatory adults with MS to improve lower extremity power by over 30% in a short period of time. Although the benefits of improved power has not been examined in adults with MS, lower extremity power is a major determinant of functional ability in older adults (Bassey et al., 1992), and was highly correlated to functional mobility in this study ($r = .577$, $p = .002$). Although changes in functional mobility were not seen following the eight-week intervention, the potential for improved power to enhance long-term mobility remains undetermined.

Lower Extremity Power

This study supports the first research hypothesis of an improvement in lower extremity power, following eight weeks of home-based exercise. The exercise group significantly improved their power 30.6% more than the control group. Thus, as been shown previously (Shaw & Snow, 1998; Winters, Shaw, Voegeli, & Snow, 1998), the women in the exercise group improved the lower

extremity power, following a resistance training program using functional exercises and weighted vests.

The improvement in lower extremity power was likely the result of the overload principle. The overload principle states that strength and fitness gains are made by providing a greater stress on the body than its' normally accustomed to (Wathen & Roll, 1994). The improvements in lower extremity power were due to the increased volume of work placed on the lower extremities. Specifically, the exercise group was asked to perform a sequence of five lower extremity exercises, by placing all of their body weight (plus the weight of the vest) on their legs. These exercises, plus the progressive resistance which was added to the weighted vests, provided enough overload to the lower extremities to improve lower extremity power.

The improvements in lower extremity power are similar to results of other training studies with adults with MS. Svensson, Gerdle and Elert (1994) found that four to six weeks of muscular endurance training improved the peak torque of the knee flexors. Five participants trained two or three days per week with an isokinetic dynamometer, weight cuffs, or pulley system either at a rehabilitation center or physical therapy department. Similarly, Kasser and McCubbin (1995) found that 10 weeks of progressive resistance exercise improved upper and lower extremity peak torque in 10 adults with MS. Participants exercised two days per week, and similar to this study, the intensity of the exercise was adjusted for each individual. Gehlsen, Grigsby, & Winant, (1984) examined the effects of a 10-week

aquatic fitness program on muscular strength and endurance with 10 adults with MS. Participants swam for one hour, three times per week. These results indicate that after five weeks peak torque of the knee extensors significantly improved, and that after 10 weeks, the total work and fatigue of the knee extensors significantly improved as compared to pre-test scores. In each of these studies, the training programs did not negatively affect the participants fatigue or MS symptoms, and the majority of the participants showed improvements in muscular strength or endurance.

Although non-significant, prior to the intervention, the exercise group had slightly less lower extremity power than the control group. Following the intervention, the exercise group had a greater improvement overall than the control group. One reason may be that the exercise group started the intervention with a greater potential for improvement. This concept which has been termed the “window of adaptation” states that the opportunity for change (or gain) is related to an individuals potential for adaptation (Fleck & Kraemer, 1997). Although pre-test scores were used as a covariate, the decreased starting point of the exercise group may have been a potential confounder.

Functional Mobility

It was hypothesized that the resistance training intervention would improve functional mobility. However, the results of this study did not support the second research hypothesis. This may have been due to the small sample size and low

statistical power. Thus, although changes were made in the exercise group, the ability to detect changes may not have been great enough, likely or perhaps because of the low sample size and statistical power.

Other research has not looked at the specific effects of exercise on functional mobility, yet they have looked at the relationship between functional measures and lower extremity power in very old women (Bassey et al., 1992). In this study of 13 very old women ($\bar{M} = 86.5$ yr., $SD \pm 6$) the relationship between leg extensor power in both legs (Watts/kg) and functional performance was significant for stair rising speed and for 6.1 meter walking speed. In this study, the pre-test lower extremity power in both legs (Watts/kg, both groups) was also significantly ($p < .01$) correlated with the Up and Go test ($r = -.576$). Some authors have suggested that leg extensor power may supersede strength as a predictor of function in older adults (Bassey et al., 1992). Although its difficult to compare the participants of this study ($\bar{M} = 49.67$ yr.; $SD \pm 8.04$), with frail elderly women the relationship between power and functional mobility may improve over time. In middle aged women, the relationship between power and functional mobility maybe less than in frail elderly women, but over time and as women age, the relationship between lower extremity power and functional mobility may increase. The true nature of the power and functional mobility relationship may also have been effected by the lack of statistical power in this study.

Physical Activity

Initial level and choice of physical activity among exercisers and controls may also have contributed to the lack of change in mobility measures. Since primary and secondary outcomes were power and mobility, respectively, participants were allowed to perform aerobic type physical activity during the study. Most participants (over 87%) documented walking as their primary source of physical activity, and 30% of the participants (both groups) walked for at least 20 minutes four or five times per week. At the start of the study, participants were asked not to alter their levels of physical activity, therefore prior to and during the study, the participants walked an average of 73.3 minutes per week (both groups). The specificity of training principle states that if one trains using a specific mode, improvements will be in that mode, and training in a different mode does not necessarily mean that the benefits will transfer to a different mode of exercise. Thus, if the both groups primarily walked for physical activity, and continued to do so during the intervention, it may be reasonable to conclude that resistance training intervention may have improved lower extremity power, but these improvements would not transfer to measures of functional mobility (Wathen & Roll, 1994).

Fatigue

The study indicates that the intervention was implemented without significantly increasing daily fatigue, as indicated by the lack of change in fatigue slope. Fatigue was measured everyday, and fatigue levels decreased slightly in the

evening (0.01 a.m. slope and -0.01 p.m. slope) for the exercise group, and decreased in the morning and evening for the control group (-0.06 a.m. slope and -0.11 p.m. slope). Participants in the exercise group routinely commented that they were sleeping better, especially during the first four weeks of the home-based intervention. These results are concurrent with the results from an aerobic exercise program in which fatigue was shown to decrease during the tenth week of a 15 week intervention (Petajan et al., 1996), yet at the end of the study fatigue was similar to the beginning of the study. During this study, the participants documented to the researcher that exercise did not influence daily fatigue levels, rather it was life events or “stressors”, (e.g. marriage, death in family, work) that increased daily fatigue.

During the study, the control groups fatigue slope slightly declined (non-significant) more than the exercise group. One reason may be that the control group was participating at a greater amount of physical activity prior to ($p < .010$), and after ($p < .025$) the intervention ($\bar{M} = 108.5$ min/wk; $SD \pm 92.3$ vs. $\bar{M} = 28.2$ min/wk; $SD \pm 56.4$). These higher rates of physical activity may have allowed the control group to perform daily activities at a lower relative intensity, whereby promoting less fatigue.

It was also found that fatigue levels were not confounded by changes in symptoms of depression. After controlling for the effects of change in symptoms of depression, an ANCOVA revealed non-significant differences in levels of daily fatigue for both groups.

The results of this study support the findings of others regarding the independence of fatigue and depression. Although both depression and fatigue are common among adults with MS (Petajan et al., 1996; Krupp, LaRocca, Muir-Nash, Steinberg, 1989), and adults with MS tended to have higher symptoms of depression (CES-D) than controls, the relationship between fatigue severity and CES-D scores was minimal ($r = .26$) (Krupp, LaRocca, Muir-Nash, Steinberg, 1989). In this study, the researcher found that our sample had lower CES-D scores ($M = 10.1$, $SD \pm 6.7$) than others ($M = 14.1$, $SD \pm 11.0$), and the relationship between CES-D and fatigue slopes was less (Spearman's rho $r = -.019$ a.m. slope; $r = -.186$ p.m. slope). Although this study examined the influence of exercise on fatigue and depression, this research also suggests that changes in fatigue were independent of changes in symptoms of depression (Table 6).

One surprising finding was that daily fatigue levels did not change very much during the study. With regard to the exercise group, the fatigue levels (both a.m. and p.m.) over the 10 weeks, varied by less than one half of a point ($-.03$ & -0.06). One explanation may be that the exercise program was individualized to the extent that it did not create undue stress for the participants. This finding may be as important as the improvements in lower extremity power. Fatigue is often the chief complaint for adults with MS (Krupp, 1983), and if resistance training programs can be designed and implemented without increasing levels of daily fatigue, then maybe physicians and health professionals will have more success in engaging adults with MS in exercise. Another reason why fatigue levels may not have varied

may be due to the adaptation of the visual analog scale. Rather than marking on a 10 cm line the fatigue felt by the participant, the participant was asked to rate her level of fatigue on a scale from 0 – 10. This changed the measurement from an objective measure, to a subjective rating. Thus, the adaptation to the visual analog scale may have decreased the ability to objectively measure variation in daily fatigue.

Limitations

One limitation of the study is the lack of full randomization of participants. Twenty-four of the 29 participants underwent stratified randomization, but the remaining five participants were assigned to either the control group (participant request) or exercise group (potential dropout) based upon specific request.

As discussed earlier, another limitation of the study is the sample size and low statistical power. Prior to the study, 25 participants per group were needed for appropriate statistical power. To maintain homogeneity among groups this study includes the results for women only. The entire project included both genders, and had a sample of 23 in the exercise group (7 males) and 19 in the control group (6 males). Thus, although the statistical power was not adequate for this portion of the study, the entire project was completed with a greater amount of statistical power.

Another limitation of the method is the modification of the visual analog scale (VAS). Although the original VAS has been determined to be reliable (in patients with sleeping disorders) and is widely used with adults with MS, the reliability or the validity of the modification had not been examined. The purpose of the VAS in our study was to ensure that the increases in the intensity of the program (added weight to the vest), were not causing extreme changes in daily fatigue, thus the subjective measurement of daily fatigue was used. A third limitation of the study may be the inherent bias in levels of physical activity between groups. The control group had a significantly greater level of physical activity prior to and during the intervention. The intervention was designed to improve muscular strength and power, thus participants were allowed to maintain participation in aerobic type activities. Previous research determined that aerobic type activities would not confound the results for the primary outcome measure, lower extremity power.

Another limitation of the study is the length of the intervention. The home-based resistance training program included two weeks of instructional sessions and eight weeks of home-based exercise. Although the length of the intervention was appropriate enough to evaluate results for lower extremity power, it may not have been long enough to determine changes in functional mobility. Lengthening the intervention by two to six months may improve the ability to determine the effects of resistance training on functional mobility.

Contributions

Despite these limitations, the study design has advantages over previously related research. Exercise studies that emphasize resistance training have been performed with adults with MS with less than 10 participants, (Svensson, Gerdle, Elert, 1994) without control groups (Gehlsen, Grisgsby, & Winant, 1984; Kasser & McCubbin, 1996), and lack results with regard to functional mobility. Although this study had less than 25 per group, each group had over ten participants. This sample size is larger than other resistance training research involving adults with MS. This study documented the results of a home-based exercise program with a control group, and examined whether resistance training affected functional mobility. Functional mobility is a primary concern for adults with MS, thus this study relates the results of resistance training to an issue that concerns adults with MS daily.

Applications and Implications

An important application of the study may be the nature of the home-based exercise program. The intervention consisted of functional exercises which could be performed at home, with inexpensive equipment (weighted vest \$45.00, ankle weights \$15.00), and little training. Over a longer period of time, such as three to six months, the functional nature of the exercises may also transfer specifically to activities of daily living. Activities such as getting out of a chair, and walking up and down steps, were performed as part of the intervention. Participants often

claimed that others noticed how much easier it was for them to get in and out of the car, and get up and down stairs. Although, the functional mobility results were not significant, participants routinely commented that they were walking better, and that their friends routinely noticed how much better they were walking. During the intervention, four participants stopped using their canes for daily ambulation.

These anecdotal results are important to consider, and may have a bigger impact on the activities of daily living and functional mobility in women with MS than the improvements in lower extremity power.

Recommendations for Future Research

The recommendations for research stem from the implications and applications. One recommendation is to extend the project, and systematically decrease the amount of contact. After the instructional sessions, one may initiate bi-monthly home visits for one month, and maintain phone contact monthly for three months. After, the participants would be asked to call if they have any questions or concerns. Another suggestion, includes providing the instructional sessions, three times a week for two weeks in a clinical or community based setting, then providing only one home visit, and following with one phone call per month after the home visit. The researcher found that the home visit was important to ensure the participants were performing the exercises correctly and safely. These suggestions may be applicable for physical therapy and/or home health care workers. Another suggestion would be to initiate training, and primarily use phone

contact for a period of three to six months, then examine the compliance and dependent measures after six months and one year. Other suggestions include extending the current project over a one, to two-year period, and examine the long term effects on functional mobility. The use of daily fatigue cards are not applicable to clinical situations, and therefore the use of the POMS and/or the CES-D at yearly, or bi-yearly medical visits may be a way to examine the long term effects of home exercise on fatigue and symptoms of depression.

Conclusions

The purpose of this study was to examine the effects of an eight-week home-based resistance training program in women with MS. The results indicate that the strength training intervention improved lower extremity power. Although there were non-significant changes in functional mobility, the anecdotal comments, led the researcher to believe that the slight improvements in mobility scores, made an impact on their daily activities. This intervention was implemented without injury or increases in MS fatigue, or negative symptoms. The nature of the home-based exercise program may provide a viable solution to those who would like to exercise at home and at a reasonable cost.

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APPENDICES

Appendix A
Informed Consent

CONSENT FORM
THE EFFECT OF AN 8 WEEK HOME-BASED EXERCISE PROGRAM ON
MOBILITY AND LEG STRENGTH IN ADULTS WITH MULTIPLE
SCLEROSIS.

It has been explained to me that the purpose of this study is to increase lower leg strength. The information obtained from this study will help other researchers, and may help other professionals prescribe exercise and home-based exercise programs to persons with multiple sclerosis (MS).

It has been explained to me the importance of the randomization of the study. I understand if I participate in the study that I may be chosen to participate in the exercise group or the control group. I understand that I will be matched with another participant based on gender, disability status and age. After matching, a coin will be flipped to determine which participant goes to the exercise group, and which one becomes part of the control group. I understand that I have a 50/50 chance for each group, and there will be no discrimination against individuals (i.e., age, race, sex, religion, or disability status).

I understand that if I am chosen to be in the exercise group this will involve my participation for approximately 11 hours. This will involve 5 testing sessions and 6 exercise sessions. At home, I understand that I will be asked to exercise three times a week for eight weeks, using the exercise sheet and videotape provided. I understand if I participate in the control group, this will involve approximately 5 hours of testing at Oregon State University.

I understand that I will be asked to record my daily level of fatigue and physical activities. I understand that I will be asked to write down my daily level of fatigue using a scale from 0 "no fatigue" to 10 "very fatigued". I will be asked to rate my level of fatigue at 10:00am and 7:00pm each day. I understand that physical activities will be accounted for in intervals of 15 minutes and will include housework, walking, swimming, exercising, and gardening. I understand that I will return the information each week, via a stamped self-addressed postcard provided by the research staff. The research staff will also be contacting me by phone once per week and bi-monthly a member of the staff will come to my house to discuss my levels of daily fatigue and physical activities.

I have received an oral explanation of the testing and study procedures, and understand that it entails the following:

1. Lower Leg Strength. The assessment of lower leg strength will involve that I sit upright in a padded seat with one leg positioned on a footplate, and the other on a footrest. I understand that I will be asked to push down on the footplate as hard and as fast as I can. I understand that I will repeat this test with alternately legs, about 5-10 times. I understand that I will have three practice trials. This test will take about 25 minutes to complete. I understand that the strength test may cause some mild muscle soreness 24-48 hours following testing.
2. Mobility. The "Up and Go" test will be used to determine the effects of exercise on functional mobility. I understand that I will be asked to stand up from standard armchair, walk a distance of 3 meters, turn, walk back to the chair, and sit down again. The test will be conducted over an indoor smooth surface. It has been explained to me that I may use an assistive device. If I choose to use an assistive device, I understand that I will be

asked to use the same device during the next testing session. This test will take about 5 minutes to complete.

3. Balance. The force platform will be used to measure balance. I understand that I will be asked to stand still on a platform for about one minute while my balance is being measured. I understand that there will be a safety bar in front of me which I may grasp if needed.

4. Mood. The Center for Epidemiological Studies Questionnaire will be used to measure my overall mood state. This will be used to determine if my mood has is related to my levels of fatigue. This will be measured once at the beginning and end of the study, the questionnaire takes less than 10 minutes.

I understand that after a one-day familiarization period, that testing will be made on two separate days, at least 48 hours apart. Testing will occur over two days at the beginning (January & February) and the end of the study (April-June). Total testing will take about 45 minutes per person during the familiarization period, and approximately 30 minutes after. Rest will be provided in between tests. Due to the variability associated with the disease, the two-day assessment will provide a more accurate measure lower extremity strength, balance, and mobility for that particular week.

5. Exercise Training Program. I understand that if selected to be in the exercise group, I will be participating in two-week exercise training program designed to increase muscular endurance of my legs. I understand that these six training sessions will involve exercising three times a week for one hour.

5. Exercise Training Program (cont'd). After the two weeks of training I understand that I will be asked to perform the same exercises at home for an hour, three times a week, for eight weeks. I understand that prior to exercising at home, I will be asked to watch a 3-4 minute video tape which shows how to perform the exercises correctly and safely.

This exercise program at the University and at home will include:

a) Participating in warm-up and cool-down stretching sessions which will take approximately 10 minutes.

b) Performing lunges, squats, chair sit to stands, toe-raises, and step-ups for 10-15 repetitions, two to three times. Prior to signing informed consent, I understand that these home exercises will be demonstrated to me either by videotape or in person.

c) Chairs may be used to help me balance while performing these exercises

d) I will wear a weighted vest adjusted for me to increase the intensity of the exercise

e) I understand that at any time I may ask to decrease the intensity of the exercise, or not perform a specific exercise for any reason. I understand that I may be asked to perform alternative exercises, which may be easier for me.

f) I will fill out an exercise sheet which includes: the vest weight, name of exercise, number of sets per exercise number of repetitions per exercise, and level of fatigue for each day.

g) I understand that weekly a member of the research staff will contact me by phone, and bi-monthly a member will come over to my home and exercise with me. At

that time he/she will review the exercise sheet and adjust the number of repetitions, sets, and weights in the vests for me.

6. Risks

I understand that the muscular training program may also result in mild muscle soreness. This may also last 24-48 hours after an exercise session. Stretching will be done prior to and following exercise to minimize muscle soreness. I understand that I may experience an increase in levels of daily fatigue.

7. Benefits

I understand that little is known regarding strength training programs for persons with multiple sclerosis. This project may provide the information necessary to disseminate this information to others with MS. The benefits of this type of training for some individuals has included: an increase in lower leg strength, a decrease in daily fatigue, an increase in mobility, improved balance, and increase in the ability to perform activities of daily living. The exercise program will be implemented free of charge. The members of the control group will also have an opportunity to participate in the six training sessions at the completion of the project (May-June). Each participant will also have the opportunity to purchase the equipment if desired.

I understand that I may be reimbursed monthly for travel costs at a rate of \$0.28 cents per mile for each of the visits to OSU (exercise group 11 sessions; control group 5 testing sessions).

I understand my confidentiality will be maintained by the use of a number coding system, and that only the researchers involved with the study will have use of the numbers. I have been informed that the results of the study may be reported in a scientific journal and that data will not be associated with my identity in any way.

I understand that the University does not provide a participant with compensation or medical treatment in the event that the participant is injured as a result of participation in the research project.

I understand that if I choose to participate I am free to withdraw at any time without, prejudice penalty or loss of benefits to which I am entitled. If I have any questions, I should contact Jeff McCubbin, Ph.D. at 737-5921 or Louisa Summers at 737-3402. Any questions regarding my rights as a research subject should be directed to Mary Nunn, OSU Research Office, 541-737-0670.

Signature

Date

Witness

Appendix B

Expanded Disability Status Scale

Appendix B

Expanded Disability Status Scale (EDSS)

<u>Functional Systems Scale</u>	<u>Grades (0-6)</u>
A. Pyramidal	6
B. Cerebellar	5
C. Brain Stem	5
D. Sensory	5
E. Bowel & Bladder	5
F. Visual	6
G. Cerebral-total	5
H. Cerebral-mentation	2

Expanded Disability Status Scale

EDSS Step 1.0 - One FS grade 1, excluding cerebral grade 1, with all others grade 0.

EDSS Step 1.5 – Two or more FS grade 1, excluding Cerebral grade 1, but no grade above 1 in any FS.

EDSS Step 2.0 – One FS grade 2, other grade 0 or 1.

EDSS Step 2.5 – Two FS grade 2, others grade 0 or 1.

EDSS Step 3.0 – One FS grade 3, or three or four FS 2, others being 0 or 1.

EDSS Step 3.5 – One FS grade 3, plus one or two grade 2, or two FS grade 3, or five FS grade 2, others being grade 0 or 1.

Appendix B

Expanded Disability Status Scale (continued)

EDSS Step 4.0 - combinations just exceeding two grade 3, or gone grade 3, plus two grade 2, or five grade 2; or one FS grade 4 alone, all others being grade 0 or 1.

“At this point, the ambulation start to take precedence over the precise FS grades” (Kurtzke, 1983). For step 4.0, there must be full ambulation (including the ability to walk without aid or rest for some 500 meters).

EDSS Step 4.5 – The same minimal FS grade requirements as 4.0, and the participant must be able to walk without aid or rest for some 300 meters.

EDSS Step 5.0 – requires ambulation for about 200 meters without aid or rest.

EDSS Step 5.5 – requires ambulation for about 100 meters without aid or rest.

EDSS Step 6.0 – requires assistance to walk about 100 meters without rest. This includes resting, the use of unilateral aids (cane) at most times, or the intermittent use of bilateral aids.

EDSS Step 6.5 – requires assistance to walk about 20 meters without rest. This includes the use of bilateral aids (cane) at most times.

EDSS Step 7.0 – essentially uses a wheelchair for mobility, with the inability to walk beyond about 5 meters with an aid.

EDSS steps 7.5 – 10.0 descriptions are not included because they do not pertain to this study.

Appendix C

Heath and Physical Activity History Questionnaire

Oregon State University
Home-Based Exercise for Adults with Multiple Sclerosis

Health and Physical Activity History

16. Have you ever had pneumonia? Yes or No

If you answered yes: when? _____

17. Do you have asthma? Yes or No

18. Do you have emphysema? Yes or No

Questions 19- 23 are for females only (for males, please skip to question # 20)

19. Have you stopped having menstrual periods? Yes or No

20. At what age did you stop having menstrual periods? Age: _____

21. Are you currently taking hormone replacement therapy? Yes or No

22. How long have you been taking hormone replacement therapy (HRT)?
Years: _____

23. If you were taking hormone replacement therapy, and have stopped,

How long were you using HRT? Years: _____

Other, please describe _____

24. Please list the medications you are now currently taking:

Oregon State University
Home-Based Exercise for Adults with Multiple Sclerosis

Health and Physical Activity History

Physical Activity. Please describe your physical activity pattern.

25. How many hours a day do you watch TV? _____

26. Do you walk outside your home for exercise? Yes or No (please circle)

of minutes per session _____ # of sessions per week _____

27. Are you involved in swimming? Yes or No (please circle)

minutes per session _____ # sessions per wk _____

28. How many hours of housework do you do per day? _____ per week _____

29. When it's not raining, are you involved in gardening or outside homecare activities?

Yes or No (please circle)

of minutes per session _____ # of sessions per week _____

30. Are you involved in any other physical activities or exercises? (stationary bike, rowing) _____

27. Prior to the holidays, please estimate the number of minutes of physical activity per week you performed. _____.

Please describe. (i.e., walk 15 mins, 3 times per week = 45 minutes of activity)

Appendix D

Center for Epidemiologic Studies Depression Scale (CES-D)

Appendix D

Center for Epidemiological Studies – Depression Scale (CES-D)

Participants were asked to respond to the questions below based on how they may have felt or behaved in the past week. Listed at the bottom are the responses that participants were asked to circle. To the left of the response is the score the participant would have received for each response. For question numbers 4, 8, 12, and 16, the scoring is reversed. The responses were summed and a total score was given for pre and post testing.

1. I was bothered by things that usually don't bother me.
2. I did not feel like eating; my appetite was poor.
3. I felt that I could not shake off the blues even with help from my family or friends.
4. I felt that I was just as good as other people.
5. I had trouble keeping my mind on what I was doing.
6. I felt depressed.
7. I felt that everything I did was an effort.
8. I felt hopeful about the future.
9. I thought my life had been a failure.
10. I felt fearful.
11. My sleep was restless.
12. I was happy.
13. I talked less than usual.

Appendix D (cont'd)

Center for Epidemiological Studies – Depression Scale (CES-D)

- 14. I felt lonely.
- 15. People were unfriendly.
- 16. I enjoyed life.
- 17. I had crying spells.
- 18. I felt sad.
- 19. I felt that people dislike me.
- 20. I could not get “going”.

<u>Responses.</u>	<u>Score.</u>
Rarely or none of the time (less than 1 day)	0
Some or little of the time (1-2 days)	1
Occasionally or a moderate amount of time (3-4 days)	2
Most or all of the time (5-7 days)	3

Appendix E
Modified Ashworth Scale

Appendix E

Modified Ashworth Scale

Grade	Description
0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of motion
2	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part(s) rigid in flexion or extension

Ashworth, B. (1964). Preliminary trial of carisoprodal in multiple sclerosis.

Practitioner, 192, 540-542.

Appendix F

Daily Fatigue and Physical Activity Postcard

Appendix G

Modifications to the Home-based Exercise Program for Adults with MS

Appendix G

Modifications to the Home-based Exercise Program for Adults with MS

Mini-squats.

- a. Mini-squats were performed with feet slightly farther than shoulder width apart, and in a toe-out position. Participants were instructed to squat down until their thighs were almost parallel to the floor, or their knees were near a 90-degree angle.
- b. Participants who were unable to perform a full squat were instructed to perform a half squat.

Hamstring curls.

- a. Participants performed the hamstring curls by standing up and lifting their lower leg up towards their buttocks.
- b. Participants who were unable to perform the hamstring curls standing up were instructed to, lie on their stomach and lift their lower leg up towards their buttocks.
- c. Participants who were unable to perform the hamstring curls as above, were instructed to sit in a chair with their leg extended, and slide their foot towards their body (knee flexion). For two participants, hamstring curls were performed in this fashion on the non-dominant side, and then on their dominant leg, as described in either (a) or (b).

Appendix H

Lower Extremity Power in Dominant and Non-dominant Legs

Appendix H

Lower Extremity Power in Dominant and Non-dominant Legs (M \pm SD)

Variable	Absolute Power Strong (Watts)	Absolute Power Weak (Watts)	Power strong/kg (Watts/kg)	Power weak/kg (Watts/kg)
EX Pre	127.16 \pm 46.92	102.89 \pm 43.83	1.78 \pm 0.69	1.89 \pm 0.69
EX Post	154.16 \pm 37.56	128.60 \pm 35.40*	2.13 \pm 0.56	2.01 \pm 0.73*
Ex % change	33.48 \pm 48.56	45.96 \pm 62.59	32.12 \pm 47.72	44.55 \pm 62.10
CON Pre	128.90 \pm 38.59	114.60 \pm 33.20	1.46 \pm 0.70	1.66 \pm 0.54
CON Post	139.43 \pm 49.81	123.85 \pm 46.57	1.85 \pm 0.61	1.76 \pm 0.58
CON % change	7.68 \pm 14.93	7.19 \pm 17.61	7.08 \pm 14.72	6.67 \pm 17.67

Note: p < .05, significantly different from control at post-test.

Appendix I
Review of Literature

Appendix I

Review of literature

This review of the literature on exercise with MS will be broken into three parts: 1) general fatigue in MS; 2) aerobic exercise in adults with MS; 3) muscular considerations in MS (muscular strength and endurance, muscle tension development, muscle activation, and intramuscular fatigue in adults with MS).

Fatigue in MS

For many adults with MS, fatigue is the most challenging symptom they battle. The etiology of fatigue in individuals with MS is unknown, and researchers have concluded that this type of fatigue was not related to depression or neurological impairment (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989). The fatigue experienced by persons with MS has been described as idiopathic lassitude. This type of fatigue is different from the “physical exertion” fatigue that the general population experiences after a hard day of physical activity. Idiopathic lassitude is described in terms of a weakness, tiredness, and lack of energy, that is disproportional to the amount of energy expended and to the level of disability (Scheinberg, et al., 1980). Other types of fatigue felt by persons with MS include: depression, which is usually associated with clinical signs of depression, and nerve impulse fatigue, which is associated with a muscle that has been worked beyond its capacity (Schapiro, Harris, Lenling, Metelak, 1987). All of these types of fatigue

may be felt by persons with MS, but idiopathic lassitude is the most common type of fatigue felt by adults with MS (Schwartz, Coulthard-Morris, Zeng, 1996). Some authors feel cardiorespiratory and metabolic factors are partially responsible for the idiopathic lassitude in MS (Freal, Kraft, & Coryell, 1984). Fatigue can manifest itself after walking, household chores, or other physical activity, and typically, if individuals rest after an activity, they can go on with other tasks.

In an attempt to further describe the fatigue associated with MS, and quantify the number of adults affected by the symptom, Freal and colleagues (1984) had 309 adults respond by questionnaire. Fatigue was described as "tiredness" or the "need to rest" in as many as 90% of persons responding ($n = 289$). For many (66%), fatigue occurred daily, and made other MS symptoms worse. Due to the neurological damage caused by the demyelination, and the high numbers of persons experiencing fatigue, it is probably not psychosomatic in nature, nor due to muscular problems (Freal et al., 1984).

Krupp and colleagues (1989) created a questionnaire that was designed to determine the severity of fatigue felt by participants with MS. This questionnaire asked participants to indicate their level of agreement (1 strongly disagree – 7 strongly agree) with nine statements regarding fatigue. The questionnaire was administered to patients with Lyme disease, systemic lupus erythematosus, multiple sclerosis, and healthy controls, to determine its sensitivity, reliability and internal consistency. The CES-D was used to determine the relationship of fatigue severity to symptoms of depression. The questionnaire had a high level of internal

consistency (Cronbach's $\alpha = .88$), and test-re-test reliability of over 16 weeks yielded non-significant changes in 11 participants (eight with MS, three with systemic lupus erythematosus) in which no clinical changes in disease status were expected. The results of the study indicated that fatigue severity was independent of symptoms of depression, and level of impairment, and distinguished the severity of fatigue between groups (Krupp, Alvarez, LaRocca, & Scheinberg, 1988).

Vercoulen and colleagues (1996) measured subjective fatigue and its relation to impairment in daily life, physical activity, depression, cognitions and attributions, sleeping problems, and neuropsychological complaints in patients' with chronic fatigue syndrome, MS, and healthy controls. Using the Subjective Fatigue subscale of the Checklist of Individuals Strength (Vercoulen et al., 1994) self-observation list, subjects measured fatigue four times a day, on a four-point scale, for two weeks. Adults with MS reported that they felt fatigued every day (51%), and it was present in 85% of the patients at least once a week. Adults with MS had daily fatigue scores, which were higher (5.4) than healthy controls (2.2), and significantly impacted daily functioning, but was not related to depression. Fatigue in MS was closely related to impairment in daily life, as measured by the Sickness Impact Profile and stable over the two-week period. Other components revealed that fatigue was associated with a sense of control and focusing on bodily sensations. Levels of physical activity and mobility were significantly lower in adults with MS as compared to healthy controls.

Others have examined similar psychosocial correlates of fatigue in MS, to reveal the relationships among various psychological factors and the impact of fatigue on role performance (Schwartz, Coulthard-Morris & Zeng, 1996). Fatigue was measured using the Multidimensional Assessment of Fatigue (Belza, Henke, Yelin, Epstein & Gilliss, 1993) which is a 16 item self-reported questionnaire. This valid and reliable (Belza et al., 1993) instrument uses a Likert scale to measure four dimensions of fatigue: severity, distress, timing, and interference, to compute a global fatigue index. The results indicated that after adjusting for sociodemographic and medical factors, environmental mastery was the best predictor of both global and fatigue related-distress. In contrast to Vercoulen et al., (1996) higher fatigue was related to more depression, and was not found to limit physical role performance (as measured by the Sickness Impact Profile). These results for physical role performance and depression are in direct opposition as those found by Vercoulen et al., (1996).

Moderate exercise has been shown to increase perceptions of fatigue (Freal, Kraft, Coryell, 1984), while others have shown that aerobic exercise performed three times per week, decreases perceptions of fatigue (Petajan, et al., 1996). In contrast to the earlier (Freal et al.; Krupp, LaRocaa, Muir-Nash, & Steinberg, 1989) research, a more recent activity based study showed that regular exercise decreased levels of fatigue (Petajan et al., 1996). This study examined the effects of a 15-week aerobic exercise program on fatigue, using an experimental design with 63 adults with MS. The Fatigue Severity Scale (Krupp et al., 1988) and the Profile of

Mood States (POMS) were used to determine the effects of exercise fatigue. The POMS has a fatigue-inertia section of the questionnaire which uses a weighted adjective scale to assess the subject's level of agreement, "not at all" to "extremely" with each test item. One interesting point was that after 10 weeks of exercise, fatigue measured by the POMS, was significantly lower than prior to exercise. Whereas, with the Fatigue Severity Scale (FSS), there were no changes found. The authors concluded that the participants might have interpreted the FSS items in a way that may not change over time, e.g. "fatigue interferes with my physical functioning". Whereas, items on the POMS, e.g. "how energetic do you feel" may be worded in a way, which may change over time.

Other researchers have used visual analog scales (VAS) to determine initial level and changes in fatigue in adults with MS (Kent-Braun, Sharma, Miller, & Weiner, 1996; Krupp, LaRocaa, Muir-Nash, & Steinberg, 1989; Sharma, Kent-Braun, Mynhier, Weiner, & Miller, 1995; Svensson, Gerdle, Elert, 1994). A visual analog scale uses a 10-cm line to gauge level of fatigue. Participants are asked to indicate the point between 0 (no fatigue) and 10 (severe fatigue) that depicts their level of fatigue. The fatigue is then scored as the distance in millimeters between 0.0 and 100.0. Although this scale is frequently used to assess fatigue in adults with MS, the reliability and validity of this scale was established using a 13 item subscale to describe fatigue in adults with sleep disorders (Lee, Hicks & Nino-Murcia, 1991). Others have used the VAS to determine functional capacity in adults with rheumatoid arthritis (Scott & Huskisson 1977).

The research that has been done with adults with MS used a one-item VAS to determine levels of fatigue (Sharma, Kent-Braun, Mynhier, Weiner, & Miller, 1995; Sharma, Kent-Braun, Mynhier, Weiner, & Miller, 1995; Svensson, Gerdle, Elert, 1994). The benefits of using the VAS are the objective nature of the measurement, versus other questionnaires which use likert type scales with adjectives at each extreme to describe fatigue. The VAS was helpful in determining changes in fatigue and five different aspects of well-being during endurance training with adults with MS (Svensson, Gerdle, Elert, 1994).

This study examined the effects of a muscular endurance exercise program on fatigue (and muscular endurance) in five adults with MS. After four to eight weeks of knee flexor strength training, three of the five participants improved their muscular endurance, and all participants improved their levels of general fatigue as measured by the one-item VAS. Sharma and colleagues examined perceived fatigue and muscle fatigability after nine minutes of intermittent isometric stimulation of the tibialis anterior in 13 adults with MS, and nine controls. The VAS and FSS were used to assess subjective fatigue, and magnetic resonance spectroscopy was used to assess changes in the intramuscular metabolites (intracellular pH, phosphocreatine, and inorganic phosphate). The results indicate that subjective fatigue was not related to the changes in muscle metabolites during exercise, yet the metabolic changes were related to clinical level of disability (EDSS). The authors conclude that the excessive muscle fatigue in adults with MS, was due to impaired excitation-contraction coupling, and abnormal energy

metabolism, which may at least in part be due to deconditioning (Sharma, Kent-Braun, Mynhier, Weiner, & Miller, 1995). Both of these studies and their results with respect to muscular strength and endurance exercise training are discussed later in the last section of the review.

Physical Activity and Exercise in Adults with MS

It has been documented that adults with MS have lower levels of physical activity than sedentary adults without MS. Ng and Kent-Braun examined three-dimensional accelerometer activity in 17 patients with MS and in 15 healthy sedentary control subjects. It was found that the accelerometer activity over seven days was significantly less in participants with MS ($\bar{M} = 121,027 \pm 59,336$ units/day), than controls ($\bar{M} = 185,892 \pm 60,556$ units/day). The authors also found that the accelerometer measures detected differences in activity levels, whereas a seven day recall activity questionnaire was not sensitive enough to detect differences in activity levels. This was the first study that actually quantitatively tested the hypothesis that adults with MS are less physically active than participants without MS.

Other Research Regarding Exercise and Adults With MS

In an attempt to address the fatigue associated with MS and its physiological effects on exercise, researchers have examined a host of different properties associated with physical activity. Olgiati, Burgunder, & Mumenthaler

(1988) examined the energy cost of walking in 33 participants with MS, and 12 controls. The participants had mild to moderate levels of disability (EDSS scores not available), and were asked to walk on a treadmill, climb stairs, and perform a ten second sit-up test. The results of the study showed that adults with MS, had a significantly greater oxygen consumption ($\underline{M} = 0.287 \text{ ml/O}_2/\text{min} \pm \underline{SD} 0.018$) than controls ($\underline{M} = 0.163 \text{ ml/O}_2/\text{min} \pm \underline{SD} 0.007$) at 1.8 km/hour. A multiple regression analysis revealed that the higher oxygen consumption was related to lower extremity spasticity and not due to abdominal weakness.

A similar study examined metabolic cost of energy in patients with mild levels of disability (EDSS 0-2). Ten participants and age matched controls, completed an incremental sub-maximal exercise test (cycle ergometer) and a complete pulmonary function test. The results of the study indicate that participants with MS had slightly less ($\underline{M} = 1886 \text{ ml/min} \pm \underline{SD} 145$) peak oxygen consumption values as compared to controls ($\underline{M} = 2246 \text{ ml/min} \pm \underline{SD} 196$). These participants with mild disability also exhibited a similar slope between VO_2 and workload ($\underline{M} = 9.9 \text{ ml/min/Watt} \pm \underline{SD} 0.6$ vs. $\underline{M} = 10.9 \text{ ml/min/Watt} \pm \underline{SD} 0.42$ in controls). In contrast to the above study, these participants with mild levels of disability did not exhibit significant differences in the metabolic cost of exercise. Yet, the two studies used two different modes of exercise, and its clear that the participants in the above study had greater levels of disability. Other results included a significantly greater pulmonary dead space ($p < .05$), and a faster respiratory rate among participants with MS. The authors concluded that

participants with mild levels of disability did not have an increased metabolic cost of energy, and the minimal differences in oxygen consumption and workload were due to poor training and deconditioning (Tantucci, Massucci, Piperno, Grassi, & Sorbini, 1996).

Others have linked the fatigue associated with MS to decreased cardiopulmonary functioning (Fragoso, Wriz, & Mashman, 1995). This case study also examined pulmonary function and oxygen consumption during a maximal incremental cycle ergometer test. One participant aged 38 years was examined due to her profound levels of fatigue (EDSS not available). The results of the study indicate a normal central cardiovascular response (radionuclide ventriculography), an early anaerobic threshold (ventilated), and a decreased maximal oxygen consumption (49% of predicted $\text{VO}_{2\text{max}}$). The authors concluded that the decreased peripheral oxygen distribution or utilization might be associated with the high levels of MS fatigue felt by this participant. It was suggested that the implication of improper oxygen utilization could provide a physiological basis for defining and treating MS fatigue.

In summary, these studies examined the cardiovascular endurance of participants with MS. In the researchers' opinion, these studies substantiate the fact that participants with MS are in poor shape, and these low levels of cardiovascular endurance, increase fatigue, increase the energy cost of walking. A further implication is that participants with mild levels of disability do not exhibit a

significant difference in oxygen consumption, yet their extertional capacity is due to deconditioning.

Aerobic Exercise in Adults with MS

Aerobic exercise has been researched more frequently than any other types of exercise involving adults with MS. Many studies were conducted early on to determine if maximal aerobic capacity testing was safe for adults with MS (Kosich, Molk, Feeney, & Petajan, 1987; Lohman, Smith, La Rocca, & Abrahams, 1992; Ponichtera-Mulcare, Glaser, Mathews, & Camaione, 1993; Ponichtera-Mulcare, Mathews, Glaser, & Gupta, 1995). These studies used stationary bike ergometers, recumbant bikes, arm ergometers, and combination arm/leg bicycle ergometers. Each of these studies were conducted with small sample sizes ranging from four to 26, but found that it was safe for adults with MS to complete a maximum aerobic capacity test. There were no adverse effects from the assessments, nor did the tests induce MS symptoms, nor exacerbations.

After the initial safety of maximum testing was determined, researchers moved into the area of aerobic exercise training. Early on, Schapiro et al., (1988) examined 16 weeks of unsupervised home exercise using with 50 adults with MS. Twenty-five adults with MS exercised 15-30 minutes, four to five times a week. They were compared to 25 non-exercising adults with MS on graded exercise time, and highest workload achieved using an arm/leg cycle ergometer. Overall, the exercise group had a modest improvement of 10% in workload. The participants

with a lower level of disability had greater improvements in exercise time and workload achieved, as compared to participants with a higher level of disability. The authors concluded that it was safe for adults with MS to engage in an aerobic exercise program, and that neurological impairment may have effected the intensity at which participants trained.

Mulcare, Mathews, Glaser, and Gupta (1994) examined aerobic capacity (VO_{2max}), power output, and maximal heart rate, before and after three months of aerobic exercise in 19 adults with MS. The supervised exercise program consisted of 30 minutes of exercise, at 65-70% of age predicted maximum heart rate, on a recumbent or upright arm/leg bicycle ergometer. Students *t*-tests were used to compare pre-test values to post-test values in 11 fully ambulatory adults with MS, and eight semi-ambulatory adults with MS. The fully ambulatory adults improved VO_{2max} by 10%, increased their age predicted max HR from 88% to 95% (post-test), and power output by 9%. The semi-ambulatory group had improvements by 7%, 4%, and 11% respectively. Although the post-test results were not statistically significant, they are still favorable with respect to exercise. The improvements in power output and VO_{2max} may be due to the greater maximum heart rate achieved during post-testing, or improved cardiovascular fitness. Although the semi-ambulatory group did not improve as much, the results were still positive. Unfortunately, the study did not have a control group, nor was the sample size large enough to generalize the results to other adults with MS.

As described earlier in the fatigue section, Petajan et al., (1996), completed a 15-week aerobic exercise-training program with 54 adults with MS. This study measured many different items including: a host of psychological parameters (Fatigue Severity Scale, Sickness Impact Profile, Profile of Mood States), blood lipids (total cholesterol level, high density lipoprotein level, low density lipoprotein level, triglyceride level), body composition, isometric strength, and VO_{2max} . This study examined scores prior to exercise, after 5, 10, and 15 weeks of exercise. This was the first study to have a large enough sample to detect significant differences among groups, and it randomized participants into two groups (exercise & control). Following a warm-up, the exercise group trained at 60% VO_{2max} for 30 minutes on arm/leg bicycle ergometers, three times a week.

The results for the psychological parameters were positive. Improvements on the Sickness Impact Profile (Berger, Bobbit, Carter, & Gilson, 1976) occurred after 10 weeks of exercise in the physical dimension subsection (ambulation, mobility, body care and movement). Mobility improvements were seen after 5 and 15 weeks of exercise as well. There were significant changes between baseline and 10 weeks of exercise in the total SIP score, and the social interaction, emotional behavior, and home management subsections for the exercise group.

After 10 weeks of exercise, the exercise group improved fatigue, depression, and anger scores on the POMS, whereas on the Fatigue Severity Scale differences in fatigue were not detected. These differences were not detected at the completion of 15 weeks of exercise, and the authors suggested that the negative

feelings as a result of “knowing the study was coming to an end”, and the loss of interaction among participants may have influenced these psychological parameters of the POMS.

Although this study was not designed to increase strength, both the upper and lower extremity isometric strength scores improved over time for the exercise group as compared to the control group. The sum of four upper and the sum of five lower extremity measures improved significantly over time as a result of the combined arm/leg bicycle ergometry.

After 15 weeks of aerobic exercise, serum triglyceride levels were significantly less (17%) as compared to baseline values for the exercise group as compared to the control group. Values for the other blood lipids did not change significantly over time. In contrast, skinfold thicknesses were significantly different from baseline for the exercise group, and percent bodyfat, approached significance, ($p = .068$). Lean mass, or body weight did not change significantly in the exercise group, or the control group.

Aerobic capacity improved after 15 weeks of training by 22% in the exercise group (1% in the control group), and maximal power output improved 48% in the exercise group (12% non-exercise group). Relationships between EDSS score and improvements in VO_{2max} were not statistically significant, implying that improvements were made regardless of neurological impairment. This is the first study that showed that adults with MS with a more severe level of disability improved at a similar rate, as adults with less disability.

Another important finding was the significant improvements in bowel and bladder function. Bowel and bladder dysfunction is a common and frustrating symptom for adults with MS, and this study may provide another mechanism for improving function. The authors suggest that improvements in circulation may have contributed to better bowel and bladder function for the exercise group. In summary, this study showed significant improvements for the exercise group as compared to the control group: for fatigue, anger, depression, triglycerides, skinfold thicknesses, isometric strength, VO_{2max} , maximum power output, and bowel and bladder function.

Muscular Considerations in MS

Muscular Strength and Endurance in MS

Research involving muscular strength and endurance with adults with MS has been limited and diverse. Armstrong and colleagues (1983) first examined the effect isokinetic dynamometry on adults with MS. This study was done to determine if isokinetic dynamometry testing was safe for adults with MS. Ten adults with MS were matched for age, sex and weight to 20 adults without MS. Peak torque testing was done at velocities ranging from 0 to 275 degrees per second, on the knee flexor and knee extensor muscles. After recovery, a fatigueability test asked participants to complete 50 contractions at a rate of one contraction every two seconds. Student's *t*-tests revealed that participants with MS

had significantly lower values for peak torque at all velocities as compared to controls. This study also examined familiarization and the reliability of repeated measurements. The test-retest reliability of peak torque measurements during one testing session were highly consistent ($r = .99$), but without familiarization, peak torque values at 0, 6, and 11 weeks were highly variable. The authors concluded that isokinetic dynamometry was safe for adults with MS, but that a learning effect may exist without familiarization of the apparatus. The authors suggest one or two familiarization sessions prior to initial data collection.

Muscular strength of the quadriceps and hamstrings were assessed using isokinetic dynamometry in nine adults with MS and nine adults without MS (Ponichtera, Rodgers, Glaser, Mathews, Camaione, 1992). Participants were matched for gender, age (31-49 years), height, weight, and lifestyle, and all adults with MS were ambulatory. At 30, 60, and 90 degrees per second the MS group had significantly less concentric peak torque in both the quadriceps and hamstrings than the control group. The difference in average peak torque ranged from 25 to 29 percent for the quadriceps and 19 to 22 percent for the hamstrings. In contrast, there were no significant differences between groups for either speed during eccentric contractions of quadriceps and hamstrings. The authors concluded that adults with MS had the greatest deficit in concentric peak torque at 90 degrees per second and that strengthening programs that emphasize concentric contractions at higher speeds may be beneficial for this population.

Muscular Strength and Endurance Training in Adults with MS

Isokinetic dynamometry was used with adults with MS to assess the effects of a 10-week aquatic fitness program on upper and lower extremity muscular force, torque, fatigue, and work (Gehlsen, Grigsby, & Winant, 1984). Ten adults with MS (mean age of 40) had both upper and lower body assessments prior to the aquatics program, after 5 weeks, and after 10 weeks of aquatics exercise. A Cybex II isokinetic dynamometer was used to assess knee flexion/extension, at velocities from 0 - 300 degrees per second. A biokinetic swim bench assessed upper body force, work and power. As compared to baseline measures, peak torque during knee extension was significantly greater for all velocities (except 0 degrees per second) after 5 weeks of the program. In contrast, there were no significant differences for knee flexion at any time during the study. Lower extremity fatigue, as measured by percent of peak torque decline, and the total work during 50 contractions improved following the 10-week aquatics program. For the upper extremities, power, work and force measurements were significantly greater at completion of the study as compared to baseline. Following the aquatics program, the adults with MS had an 82% improvement in total work for the upper extremities, and a 330% improvement for the lower extremities. Unfortunately, this study did not employ a control group, nor was the sample large enough for the multiple comparisons made.

In the 1990's, Swensson, Gerdle and Elert (1994) implemented an endurance training program of the knee flexors in five adults with MS. Five participants used weight cuffs, pulley apparatus, or an isokinetic dynamometer two

or three days per week, for four to eight weeks. The training program took place either at a rehabilitation clinic, or physical therapy clinic. Pre and post-testing consisted of 50 repeated maximal repetitions of the knee flexors, measurements of peripheral muscle fatigue using a Borg 10 point scale, and five aspects of general well-being were measured with visual analog scales. After training, three of the five participants increased the peak torque of the knee flexors and perceptions of fatigue were decreased after training. Aspects of general well-being (fatigue, health, physical fitness, somatic health, and mood) also improved. The authors concluded that training improved aspects of well-being, and that more comprehensive studies of exercise prescription in adults with MS were needed.

A similar study examined the effects of progressive resistance exercise on muscular strength in nine adults with MS. The 10-week community based exercise program utilized machine-based resistance and free weights, two days per week. Assessments of peak force were made prior to and following the exercise program, with an isokinetic dynamometer set at 60 and 120 degrees per second. The results of the study indicated that the participants improved their knee flexors/extensors by 16 - 57%, elbow flexors/extensors by 6 - 29%, and shoulder abductors/adductors by 3 - 11%. The authors concluded that although some participants did not improve, the results indicate that overall, the majority of the participants improved their muscular strength (Kasser & McCubbin, 1996).

Muscle Tension Development

Others have used isokinetic dynamometry to examine the rate of muscle tension development in the knee flexors and extensors of adults with MS (Chen, Pierson, & Burnett, 1987). Fifteen ambulatory adults with MS were compared to 17 adults without MS (of similar age), during isometric contractions of the quadriceps and hamstrings at 45 degrees of knee flexion at speeds of 30 and 90 degrees per second. The variables of interest were: 1) time-rate of muscle tension development, 2) muscle maintaining capacity, and 3) the reciprocal inhibition time. Reciprocal inhibition time was defined as the time between the two points of peak isokinetic torque produced by a reciprocal contraction of knee extension and flexion (Chen, Pierson, & Burnett, 1987). Adults with MS had significantly less peak torque in both muscle groups, and it took longer to reach maximum peak torque than controls. Thus, the rate of muscle tension development was significantly less than controls. These findings of less peak torque in adults with MS were similar to those of Armstrong et al., (1983). In contrast, the reciprocal inhibition times for the two groups were not significantly different. These findings indicate that muscle torque, the development of torque, and the maintenance of peak torque is all less in adults with MS than adults without MS. These findings may be applied to activities such as chair raises, where the rate of muscle tension development is important. During chair raises, a large percentage of peak torque may be needed for adults with MS to lift themselves out of a chair. Thus, it may take longer for the adult with MS to perform that activity. Unfortunately, the adults with MS were unfamiliar with

isokinetic dynamometry, thus, the differences between groups may be less, if a familiarization period was given to the adults with MS.

Muscle Activation in Adults with MS

Rice, Vollmer, & Bigland-Ritchie (1992) examined the intramuscular rate of isometric muscle tension development, the percent of maximum activation by a voluntary effort (assessed by twitch occlusion), and motor neuron firing rates during voluntary contractions of the quadriceps. Four ambulatory adults with MS were compared to 16 controls using electrical stimulation, surface electromyography (EMG) electrodes, and intramuscular microelectrodes. The adults with MS had less quadriceps maximum voluntary contraction (MVC) force in relation to body weight, and their muscles were not able to generate a maximum contraction, due to reduced maximum motor neuron firing rates. For adults with MS, the percentage of maximum voluntary activation ranged from 47% to 93%. Although the authors concluded that a substantial cause of muscle weakness was the inability to excite spinal motor neurons, they also stated that if fully activated, the values for intrinsic muscle strength were still below the mean for normal subjects (Rice, Vollmer, & Bigland-Ritchie, 1992). Thus, some of the weakness was also due to muscle deterioration. The authors also pointed out that little research exists in the area of strength training in persons with MS.

Similar research examined the EMG output during voluntary isometric contractions of tibialis anterior in 14 participants with MS, and 18 controls (Ng,

Miller and Kent-Braun, 1998). The EMG output was obtained during contractions at 10-100% of MVC, incremented by 10% MVC. Participants with MS had a significantly greater EMG output as compared to controls throughout the range of contractions. Although there were not significant differences between groups for the initial or final MVC, the EMG was elevated at each force level. This implies that a greater central motor drive was needed for participants with MS to achieve the same force as those without MS. Disease severity, as measured by the EDSS scale, was significantly correlated to the slope of the EMG/force relationship ($r = -.087$, $p < .05$). The authors concluded that central motor drive is increased during voluntary muscle contractions in participants with MS (Ng, Miller and Kent-Braun, 1998). This research compares with that of Rice et al. (1992), who found that motor neuron firing rates were less in participants with MS, than controls. Therefore, participants with MS may have a decreased motor unit firing rates, which may put more reliance on motor unit recruitment, which would increase the EMG/force relationship and the central motor drive.

Intramuscular Fatigue in Adults with MS

Many research projects have taken the EMG data one step further, and examined the intrinsic properties of the muscle and metabolites during voluntary and involuntary muscular contractions. Much of this research has focused on the intramuscular fatigue associated with MS. Lehman, Tulley, Vrbova, Dimitrijevic, Towle, (1989) examined the fatigue ability of the tibialis anterior in adults with MS

and spinal cord injury. Fatigue was induced by repetitive electrical stimulation.

The results of the study indicate that there was an increase in half relaxation time in these participants. The authors concluded that the inactivity affected the efficiency of the calcium uptake mechanism of the muscle fibers, and exaggerated the slowing of muscle relaxation after prolonged exercise.

During the 1990's, Kent-Braun, Sharma, Miller, and Weiner completed a series of studies examining the metabolic properties of muscle during and after exercise in adults with MS. One of their first studies (Kent-Braun, Sharma, Miller, & Weiner, 1994) examined the rate of oxidative metabolism during and after exercise in 13 adults with MS. Phosphocreatine (PCr) levels were measured using phosphorus magnetic resonance spectroscopy (MRS) during electrically stimulated isometric tetanic contractions of the dorsiflexor muscles. Eight healthy controls performed voluntary isometric contractions of the same muscles to induce similar metabolic responses as the adults with MS. Students *t*-tests were used to analyze the differences in PCr recovery between groups. Following exercise, PCr and pH were reduced to similar levels in both groups. After exercise, the half time of PCr re-synthesis during the first 10 minutes of recovery was significantly slower in adults with MS ($\bar{M} = 2.3 \text{ min.} \pm 0.3$) as compared to controls ($\bar{M} = 1.2 \text{ min.} \pm 0.1$). Although there was relationship to EDSS score, a toe-tapping activity designed to indicate neurological impairment, was moderately related to the reduced PCr recovery. The authors suggested these results indicated an impaired intramuscular oxidative capacity, similar to physically inactive or deconditioned muscles. The

authors discussed how PCr recovery was slowed in other ailments (which develop mitochondrial myopathies), such as peripheral vascular disease (Zatina, Berkowitz, Gross, Maris, & Chance, 1986) and heart failure (Mancini, et al., 1992), but was not seen in adults with chronic fatigue syndrome (Kent-Braun, Sharma, Weiner, Massie, & Miller, (1992). As a result of the findings, the authors conclude that the oxidative capacity of some adults with MS may be impaired, may be partly due to deconditioning, and may be reversible.

Another study by this group, examined the metabolic factors of muscle fatigue during voluntary isometric exercise in 6 adults with MS, as compared to 8 controls (Kent-Braun, Sharma, Weiner, & Miller, 1994). Muscle fatigue was defined as, the decrease in force from a maximum voluntary contraction during intermittent, progressive contractions of the ankle dorsiflexors. Phosphocreatine, pH, and inorganic phosphate were measured as in the study above. The muscle twitch force, and twitch tension were measured by compound muscle activation potential (CMAP) measurements via surface electrodes. The results indicated that there was no impairment at the neuromuscular junction. During exercise, the MVC fell sooner in adults with MS, although by the end of exercise the relative MVC decreases were not significantly different between groups. Although, the adults with MS had a much smaller metabolic response throughout the fatiguing exercise than the controls (higher pH, lower inorganic phosphate/phosphocreatine), the authors concluded that “metabolic factors did not play a significant role in muscle fatigue during voluntary isometric exercise”. Rather, they suggest that “activation

failure beyond the muscle membrane, specifically, excitation-contraction coupling may be impaired in adults with MS” (Kent-Braun, Sharma, Weiner, & Miller, 1994). Throughout the paper the authors suggest that deconditioning or immobilization may play a role in the muscle fatigue of MS, and may be somewhat reversible with exercise.

A third study, (Sharma, Kent-Braun, Mynhier, Weiner, & Miller, 1995) used intermittent electrical stimulation to examine intramuscular muscle fatigue and its relation to disability status, and perceived fatigue in 28 adults with MS and 14 controls. Muscle twitch force, and metabolic changes (PCr, inorganic phosphate, ph) within the muscle were measured as in the previous study (Kent-Braun, Sharma, Weiner, & Miller, 1994). They found that following intermittent electrical stimulation, the recovery force was slower in adults with MS, but the metabolic changes were similar to controls. The disability level of participants (EDSS score) was related to the level of muscular fatigue, but not perceived fatigue (Fatigue Severity Scale & visual analog scale). As in the study above, the authors conclude that there was no impairment at the neuromuscular junction, but that muscle fatigue in MS may be due to impaired excitation-contraction coupling, and intramuscular metabolism (Sharma, Kent-Braun, Mynhier, Weiner, & Miller, 1995).

Another study from this group examined the increased energy demand of contraction, as indirectly assessed by myofibrillar actomyosin calcium ATPase activity (qATPase). This study had biopsies taken from seven participants with MS

and five controls after intermittent isometric contraction of the tibialis anterior. The (qATPase) activity did not differ significantly between participants with MS or controls. The authors concluded that muscle fatigue in MS does not reflect increased energy demand of contraction (Castro, Kent-Braun, Ng, Miller, & Dudley, 1998).

Kent-Braun and colleagues (1996) used isometric endurance training via electrical stimulation to improve muscle fatigue ability. Six participants with MS trained with electrical stimulation for 60 minutes a day, six days a week, for eight weeks. Metabolic changes (ph & PCr) within the muscle were measured by MRS, and electromyography was used to evaluate tetanic force. Muscle fatigue was defined as a percentage of the pre-exercise levels. For the group, there were not significant changes in mean muscle fatigue or metabolic data. Although, during post-testing, four of the six participants had less muscle fatigue during exercise, and less of a decrease in ph. In contrast, two participants responded negatively to the training. These participants were not different in ability level or subjective fatigue scores prior to the study, but exhibited greater fatigue, and a greater decrease in muscle ph. The authors discuss the positive results regarding the intrinsic muscular adaptations (decreased ph during exercise) that occurred with exercise, as well as the high compliance rate among participants. Lastly, the authors cautioned researchers to be aware that exercise protocols designed for other samples may not be tolerated as well by adults with MS.

Summary

In summary the research surrounding issues of exercise and exercise training for adults with MS, has had a good start. First, researchers established that exercise testing was safe for persons with MS. Strength differences between participants with MS and controls was evaluated and established. Similarly, aerobic exercise testing and safety was first established prior to intervention studies. Many studies were completed to determine the differences in aerobic capacity between adults with MS and adults without MS. Recently, research has begun to focus on the benefits of moderate aerobic exercise for persons with MS. The work by Kent-Braun and colleagues has determined many differences in intramuscular and metabolic properties in participants with MS. Yet, although the authors have consistently concluded that many of these differences may be due to deconditioning, little research has been done to examine the benefits in the area of strength training for adults with MS. The limited research that has been done on progressive resistance exercise has used small samples, no control groups, and lacked functional dependent measures. The need for establishing exercise and physical activity protocols for this population is apparent, more research is needed to clarify the value of exercise for adults with MS.