Improvement in strength following resistance training in MS patients despite varied disability levels

Mary L. Filipi\textsuperscript{a,b,*}, Daryl L. Kucera\textsuperscript{c}, Eric O. Filipi\textsuperscript{d}, Alanson C. Ridpath\textsuperscript{e} and M. Patricia Leuschen\textsuperscript{f}

\textsuperscript{a}University of Nebraska Medical Center, College of Nursing, Omaha, NE, USA
\textsuperscript{b}Neurology Associates, PC, Lincoln, NE, USA
\textsuperscript{c}Past Forward Gym, Omaha, NE, USA
\textsuperscript{d}Valmont Industries, Valley, NE, USA
\textsuperscript{e}University of Kansas, Department of Statistics, KS, USA
\textsuperscript{f}University of Nebraska Medical Center, Department of Allied Health, Omaha, NE, USA

Abstract. Strength and endurance data from 67 participants with multiple sclerosis (MS) were compared before, during and after a 6-month program of standardized resistance training. The hypothesis was that a standardized, structured resistance training exercise program improves strength in MS patients with different levels of disability. The range of EDSS scores was 1–8: (40% – EDSS of 1–4.5), (35% – EDSS of 5–7) (25% – EDSS of 7.5 or higher). This unique study evaluated patients with differing levels of disability for a change in strength and endurance following a 6-month training program. Data were analyzed by repeated measures and analysis of variables using Proc GLM in SAS to account for variability between subjects, and within subjects, due to repeated measures at 3 time points. Each treatment was blocked by disability class. Every within-treatment analysis was significant. Each exercise showed significant improvement in strength for participants, despite disability levels. Increases in strength followed parallel improvement pathways, at all disability levels. All but one treatment displayed highly significant improvement (p-value < 0.0001). The results demonstrated that all individuals with MS, despite disability levels, show parallel improvement in strength and endurance. This study supports the use of exercise, including resistance programs, for all MS patients.

Keywords: Resistance training, strength, multiple sclerosis, varied disability

1. Introduction

Exercise has long been felt to be the cornerstone of a long and healthy life style. However, as people age or accumulate disability, the idea of regular exercise diminishes for no apparent reason other than it becomes increasingly difficult to facilitate. Most healthcare providers switch recommendations from conditioning exercise to stretching exercise only, as aging and disability accumulate.

Muscle weakness and fatigue have long been hallmarks of multiple sclerosis (MS). Individuals with MS were advised in the past not to exercise, because exercise was believed to bring on fatigue, thereby decreasing quality of life (QOL) indicators [1]. Contrary to this historic opinion, muscles weakened by MS appear to improve from strength training programs [2]. This improvement in strength can make daily activities easier to perform, less fatiguing and therefore decrease the degree of disability and increase QOL [2–5]. Exercise is being recognized as an important part of the symptomatic treatment of MS. There is, however, some indication that exercise may go beyond symptomatic treatment and could impact the disease state itself. Recent studies make it clear that MS patients benefit from
physical exercise with profound effects on immune and endocrine parameters [6–8], making exercise as important as early pharmalogical intervention.

2. Review of effects of exercise in inflammation and MS

Over the last 16 years, pharmacologic treatments for relapsing/remitting multiple sclerosis (RR-MS) decreased the number of MS relapses and their severity in many MS patients. However, despite treatment, patients continue to report fatigue, muscle weakness, lack of endurance and balance problems due either directly to their MS or as a side effect of the immunotherapy treatment [9,10].

Numerous current studies report that physical rehabilitation has a positive effect in MS patients [3,8,11,12]. Earlier studies evaluated inpatient rehabilitation programs [13] that are not routinely available or covered by insurance in this country. With the introduction of newer and increasingly effective treatments, more RR-MS patients maintain low levels of disability, remain in the work force and out of care facilities. These individuals, however, continue to report ongoing fatigue, muscle weakness and balance problems [14]. Earlier studies concentrated on maintaining or improving quality of life and disability outcome measures in RR-MS patients but did not evaluate traditional strength and endurance outcome measures.

The skeletal muscle of people with MS displaying moderate impairment and muscle weakness, have similar muscle fiber characteristics as age-matched sedentary control [15]. This supports the hypothesis that the quality of skeletal muscle is unaffected by MS, at least in the early stages of the disease. Lower lactate levels occur during training, despite higher workload levels, indicating a training effect. Balance, fatigue, depression and fear of falling improve with progressive resistance training [16]. QOL improves through pathways that include decreased fatigue and pain and increase in social support and self-efficacy [3,17].

Rietberg et al. [8], and Rimmer et al. [13] reviewed controlled trials dealing with exercise and MS from 1986-2006. The current literature on exercise and disability in MS is extremely broad in scope and has limited generalizability to any specific disability group [13]. Best evidence synthesis showed strong evidence in favor of exercise therapy compared to no exercise in terms of muscle power function, exercise tolerance functions and mobility-related activities. Moderate evidence was found for improving mood. In these studies, no evidence was observed or primarily monitored for exercise related benefit on fatigue and perception of handicap. No specific exercise therapy programs were shown to be more successful in improving activities and participation than other exercise treatments. No evidence of deleterious effects of exercise therapy was described in the included studies.

Romberg et al. [18] reported that individuals who maintain the ability to walk, with EDSS scores between 1.0–5.5, could increase their walking speed following a progressive 6-month exercise program. Dalgas [4] and Cakt [16] conclude that MS patients are capable of making positive adaptations to resistance training improving balance, fatigue and fear of falling. The beneficial effect appears to be maintained for at least 12 weeks after the end of intervention [17].

Dynamic strength training, combined with endurance type physical activity, improves muscle strength and physical function in patients with early rheumatoid arthritis which shares many inflammatory features with MS [19]. There were no differences in specific force, contractile properties, voluntary activation capacity and contraction velocity.

While exercise was found to be safe for MS patients with mild to moderate disability, no data are available for those individuals more disabled. This current study is unique because no previous study evaluated and showed improvement in individuals with MS who displayed Expanded Disability Status Scale (EDSS) scores of > 5.5. All previous study participants were able to ambulate with little or no assistance. In this study, all levels of MS patients, even those with significant disability, were evaluated for change in strength and endurance despite the degree of their original disability.

3. Hypothesis/objectives

It was hypothesized that there is a significant muscle training effect in all individuals with MS, despite disability levels because muscles respond normally with training. The primary objective of this study was to evaluate the effectiveness of weight resistance exercise in a group of MS patients with varied disability levels as measured by changes in strength and endurance at baseline, during and at completion of a six-month training program. A secondary objective was to determine if the pattern of training effect was similar within groups, despite differences in disability levels.
4. Methods

This was a retrospective evaluation of specific outcome measures related to strength and endurance. This particular exercise protocol was initiated in 6 individuals to provide preliminary data to guide the clinical treatment protocols. Numbers of participants rapidly grew due to the significant improvement that was verbally reported by those participating in the exercise program. Data were available on 67 participants due to standard record keeping of program progression combined with information from clinical notes. Specific strength and endurance outcome measures were evaluated for designated muscle groups, before, during and at completion of a six-month resistance program developed for MS patients.

The study population consisted of consecutive MS patients at a Midwestern Multiple Sclerosis Clinic, recommended for exercise therapy to include a specific regime of conditioning and strength training. Individuals were included irrespective of their EDSS score on entry. Subjects had to complete at least 6 months of a regular bi-weekly exercise intervention to be included in the study.

4.1. Inclusion criteria

1. Subjects met all required areas of McDonald criteria as well as clinical history for a diagnosis of laboratory supported MS (MRI evidence of dissemination in time and space).
2. Age between 19 and 75 years.
3. Subjects were willing to complete a structured 6-month exercise program.
4. Participation in the study would not put the subject’s health at undue risk.

General demographic information on all subjects was collected to insure that the study population was consistent with the general MS population. The primary outcome was to evaluate whether weight resistance exercise was more effective in MS patients with low disability than those with moderate or severe disability. The demographic data included: gender, age, age at diagnosis, time since diagnosis of MS, type of immunotherapy for MS (if any) at the time of participation in the exercise program and number of relapses (if any) during the 6-month weight resistance study period. The disability level of the MS patients at the time of the exercise initiation dictated placement into one of three groups:

1. Minor disability, able to walk without aid, EDSS 1–4.5,
2. Moderate disability, able to walk with an aid (cane or orthotic device), EDSS 5–7,
3. Severe disability, unable to walk 25 feet, wheelchair confined, EDSS 7.5 or above.

Weight resistance exercise outcome data were collected from training records at the initiation of the resistance exercise program, after 3 months participation and after completion of 6 months of bi-weekly training. The data included the following:

a. strength: maximum pounds lifted
b. endurance: measurement of output at certain stations recorded as repetitions with specific low weights over a set time period.

4.2. Exercise program

The program was designed and supervised by ACE certified trainers, with no more than a 3:1 subject to trainer ratio. The exercise protocol was reviewed by the PI and Physical Therapy for safety, completeness and appropriateness in this patient population. A full complement of dynamic stretching exercises was done as a warm-up and a static stretch was performed after the main program, involving the arms, shoulders, calves, hamstrings; and quadriceps. A variation of all the stretches could be performed standing, sitting in a chair, or on a floor mat. The program breakdown consisted of: 5–10 minutes of warm-up (dynamic stretch), 30 minutes of strength circuit and 5–10 minutes of cool down (static stretch).

The resistance program consisted of twice-weekly exercise sessions lasting 50 minutes each for a total of 6 months. To be included in the data, each participant was required to attend the full exercise program. Starting resistance or weight was determined by each individual’s ability to perform 10 repetitions of the designated exercise within 30 seconds using correct form. Progression in weight or resistance was implemented when the final repetition of a 10 repetition set could be done with the same effort as the first. The entire training program consisted of three phases (Table 1) [20]. A single phase was used at each exercise session and a rotational order was used to insure that subjects participated in each phase equally. Phases were rotated to provide muscle confusion and allow for better conditioning. Extremities were exercised separately/unilaterally to allow both hands to be used for weight stabilization, if needed, and to provide adequate attention and
training to weakened extremities. Each phase was designed to address balance and muscle strength, issues of special concern to MS patients, rather than overall conditioning. Trainers assisted with one-on-one help, as needed, during the workouts.

The first phase focused purely on strength improvement, with the participants spending the entire time on stationary machines, with each machine working different areas, including the back (upper and lower), shoulders, chest triceps, biceps, abdominals and legs. Machines were modified and arranged to allow handicap accessibility.

The second phase was divided between the machines and exercises to improve balance and dexterity. Balance exercises were conducted in squat cages, providing stability, and security, allowing the participants to work on balance, strength and to increase conditioning, agility and strength.

The third phase used free weight movements. Each participant utilized weight benches to complete their activity, with balance and coordination as the goal. The goal of each phase was to recognize and improve on the imbalance problems MS often causes. Each activity was completed unilaterally to ensure the stronger body parts were not assuming all the work.

The program was circuit based with each participant completing 2–3 sets of approximately 10 repetitions at each exercise station before moving onto the next. This was done to reduce any undue physical fatigue caused by rapidly moving between stations. Ten exercise stations made up each circuit. Completing multiple sets on each station with limited rest between each set allowed for the anaerobic benefits that result from strength training. The limited rest between exercises allowed the heart rate to remain elevated throughout the duration of the routine. Data was collected on 12 interventions to include: triceps extensions, arm curls, abdominal crunches, back extensions, shoulder raises, wrist curls, leg curls, back rows, leg extensions, lateral pulldowns, shoulder press and chest press.
4.3. Data analysis

Data were collected on all activities, including time spent in the standing frame for those who were wheelchair confined as well as strength, endurance, and conditioning information. Due to the inability of some participants to complete specific exercises, full program comparisons between subjects could not be done.

Data were analyzed by repeat measures and analysis of variables using Proc GLM in SAS to account for variability between subjects, and within subjects, due to repeated measures at baseline, 3 months and 6 months. Each treatment was blocked by disability class and weights modeled at each time point (baseline, 3 months and 6 months). The assumption that improvement performance occurs in all classes of subjects despite levels of disability for each treatment was tested using Huynh-Feldt epsilon. Sphericity assumption was satisfied.

5. Results

5.1. Characteristics of the study population

A total of 67 subjects were enrolled and completed the 6 month exercise program. Individuals were excluded if a total time of ≥ 2 weeks were missed at any time during the 6 months of exercise or if attendance dropped below weekly participation. Participant's age range was 24–75 years of age with mean subject age of 49.5 years. There were 18 males and 49 females with a female bias of 2.7:1. MS is a predominately female disease with a 2:1 or 3:1 female to male ratio. Three subjects were black (4.7%) and 64 were Caucasian (95.3%), reflecting Nebraska’s population prevalence of 4% blacks. Participants included relapsing/remitting MS (RR-MS) patients as well as those considered secondary progressive. The range of EDSS scores was 1–8: 40% (n = 27) had an EDSS of 1–4.5, 35% (n = 23) had an EDSS of 5–7 and 25% (n = 17) an EDSS of 7.5 or higher. Time since diagnosis ranged from 1 to 45 years, with 43 participants (64%) diagnosed 10 years or less.

MS treatment varied: 6 (9%) were on no treatment, 33 (49%) were on Avonex, 6 (9%) were on Betaseron, 12 (18%) were on Copaxone, 6 (9%) were on Rebif and 4 (6%) were on Novantrone. There was no significant impact of treatment choice on exercise outcome. Only two individuals had an MS relapse during the exercise program and both responded to standard steroid therapy with a return to baseline status within 2 weeks.

5.2. Effects of exercise

As expected, between subjects analysis demonstrated that individuals with Disability Level 1 (mildly disabled) start at a higher training weight or resistance level than those with Disability Level 2 (moderately disabled) and those with Disability Level 3 (severely disabled). They also continue throughout the program to perform at proportionally higher levels. Subjects with Disability Level 2, likewise, out-perform subjects in Disability Level 3. This performance difference was maintained throughout each treatment. Leg curls were not recorded by subjects with EDSS scores 7.5 or greater due to the amount of lower extremity involvement consistent with a disability score of this level. A decrease in the number of subjects able to perform exercises requiring core strength within the severe disability group were expected and noted.

Each within-treatment analysis was significant for improvement from baseline to 6 months. Each specific exercise showed significant improvement in strength for participants, despite their disability levels. Increases in muscle strength followed parallel improvement pathways, reflected at all disability levels (Fig. 1). All but one treatment displayed highly significant improvement over the exercise course with a p-value < 0.0001. “Abdominal Crunches” had a p-value = 0.0142 but remained significant at an α = 0.05 level. A higher than anticipated strength level for one participant in a Disability Level 3 at baseline was recorded, but could not be replicated at any other level or in any other time. This value, however, was recorded with only one participant and should not be generalized to that population. Upper extremity strength was at times very comparable between the moderate and severe disability levels (tricep extensions, back extensions, shoulder raises, wrist curls, back rows, lateral pulldowns and chest press) possibly reflecting the subsequent upper body strength secondary to the constant use required of those muscles in patients with severe lower extremity weakness.

These findings support the hypothesis that a strength training program improves strength and endurance in subjects with MS, despite varying degrees of disability.

6. Discussion

6.1. Outcome measures specific to exercise physiology

The functional unit of the neuromuscular system motor unit consists of the α motor neuron and the asso-
associated muscle fibers it activates. When maximal force is desired from a muscle, all the available motor units must be activated. Different types of motor unit firing rates, or frequencies, affect muscle force by an adaptive mechanism called the “size principle”. This, in turn, is affected by resistance training. With resistance training, muscle fibers increase in size and are recruited in consecutive order by their size to produce high levels of force. The CNS may adapt, in trained individuals, by not recruiting some motor units in consecutive order but by recruiting larger units to help with a greater production of power or speed [21,22]. This improvement of speed and power of muscle response would increase performance in anyone training, despite disabil-
ity level, as long as the muscle is not damaged. This type of adaptation is hypothesized to be the mechanism for how muscle strength training might help those with MS.

When starting a training program, a variety of alterations must take place to increase the strength, power, and size of the muscles trained. The CNS, motor neurons and associated muscle tissue are the primary physiological systems involved with the needed adaptations for increased force production. High intensity (5RM and lower) and low-volume multi-joint lift training programs primarily affect neural factors (e.g., recruitment patterns, activation, and inhibition). Resistance training normally increases performance by in-
creasing muscle strength, muscle endurance, aerobic power, maximal rate of force production, muscle fiber size, capillary density, mitochondrial density and subtype conversion to Type II muscle fiber [21,22].

The neuromuscular junction (NMJ) is a major site of plasticity. While data describing the molecular mechanisms involved with neural adaptation to general exercise training are limited, it is hypothesized that heavy resistance exercise training produces morphological changes in the NMJ. Changes related to heavy resistance exercise training are of a greater magnitude than adaptations to low-intensity aerobics. During progressive overload in resistance training, neural factors may mediate greater strength increases without large increases in cross-sectional muscle area. In healthy individuals, increases in muscle strength from pre-training values can range from 7% to 45%: the increase for a given person depends largely on the starting level of strength [21,22]. It is hypothesized that the use of resistance exercise training will produce a similar increased muscle strength and endurance in MS patients, independent of disability level.

6.2. Significance of the present study.

Individuals with MS, regardless of the degree of disability or EDSS scores, benefit from an individualized exercise program of endurance and strength training in select areas of performance. The exact mechanism is unknown. Data from within subject trials at 3 time points (baseline, 3 months and 6 months) show strength improvement on similar trajectories independent of established disability levels in all but one treatment, that of abdominal crunches. This data supported the hypothesis that individuals with MS benefit from strength and endurance training, demonstrating that muscles of those with MS respond to training intervention much like unaffected individuals. Initial increases in strength and endurance are greater in those subjects who are more deconditioned but improvements are significant in all groups. Any training advantage disappears as conditioning continues.

Clinical observations of moderate to severely disabled MS patients describe a decline in core strength with subsequent loss of balance related to muscle weakness. Weakness is most easily observed in the hip flexors, but is also significant in the abdominal muscles. It is reasonable to predict that the exercise area least likely to show improvement in the severely disabled would involve these particular muscles, as is evident in this study.

Interventions for individuals with MS, by health care providers, are generally limited to brief interactions with physical therapy and occupational therapy programs, particularly if disability is moderate to severe. The driving force for being able to remain in these programs are maximum or continued improvement after an acute event, not maintenance of function during a chronic process. Individuals are “counseled to leave the program” or payment is denied when maximum improvement is reached. The difference in utilizing physical therapy for a condition like MS rather than an acute disability is that maintenance of abilities is the primary outcome. Many programs are not incorporated into the lifestyles as practiced health habits. The exceptions are specific individuals who have intense personal goals and persistence and are capable of carrying out the exercise program by themselves in an atmosphere of isolation. Unfortunately, few people are that driven and most need a defined program, facility, exercise group or personal trainer to carry out a routine exercise program.

Another challenge is that most private exercise facilities cater to the young and healthy but do not allow for those individuals that need time and attention to complete exercise programs, even if those individuals may be the ones that would benefit the most. Individuals with disability clog the system and do not allow for fast turnover of equipment or space. This fast turnover is often the cornerstone of business development in the world of fitness. One of the most common complaints among the disabled is that they do not feel welcome in the new age, high tech exercise arena. Medically affected individuals need “a place of their own” that understands their needs and are designed for their use.

Only three relapses were noted overall in the participants throughout the length of the study which is significantly lower than the expected relapse occurrence of 1.6–2.0 per person per year and relapse recovery was rapid and complete. The reason for this decreased relapse rate is unknown. This anecdotal report gives pause for consideration. Even while attempting to maintain a healthy lifestyle, individuals will experience flares or relapses from MS in which symptoms worsen and disability progresses. It is uncertain whether symptoms will improve or disability remains permanent. During a relapse, areas of axons are damaged or destroyed during the inflammatory process. It is speculated that nerve rootlets are present for a limited time at the site of injury and can possibly be stimulated to grow, replacing the destroyed fibers, establishing new collateral impulse pathways: If this is the case, the
use of significant, regimented exercise to stimulated growth and subsequent use of these pathways would decrease the degree and extent of permanent injury. It would be comparable to building collateral circulation to the cardiac muscles following a myocardial infarct. It would suggest that the immediate decrease of inflammation followed by aggressive physical therapy or exercise training would positively impact final outcome of these flares and decrease further disability. No research in this area has been done. Structured evaluation should be considered.

The retrospective design of the current study is a limitation. There is a need for prospective studies with randomized controls to replicate and support the current study outcomes. Due to anecdotal reported improvements in fatigue levels, fatigue measures should also be noted to determine what type of measurable impact exercise plays in this area.

By anecdotal report, training sessions have given participants a feeling of self-worth and fulfillment and have been referred to as a type of proactive support group for those involved. Further studies should be designed to include assessments of quality of life indicators as compared to parameters of strength and conditioning improvements. Consideration should be given to include depression screenings both pre and post training to quantify changes in their perceptions.

Since many research studies have excluded those individuals who have reached wheelchair dependency as being too disabled or difficult to observe for changes, it becomes imperative that all levels of disability be considered. Disabled individuals should be included in research that can significantly impact their quality of life. Causing any positive change in their condition even minimally, may affect them considerably more than those less disabled.

7. Summary

Regular resistance exercise programs:

1) Show benefit in individuals with MS despite varying levels of disability. A parallel response curve is seen despite level of disability and lower weight resistance thresholds.

2) Individuals participating in a regular exercise routine appear to have a shorter recovery time from MS flairs, returning to pre-relapse activity more quickly. The routine use of weight resistance and balance exercises as an adjunct treatment in the fight against MS should be considered.

3) A positive psychosocial impact is reported by participants. The use of quality of life indicators as well as fatigue and depression scales should be included in further studies to further explore this type of improvement.

4) Further randomized control trials are needed to prove the effect of the current intervention program.

References


Journal of Physical and Medical Rehabilitation 89(3) (2010), 240–263.


