EFFECTS OF AN EIGHT-WEEK PROGRESSIVE RESISTANCE TRAINING PROGRAM ON BALANCE IN PERSONS WITH MULTIPLE SCLEROSIS

By

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Multiple sclerosis (MS) is an autoimmune disorder of the central nervous system, which leads to degeneration of the myelin sheaths that protect the neural axons. MS can affect any part of the central nervous system, so persons with MS experience a wider variety of symptoms than most neurological disorders, including problems with balance and strength loss. The aim of this study was to determine if a strength training program, designed to increase muscle strength, could improve postural sway measures in persons with MS. Nine MS subjects and four non-MS controls participated in an eight-week strength-training program. They were tested for isometric strength for their knee extensors, knee flexors, plantar flexors, and dorsiflexors prior to and following the strength-training program. Postural sway was also evaluated before and after training in 5 different stance conditions: 1) self-selected, 2) feet 6 inches apart, 3) feet 6 inches apart on a foam pad, 4) semitandem, and 5) tandem. Four dependent variables were calculated from the tests of postural sway: path length (PL), average speed (AS), antero-posterior
amplitude (AP), and medio-lateral amplitude (ML) of the COP movement. Wilcoxon signed rank tests were performed on all strength and balance variables to determine if changes occurred due to the strength-training program with a conventional significance level of 0.05. For the MS training group, the Wilcoxon signed rank tests revealed a significant increase in PL and AS for the self-selected stance and an increase in isometric strength in the knee flexors. The non-MS control training group had no significant differences in strength or balance after training. The results indicate that strength training is safe for persons with MS and may lead to an increase in muscular strength. However, it does not appear to have a significant effect on standing balance in the stance positions studied. A training program more specific to balance may demonstrate more significant improvement in balance for persons with MS.
CHAPTER 1
INTRODUCTION

Multiple sclerosis (MS) is the most common cause of nontraumatic neurological disability affecting young adults in the northern hemisphere (Goodkin, 2000). MS is an autoimmune disorder of the central nervous system that leads to widespread degeneration of the myelin sheaths that encase axons in the central nervous system. The loss of the protective myelin layer causes lesions to form on the axons, which can eventually develop into hardened *scleroses* that inhibit the normal conduction of nerve impulses down the axons (Herndon, 2000). The extent of axonal loss is variable, but usually substantial, with some axonal loss occurring in every lesion (Trapp et al., 1998). Symptoms from axonal loss cannot be alleviated. However, experimental efforts to improve conduction in neurons without axonal loss have been promising (Herndon, 2000).

The four accepted patterns of pathology in MS as defined in 1996 are: 1) relapsing-remitting, 2) secondary progressive, 3) chronic progressive and 4) progressive relapsing MS (Goodkin, 2000). However, specific lines separating these disease patterns are not completely clear thus making specific diagnoses challenging. Furthermore, the variable nature of the disease leads to a difficulty in creating an ideal outcome assessment measure for patients with MS. In all patterns of MS, the level of disability in patients is typically categorized using the Expanded Disability Status Score (EDSS). The EDSS scale was designed by John F. Kurtzke and is based on the maximum function of a patient as limited by their neurological deficits (Kurtzke, 1955). Aside from a few
shortcomings, it serves as a familiar and quantifiable method of communication amongst healthcare professionals concerning individuals with MS.

MS lesions occur in different areas of the central nervous system and due to this variable distribution of demyelination, people with MS may experience a wider variety of symptoms than any other neurological disease including balance, coordination, strength and sensation disorders (Cattaneo et al., 2002). Furthermore, individuals with MS have been found to have a reduced amount of skeletal muscle and a tendency to supply energy through anaerobic pathways (Kent-Braun et al., 1997), which implies a decrease in the number of slow-twitch muscle fibers. Along with a decrease in skeletal muscle fiber size, persons with MS also face a reduced ability to activate muscle (Lambert et al., 2001), which is associated with the demyelination of nerves (Kent-Braun et al., 1997). This reduced muscle size and compromised motor unit activation cause the muscle weakness associated with MS, which coupled with spasticity, further compromises the ability to balance by affecting the sequencing and force of muscle contraction (Frzovic et al., 2000).

Inability to maintain standing balance impacts a patient’s ability to perform activities of daily living (ADLs) and puts them at an increased risk of falling and subsequent injury, which contributes to the development of a fear of falling that may lead to a change in quality of life (Cattaneo et al., 2002). Therefore, balance assessment and implementation of rehabilitation strategies to improve balance is important in attempting to maintain a favorable quality of life for persons with MS.

Patients with MS demonstrate reduced physical activity when compared to non-MS individuals (Ng & Kent-Braun, 1997), which is usually attributed to muscle weakness
and fatigue, but could also be due to a patient’s fear of falling (Cattaneo et al., 2002). When balance is compromised, even simple ADLs such as dressing, walking, and standing become challenging, which may contribute to the anxiety and depression that affects about 65% of patient’s with MS (Joffè et al., 1987).

The muscle weakness and fatigue demonstrated in persons with MS is consistent with human models of disuse and provides a rationale for therapeutic intervention in the form of exercise training as a means of reversing some of the reduced sensory and motor functions in individuals with MS (Kent-Braun et al., 1997). Individuals with MS experience muscle weakness and more symptomatic fatigue with exercise, however Kent-Braun and colleagues found that they were not weaker compared to healthy individuals when the amount of fat-free mass was taken into account. Therefore, an exercise-training program designed to enhance muscle strength and endurance is a reasonable therapeutic intervention in persons with MS and may be helpful in improving the functional capacity of individuals with MS and offsetting the deleterious effects of their disease.

Furthermore, the demyelination associated with MS is not always permanent; remyelination has been documented in MS (Chang et al., 2002). However, these remyelinated nerves often fail to return to baseline functioning because of the decline in activity following an acute MS attack (Herndon, 2000). Strength training may assist in both promoting strength that may have been lost because of physical inactivity and returning proper neural function to the remyelinated tissue. In addition, physical activity has an important benefit in reducing the risk of secondary diseases and improving overall health.
As stated earlier, persons with MS often face a reduced ability to balance, meaning they are frequently unable to maintain the body’s position over its base of support (Rogers et al., 2001). Quantifying a patient’s level of balance impairment is important, therefore many different techniques have been proposed to measure a person’s ability to maintain static or dynamic balance. In research settings, postural sway analysis is widely accepted as a reliable way to quantify the complex and multidimensional nature of a person’s standing balance (Tillman & Chow, 2002); however little research has been conducted using postural sway in persons with MS. In addition, the influence of strength training in MS patients has not been evaluated. Thus, the primary aim of this study is to determine whether an eight-week program of progressive resistance training is tolerable for persons with MS and if it could enhance standing balance in ambulatory individuals with MS.
CHAPTER 2
LITERATURE REVIEW

A review of the literature revealed a significant shortage of relevant information concerning strength training and balance in persons with MS. This work is intended to fill that void. More specifically, it aims to provide more data regarding the effects of resistance training on balance in individuals with MS.

**Multiple Sclerosis**

Multiple sclerosis (MS) is the most common progressive neurological disease in young adults (Kraft & Wessman, 1974), usually diagnosed in individuals between the ages of 20 and 40. MS is a degenerative inflammatory autoimmune disorder of the central nervous system that destroys the myelin sheaths that encase and insulate the neural axons (Chang et al., 2002; Kidd, 2001). The etiology of MS is not known, however the most widely accepted hypothesis is that it is a virus-induced autoimmune disorder (Herndon, 2000). The myelin in the central nervous system and the cells that form that myelin, the oligodendrocytes, are the primary targets of attack (Herndon, 2000). Lesions form on the myelin sheaths and can eventually develop into hardened *scleroses* that inhibit the normal conduction of nerve impulses down the axons (Herndon, 2000).

MS lesions occur in different areas of the central nervous system and can range from acute plaques with active macrophages containing lipid and myelin degenerating products to chronic, inactive glial scars. The plaques appear to begin with the macrophages and lymphocytes forming perivascular cuffs about the capillaries and venules (Herndon, 2000). This is followed by diffuse infiltration by inflammatory cells,
edema, astrocytic hyperplasia, and macrophages consuming the myelin off the axons causing an increasing number of lipid-filled macrophages and demyelinated axons (Prineas, 1975). The extent of axonal loss is variable, but usually substantial (Trapp et al., 1998), with some axonal loss occurring in every lesion. Experimental efforts to improve conduction in neurons without axonal loss may produce dramatic improvements in many symptoms that result from conduction failure in unaffected axons, however the symptoms that result from axonal loss cannot be alleviated by these interventions (Herndon, 2000).

There are four accepted patterns of pathology in MS that were defined in 1996, which include: 1) relapsing-remitting, 2) secondary progressive, 3) chronic progressive and 4) progressive relapsing MS. The relapsing-remitting form of MS is the best understood and is more common in younger patients. Approximately 85% of MS patients experience an exacerbation at disease onset (Goodkin, 2000). Multifocal discrete inflammatory demyelinating lesions in both the gray and white matter of the CNS are characteristic of this pattern (Herndon, 2000) and patients are usually stable between exacerbations (Goodkin, 2000). Secondary progressive MS has characteristics consisting of a combination of both relapsing-remitting and chronic progressive MS (Herndon, 2000). In these individuals, old, inactive, multifocal lesions coexist with progressive diffuse demyelination (Herndon, 2000). Chronic progressive MS (also known as primary progressive MS) is more typical in older patients and is less dramatic than relapsing-remitting MS. The demyelination is diffusely scattered involving individual fibers or small groups of fibers interspersed with normal appearing myelinated fibers. The inflammatory infiltrates and macrophages are much more limited and diffuse than in
relapsing-remitting MS (Herndon, 2000). Chronic progressive MS involves a gradual progression of disability without superimposed relapses (Goodkin, 2000). The fourth pattern is termed progressive relapsing MS in which patients experience gradual disability progression accompanied by one or more relapses (Goodkin, 2000). However, specific lines separating these disease patterns are not completely clear which makes specific diagnoses challenging.

During the process of demyelination, some conduction failure is unavoidable in the affected fibers. Some lesions are known as clinically silent lesions, which occur when a minority of fibers in a conduction path become demyelinated at any one time, leaving intact conduction in the unaffected fibers in the path (Herndon, 2000). The causes of conduction failure associated with demyelination are not completely understood, but it is hypothesized that it may be due to 1) damage to the nodal sodium channels (Kaschow et al., 1986a & 1986b), 2) a virtual absence of these sodium channels (Ritchie et al., 1977), and/or 3) increased membrane capacitance in the demyelinated region (Waxman, 1995). There is substantial evidence that the nodal membranes are damaged by various enzymes released by the inflammatory cells that appear to produce extensive damage to the myelin. Furthermore, an increased membrane capacitance causes the amount of current required to depolarize the axon to be higher and therefore make impulse conduction slower or in some cases blocked. These characteristics of demyelinated fibers help explain some of the features of the motor fatigability and activity related failure of neurological processes that affect individuals with MS (Herndon, 2000).

**Expanded Disability Status Score (EDSS)**

The very nature of the disease leads to a difficulty in creating an ideal outcome assessment measure for patients with MS. In all patterns of MS, level of disability in
patients is typically categorized using the Expanded Disability Status Score (EDSS). The Disability Status Score (DSS) was designed in 1955 by John F. Kurtzke and measures the maximum function of a patient as limited by their neurological deficits (Kurtzke, 1955). The DSS was expanded in 1983 to include more extensive criteria and is now known as the Expanded Disability Status Score. The EDSS scale is based on any lack of function in eight functional systems: 1) Pyramidal (degree of paralysis), 2) Cerebellar (coordination of movement), 3) Brain Stem (cranial nerve functioning), 4) Sensory, 5) Bowel and Bladder, 6) Visual (optic), 7) Cerebral (mental), and 8) Other neurological deficits attributed to MS. The scale ranges from 0 to 10, where 0 is normal functioning and 10 is death due to MS (Kurtzke, 1983). The scale is primarily based on the patient’s ability to ambulate and deficiencies in any of the eight functional systems make the score more specific to the patient’s actual disability level.

The most favorable aspects of the EDSS scale lie in the coverage of four of the eight functional systems: the pyramidal, cerebellar, visual, and mental systems (Coulthard-Morris, 2000). The pyramidal scale measures disability in the appendages (i.e. paralysis in a limb). Cerebellar function is measured by the ability to coordinate movements, which can be affected by the ataxia suffered by MS patients. Visual impairments are characterized by a loss of visual acuity and/or temporal pallor. Finally, mental functioning is measured by decreases in mentation leading to dementia. Although we will not be directly testing disability level in any of the eight functional systems, the ones that are most important for maintaining balance include the pyramidal, cerebellar, sensory and visual systems.
Even though the EDSS scale is the most widely accepted MS impairment measure and provides a familiar and quantifiable method of communication among health care professionals, it lacks the sensitivity needed to detect the small changes in disease status experienced by people with MS over short time periods. Furthermore, low interrater reliability makes reproducible assessments more challenging. The EDSS scale predominantly measures ambulation and many clinicians feel it does not adequately assess impairment and disability in persons with MS (Coulthard-Morris, 2000). Aside from its few shortcomings, the EDSS scale is the best measure available for quantifying disability in persons with MS to date. However, more comprehensive scales for balance deficits in MS would be beneficial. (See Appendix B for the complete breakdown of the EDSS scale).

**Symptoms**

Without proper neural functioning, individuals with MS may suffer from a variety of symptoms, including sensory loss in the appendages, slowly progressive motor deficit, acute motor deficit, optic neuritis, and/or a variety of other ailments (Paty, 2000). Due to the variable distribution of demyelination throughout the central nervous system (Cattaneo et al., 2002), people with MS may experience a wider variety of symptoms than any other neurological disease. These symptoms can lead to problems with balance, coordination, walking mechanics (gait), and postural control. Much of the disability associated with MS results from axonal destruction in very long pathways, such as the pyramidal tract, which supplies the legs and dorsal column with efferent and afferent signals. The imbalance and coordination issues encountered by individuals with MS are due to the slowed conduction in these tracts of proprioceptive impulses and the inability to monitor motor processes that pass through the demyelinated areas (Herndon, 2000). In
many of these individuals, symptoms are exacerbated by an increase in core body temperature of as little as 0.5° C (Paty, 2000).

The combination of factors causes individuals with MS to have reduced skeletal muscle fiber size, lower oxidative capacity per unit volume, and a greater tendency for the muscle to supply energy via anaerobic pathways (Kent-Braun et al., 1997). The variability in muscle strength in MS patients appears to be the result of reduced ability to activate muscle (Lambert et al., 2001), in part, because of poor motor unit activation associated with demyelination of nerves (Kent-Braun et al., 1997). Also, MS often results in muscle atrophy and high fatigueability associated with reduced physical function during MS relapses. Following an acute MS attack, intact motor units may not function fully because of disuse, and coupled with spasticity, further compromise the patient’s ability to balance themselves, affecting both the sequencing and force of muscle contraction (Frzovic et al., 2000).

**Risk of Falls**

Balance assessment in conjunction with the implementation of rehabilitation strategies is important in a clinical setting to improve mobility and reduce the risk of falls and subsequent injury in persons with MS. Patients with MS, even those only mildly affected, demonstrate reduced physical activity patterns compared to healthy individuals (Ng & Kent-Braun, 1997). This reduced physical activity is usually attributed to muscle weakness and fatigue, but could also be due to poor balance, frequent falling, fear of falling, thermoregulatory issues and a global decline in functional capacity (Cattaneo et al., 2002). Recreational and social activities may also be reduced, especially when considering that leisure activities are the first lost when an illness is present (Petajan et al., 1999).
In patients with compromised neurological function, falling has a multifactorial origin and consequently there are many reasons why these individuals face an increase risk of falling (Cattaneo et al., 2002). The role of improved balance in decreasing the risk of falls has important implications in reducing injury and long-term disability. Unfortunately, little research has been performed on falling behavior in persons with MS, however the risk of falls in MS is comparable to that of the elderly (Cattaneo et al., 2002). Gryfe and colleagues (1977) reported that 45% of adults age 65 and older experience on average one fall per year. Furthermore, falling is the leading cause of injury related deaths in older adults with 27.2% of injury related deaths in persons age 70-79 being attributed to falling behavior (National Safety Council, 2000). Most published studies have found that balance impairment is an important risk factor in predicting falling behavior (Cattaneo et al., 2002).

MS has a global impact on patients and impairs their ability to perform even the simplest ADLs. When balance is compromised, many common activities such as standing, dressing, and walking become challenging. Inability to maintain balance when performing ADLs can lead to anxiety and depression, which already affects about 65% of patient’s with MS (Joffe et al., 1987).

**MS, Exercise and Remyelination**

The muscle weakness and fatigue demonstrated in persons with MS is consistent with human models of atrophy, which provide the rationale for exercise as a therapeutic intervention to reverse reductions in functional capacity in individuals with MS (Kent-Braun et al., 1997). Kent-Braun also found that even though individuals with MS experience more symptomatic fatigue with exercise, they were not weaker when compared to control subjects when differences in fat-free mass were taken into account.
The finding that MS patients are in fact not weaker than control subjects also supports the idea that strength training to increase the quantity and quality of skeletal muscle is a viable means of improving the function and quality of life in individuals with MS. Improvements in muscle strength, endurance, range of motion, and coordination may improve balance in individuals with MS (Armstrong et al., 1983).

An exercise-training program designed to enhance these variables may improve the functional capacity of individuals with MS and offset the deleterious effects of their disease. Unfortunately, little research is available on resistance training in MS, however there is information available concerning MS and exercise, specifically aerobic exercise. Several studies have found that even a short term aerobic exercise program can improve aerobic fitness and fatigue, and may lead to an increased level of physical activity and an improved perception of health status in persons with MS (Mostert & Kesselring, 2002; Petajan et al., 1996; Gehlsen et al., 1984). This strengthens the rationale that an exercise-training program may improve quality of life in persons with MS.

Furthermore, the demyelination associated with MS is not always permanent; remyelination has been documented in MS (Chang et al., 2002). Bunge and colleagues (1961) demonstrated that central nervous tissue could be remyelinated in a cat and this was later proven to be true in other species including the tadpole, rat, mouse, rabbit and dog (Hommes, 1980). Remyelinated areas in experimental animals show 1) an increased number of oligodendrocytes, which contrary to traditional beliefs can proliferate (Ludwin, 1984), 2) thin myelin sheaths of uniform thickness, and 3) short internodes (Herndon, 2000). Demyelinated areas that become remyelinated are often unused after an MS attack and thus do not reestablish baseline function. Furthermore, demyelination
of newly remyelinated areas may result in scarring that prohibits further remyelination, creating a glial scar. The progressive accumulation of demyelination, axonal damage, and increasing disability provides a rationale for early implementation of therapeutic interventions (Herndon, 2000).

Following an acute MS attack, intact motor units may not function fully because of disuse, thus neural recruitment through activity may contribute to positive neural adaptations. Exercise training may facilitate positive neural adaptations and help regain strength that may have been lost because of physical inactivity. Although remyelination has been documented in MS, it will not be evaluated in this study. However, if resistance training contributes to remyelination or improves conduction and recruitment in remyelinated fibers, improvements in strength and function could be significant. Moreover, improving the function of unaffected skeletal muscle may also improve overall physical function and help attenuate disability. Furthermore, physical activity has an important benefit in reducing the risk of heart disease and improving insulin sensitivity.

**Balance**

As stated previously, maintaining balance is a major concern for persons with MS. Balance is the ability to maintain the body’s position over its base of support (Rogers et al., 2001). The study of human standing balance has provided insight into the basic mechanisms of neurological integration and into biomechanics in both health and disease (Kirby et al., 1987). For this reason, many different techniques have been proposed to quantify a person’s ability to maintain static or dynamic balance. In clinical settings, balance tests must be reliable and valid, use readily available equipment, and be easy to administer and master (Smithson et al., 1998). However, in a research laboratory,
postural sway analysis has been widely accepted as a reliable way to quantify the complex nature of a person’s standing balance in both healthy individuals and in special populations (Tillman & Chow, 2002).

The center of gravity (COG) of the body shifts continuously even during quiet standing. Postural sway is the corrective actions made by the body in an attempt to control body position and is measured by observing the vertical projection of the COG onto their base of support using force platform technology (Rogers et al., 2001). This vertical projection of the COG onto the force platform is commonly referred to as the center of pressure (COP). Increased sway as measured by the path length, speed of sway, and the amplitudes in the sagittal and coronal planes indicates greater effort to maintain upright position and therefore poorer balance (Rogers et al., 2003). Individuals who have sustained multiple falls demonstrate greater postural sway than age-matched peers (Era, 1985). Analysis of postural sway is a valid measure of standing balance control in many populations, but little research has been conducted using postural sway in persons with MS.

Postural control is dependent on complex, integrative processing from a variety of sensory and motor inputs (Teasdale et al., 1991) and it is therefore difficult to quantify the origin of poor balance. There is no single global clinical test that can reflect the complexity and multidimensional nature of balance (Horak, 1987). Instead, balance measurements should test a patient’s ability to maintain steady standing in a variety of different stance conditions and their ability to remain stable during and after self-generated perturbations (Frzovic et al., 2000). Sway velocity has been found to be higher when the feet are positioned close together resulting in a functionally small base of
support (i.e., semitandem, tandem, or unilateral stances), which indicates that in these conditions there is a higher likelihood of falling and subsequent injury (Rogers et al., 2001).

The effect of a strength-training program on balance has not been evaluated in MS patients. However, none of the training in this study is designed to be balance specific. The goal of this study was to evaluate the efficacy of a resistance training program on improving balance in persons with MS without specifically concentrating on balance training so as to provide a rehabilitative intervention available to all individuals with MS without the need for special balance training equipment.
CHAPTER 3
METHODOLOGY

This experiment investigated the effects of resistance training on balance control in persons with MS. Postural stability in a series of different stance positions and altered support surface and isometric strength was measured before and after an 8-week resistance-training program.

Subjects

Nine MS subjects (7 female and 2 male, mean ± SD, age: 43.3 ± 12.1 yrs; weight: 69.6 ± 10.3 kg; height: 1.69 ± 0.08 m; EDSS: 4.44 ± 1.67) and four non-MS controls (3 female and 1 male; age: 46.8 ± 11.4 yrs; weight: 82.0 ± 9.1 kg; height: 1.71 ± 0.07 m) were recruited from the local Gainesville population. The subjects were examined by a neurologist for disability status and cleared for participation prior to the outset of the experiment. For participation in this study, the subjects were required to meet the following criteria:

- Subjects must have been able to walk a distance of at least one city block (100m)
- Subjects could not have any coexisting orthopedic disorders, visual impairments (blindness, diplopia, blurred vision, severe nystagmus, etc.) or tremor that would adversely affect their ability to balance.

Each subject was asked to sign an informed consent agreement approved by the Institutional Review Board of the University of Florida prior to participation. The subjects were asked to fill out a Physical Activity Readiness Questionnaire (PAR-Q), a RISKO: Heart Health Appraisal, and a Health Risk Questionnaire to assure that they were healthy enough to participate in a resistance-training program.
Instrumentation

Force Platform

A Bertec® 4060-10 Force Platform System (Bertec Corporation, Columbus, OH), Peak Motus® 2000 Motion Analysis System (Peak Performance Technologies, Englewood, CO), and a Motion Analysis® Hawk Realtime system (Motion Analysis Corp., Santa Rosa, CA) were utilized to measure postural stability of each subject prior to and after an 8-week progressive resistance-training program. The force platform is capable of measuring forces and moments in the x, y, and z directions, which allows for the center of pressure to be tracked in the frontal and sagittal planes. The analog data were sampled at 40 Hz with the amplifier set at a gain of 5.

Isokinetic Dynamometer

A Kincom® isokinetic dynamometer (Model AP125, Chattecx Corp., Chattanooga, TN) was used to perform all isometric strength testing. Isokinetic dynamometers can be used to measure isometric force production at a preset joint angle for each exercise. The dynamometer sampled data at 100 Hz. Even though subjects trained isotonically, isometric testing was preferred because it has been found to be more reliable (Todd et al., 2004) and data are readily available in the literature for comparison purposes (Chetlin et al., 2004). Subjects were seated and restrained using shoulder and lap belts and the axis of the joint being studied was aligned with the axis of the dynamometer. Seat position and orientation on the dynamometer were stored in the computer database as well as on data sheets to ensure reproducibility of body position for all testing.

Experimental Setup

Subjects performed the tests of standing balance and muscular strength in the Biomechanics Laboratory in the Center for Exercise Science in the Florida Gym at the
University of Florida prior to and following an eight-week resistance-training program. They were advised to wear comfortable clothing and footwear, although the balance testing was performed with the subjects barefoot. Prior to data collection, the purpose of the study and procedures were explained to the subjects and all questions were answered. Sex, age, height, weight, and lower limb dominance (as ascertained by asking “Which foot would you kick a ball with?”) was recorded.

**Postural Sway**

For the tests of static balance, the subjects were asked to stand on a force platform for two trials lasting 20 seconds each in five different stance positions. The subjects were asked to stand quietly with their hands at their sides in a neutral position for each 20-second trial. All five conditions were administered in a randomized testing order and subjects were allowed to rest as much as needed between trials. The five different stance conditions were:

- **The self-selected (E) stance** – feet apart at a self selected distance (See Figure 1). Distance between the toes and heels were measured.
- **The feet apart (F) stance** – feet 15.2 cm (6 in.) apart (See Figure 2)
- **The foam pad (P) stance** – feet 15.2 cm (6 in.) apart on a foam balance pad; to simulate altered support (See Figure 3).
- **The semitandem (S) stance** – feet 15.2 cm (6 in.) apart and the heel of their dominant leg in line with the toe of their non-dominant leg (See Figure 4a and 4b)
- **The tandem (T) stance** – feet inline heel-to-toe and the dominant limb in front. (See Figure 5a and 5b)
Figure 1 – The self-selected (E) stance.

Figure 2 – The feet apart (F) stance.

Figure 3 – The foam pad (P) stance.
Figure 4 – The semitandem (S) seen from a A) frontal view and B) sagittal view.

Figure 5 – The tandem (T) stance seen from a A) frontal view and B) sagittal view.

**Strength Testing**

The subjects were tested for isometric strength prior to and following an 8-week study period. The muscle groups and corresponding joint angles are depicted in Table 1.

The subjects were asked to contract their muscles to attempt to produce maximal force.

<table>
<thead>
<tr>
<th>Muscle Group Tested</th>
<th>Exercise</th>
<th>Joint Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadriceps</td>
<td>Knee Extension</td>
<td>Knee Angle = 90</td>
</tr>
<tr>
<td>Hamstrings</td>
<td>Knee Flexion</td>
<td>Knee Angle = 90</td>
</tr>
<tr>
<td>Ankle Plantarflexors</td>
<td>Plantarflexion</td>
<td>Ankle Angle = 0 (neutral)</td>
</tr>
<tr>
<td>Ankle Dorsiflexors</td>
<td>Dorsiflexion</td>
<td>Ankle Angle = 0 (neutral)</td>
</tr>
</tbody>
</table>

*Table 1* – Muscle groups being tested, the movement they produce, and the corresponding joint angles.

To normalize the force measurement to leg length, the highest force (F) reading was multiplied by the moment arm (r) to determine the maximum torque (T) produced.

\[ T = F \times r \]
Functional Tests

Functional tests were also performed prior to and following the strength-training program. These tests included a 100 ft. walk test and a 3-min step test. For the walk test, subjects were asked to walk a distance of 100 ft as quickly and as safely as possible. The time taken to complete the walk was recorded. For the step test, subjects were asked to step up onto a platform 15.2 cm (6 in.) above the ground with both legs as many times as possible in a 3-min period and total number of steps were recorded. Subjects were allowed any assistance necessary to complete the step test.

Resistance Training

During the next eight weeks of the study period, MS and non-MS control subjects were asked to visit the Center for Exercise Science or Living Well Fitness and Wellness Center twice a week, either Monday/Thursday or Tuesday/Friday sessions to perform resistance training exercises. Exercises were performed under the supervision of staff trained in cardiopulmonary resuscitation, emergency procedures, and proper exercise safety for individuals with disabilities. A training protocol was established using recognized criteria for load assignment in older/disabled persons (ACSM, 2000).

During the first training session, subjects were asked to lift a submaximal load until they could no longer complete a full repetition for each exercise (2-20 repetitions). A predicted 1-repetition maximum (1-RM) was determined using the Kuramoto and Payne (1996) prediction equation for older women. During the second training session, subjects performed one set of 6-10 repetitions at 50% of the predicted 1-RM. In subsequent sessions, subjects completed one warm-up set and one training set for each exercise. Their warm-up consisted of five repetitions at 40% of the predicted 1-RM on each of the weight-machines. The training set consisted of 10-15 repetitions at 70% of predicted 1-RM.
RM for lower limb exercises (using one leg at a time leg) including knee flexion and extension, plantar flexion, trunk flexion and trunk extension; in that order every time. Exercises were performed at a self-selected, comfortable pace with at least one minute of rest between exercises. Each training session did not exceed 60 minutes. When subjects were able to complete 25 repetitions for any exercise in consecutive sessions, the resistance was increased by 2-5%. All training sessions were supervised.

**Data Reduction**

The COP was tracked for all trials and the average COP path length (PL) - the sum of the displacement vectors, average path speed (AS) - the PL divided by the total time, and the amplitudes in the medio-lateral (ML) - frontal plane, and antero-posterior (AP) - sagittal plane directions were calculated for each of the five conditions. A representative diagram of COP movement throughout a trial is depicted in Figure 6.

![Figure 6 - Diagram depicting the movement of the COP throughout a balance trial.](image)
Design/Analysis

This study was a pretest-posttest control group design. Descriptive statistics (means and standard deviations) were calculated for each of the four dependent variables (total sway path length, average sway speed, and sway amplitude in the AP and ML directions) in each of the five stance conditions. Due to the small sample size, nonparametric Wilcoxon signed ranks tests were performed to determine if any changes occurred in any balance and/or strength measures following eight weeks of strength training. Descriptive statistics were calculated for the functional tests, however no statistical tests were performed on the data. All statistical tests were conducted with the conventional level of significance, $\alpha=.05$. 
CHAPTER 4
RESULTS

All subjects completed the eight-week resistance-training program (16 sessions) with no MS-related exacerbations reported. The protocol was occasionally adjusted when subjects missed days between workouts for personal reasons, although adherence remained at 100%.

Strength

Eight of the nine MS subjects were tested for strength prior to and following the strength-training program. One subject was unable to produce muscular force from several lower extremity muscle groups at the time of the day the pre-testing took place, therefore he was excluded from the isometric strength analysis. The MS training group significantly increased strength in the knee flexors (p<0.05). Although not statistically significant, all other muscle groups also increased isometric strength (Table 2).

<table>
<thead>
<tr>
<th>Stance</th>
<th>Pre</th>
<th>Post</th>
<th>% Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee Extension</td>
<td>66.8 ± 29.5</td>
<td>81.6 ± 38.7</td>
<td>+ 22.17 %</td>
<td>0.069</td>
</tr>
<tr>
<td>Knee Flexion</td>
<td>34.9 ± 17.2</td>
<td>42.7 ± 14.4</td>
<td>+ 22.02 %</td>
<td>0.012*</td>
</tr>
<tr>
<td>Plantar Flexion</td>
<td>45.6 ± 28.9</td>
<td>68.2 ± 33.5</td>
<td>+ 49.54 %</td>
<td>0.069</td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>25.7 ± 10.8</td>
<td>28.2 ± 9.5</td>
<td>+ 9.89 %</td>
<td>0.484</td>
</tr>
</tbody>
</table>

Table 2 – Strength measures for the MS training group (mean ± SD). All strength (torque) measures in Nm. * denotes p<0.05.

<table>
<thead>
<tr>
<th>Stance</th>
<th>Pre</th>
<th>Post</th>
<th>% Change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee Extension</td>
<td>94.4 ± 24.5</td>
<td>112.5 ±30.3</td>
<td>+ 19.15 %</td>
<td>0.068</td>
</tr>
<tr>
<td>Knee Flexion</td>
<td>43.5 ± 9.8</td>
<td>50.7 ± 18.3</td>
<td>+ 16.54 %</td>
<td>0.144</td>
</tr>
<tr>
<td>Plantar Flexion</td>
<td>71.1 ± 24.7</td>
<td>92.5 ± 47.6</td>
<td>+ 30.13 %</td>
<td>0.144</td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>42.7 ± 9.7</td>
<td>45.1 ± 10.7</td>
<td>+ 5.45 %</td>
<td>0.144</td>
</tr>
</tbody>
</table>

Table 3 – Strength measures in the non –MS control training group (mean ± SD). All strength (torque) measures in Nm.
The non-MS control training subjects displayed increases in isometric muscle strength similar to those seen in the MS group, although again not statistically significant (Table 3).

**Balance**

Several of the MS subjects could not complete certain stances for the entire 20 seconds, primarily the more difficult stances, such as the T and P stances. However, subjects that did require assistance required a similar amount of assistance in the pre-test and post-test. In the MS subjects, a significant increase was noted in the path length and average speed for the E stance ($p=0.028$), however none of the other dependent variables for any of the other stances changed significantly (Table 4). Furthermore, the control subjects did not significantly change any of the dependent balance variables evaluated (Table 5).

<table>
<thead>
<tr>
<th>Stance</th>
<th>PL pre</th>
<th>PL post</th>
<th>p</th>
<th>AP pre</th>
<th>AP post</th>
<th>p</th>
<th>ML pre</th>
<th>ML post</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>0.780</td>
<td>1.068</td>
<td>0.028*</td>
<td>0.041</td>
<td>0.046</td>
<td>0.139</td>
<td>0.026</td>
<td>0.032</td>
<td>0.214</td>
</tr>
<tr>
<td>F</td>
<td>0.841</td>
<td>1.001</td>
<td>0.066</td>
<td>0.051</td>
<td>0.050</td>
<td>0.767</td>
<td>0.033</td>
<td>0.036</td>
<td>0.374</td>
</tr>
<tr>
<td>P</td>
<td>1.109</td>
<td>1.297</td>
<td>0.374</td>
<td>0.084</td>
<td>0.071</td>
<td>0.859</td>
<td>0.062</td>
<td>0.057</td>
<td>0.859</td>
</tr>
<tr>
<td>S</td>
<td>1.100</td>
<td>1.234</td>
<td>0.441</td>
<td>0.054</td>
<td>0.044</td>
<td>0.374</td>
<td>0.067</td>
<td>0.045</td>
<td>0.767</td>
</tr>
<tr>
<td>T</td>
<td>1.305</td>
<td>1.329</td>
<td>0.953</td>
<td>0.062</td>
<td>0.069</td>
<td>0.260</td>
<td>0.047</td>
<td>0.038</td>
<td>0.314</td>
</tr>
</tbody>
</table>

Table 4 – Mean balance measures for the MS training group. All balance measures in m. * denotes $p<0.05$.

<table>
<thead>
<tr>
<th>Stance</th>
<th>PL pre</th>
<th>PL post</th>
<th>p</th>
<th>AP pre</th>
<th>AP post</th>
<th>p</th>
<th>ML pre</th>
<th>ML post</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>0.395</td>
<td>0.681</td>
<td>0.068</td>
<td>0.018</td>
<td>0.019</td>
<td>0.715</td>
<td>0.009</td>
<td>0.008</td>
<td>0.715</td>
</tr>
<tr>
<td>F</td>
<td>0.416</td>
<td>0.663</td>
<td>0.144</td>
<td>0.020</td>
<td>0.016</td>
<td>0.144</td>
<td>0.009</td>
<td>0.012</td>
<td>1.000</td>
</tr>
<tr>
<td>P</td>
<td>0.608</td>
<td>0.813</td>
<td>0.144</td>
<td>0.046</td>
<td>0.042</td>
<td>0.144</td>
<td>0.030</td>
<td>0.025</td>
<td>0.273</td>
</tr>
<tr>
<td>S</td>
<td>0.545</td>
<td>0.766</td>
<td>0.144</td>
<td>0.028</td>
<td>0.022</td>
<td>0.144</td>
<td>0.029</td>
<td>0.025</td>
<td>0.144</td>
</tr>
<tr>
<td>T</td>
<td>0.829</td>
<td>0.911</td>
<td>0.465</td>
<td>0.044</td>
<td>0.025</td>
<td>0.144</td>
<td>0.038</td>
<td>0.034</td>
<td>0.715</td>
</tr>
</tbody>
</table>

Table 5 – Mean balance measures for the Control training group. All balance measures in m.
Functional Tests

Prior to strength training the MS group was able to complete the 100 ft walk in an average time of 33.9 s and following training that time decreased to 31.5 s. The control group was able to complete the walk in 14.3 s, which decreased to 13.8 s after training. The MS group completed 58.1 steps in the 3-min period prior to training, which increased to 68.2 following training. The control group began the training able to step an average of 111.6, which increased to 127.3 after training.
The aim of this study was to evaluate the effects of an eight-week progressive resistance-training program on postural sway in persons with MS. More specifically, the efficacy of a training program that is not balance specific in improving the balance of persons with MS was evaluated. Furthermore, little research is available concerning lower extremity muscle strength training in persons with MS, therefore the study was also designed to determine whether persons with MS could adhere to and endure a resistance training program. The results indicate that persons with MS can complete an eight-week resistance-training program, with no MS exacerbations, and increase lower extremity muscle strength. However, it remains unclear whether a strength training program, not designed to be balance specific, can positively influence balance in individuals with MS.

**Strength**

A statistically significant increase was noted in only one of the muscle groups tested in this experiment. Although not statistically significant, strength increased in all muscle groups for both the MS subjects and the controls. In fact, the plantar flexor isometric muscle strength increased 45% in the MS training group. Increases in muscle strength were expected from the training program, in that it was designed to increase lower extremity muscle strength. The lack of statistical significance may be due to the limited sample sizes in both the MS and control groups and high variability.

Debolt and McCubbin (2004) found that a home-based resistance-training program was well tolerated by persons with MS, and improved their lower extremity muscle
power. Furthermore, Kraft et al. (1996a & 1996b) resistance trained arms and legs in MS subjects for eight weeks and also found improvements in strength, along with improved function and psychosocial well-being. Most recently, White et al. (2004) found increased strength and function, along with a decrease in daily fatigue after eight weeks of lower extremity strength training. These studies, along with the findings of this research support the practicality of a strength-training program as a viable means to increase strength in individuals with MS.

Increased strength is desirable in this population because they are often faced with an increased level of fatigue, which decreases their daily activity levels, and eventually causes muscle atrophy. An increase in strength due to strength training may help to counteract the atrophic changes noted in the musculature of individuals with MS, and perhaps increase their daily activity levels. Furthermore, it is known that the first neuromuscular adaptations to strength training are more neural than muscular. Positive neural changes are especially important in a population afflicted with a neurological disorder. Neural recruitment gained through physical activity may have a favorable functional outcome, although this may be limited by the severity the MS lesions already present. This suggests that resistance training may be an early intervention strategy in persons with MS that may help to maintain function and hopefully, limits exacerbation of MS symptoms. In fact, in all research previously mentioned concerning strength training in individuals with MS, no MS related exacerbations were reported and there were no reports of increased MS-related symptoms (Kraft et al., 1996a & 1996b; Debolt and McCubbin, 2004; White et al. 2004).
Strength training is known to have many benefits, including, but not limited to, increasing bone mineral density (Asikainen et al., 2004). Since most individuals who suffer from MS are female, and females are at a higher risk of osteoporosis, strength training to increase bone mineral density may have profound effects on the quality of life of these individuals as they age. Furthermore, the performance of the subjects in the functional tests also lends itself to supporting strength training in this population. All subjects were able to walk faster and step more following training. This should be expected from a strength-training program designed to enhance muscle strength and endurance.

**Balance**

Decreased ability to maintain balance is a concern in individuals with MS, which may lead to an increased susceptibility to falls. For this reason, an intervention strategy to improve balance is desirable for individuals with MS. This study was intended to determine if static balance could be improved with a training program that is not balance specific. As stated earlier, the training protocol in this study was designed to increase lower extremity muscle strength. A significant increase was noted in the strength of knee flexors after strength training, and the knee extensors and plantar flexors also tended to be stronger after the strength training, however only two measures of postural sway were significantly different following training, and that change represented a decrease in postural stability. The results suggest that strength training has little effect on postural sway in persons with MS or control subjects.

The MS subjects who participated in this study represented a broad spectrum of disability levels, which is common for a condition like MS. Some subjects had little or no visible or obvious disability, while others required assistance to complete the tests of
standing balance. For those who did require assistance to complete the tests of standing balance, the amount of assistance required did not change for between the pre and post-tests. Furthermore, the data indicate that the strength training did not improve postural sway characteristics in these subjects. This could be due to a couple of different possible explanations: 1) the subjects were perhaps too disabled, more specifically, their loss of function was already too extensive, to have dramatic improvements in just eight weeks, or more likely 2) the training was not specific enough to the stances studied to cause positive alterations in postural sway. Even though strength did increase in these subjects, that increase did not result in improvements in static balance.

The finding that increased strength does not significantly influence balance is supported by the work of Katayama et al. (2004), who found that knee and toe muscle power does not appear to be a dominant factor in maintaining balance. This corroborates the assertion that lower extremity muscle strength training may not have a significant influence on postural sway. On the other hand, Judge and colleagues (1993) found that an exercise program emphasizing postural control, moderate resistance training and walking improved single leg static balance in neurologically intact elderly individuals, however double leg static balance measures did not improve. Two important conclusions can be dawn from this work: 1) a training intervention intended to improve balance should be focused on training for balance, and 2) double leg static stances may not be sufficiently challenging to unimpaired individuals to show significant changes after any training program. Although most subjects in this study were impaired in some way, some of the MS subjects had no obvious disability and may not have been challenged enough with the stances tested to change postural sway characteristics significantly. This
assertion is supported by the performance of the control group, who showed no significant changes in any of the balance measures tested.

Limitations

There are limitations in the experimental design that may account for the lack of significant changes in postural sway characteristics. As stated earlier, eight weeks may not have been a sufficient amount of time to significantly influence balance. Therefore, a more elongated and extensive strength-training program may have elicited more significant responses. Furthermore, a larger subject pool may help eliminate some of the variability, which could account for the lack of statistically significant differences. With such a small sample size, even a small amount of variability would eliminate statistical significance. The strength gains should be interpreted cautiously because the training was isotonic and the testing was isometric, so strength gains noted in this work may not be clinically applicable. Another possible origin of variability is the change in motion analysis systems used to collect the postural sway data midway through the study protocol. Unfortunately, several subjects were pre and post-tested on different motion analysis systems, therefore some inherent variability between the two systems may have changed the final data enough to account for the lack of statistical significance. Additional work with larger sample sizes, longer training protocol, more intense training, and more balance specific training is desirable and could lead to promising intervention strategies to improve balance and reduce the risk of falls in individuals with MS.

Summary and Conclusions

This study was designed to determine the efficacy of a progressive resistance-training program on postural sway in persons with MS. The training program was not intended to be balance specific. It was designed to focus on increasing general lower
extremity muscle strength. Only two out of 20 postural sway characteristics evaluated significantly changed following strength training in the MS group. Strength increased significantly in the knee flexors and tended to increase for the knee extensors and plantar flexors. It appears that the increased strength in the lower extremity may not influence static balance in individuals with MS. Additional research with larger sample sizes for both groups, and increased duration and/or intensity of training is recommended. A training program designed to focus specifically on balance would potentially demonstrate more significant changes in balance and could present a promising intervention strategy to improve balance and reduce the risk of falls in persons with MS, or any other neurological disorder.
Informed Consent to Participate in Research

You are being asked to take part in a research study. This form provides you with information about the study. The Principal Investigator (the person in charge of this research) or a representative of the Principal Investigator will also describe this study to you and answer all of your questions. Before you decide whether or not to take part, read the information below and ask questions about anything you do not understand. Your participation is entirely voluntary.

1. Name of Participant ("Study Subject")

_____________________________________________________________________

2. Title of Research Study

Resistance Training Effects on Muscle Function in Multiple Sclerosis

3. Principal Investigator and Telephone Number(s)

Lesley J. White, Ph.D., Assistant Professor
Department of Exercise and Sport Sciences
College of Health and Human Performance
University of Florida
(352) 392-9575 ext. 1338
Email: lwhite@hhp.ufl.edu
4. Source of Funding or Other Material Support

National Multiple Sclerosis Society

What is the purpose of this research study?

The primary purpose of this study is to determine whether a sixteen-week progressive resistance training exercise program influences measures of your muscle’s performance and your ability to walk and balance more effectively. This study is part of a project to learn more about your muscles ability to become more effective in producing energy during activities after you exercise train. We plan to measure your walking mechanics and your balance before and after you exercise train. We will also get pictures of your leg muscles using a technique called magnetic resonance imaging (MRI). Then we can get information about the chemistry of your muscle using a technique called magnetic resonance spectroscopy (MRS).

6. What will be done if you take part in this research study?

If you volunteer for this study you will be asked to participate in a 21 week experimental period that consists of evaluation of several functional measures such as muscle strength, balance, and walking mechanics, followed by a sixteen week exercise program. Midpoint evaluation will occur after 8 weeks of resistance training. Follow-up evaluation will occur after sixteen weeks of exercise training program. Listed below are descriptions of each visit should you choose to participate in this study.

Visit #1
On the first visit of week one of the study, you will be familiarized with the experimental protocol and be examined by a neurologist. Your disability status and physical readiness to participate in an exercise protocol will be assessed. If you are cleared to participate in this study, you will be asked to read and sign an informed consent, which will inform you of all the risks/benefits of participation in the experiment. The approximate time required for this visit will be 60 minutes.

Visit #2
On the second visit of week 1, you will have an MRI/MRS performed on your legs. During the MRI/MRS you will lie on a bed, which rolls in the opening of a large magnet. A flat coil of wire (a radiofrequency coil) will be placed on your thigh and calf. A computer will look at the radio waves passing through your leg and constructs pictures and chemical information of your muscles. The total procedure will last approximately 45 minutes. An MRI/MRS is used routinely to detect structures or gain chemical information about the muscles of healthy subjects or hospital patients. Just prior to and following the MRI, we will draw 20ml of blood (about 4 teaspoons) by venipuncture to test levels of blood sugar, triglycerides, and cholesterol. This will take an additional fifteen minutes. The total time of this visit, including MRI/MRS and blood sampling, will take approximately 60 minutes.

Visit #3

During the third visit in week 2 of the experimental period, you will have your body composition assessed using a three-site skinfold technique, and measurements of the waist and hip circumference will be taken. You will then be asked to perform muscular strength and endurance tests on a Kin-Com isokinetic dynamometer for the following exercises: abdominals, back, leg extensions, leg curls, and ankle flexion exercises. The Kin-Com is a muscle testing machine commonly used for evaluating muscle function in healthcare settings. During the testing, you will be asked to be seated on the machine and you will be asked to perform a muscle contraction at a constant, predetermined speed. The discomfort associated with this procedure is minimal, but will require you to put forth a strong effort. In conjunction with the muscle testing, two self-adhesive electrodes (2” x 4”) will be placed on your thigh close to your knee and hip. During your knee extension strength evaluation an electrical pulse will be delivered to your thigh muscle. The level of stimulation should not be painful, though it may cause a prickly sensation on your skin and will make your muscle feel like it is being squeezed. The feeling will be very similar to what you experience when you climb stairs or ride a bicycle for an extended period of time. The procedure is used to evaluate the ability of your muscle to generate force during the strength testing. The strength testing will be used to determine your 10-repetition maximum, which will be used in the training aspect of the study. Testing is expected to take 60 minutes.

Visit #4

During the fourth visit, in week 2 of the experimental period, you will be asked to perform tests of balance, and gait (walking mechanics). For the balance test, you will be asked to stand on a force plate without support for 20 seconds. You will be asked to repeat this test 3 times. Balance tests will be completed with your eyes open and closed. A test of your functional reach will be completed after a brief rest period following the balance test. During the functional reach test you will reach forward as far as you can until your heels come off the floor. A safety harness will be used to ensure your safety during functional tests. The harness may cause minor skin irritation. For the gait analysis you will be asked to walk on an 8-meter walkway twice. The gait testing will require you to have special sensors and reflective markers placed on your lower back and legs. The special sensors will measure your muscle activity during walking. Your skin preparation will include shaving areas displaying body hair with an electric razor that causes no skin
irritation. Your skin will then be sanitized with an alcohol swab. There is not any expected irritation or discomfort associated with the shaving or alcohol swabbing. Testing will also consist of a timed 25-foot walk test where you will be asked to walk as fast as possible within your comfort. Lastly, you will be asked to perform a three-minute step test where you will be asked to step up onto a platform as many times as possible in the allotted three minutes. During this visit we will ask you to wear shorts and exercise shoes. These tests will be conducted in the Biomechanics Laboratory in the Center for Exercise Science and will take will take approximately 60 minutes to complete.

Visits #5 and #6

During the fifth and sixth visits, in week 3 of the experimental period you will be asked to repeat all the testing performed in week 2. This is designed to more accurately quantify baseline measures. These visits will each take approximately 60 minutes to complete.

Visits #7 through #22

During the next eight weeks of the study period (weeks 4-11) you will be asked to visit the Center for Exercise Science or Living Well Fitness and Wellness Center, or North Florida Regional YMCA twice a week, either Monday/Thursday or Tuesday/Friday sessions to perform resistance training exercises. Twenty milliliters (4 teaspoons) of blood will be drawn before and after exercise to determine the effect of training on glucose, triglycerides, and cholesterol. Subjects will be required to attend strength training sessions requiring blood draws at the Center for Exercise Science. All training will occur in a supervised exercise environment with staff trained in cardiopulmonary resuscitation and emergency procedures. The staff will also be trained in proper exercise safety for individuals with disabilities.

During each exercise session you will be asked to perform one set of 15-20 repetitions at 70% of your 10-repetition maximum (RM) for each of the following exercises: leg extensions, leg curls, ankle plantarflexion, and an abdominal/lower back regimen using free-weight machines or a Kin-com isokinetic dynamometer. This is not a maximal exercise protocol and is not designed to be exhaustive. When you are able to complete 15 repetitions with proper technique, for two consecutive sessions, the resistance will be increased by 10% of your 10-RM. To assess your level of fatigue you will be asked to rate your level of effort (perceived exertion) at the end of each exercise. Because of the functional variability of MS individuals, the protocol may be adjusted on an individual basis to maintain your comfort and safety. A Certified Strength and Conditioning Specialist (CSCS) or exercise physiology research assistant will supervise all training sessions. Each training session will last 30-45 minutes.

You will be asked to perform a self-reported dietary recall at weeks 2, 4, 8, 12, and 16 of the experimental period when you come to the laboratory for exercise training. You will be asked to follow the dietary guideline established by the American Heart Association for the duration of the study to ensure that the appropriate amounts of nutrients are being consumed to meet the nutritional needs associated with a strength-training program. These guidelines are similar to those suggested for the MS population.
You will also be asked to complete a functional independence measure at weeks 1, 5, 7, 9, 11, 16, and 20. We will also randomly ask you to wear an accelerometer throughout one day during weeks 2, 12, and 20 to assess your level of activity. The accelerometer is a small device that will be worn around the waist to measure your activity throughout the day.

Visit #23 (Midpoint evaluation)

On the first visit of week 12 of the study period, following first phase of the exercise training period, you will be asked to perform all testing measures as performed at the beginning of the study. Again, you will be asked to perform self-reported questionnaires examining functional independence and fatigue impact. The completion of these questionnaires will take approximately 10 minutes. Following questionnaire completion, your body composition will be reassessed via the three-site skinfold technique, and measurements of the waist and hip will be taken. Twenty milliliters (about four teaspoons) of blood will be taken before and after exercise to determine if any changes in your resting levels of blood glucose, triglycerides, and cholesterol occurred. Again, these factors will be examined for experimental use and for your own personal information. This portion of the study will take 45 minutes. The total time for this visit will be approximately 90 minutes.

Visit #24

During the second visit of week 12 of the study period, you will be asked to perform tests of muscle strength and endurance on a Kin-com isokinetic dynamometer with electrical stimulation. This testing will follow the same procedure and include the same exercises as was performed in weeks 2 and 3 of the study. Testing will take approximately 60 minutes.

Visit #25

During the first, and only, visit of week 13 of the study, you will be asked to perform follow-up tests of balance, and gait. Testing will also consist of a timed 25-foot walk and the three-minute step test. These tests will again be conducted in the Center for Exercise Science Biomechanics Laboratory and will take approximately 60 minutes to complete.

Visit #26-42

During the next eight weeks of the study period (weeks 13-21) you will be asked to continue twice weekly exercise training sessions until you have completed 16 consecutive weeks of training. Twenty milliliters (4 teaspoons) of blood will be drawn before and after exercise at week 20 to determine the effect of training on glucose, triglycerides, and cholesterol. Any special needs that you require will be accommodated throughout the duration of the study. All data collected in the post-testing phase will be compared to the information gathered in the pre-testing to determine if any improvements were made in any of the factors that were studied in this experiment.

7. What are the possible discomforts and risks?
The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure. The risk from having a catheter inserted into an arm vein for time needed in this study is possible infection of the vein, but the risk is very low because we will have a trained phlebotomist collecting the blood samples. The amount of blood we will take should have no negative effects. You will be closely watched for any possible ill effects.

There is also a risk of mild muscle soreness associated with the initiation of any strength-training program, however this risk is minimal. Potential soreness may last for three days but is not expected to limit any activities. There is also a slight risk of skin irritation associated with electrode and reflective marker placement for the electromyographic analysis. Balance and gait testing with the safety harness may cause some mild skin irritation. There is also a risk of skin irritation associated with the electrical pulses to your thigh, however, the equipment used is highly reliable with safety features to minimize pulse strength. The short duration pulses may contribute to mild muscle soreness, however the risk is minimal.

The risks of MRI/MRS are: the MRI/MRS scanner contains a very strong magnet. Therefore, you may not be able to have the MRI/MRS if you have any type of metal implanted in your body, for example, any pacing device (such as a heart pacer), any metal in your eyes, or certain types of heart valves or brain aneurysm clips. Someone will ask you questions about this before you have the MRI/MRS. There is not much room inside the MRI/MRS scanner. You may be uncomfortable if you do not like to be in close spaces ("claustrophobia"). During this procedure, you will be able to talk with the MRI/MRS staff through a speaker system, and in the event of an emergency, you can tell them to stop the scan.

The MRI/MRS scanner produces a loud hammering noise, which has produced hearing loss in a very small number of patients. You will be given earplugs to reduce this risk.

If you are a woman of childbearing potential, there may be unknown risks to the fetus. Therefore, before you can have the MRI/MRS, you must have a pregnancy test. This test will be done at no charge.

8a. What are the possible benefits to you?

It is possible that you may experience improvements in gait, balance, muscular strength, and endurance. You will also receive eight weeks of personal exercise training. Blood cholesterol, nutritional profile and analysis, will be provided for your own personal records.

8b. What are the possible benefits to others?
Research findings from this study may help in the design and use of therapeutic exercises designed to help other individuals with MS.

9. **If you choose to take part in this research study, will it cost you anything?**

   All costs associated with the assessment of your percent body fat, gait analysis, and quality of your diet will be paid for by the Center for Exercise and Sport Sciences. Additional measurements of blood cholesterol, glucose, and insulin levels will be absorbed by funding supporting the principal investigators of the study. The principal investigator will also pay for the MRI/MRS and any required pregnancy test.

10. **Will you receive compensation for taking part in this research study?**

   At the completion of the study, subjects with multiple sclerosis will receive $200.00. Subjects who do not have multiple sclerosis will not receive monetary compensation for study participation.

11. **What if you are injured because of the study?**

   If you experience any injury that is directly caused by this study, only professional consultative care that you receive at the University of Florida Health Science Center will be provided without charge. However, hospital expenses will have to be paid by you or your insurance provider. No other compensation will be offered.

12. **What other options or treatments are available if you do not want to be in this study?**

   The exercise training and dietary counseling are in addition to standard therapy for your condition. You may choose to continue with your current therapy.

13a. **Can you withdraw from this research study?**

   You are free to withdraw your consent and to stop participating in this research study at any time. If you do withdraw your consent, there will be no penalty, and you will not lose any benefits you are entitled to.

   If you decide to withdraw your consent to participate in this research study for any reason, you should contact Dr. Lesley White at (352) 392-9575 ext 1338.

   If you have any questions regarding your rights as a research subject, you may phone the Institutional Review Board (IRB) office at (352) 846-1494.
13b. If you withdraw, can information about you still be used and/or collected?

If you withdraw from the study, information about you will not be used or collected any further.

13c. Can the Principal Investigator withdraw you from this research study?

You may be withdrawn from the study without your consent for the following reasons: failure to make scheduled training visits and cardiovascular risk factors contraindicating your participation in a strength training program.

14. How will your privacy and the confidentiality of your research records be protected?

Authorized persons from the University of Florida, the hospital or clinic (if any) involved in this research, and the Institutional Review Board have the legal right to review your research records and will protect the confidentiality of them to the extent permitted by law. Otherwise, your research records will not be released without your consent unless required by law or a court order. If the results of this research are published or presented at scientific meetings, your identity will not be disclosed.

15. How will the researcher(s) benefit from your being in this study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigators may benefit if the results of this study are presented at scientific meetings or in scientific journals.
16. Signatures

As a representative of this study, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study, the alternatives to being in the study, and how privacy will be protected:

___________________________________________ _____________________
Signature of Person Obtaining Consent                   Date

You have been informed about this study’s purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your privacy will be protected. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

You voluntarily agree to participate in this study. By signing this form, you are not waiving any of your legal rights.

____________________________________________ _____________________
Signature of Person Consenting             Date
Consent to be Videotaped and to Different Uses of the Videotape(s)

With your permission, you will be videotaped during this research. Your name or personal information will not be recorded on the videotape, and confidentiality will be strictly maintained. When these videotapes are shown, however, others may be able to recognize you.

The Co-Principal Investigator of this study, John Chow, Ph.D., will keep the videotape(s) in a locked cabinet. These videotapes will be shown under his direction to students, researchers, doctors, or other professionals and persons.

Please sign one of the following statements that indicates under what conditions Dr. John Chow, Ph.D has your permission to use the videotape.

I give my permission to be videotaped solely for this research project under the conditions described.

________________________________________ Signature ____________________________ Date

I give my permission to be videotaped for this research project, as described in the Informed Consent Form, and for the purposes of education at the University of Florida Health Science Center

________________________________________ Signature ____________________________ Date

I give my permission to be videotaped for this research project, as described in the Informed Consent Form; for the purposes of education at the University of Florida Health Science Center; and for presentations at scientific meetings outside the University.

________________________________________ Signature ____________________________ Date
The EDSS quantifies disability in eight Functional Systems (FS) and allows neurologists to assign a Functional System Score (FSS) in each of these systems:

- pyramidal
- cerebellar
- brainstem
- sensory
- bowel and bladder
- visual
- cerebral
- other

EDSS steps 1.0 to 4.5 refer to people with MS who are fully ambulatory, while steps 5.0 to 9.5 are defined by the impairment to ambulation.

<table>
<thead>
<tr>
<th>Kurtzke Expanded Disability Status Scale</th>
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<tbody>
<tr>
<td>0.0</td>
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<tr>
<td>1.0</td>
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<td>5.0</td>
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43
<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
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<tbody>
<tr>
<td>4.5</td>
<td>Impair full daily activities (work a full day without special provisions)</td>
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<tr>
<td>5.5</td>
<td>Ambulatory without aid or rest for about 100 meters; disability severe enough to preclude full daily activities</td>
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<tr>
<td>6.0</td>
<td>Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk about 100 meters with or without resting</td>
</tr>
<tr>
<td>6.5</td>
<td>Constant bilateral assistance (canes, crutches, braces) required to walk about 20 meters without resting</td>
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<tr>
<td>7.0</td>
<td>Unable to walk beyond approximately five meters even with aid, essentially restricted to wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day</td>
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<tr>
<td>7.5</td>
<td>Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self but cannot carry on in standard wheelchair a full day; May require motorized wheelchair</td>
</tr>
<tr>
<td>8.0</td>
<td>Essentially restricted to bed or chair or perambulated in wheelchair, but may be out of bed itself much of the day; retains many self-care functions; generally has effective use of arms</td>
</tr>
<tr>
<td>8.5</td>
<td>Essentially restricted to bed much of day; has some effective use of arms retains some self care functions</td>
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<tr>
<td>9.0</td>
<td>Confined to bed; can still communicate and eat.</td>
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<tr>
<td>9.5</td>
<td>Totally helpless bed patient; unable to communicate effectively or eat/swallow</td>
</tr>
<tr>
<td>10.0</td>
<td>Death due to MS</td>
</tr>
</tbody>
</table>
LIST OF REFERENCES


Rogers ME, Rogers NL, Takeshima N, Islam MM. Methods to Assess and Improve the Physical Parameters Associated with Fall Risk in Older Adults. *Preventive Medicine*. 2003, 36: 255-64.


BIOGRAPHICAL SKETCH

Gregory M. Gutierrez has an innate drive that has allowed him to succeed in many aspects of his life. His competitive nature has helped him succeed on the field of play, and in the classroom. He received his bachelor’s degree in exercise and sports sciences in December of 2002 from the University of Florida. He immediately began his master’s degree in biomechanics in the same department. Under exceptional guidance, he has matured in many ways and is ready to pursue a Ph.D. in biomechanics. Gregory’s long-term goal is to one day become an orthopedic surgeon, while still contributing to research as a biomechanist.