The Effect of a Single Bout of Physical Exertion on Expressive Language and Word Finding in Individuals with Multiple Sclerosis

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THE EFFECT OF A SINGLE BOUT OF PHYSICAL EXERTION ON EXPRESSIVE LANGUAGE AND WORD FINDING IN INDIVIDUALS WITH MULTIPLE SCLEROSIS

by

Marissa A. Barrera

A dissertation submitted to the Graduate Faculty in Speech-Language-Hearing Sciences in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

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by

Marissa A. Barrera

This manuscript has been read and accepted for the Graduate Faculty in Speech-Language-Hearing Sciences to satisfy the dissertation requirement for the degree of Doctor of Philosophy.

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ABSTRACT
The Effect of a Single Bout of Physical Exertion on Expressive Language and Word Finding in Individuals with Multiple Sclerosis
by
Marissa A. Barrera

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To date, little research has been conducted on the relationship between fatigue and expressive language among Multiple Sclerosis patients (MS). This study was a response to this knowledge gap. A nonrandom, matched-subject, mixed-factor design model was used with a purposive sample of 17 individuals with MS (five had primary-progressive (PP) MS, and 12 had relapsing-remitting (RR) MS). The research design was subjected to pretesting to ensure validity. Participants were assessed on a range of language tasks after undergoing one bout of cardiovascular exercise (NuStep T5 Recumbent Cross Trainer) and asked to provide a subjective fatigue score. The expressive language tests included confrontation naming, assessment of expressive-language skills, verbal fluency, and assessment of a picture description. The tasks were replicated after a fatigue-equivalent rest period. Statistical analyses involved the testing of assumptions for one-way MANOVA/MANCOVA. Gender and subtypes of MS were subject to chi distribution.

Analysis of the intervention and control groups for differences in gender, ethnicity and years of education revealed no significant difference. The mean number of years with a MS diagnosis was 12.82 with a median EDSS score of 5.50. The Intervention Fatigue Group had a significantly higher confrontation naming errors score in comparison to the Control Fatigue Group, the Control Rest Group and the Intervention Rest Group. Analysis of verbal fluency revealed that the Intervention Fatigue Group generated significantly fewer words when given a
letter of the alphabet or asked to generate words within an abstract category compared to the Control Fatigue Group, the Control Rest Group and the Intervention Rest Group. Analysis of narrative production skills revealed the Intervention Fatigue Group and the Intervention Rest Group illustrated a similar reduced performance compared to the Control Fatigue Group and Control Rest Group. For tasks concerning confrontation naming, the Intervention Fatigue Group took significantly longer time to verbally name colors and objects compared to the Control Fatigue Group and the Control Rest Group; however, the Intervention Fatigue Group was not statistically different from the Rest Group. The Intervention Fatigue Group had a significantly higher fatigue change score in comparison to the Intervention Rest Group and the Control Rest Group. However, the Intervention Fatigue Group did not significantly differ from the Control Fatigue Group.

Overall, the results indicate that when working with language skills in persons with MS, clinicians should account for the presence of fatigue on performance measures and consider testing skills in conditions.
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CHAPTER 1:
INTRODUCTION

Multiple sclerosis (MS) is one of the most common chronic neurological diseases, yet its cause is unknown and its course unpredictable. MS is a progressive disorder of the central nervous system that results in demyelination of nerve fibers and axonal injury (Bjartmar & Trapp, 2001). MS affects the white matter of the central nervous system and is characterized by progressive neurological deficits with a relapsing/remitting disease course (Sliwa & Cohen, 1998). The development of scattered lesions, plaques, or both, within the brain produces varying combinations of motor, sensory, and cognitive-communication impairment (Yorkson, Klasner & Swanson, 2001).

Many researchers have investigated motor and sensory disorders in MS. However, cognitive-communication deficits associated with MS have received little attention, despite an estimate that between 45% and 65% of individuals with MS experience problems with memory, attention, distractibility, problem solving, word finding, and other cognitive functions as symptoms of the disease (Rao, Leo, Bernardin, & Unverzagt, 1991). Verbal fluency, in particular, word finding in individuals with MS, has not been studied, leaving knowledge gaps in the scientific literature. The cognitive resource allocation model developed by Kahneman (1973) served as a theoretical framework to investigate the idea that humans have a fixed cognitive resource capacity requiring conscious allocation of attention to competing stimuli.

When a person is presented with simultaneous cognitive tasks, the theory indicates one of the tasks will likely be performed suboptimally (Kahneman, 1973, Tversky & Kahneman, 1992). The cognitive resource allocation theoretical framework, examined in conjunction with reduced verbal fluency skills, forms the basis for the study’s hypotheses concerning the effects of fatigue and disease severity on word finding skills in individuals with MS. Before presenting a
discussion of the effects of MS and fatigue on cognitive-communication and word-finding skills, a clear understanding of the disease is essential.

The exact cause of MS is unknown, but researchers believe it is most likely an autoimmune disease (Kalb, 2004). Four experimental models of autoimmune demyelination have been developed to explain MS; however, each of these theories contains only a piece of the larger MS puzzle. Although to date no single theory can account for the complete etiology of MS, researchers have agreed that MS is likely the result of a complicated interaction of four factors: the immune system, the environment, infectious diseases, and genetics (Murray, 2005).

Prevalence

In the United States, an estimated 400,000 people live with MS, and 10,000 cases are diagnosed each year (NMSS, n.d.). Although more people have a diagnosis of MS today than in the past, the explanation for this is not clear. Likely contributors include greater awareness of the disease, increased access to medical care, and improved diagnostic capabilities (NMSS, n.d). Most individuals diagnosed with MS are between 20 and 50 years old, although it can occur in young children and in older adults (NMSS, n.d).

MS is approximately 2 to 3 times more common in women than in men, indicating that hormones may play a role in determining susceptibility to MS (Cook, 2006). In addition, genetic factors are thought to play a significant role in who develops MS; however, additional factors such as geography, ethnicity, and infectious agents are also likely to be involved (Ebers, Sadovnick, & Risch, 1995).

Diagnosis

For decades, scientists have been searching for an infectious agent responsible for triggering MS. Many different viruses have been investigated (including rabies, herpes simplex
virus, measles, corona virus, canine distemper virus, HTLV-1, and Epstein-Barr virus), but none has been confirmed (Murray, 2005). Although the trigger for MS has not yet been identified, most MS experts believe some infectious agent is involved in initiating the disease process (Cook, 2006).

MS is difficult to diagnose on the basis of symptoms alone because symptomatology varies considerably from person to person (DeJong, 1970; Kalb, 2004). Some common reasons for misdiagnosis can be attributed to (a) a large number of symptoms, (b) symptoms that appear singly or in combination, (c) symptoms that vary in severity, (d) symptoms that appear and disappear suddenly, and (e) symptoms of MS that are common to other neurological diseases (e.g., Parkinson’s disease, amyotrophic lateral sclerosis, Alzheimer’s disease, Creutzfeldt-Jakob disease, Huntington’s disease, and cerebral vascular accident; Cook, 2006; Rao, 1986).

**Types of MS**

There are four subtypes of MS: relapsing-remitting (RR), secondary-progressive (SP), primary-progressive (PP), and progressive-relapsing (PR; Murray, 2005). Relapsing-remitting MS occurs in the majority of cases (about 85%). Additionally, over 50 symptoms are associated with MS and can vary in severity and duration (Murray, 2005; National MS Society, n.d.). The most notable symptoms associated with MS include extreme fatigue, depression, bladder dysfunction, numbness and/or tingling of the extremities, sexual dysfunction, bowel dysfunction, pain, vertigo, spasticity, tremor, vision impairment, cognitive dysfunction, dysarthria, and dysphagia (Cook, 2006; Lumsden, 1970; Murray, 2005).

Many of the symptoms associated with MS can be treated through drug therapy and a multidisciplinary approach to medical management, including intervention by neurologists, psychologists, urologists, ophthalmologists, movement disorder specialists, neuropsychologists,
physical therapists, occupational therapists, and speech-language pathologists (National MS Society, n.d.).

**Disease Severity**

The Kurtzke Expanded Disability Status Scale (EDSS) is a method of quantifying disability in multiple sclerosis regardless of the disease subtype (Kurtzke, 1983). The EDSS is one of the most widely used rating systems used by physicians and MS specialists for judging the clinical status of people with MS (Kurtzke, 1983). The test quantifies disability in eight functional systems (pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral, and communication skills) and allows neurologists to assign an overall functional system score (FSS; Kurtzke, 1983). The EDSS is an ordinal clinical rating scale ranging from 0 (normal neurologic examination) to 10 (death attributable to MS) in half-point increments (Kurtzke, 1983). For example, FSS scores ranging from 1.0 to 4.5 generally refer to people with MS who are fully ambulatory, and FSS scores ranging from 5.0 to 9.5 indicate impairment to ambulation (Kurtzke, 1983).

**Fatigue and MS**

Fatigue is a common symptom of multiple sclerosis (Claros-Salinas et al., 2013; Schwid, Covington, Segal, & Goodman, 2002) and one of the main causes of impaired quality of life amongst MS patients (Bakshi et al., 2000). Fatigue has been reported by at least 75% of MS patients at some point in the disease course (Bailey et al., 2013).

For many MS sufferers, fatigue is the single most debilitating symptom, surpassing pain and even physical disability (Parmentier, Denney, & Lynch, 2003; Penner et al., 2007). Fatigue also imposes significant socioeconomic consequences, including loss of work hours, and in some

Nonetheless, fatigue in MS remains poorly understood and is often underemphasized for several reasons (Schwid et al., 2002). First, fatigue is a subjective symptom (Matotek, Saling, Gates, & Sedal, 2001) without a unified definition (Claros-Salinas et al., 2013), and the underlying mechanisms remain unknown (Schwid et al., 2002). Common descriptions include a sense of exhaustion, lack of energy, tiredness, or a subjective lack of physical and/or mental energy perceived by the individual or caregiver as interfering with or limiting normal or desired activities (Fisk, Pontefract, Ritvo, Archibald, & Murray, 1994; National MS Society, n.d.). In addition, the terms used to describe fatigue and the expectations of disablement through fatigue may be interpreted differently according to the individual’s cultural or educational background, thereby heightening subjectivity (Bailey et al., 2007). Ambiguity also arises because there is no “gold standard” by which to measure fatigue (Penner & Calabrese, 2010). Using multiple questionnaires does not overcome these definitional issues. Therefore, quantifying a multifactorial symptom is challenging when objectivity is elusive (Holtzer & Foley, 2009).

The most commonly proposed primary mechanisms of fatigue in MS involve the immune system and central nervous system damage (Penner et al., 2007). Specific causes are thought to include proinflammatory cytokines, endocrine influences, axonal loss, and altered patterns of cerebral activation. Secondary fatigue in MS is associated with medical conditions and/or the accumulation of the disease burden. Specific causes can include sleep disorders, depression, and disability status (Penner et al., 2007). Tasks such as dressing, brushing teeth, bathing, or preparing meals can require considerable effort for MS patients, thus making simple daily tasks fatiguing (Fisk, Pontefract, Ritvo, Archibald, & Murray, et al. 1994).
In addition to these sources of fatigue, another type of fatigue associated with persons with MS is lassitude. Also known as MS fatigue, lassitude is different from the fatigue experienced by persons without MS. Lassitude is thought to result from poor nerve conduction caused by damage to the myelin around the nerve fibers in the central nervous system (CNS). Because of the demyelination, the body must work harder to transmit messages between the brain and other parts of the body (Schwid et al., 2002). Unlike normal fatigue, MS lassitude tends to come on suddenly, can occur at any time of day as well as immediately following a restful night’s sleep, generally increases as the day progresses, worsens temporarily in the presence of heat and humidity, and can interfere with the everyday activities of daily living in both ambulatory and sedentary tasks (Schwid et al., 2002).

**Cognitive Decline in MS**

Cognitive difficulties can be particularly distressing for individuals with neurological disorders because the difficulties are often not obvious to friends and family (Beatty, Goodkin, Monson, & Beatty, 1989) or even to themselves. Frequently, individuals with MS do not recognize that their difficulties with cognition are MS-related (Rao et al., 1991). Individuals with MS typically experience deficits in attention and concentration, processing speed, memory and problem solving (Cook, 2006; Jennekens-Schinkel et al., 1990; Murray, 2005; Rao, 1986). For a typology compilation, see Table 1 in the Tables section of this dissertation.

Cognitive deficits vary greatly, depend upon the location and number of brain lesions, and correlate with increasing lesion load on MRI. However, little relationship exists between the severity of physical symptoms and the severity of cognitive problems (Rao, 1985; Rao et al., 1985; Sliwa & Cohen, 1998). Analysis of multiple studies dating back to 1983 indicates that
neurocognitive impairments were evident in several areas, including verbal fluency, information processing speed, memory, and cognitive flexibility (Zakzanis, 2000).

Estimates of the proportion of individuals with MS experiencing cognitive difficulties vary depending upon how the estimates are generated. Self-reports of a large group of individuals with MS indicated that 38% reported significant cognitive problems (Sullivan, Edgley, & Dehoux, 1990). When neuropsychological testing was used to estimate the occurrence of cognitive changes, prevalence rates increased from 50% to 70% (Heaton, Nelson, Thompson, Burks, & Franklin, 1985; Rao et al., 1991). With a few notable exceptions (Foley et al., 1994; Friend et al., 1999; Wallace & Holmes, 1993), the impact of cognitive deficits on communication has not been studied.

**Communication Disorders in MS**

Though less commonly studied, a variety of communication disorders have been identified in individuals with MS, including dysarthria, aphasia, and cognitive impairment affecting communication (Achiron et al., 1992; Kujala, Portin, & Ruutiainen, 1996; Lethlean & Murdoch, 1993; Olmos-Lau, Ginsberg, & Geller, 1977; Wallace & Holmes, 1993). Self-report questionnaires concerning communication difficulties associated with MS have indicated that approximately 45% of respondents experienced changes in speech and/or communication, and 33% of MS patients reported impairments of voice, chewing, and swallowing capabilities (Beukelman, Kraft, & Freal, 1985; Hartelius & Svensson, 1994). Despite these overwhelming figures, only a small number of MS patients (2%) are appropriately referred for treatment of speech, language, voice, and swallowing disorders (Hartelius & Svensson, 1994).

Cross-sectional investigations have provided limited evidence of language dysfunction in patients with MS compared to healthy controls (Lethlean & Murdoch, 1993). Much of the
information in the research literature on communication impairments has focused on limitation in activities. For example, in a study of language impairments in MS, impaired naming, reduced word fluency, and poor sentence construction decreased independence and interfered with the activities of daily living (Lethlean & Murdoch, 1993, Blaney & Lowe-Strong, 2009).

Additionally, reductions in expressive language by patients with MS have also been reported (Beukelman et al., 1985). Specifically, compared to controls, patients with MS produce fewer utterances per minute, use fewer grammatically correct utterances per minute, and use shorter utterances (Lethlean & Murdoch, 1993). These symptoms contribute to depression and isolation from the community (Beukelman et al., 1985; Wallace & Holmes, 1993). Clearly, many unknowns remain, including information about the prevalence of various communication disorders and the progression of these disorders over the course of the disease.

Aphasia occurs infrequently as a clinical manifestation of MS because MS primarily affects the white matter of the brain and the spinal cord (Achiron et al., 1992; Cook, 2005; Friedman, Brem, & Mayeux, 1983). Because aphasia is usually associated with diseases of the gray matter of the brain, it is not an expected presentation of MS (Achiron et al., 1992; Friedman, Brem & Mayeux, 1983; Cook, 2005). Aphasic disorders may be observed in two different situations in MS. The first includes aphasic disorders attributable to cognitive impairment after a long disease course. The second is acute aphasia following an exacerbation. Estimates of the frequency of acute aphasia based on a meta-review of several studies ranged from 0.7% to 3% (Olmos-Lau et al., 1977). To date, only 38 case reports have been published in the literature (Arnett et al., 1996; Damasio & Damasio, 1980; Friedman, Brem & Mayeux, 1983; Olmos-Lau et al., 1977; Trinka et al., 2001; Wallace & Holmes, 1993).
Among these 38 cases, 12 experienced acute aphasia as the first clinical manifestation of the disease, eight presented aphasic status epilepticus documented by EEG, and 18 had MRI findings of giant plaques in the left hemisphere. As a result, 41% of documented cases presented with Broca’s aphasia, 22% with mixed transcortical aphasia, 18% with conduction aphasia, 15% with transcortical motor aphasia, and 4% with global aphasia (Arnett et al., 1996; Damasio & Damasio, 1980; Friedman, Brem & Mayeux, 1983; Olmos-Lau et al., 1977; Trinka et al., 2001; Wallace & Holmes, 1993).

Although bona fide aphasia, defined by the American Speech-Language-Hearing Association (ASHA) as a difficulty in speaking, listening, reading, and writing (ASHA, n.d.) is typically not considered a clinical manifestation of MS, in a multicenter study investigating the prevalence of aphasia in MS, researchers found nearly 1% of patients presented with aphasia, and nearly 40% demonstrated markedly reduced word-finding skills (Lacour et al., 2004). These findings indicate aphasia is not as rare in MS as previously thought. One possible explanation for the presence of aphasia in the MS population is an increased understanding that damage occurring in white matter connected to the cortical language centers results in a breakdown of language (Cook, 2006).

MS patients have repeatedly complained about word-finding difficulties (Friend et al., 1999). Deficits in the recall of object labels (confrontation naming), people, and events, as well as deficits in semantic fluency, have been reported in selected studies but are not well-defined or documented (Beatty, 2002). In fact, to date, only three studies exist that have focused on word-finding skills in individuals with MS (Beatty et al., 1988; Friend et al., 1999; Pozzilli et al., 1991). Both Beatty et al. (1988) and Friend et al. (1999) documented the naming of deficits in patients with progressive-relapsing and relapsing-remitting MS as a part of a larger
neuropsychological study. However, neither of these studies showed the prevalence of word-finding difficulties or classified error types (e.g., semantic paraphasias, phonemic paraphasias).

Additionally, in a study investigating 25 individuals with progressive-relapsing and relapsing-remitting MS, naming impairments measured by the Visual Naming Test (Benton & Hamsher, 1978) were more often observed in progressive-relapsing patients than in relapsing-remitting patients, indicating that the disease course may play a role in deterioration of language function (Pozzilli et al., 1991).

**Verbal Fluency**

Tests of verbal fluency in individuals with MS are consistently sensitive to impairment relative to other language measures. *Verbal fluency* refers to how quickly an individual can name items within a given category (Beatty, 2002). For example, to test verbal fluency, a researcher might ask, “How many animals can you name in 30 seconds?” Some researchers have reported comparable deficits on measures of phonemic fluency (words that start with the same phoneme) and semantic fluency (Beatty, 2002; Parry, Scott, Palace, Smith, & Matthews, 2003). Other researchers have found MS affected phonemic fluency (Nocentini et al., 2001). Foong et al. (1997) reported that semantic fluency showed the greatest impairment in patients with MS.

An analysis of the literature examining MS and verbal fluency revealed conflicting information. Some discrepancies in previous findings may be explained by several factors:

1. Failing to distinguish study groups by either MS disease course or disease severity
2. Using abbreviated tests (short forms) for assessing language functions, rather than the complete version
3. Using diversity and inconsistency of measures to assess language functions
4. Using language processes sensitive to disruption by impairments in other cognitive domains

**Effects of Fatigue on Language Function in Persons with MS**

Multiple sclerosis affects executive function, semantic memory, and verbal fluency (Friend et al., 1999; McKenzie & Green, 2009). This disparity includes a reduction in speed of information processing (Huijbregts et al., 2004), leading to reduced semantic retrieval and a reduction in expressive language (Beatty, 2002). Further identified impacts on language function have included impaired naming, verbal expression, and verbal fluency (Friend et al., 1999). Tests of verbal fluency are particularly sensitive to cognitive impairment resulting from MS (Beatty, 2002; Henry & Beatty, 2006).

Until recently, the impact of MS fatigue upon language function has been less fully documented than has the impact of MS fatigue on cognition (Lethlean & Murdoch, 1993). Research on the language abilities of people with MS has tended to focus on the motor aspects of speech production rather than on the cognitive aspects of semantic recall and verbal fluency (Lethlean & Murdoch, 1993). Although implicit fatigue is well recognized as the expected outcome of physical exertion, the impact of fatigue on verbal fluency has been notably under-researched (Henry & Beatty, 2006). The current study was intended to help close the gap in the literature regarding the effect of fatigue on expressive-language function in patients with MS.

The purpose of this study was to measure the effect of a single bout of fatigue activity in MS patients on expressive-language function. Little research exists regarding this effect; however, seminal studies on fatigue in relation to other aspects, such as gait and balance (Karaptkin et al., 2013), have provided some indication that fatigue may reduce cognitive function (Holtzer & Foley, 2009) and thus provided a justification for conducting this research.
Karpatkin et al. (2013) found that intermittent walking, with rest intervals between, was less fatiguing for patients with MS than was continuous walking, indicating the effects of fatigue can be mitigated by paying attention to the context and duration of the exercise regime, in this case, walking. In addition, Krupp and Elkins (2000) tested 45 MS patients (14 controls) to determine whether verbal memory and conceptual planning were enhanced or diminished by cognitive activities. The scores for the controls increased, but the MS participant scores declined, indicating that in people with MS, cognitive tasks triggered fatigue and led to a decline in cognitive abilities and verbal fluency (Krupp & Elkins, 2000).

Holtzer and Foley (2009) used an equal (20 participants per group) sample to examine the hypothesis that subjectively identified fatigue correlated with impaired executive control. Holtzer and Foley used the Delayed Item Recognition (DIR) paradigm to substantiate their findings. The task consisted of three modules all requiring executive control, and fatigue was assessed using the Fatigue Severity Scale (FSS; Holtzer & Foley, 2009). The study showed that fatigue and executive control, necessary in the manipulation of language, are linked for persons with MS (Holtzer & Foley, 2009).

The FSS has become a widely used instrument in multiple sclerosis research to examine episodes of fatigue. It is important to consider fatigue when conducting language assessments for persons with MS. Fatigue—as a symptom of MS or as a result of carrying out activities of daily has been shown to influence cognitive-linguistic performance (Krupp & Elkins, 2000).

Parmentier et al. (2003) investigated the effects of fatigue in individuals with MS who performed a series of tasks from the Stroop test and found that MS subjects scored low in the areas of word reading, color naming, and word naming. The higher order cognitive functions,
which included language, demanded more focused attention and information processing (Parmentier et al., 2003).

From these findings, a hypothesis was developed for the present research: Those tasks requiring high linguistic demands are most vulnerable to the effects of a single bout fatigue when undertaken by individuals with multiple sclerosis. Although the Parmentier et al. (2003) study differed from other studies (e.g., Karpatkin, 2013) in the sense that different aspects of fatigue were investigated, nevertheless, the findings indicate the value of further investigation into the effects of fatigue on expressive language. This research study was designed to investigate these effects.

Even though physical exercise has potential benefits for patients with MS fatigue (Karpatkin, 2005), whether the fatigue is a trait inherent in the disease or a consequence of physical or cognitive activity, the impact of exercise on the language domain is not fully understood. Because fatigue has been a neglected aspect of language research for people with MS, and because the fatigue–language dyad has been under-researched, an opportunity arose to obtain crucial insights while radically transforming the manner in which speech-language pathologists (SLPs) administer assessment batteries to individuals with MS. Fatigue, whether it is a trait inherent in the disease or induced by circumstance (i.e., physical exertion), may affect performance scores and outcomes and influence the way in which language professionals work with patients with MS.

The findings of this research study may be valuable especially for professional practitioners. Investigating the relationship between fatigue (trait or induced) and language applications such as word reading, color naming, and word naming builds upon existing research. The study fills the gap in the relative paucity of research in the fatigue–expressive
language and MS domains and may affect the quality of life of MS patients directly as well as help speech language pathologists serve their patients effectively.

**Purpose and Research Questions**

To date, studies specifically focused on the influence of a single bout of physical exertion on language function are missing in the research literature. The purpose of the current investigation was to answer the following research questions:

1. Does a single bout of physical exertion cause a decline in expressive language skills in individuals with MS?
2. Does a single bout of physical exertion cause a decline in word-finding skills in individuals with MS?
3. Does a single bout of physical exertion increase the length of time needed to complete confrontation naming performance measures?
4. Do subjective patient ratings of fatigue (VAS-F) and objective EDSS scores correlate with test performance on the FAS task (verbal fluency)?

The hypothesis was that perceptually small amounts (a single bout) of fatigue would affect word-finding and expressive-language skills in people with MS, compared to the skills of neurologically intact adults. Further, it was hypothesized that there would be no correlation between disease severity as scored on the EDSS and expressive language deficits. In general, neurologic disability as measured by the EDSS is a poor predictor of the degree of cognitive dysfunction for persons with MS. Individuals may have mild physical impairment but present with significant cognitive dysfunction. The opposite is also true—some individuals with MS are severely physically impaired and yet grossly intactdisplay cognitive skills (Benedict & Zivadinov, 2011). Given that exercise has been shown to improve cognition in non-
neurologically impaired adults (Chapman et al., 2013), it was anticipated that the control group would perform better in the fatigue-creating setting, compared to performance in the at-rest setting. After having undergone fatigue-inducing activities, in contrast, neurologically impaired adults (patients with MS) would perform less well in expressive-language tests. Support for this hypothesis would demonstrate that fatigue correlates positively with expressive-language deficits in adults diagnosed with MS.
CHAPTER 2:

METHODS

Sample

A convenience sample of 17 individuals with multiple sclerosis and varying ratings on the Expanded Disability Status Scale (EDSS) was recruited from the New York City Chapter of the National Multiple Sclerosis Society via flyers posted in MS centers. All participants had been clinically diagnosed with MS by a neurologist based on the McDonald (2010) criteria. Healthy, age-matched participants served as controls. All participants were English monolingual and were required to pass these minimum performance tests:

1. Vision Pass Criteria: Visual acuity of at least 20/70 in one or both eyes (Snellen Exam)

2. Physical Pass Criteria: Complete 90 seconds of physical exertion on the NuStep T5 Recumbent Cross Trainer set to provide 25% resistance without the subject demonstrating shortness of breath, dizziness, and an unsafe body posture on the equipment

Criteria for exclusion from the study included (a) having a known cardiac condition, (b) having one or more additional neurological conditions (e.g., Parkinson’s disease or myasthenia gravis), (c) having an orthopedic condition that could affect physical performance, (d) receiving a recent course of Solu-Medrol (a high-dose intravenous corticosteroid) for the treatment of an exacerbation within 2 weeks of study participation, or (e) failing one or both of the minimum performance measures.
**Pretesting**

Demographic and subject characteristics were collected in a brief investigator-facilitated interview prior to formal testing. Data collected included each subjects’ name, age, gender, highest level of education, medical history, current medications, date of diagnosis (converted to duration of MS in years), MS subtype, and EDSS severity rating were calculated by a multiple sclerosis certified specialist (MSCS). Participants then completed two commonly used and validated subjective (self-report) questionnaires specific to MS: the Fatigue Severity Scale (FSS; Krupp, LaRocca, Muier-Nash, & Steinberg, 1989) and the MS Quality of Life-54 (MSQOL-54; Vickrey, Hays, Harooni, Myers, & Ellison, 1995).

After participants completed the subjective measures, they practiced completing the Visual Analogue Scale for Fatigue (VAS-F) in order to increase their understanding and familiarity with the procedure (Lee, Hicks, & Nino-Murcia, 1991; Shahid, Wilkinson, Marcu, & Shapiro, 2011). Next, they participated in the minimum performance tests (Snellen vision test and physical exertion test). Upon successfully achieving all pretest conditions, participants were invited to participate in Phase 1, the “fatigue” condition of the study.

**Testing**

**Phase 1: Fatigue Condition**

For the fatigue condition of the study, participants were instructed to sit comfortably on the NuStep T5 Recumbent Cross Trainer. The NuStep T5 is a cardiovascular device that simulates a natural walking motion while eliminating joint stress and promoting functional fitness. It utilizes a natural and ergonomic body position while creating a smooth stepping motion. The NuStep T5 accommodates users from 4 feet 6 inches to 6 feet 4 inches tall with a weight range from 90 to 400 pounds. Once safely seated with their feet strapped on to the
equipment, participants’ core body temperatures were measured at the tympanic membrane with The Genius 2 tympanic thermometer (Covidien Item # 303000). Body temperatures were collected as changes in core body temperature can be used to signify that participants had completed adequate physical exertion associated with physical fatigue (Gonzalez-Alonso et al., 1999).

In the next stage, participants were presented with the VAS-F instrument to determine their baseline fatigue values. The participants were given the following instruction: “Draw on the line how much fatigue you are feeling at this exact moment in time.” Before participants began pedaling, the NuStep T5 Recumbent Cross Trainer was set to provide 25% resistance. The participants were instructed to pedal at their “best comfortable pace” while the researcher assessed their fatigue levels after 3 minutes of exercise and every 30 seconds thereafter using the VAS-F until they met discontinuation requirements. The exercise task was discontinued when the participants’ VAS-F values increased 50% from baseline or when the VAS-F scale reached its maximum value. Core temperatures were collected again upon completion of the physical exercise task. The total amount of time spent exercising was documented for each participant.

A single bout of physical exertion is sufficient to generate fatigue in individuals with MS and was therefore sufficient to provide the basis for this research. Similar to Karpatkin et al.’s (2013) model, their research study used the Berg Balance Scale, a process often used to identify risk for falls among MS patients. A single bout or episode of fatigue-inducing activity was sufficient to increase the likelihood of falls. Therefore, the methodological justification of this research was grounded in prior research indicating that a single episode of activity resulting in fatigue would likely affect efficacy of language use in individuals with MS (Karpatkin et al., 2013).
Phase 2: Rest Condition

Upon completion of Phase 1, the fatigue-condition individuals were invited to schedule a follow up appointment within 7 to 14 days in order to participate in Phase 2, the rest condition. At the beginning of testing for Phase 2, participants completed a short case history to determine if they had experienced any significant medical changes (e.g., a MS flare or new medication) since their initial participation in Phase 1. For the rest condition of the study, participants’ core body temperature was measured while they were seated comfortably in an armchair.

Next, their baseline fatigue levels were established using the VAS-F. The participants continued to sit comfortably; their fatigue levels were monitored at 3 minutes and every 30 seconds thereafter using VAS-F. They remained seated until the total amount of time to increase their fatigue by 50% from baseline in Phase 1 had elapsed. For example, if the participant had required 3 minutes and 57 seconds to increase his or her baseline fatigue 50% while exercising in Phase 1, he or she rested comfortably for 3 minutes and 57 seconds during the rest condition in Phase 2. Upon completion of resting, core body temperature was measured.

Language Performance Measures

The language performance measures were completed while participants were seated comfortably in an armchair. After the fatigue condition in Phase 1, participants were immediately moved from the recumbent cross trainer to an armchair placed beside the exercise equipment. Assistance transferring to the armchair was provided upon request. After Phase 2, participants remained seated in the same armchair in which they had completed the rest condition. The testing environment for all participants during the language assessments consisted of a climate- and noise-controlled room outfitted with a table, two chairs, and overhead lighting.
Once safely seated, four language performance measures were administered in a counterbalance method. Table 2 shows the language performance measure administered in each condition of the study. See Tables 3 and 4 for the counterbalanced procedure. A flow chart illustrating the study procedure can be found in the appendix.

**Comprehensive Test of Phonological Processing (CTOPP)**

The Rapid Digit, Rapid Letters, Rapid Colors, and Rapid Objecting Naming subtests of the Comprehensive Test of Phonological Processing (CTOPP) were administered. Participants received Form A in Phase 1, the fatigue condition, and Form B in Phase 2, the rest condition. These subtests were designed to evaluate an individual’s ability to accurately and rapidly verbally identify visual symbols such as digits, letters, colors, and objects (Wagner, Togensen, & Rashotte, 1999). The letters, numbers, colors, and objects subtests contained six high-frequency stimuli randomly repeated nine times in four rows for a total of 36 stimulus items (Wagner, Togensen, & Rashotte, 1999). For each subtest, the participant was asked to name each stimulus item as quickly as possible without making any mistakes. The total number of errors and percentage correct for each subtest was tallied, as well as the amount of time required to complete each task.

**Expressive Vocabulary Test 2nd Edition (EVT-2)**

The Expressive Vocabulary Test Second Edition (EVT-2) content covers a broad range of expressive vocabulary levels, with words representing 20 content areas (e.g., actions, vegetables, tools), parts of speech (nouns, verbs, or attributes), and home and school vocabularies (Williams, 2007). For each item, the researcher presented a picture and read a stimulus question, and the participant responded with one word that provided an acceptable label, answered a specific
question, or provided a synonym for a word that fit the picture. The total number of errors and percentage correct for each subtest was tallied, as well as the amount of time required to complete each subtest.

**Measures of Cognitive Linguistic Ability (MCLA)**

The verbal fluency subtest of the Measures of Cognitive Linguistic Ability (MCLA) is a widely utilized, normed task designed to quantify how many items an adult can correctly name within a given category in a prescribed amount of time (Ellmo, Graser, Krchnavek, Hauck, & Calabrese, 1995). This subtest is appropriate for individuals aged 16 to 75 years old. Administration of the verbal fluency subtest of the MCLA allows participants one minute for each task. Verbal fluency tasks can be further classified as phonemic (i.e., “list as many words you can think of that start with the letter F”), categorical (“list as many countries as you can within one minute”), or divergent (“list as many items you can think of that that can close”; Ellmo, Graser, Krchnavek, Hauck, & Calabrese, 1995).

In Phase 1, the fatigue condition, participants were administered the tasks in the following order: phonemic, categorical, and divergent. In Phase 2, the rest condition, participants were administered the tasks in the following order: categorical, divergent, and phonemic. The total responses for each task were tabulated. The responses were analyzed for appropriateness and a percentage correct calculated for each of the tasks.

**Assessment of Picture Description**

A picture description task is one the simplest ways to elicit expressive language. This task has the added benefit of generating predictable content and yielding relatively brief language samples that require little time to transcribe. The Cookie Theft picture from the Boston Diagnostic Aphasia Examination (BDAE; Kaplan, Goodglass & Weintraub, 1983) and the Office
Scene from the Measures of Cognitive Linguistic Ability (MCLA; Ellmo, Graser, Krchnavek, Hauck, & Calabrese, 1995) are normed and validated picture description tasks for adults. Participants received the Office Scene picture in Phase 1 and the Cookie Theft in Phase 2 with the following instruction: “Please tell me what you see happening in this picture. Remember to give your best and most complete response. This is important as I am unable to cue you for additional details or provide you with assistance.” The Discourse Rate Scale (DRS) from the MCLA is a 9 item, 45-point scale that allows researchers to qualify and quantify the quality of an expressive language sample (Ellmo, Graser, Krchnavek, Hauck, & Calabrese, 1995). The quality of each participant’s picture description was judged in nine skill areas including organization, verbal fluency, referential language, word usage/word finding, vocabulary usage, syntax, coherence, presupposition and elaboration. Participants could achieve a maximum of five points in each of the nine skill areas, allowing for a total score of 45 points (Ellmo, Graser, Krchnavek, Hauck, & Calabrese, 1995).

**Data Analysis**

The study was a nonrandom, matched-subject, mixed-factor design with covariates. The study was conducted with participants diagnosed with MS, either primary-progressive (PP) or relapsing-remitting (RR). Participants were placed into either an intervention or control condition, each condition having both a fatigue group and rest group. Statistical tests used for hypothesis testing included one-way MANOVAs and MANCOVAs followed by Tukey HSD post hoc tests to examine condition differences with regard to language skills, specifically (a) phonemic, categorical, and divergent verbal fluency, as measured by the FAS (MCLA); (b) expressive vocabulary, as assessed by the EVT-2; (c) rapid naming of letters, numbers, colors, and objects, as measured by the CTOPP-2; and (d) skills in narrative composition,
assessed by the Picture Description test. Pearson bivariate correlations were used as necessary to augment the one-way MANCOVA for the fourth research question (Do subjective patient ratings of fatigue (VAS-F) and objective EDSS scores correlate with test performance on the FAS verbal fluency task?).

The one-way MANCOVA was the appropriate statistical test for this study, because it involves the examination of between-subject factors—that is, comparisons between intervention means for the four families of variables (i.e., CTOPP-2, MCLA, EVT-2, and Picture Description) against means on those same variables for the control conditions. Because the sample size was expected to be small (fewer than 30 participants), a decision was made to use bootstrapping to resolve the issue of a small sample size (Konietschke, Bathke, Harrar, & Pauly, 2015). As outlined earlier, the order in which participants experienced these measures was counterbalanced. All data in this project were analyzed using the Statistical Package for Social Sciences (SPSS 22.0).

The data analyses for the study produced descriptive and inferential statistical results. The first set of analyses involved descriptive statistics of study participants, specifically inferential statistics (chi-square tests of independence and independent-samples t tests) conducted to determine any significant demographic and MS-related differences between participants in the study conditions. Descriptive statistics were also conducted with the study variables.

Preliminary statistical analyses involved the testing of assumptions for one-way MANOVA and MANCOVA. The first assumption was normality in the distribution of scale scores. A zskewness value was computed for each scale to determine skewness. A zskewness value that is less than 3.28 is indicative of relative normality (Doane & Seward, 2011). The assumption of
lack of multicollinearity between dependent variables was assessed by calculating Pearson bivariate correlation coefficients among the measures within each assessment category. Multicollinearity is evident if the Pearson correlation coefficient is equal to or greater than .80 (Alin, 2010). Spearman’s rho correlations were conducted for the testing of covariates (demographic and MS-related variables). If the Spearman’s rho analysis yielded no significant associations between demographic and MS-related variables and the dependent variables, one-way MANOVAs were used for hypothesis testing. The reporting of one-way M ANCOVA and MANOVA results included Wilks λ for overall model significance and F values and associated significance (p) values for between-subjects effects. Mean scores and standard deviations were reported for study conditions. Partial eta squared (ηp²) was utilized as an indicator of effect size.

Numerous between-subjects tests were conducted in this study. Each assessment had numerous subtests, ranging from four for the Picture Description assessment to 16 for the FAS (MCLA); thus, the differences were examined across all assessment subtests. To prevent the likelihood of committing a Type I error, that is, rejecting the null hypothesis when in fact it was true, the Bonferroni approach, a multiple-comparison correction, was used to adjust the level of significance, with p set at α/n (Armstrong, 2014).

A sample size estimation for a one-way MANOVA for four groups, with a large effect size, Cohen’s f = .40, significance set at p < .05, and power (1 – β), with examination of 20 dependent variables required a sample size of N = 146 (Woolson & Clarke, 2011). If the effect size, Cohen’s f, was set to medium, f = .25, the required sample size was N = 351. Bootstrapping was conducted to address the small sample size issue, with the data replicated across 1,000 samples (Woolson & Clarke, 2002).
CHAPTER 3:

RESULTS

Descriptive Statistics: Study Participants

The study had a total of 24 participants, $n = 17$ in the intervention group and $n = 7$ in the control group. The individuals in the control group were healthy age-matched participants. In the intervention group, all participants had clinically diagnosed multiple sclerosis. Five had primary-progressive (PP) MS, and 12 had relapsing-remitting (RR) MS (see Table 5). Participants in both the intervention and control groups were asked to provide their gender, ethnicity, age, and years of education (see Tables 6 and 7). The intervention group was composed of 70.6% females, and the control group consisted of 28.6% females. The participants in the intervention group were predominantly White/Caucasian (64.7%), as were a plurality of the participants in the control group (42.9%).

Descriptive statistics for participants' age and educational level are presented in Table 7. Participants in the intervention group had a mean age of 51.41 years ($SD = 9.57$ years), and their ages ranged from 32 to 65 years; participants in the control group had a mean age of 48.15 years ($SD = 12.00$ years), with ages ranging from 31 to 64 years. The education level for participants in the intervention group was 15.59 years ($SD = 1.94$ years), indicating that on average, participants had 3.5 years of college. The education level of intervention group participants ranged from 9 to 17 years. The education level for participants in the control group was 14.71 years ($SD = 2.06$ years), indicating that on average, participants had slightly less than 3 years of college. The education level of control group participants ranged from 12 to 17 years.

Participants reported the number of years they had lived with a MS diagnosis. The mean number of years with MS diagnosis among participants was 12.82 ($SD = 10.16$). The large
standard deviation was attributable to the wide range of years with MS diagnosis, 1 to 37. Participants were administered the Expanded Disability Status Scale (EDSS) by a trained examiner (see descriptive statistics for this scale in Table 8). The mean EDSS score for the 17 participants were 5.50 (SD = 1.36), equivalent to ambulatory without aid or rest for a maximum of 100 meters and with a disability severe enough to preclude them from participating in full activities of daily living (Kurtzke, 1983). The EDSS scores ranged from 3.0, indicating moderate disability with ambulatory ability, to 7.5, indicating severe disability consisting of the inability to take more than a few steps and restriction to a wheelchair. One participant had an EDSS score of 3.0, and three participants had EDSS scores of 7.5.

**Analysis: Study Participants**

Analysis of the intervention and control groups for gender differences revealed no significant difference, as determined by a chi-square ($\chi^2$) test of independence, $\chi^2(1) = 3.60, p = .058$. When analyzing ethnicity between groups using a chi-square ($\chi^2$) test of independence, it was determined that the participant groups did not significantly differ by ethnicity, $\chi^2(3) = 5.33, p = .149$. Independent-samples $t$ tests showed that the intervention and control group participants were similar in age, $t(22) = 0.72, p = .481$, and did not differ with regard to years of education, $t(22) = 0.99, p = .334$.

A chi-square ($\chi^2$) test of independence determined that significant gender differences existed across MS types, $\chi^2(1) = 8.73, p = .003$, with 91.7% of females having RR MS and 80.0% of males having PP MS. However, no significant ethnic differences were found with regard to type of MS, $\chi^2(1) = 0.73, p = .394$.

As determined by an independent-samples $t$ test, no gender differences were found with regard to years with MS diagnosis, $t(15) = -0.16, p = .876$, nor were there any significant ethnic
differences, \( t(15) = 0.09, p = .926 \). With regard to EDSS scores, results from an independent-samples \( t \) test showed no significant gender differences, \( t(15) = 0.19, p = .852 \); however, a significant ethnic group difference was found, \( t(15) = -2.96, p = .010 \). African American participants \((n = 6)\) had a significantly higher EDSS score \((M = 6.58, SD = 1.11)\), compared to Caucasian participants \((n = 11, M = 4.91, SD = 1.11)\). Indeed, on average, African American participants were at stage 6.5 of the EDSS, indicating a need for constant bilateral assistance to walk 20 meters without resting, compared to Caucasian participants, who were on average at stage 5.0, or ambulatory without aid or rest for 200 meters (Kurtzke, 1983).

**Study Variables**

Four assessments were used to measure the study variables. These assessments were:

1. FAS (Measure of Cognitive Linguistic Abilities [MCLA]), which assessed phonemic, categorical, and divergent verbal fluency
2. EVT-2, which measured expressive vocabulary
3. CTOPP-2, which assessed rapid naming of letters, numbers, colors, and objects
4. Picture Description, which assessed narrative composition skills.

The FAS (MCLA), EVT-2, CTOPP-2, Picture Description, and VAS-F scale results representing the entire sample \((N=24)\) are presented in Tables 9 through 13.

**Testing of Assumptions for a One-Way MANOVA**

Study scales were examined to guard against violations of two key assumptions for a one-way MANOVA, the analysis used for hypothesis testing. The first assumption was normality in the distribution of scale scores. A \( z_{\text{skewness}} \) value was computed\(^1\) for each scale to determine skewness. A \( z_{\text{skewness}} \) value less than 3.28 is indicative of relative normality (Doane & Seward, 2011).

\(^1\) \( Z_{\text{skewness}} \) scores are derived by dividing scale skewness by the skewness standard deviation (Doane & Seward, 2011).
2011). As shown in Table 9, numerous scales displayed non-normality, as evidenced by a $z_{\text{skewness}}$ value higher than 3.28. A decision was made to use only those FAS (MCLA) scales that displayed normality, because of the large number of FAS (MCLA) scales. The two EVT-2 scales were normal (see Table 10). The four CTOPP-2 and Picture Description scales were all substantially skewed (see Tables 11 and 12), resulting from most scores having only one participant response. The four CTOPP-2 scales and the three Picture Description scales were recoded into categories, which resulted in greatly reduced $z_{\text{skewness}}$ values, and thus, normality was acceptable. The three VAS-F scales displayed normality (see Table 13).

The second assumption tested in the MANOVA analyses was lack of multicollinearity between the dependent variables. Because the MANOVA analyses were conducted with each of the four assessment categories, multicollinearity was assessed by calculating Pearson bivariate correlation coefficients among the measures within each assessment category (i.e., FAS [MCLA], EVT-2, CTOPP-2, Picture Description, and VAS-F). Multicollinearity is evident if the Pearson correlation coefficient is equal to or greater than .80 (Alin, 2010). Pearson bivariate correlation coefficients were first calculated for the FAS (MCLA) verbal fluency measures. Sixteen relationships between the FAS (MCLA) variables showed multicollinearity, as evidenced by $r_{(48)} \geq .80, p < .001$ (see Table 14). This resulted in the testing of eight FAS (MCLA) variables (shown in bold font in Table 9).

Multicollinearity was also evident between the CTOPP-2 C4TT rapid digit naming total time and C6TT rapid letter naming total time variables, $r(48) = .83, p < .001$, requiring that one of these two CTOPP-2 variables be excluded from analyses for hypothesis testing. Because the C4TT variable was less significantly associated with the C7TT rapid color naming total time and C9TT rapid object naming total time variables, compared to the C6TT variable, the C6TT
variable was excluded from analyses for hypothesis testing. The EVT-2 variables did not show evidence of multicollinearity (see Table 15), nor did the Picture Description and VAS-F variables; all these variables were included in analyses for hypothesis testing.

**Testing for Covariates**

To examine correlations between categorical and continuous variables a series of Spearman’s rho correlations were conducted with the variables of participant gender, ethnicity, age, and number of years of education with the dependent variables (i.e., the EVT-2 scales, FAS (MCLA) scales, CTOPP-2 scales, Picture Description scales, and VAS-F scales). Results from the Spearman’s rho correlation analyses showed no significant associations between the four demographic variables and the CTOPP-2, Picture Description, and VAS-F variables and the majority of the FAS (MCLA) and EVT-2 variables. Participant ethnicity was significantly associated with the CS1TC variable rapid country naming total correct, \( r_s(24) = -0.45, p = 0.028 \), and participant age and education in years were significantly associated with the PS1Mean phonemic category manual mean variable, \( r_s(24) = 0.42, p = 0.041 \), and, \( r_s(24) = 0.76, p < 0.001 \), respectively. Participant ethnicity was significantly associated with the EVT-2 time in seconds variable, \( r_s(24) = 0.42, p = 0.045 \). Because of the few significant and consistent associations between demographic and dependent variables and to enhance statistical power, no covariates were included in analyses for hypothesis testing.

**Hypothesis Testing**

**Research Question 1.** The first research question was, “Does a single bout of physical exertion cause a decline in expressive language skills (as measured by the EVT-2 scales) in individuals with MS?” To address this question, a one-way MANOVA was conducted. Results showed that the overall multivariate model was significant, Wilks \( \lambda = 0.66, F(6,86) = 3.29, p = \)
Tests of between-subjects effects showed that one variable drove the model significance, the EVT-2. Groups differed with regard to EVT-2 scale scores, $F(3,44) = 4.97$, $p = .005$, $\eta^2_p = .253$ (see Table 15). A Tukey HSD post hoc test determined that the Intervention Fatigue Group had a significantly higher confrontation naming errors score on the EVT-2 ($M = 48.82$, $SD = 16.31$) in comparison to the Control Fatigue Group ($M = 33.43$, $SD = 13.30$), the Intervention Rest Group ($M = 35.12$, $SD = 14.02$), and the Control Rest Group ($M = 38.44$ $SD = 16.48$). There were no significant differences across groups with regard to the EVT-2 time in seconds variable, $F(3,44) = 1.74$, $p = .173$, $\eta^2_p = .106$.

**Research Question 2.** The second research question was, “Does a single bout of physical exertion cause a decline in word finding skills in individuals with MS?” The second question was addressed by conducting two one-way MANOVAs, one for the set of FAS (MCLA) variables and one for the set of Picture Description variables. Results showed that the overall multivariate model was significant, Wilks $\lambda = .35$, $F(1.99, 24) = 1.99$, $p = .009$. Tests of between-subjects effects showed that, of the eight FAS (MCLA) variables, only two were significant (see Table 16). The four groups differed significantly on their ability to generate words when given a letter of the alphabet (PS1M – phonemic category mean comparison score) scores, $F(3,44) = 3.44$, $p = .025$, $\eta^2_p = .190$. A Tukey HSD post hoc test determined that the Intervention Fatigue Group had a significantly lower PS1M score, indicating fewer words generated ($M = 0.53$, $SD = 0.51$) in comparison to the Control Fatigue Group ($M = 1.00$, $SD = 0.00$), the Intervention Rest Group ($M = 0.59$, $SD = .507$), and the Control Rest Group ($M = 1.00$, $SD = 0.00$). A Tukey HSD post hoc test also determined significant group differences on DS1M divergent naming mean comparison score scores, $F(3,44) = 6.44$, $p < .001$, $\eta^2_p = .305$. The Intervention Fatigue Group had a significantly lower DS1M score ($M = 0.35$, $SD = 0.49$),
indicating they generated fewer items within a abstract category (i.e., list items that can be closed) in comparison to the Control Fatigue Group \((M = 1.00, SD = 0.00)\), the Intervention Rest Group \((M = 0.71, SD = .470)\), and the Control Rest Group \((M = 1.00, SD = 0.00)\).

The overall multivariate model was significant, Wilks \(\lambda = .48\), \(F(2.90, 12) = 2.90, p = .002\). Tests of between-subjects effects showed that of the four Picture Description variables, only one was significant (see Table 17). Groups significantly differed on the discourse rating scale participant SD from manual variable \((RS1SDM recoded)\), \(F(3,44) = 6.56, p < .001, \eta^2_p = .402\). A Tukey HSD post hoc test determined that the Intervention Fatigue Group \((M = 2.47, SD = 0.87)\) and the Intervention Rest Group \((M = 2.76, SD = 0.90)\) had significantly lower recoded RS1SDM scores, illustrating that persons with MS had a similar narrative skill performance in both testing conditions, compared to the Control Fatigue Group and Control Rest Group \((M = 4.00, SD = 0.57)\).

**Research Question 3.** The third research question was, “Does a single bout physical exertion increase the duration of time needed to complete confrontation naming performance measures?” A one-way MANOVA was conducted to address this question. The overall multivariate model was not significant, Wilks \(\lambda = .72\), \(F(9, 102.37) = 1.66, p = .107\). Tests of between-subjects effects showed that two of the three CTOPP variables were significant (see Table 18). Groups differed significantly on the C7TT variable rapid color naming total time, \(F(3,44) = 2.97, p = .042, \eta^2_p = .168\). A Tukey HSD post hoc test determined that the Intervention Fatigue Group had a significantly higher C7TT score \((M = 29.85, SD = 8.44)\), indicating they required more time to complete the rapid color naming task in comparison to the Control Fatigue Group \((M = 22.92, SD = 3.18)\) and the Control Rest Group \((M = 22.90, SD = 3.89)\); however, the Intervention Fatigue Group did not significantly differ from the Intervention Rest Group \((M = 22.92, SD = 3.18)\).
28.12, \(SD = 6.32\). Thus, the Intervention group had intrinsically longer C7TT naming times that were unaffected by fatigue.

Groups also differed significantly on the C9TT variable \textit{rapid object naming total time}, \(F(3,44) = 3.20, p = .032, \eta_p^2 = .179\). A Tukey HSD post hoc test determined that the Intervention Fatigue Group (\(M = 33.03, SD = 8.84\)) had a significantly higher C9TT score, indicating they required more time to complete the rapid object naming task in comparison to the Control Fatigue Group (\(M = 26.44, SD = 5.01\)) and the Control Rest Group (\(M = 23.80, SD = 4.29\)); however, the Intervention Fatigue Group did not significantly differ from the Intervention Rest Group (\(M = 30.05, SD = 7.14\)). As with C9TT, the Intervention group was intrinsically slower on this task regardless of fatigue.

\textbf{Research Question 4}. The fourth research question was, “Do subjective patient ratings of fatigue (VAS-F) and objective EDSS scores correlate with test performance on the FAS task (verbal fluency)?” The fourth research question was addressed in two ways. The first set of analyses was a series of Pearson bivariate correlations between the FAS (MCLA) variables and the VAS-F and EDSS variables for each group. The second analysis was a one-way MANOVA with VAS-F variables examined across the four study groups.

\textit{Pearson bivariate correlations}. The first set of correlations was conducted with the Intervention Fatigue group (see Table 19). Only one significant association emerged: the PS1M variable (\textit{phonemic category naming mean comparison score}) was significantly associated with the VAS-F change score\(^2\), \(r(17) = -.53, p = .031\). Higher PS1M scores were significantly associated with lower VAS-F change scores, meaning smaller perceived changes in fatigue while exercising for the Intervention Fatigue Group.

\(^2\) VAS-F change scores were calculated by subtracting baseline VAS-F scores from VAS-F end scores.
The second set of Pearson bivariate correlations was conducted with the Control Fatigue Group (see Table 20). The EDSS variable was not included in the analyses because it was a constant variable—that is, all participants provided the same score because they did not have multiple sclerosis. The PS1M phonemic category naming mean comparison score and DS1M divert naming mean comparison score variables were also not included in the analyses because the values were constant. Results from the Pearson bivariate correlations showed no significant associations between variables. Some of the correlations were quite high; however, lack of significance between variables was likely attributable to the relatively small sample size.

The third set of correlations was conducted with the Intervention Rest Group (see Table 21). The EDSS variable was not included in the analyses because the variable was constant (i.e., all participants provided the same score). Two significant associations emerged from the analyses. The CS1TC rapid country naming total correct variable was significantly associated with the VAS-F change score, $r(17) = -.63, p = .007$. As the VAS-F change score decreased, the CS1TC scores increased. The PS1Mean variable was significantly associated with the VAS-F change score, $r(17) = -.58, p = .014$. As the PS1Mean scores increased, the VAS-F change score decreased.

The fourth set of Pearson bivariate correlations was conducted with the Control Rest Group (see Table 22). The EDSS variable was not included in the analyses because the variable was constant (i.e., all the scores on the EDSS variable were the same for each of the seven participants). The PS1M phonemic category naming mean comparison score and DS1M divert naming mean comparison score variables were also not included in analyses because they too were constant values. Results from the Pearson bivariate correlations showed three significant associations between variables. The DS1T variable divergent naming total was significantly
associated with the VAS-F 3 minute fatigue variable, \( r(7) = .79, p = .035 \). As the DS1T scores increased, so did the VAS-F 3 minute fatigue scores. The PS1Mean variable was significantly associated with the VAS-F change score, \( r(7) = -.93, p = .035 \). As the PS1Mean scores increased, the VAS-F change scores decreased. The PS1SD variable was also significantly associated with the VAS-F change score, \( r(7) = -.85, p = .014 \). As the PS1SD scores phonemic category naming \( SD \) increased, the VAS-F change scores decreased.

The summary of results from the Pearson bivariate correlations conducted for each group is presented in Table 23. For all but the Intervention Fatigue Group, scores on the EDSS variable were the same across participants and thus were not included in analyses. Of the three VAS-F variables, the VAS-F change score had the most significant associations with the FAS (MCLA) variables. The VAS-F change score variable was significantly and negatively associated with the PS1M variable for the Intervention Fatigue Group; significantly and negatively associated with the CS1TC and PS1Mean variables for the Intervention Rest Group; and significantly and negatively associated with the PS1Mean and PS1SD variables for the Control Rest Group. The VAS-F change score variable was significantly and negatively associated with the PS1Mean variable for both the Intervention Rest and Control Rest Groups. No significant associations were found for the Control Fatigue Group.

**One-way MANOVA.** A one-way MANOVA was conducted to determine if the three VAS-F variables significantly differed across the four study groups (see Table 24). The overall multivariate model was significant, Wilks \( \lambda = .43, F(9, 102.37) = 4.65, p < .001 \). Tests of between-subjects effects showed that groups differed significantly on the VAS-F change score variable, \( F(3,44) = 14.87, p < .001, \eta^2_p = .503 \). A Tukey HSD post hoc test determined that the Intervention Fatigue Group had a significantly higher VAS-F change score \( (M = 29.24, SD = \)
14.84) in comparison to the Intervention Rest Group ($M = -2.47, SD = 9.72$) and the Control Rest Group ($M = 1.86, SD = 25.77$). However, the Intervention Fatigue Group did not significantly differ from the Control Fatigue Group ($M = 28.14, SD = 17.40$). Therefore, fatigue affected VAS-F regardless of medical status.
CHAPTER 4:
DISCUSSION

The purpose of this study was to investigate the relationship between physical fatigue and expressive-language capabilities in MS patients to determine the extent to which such fatigue compromised linguistic competence. The hypothesis was that even a single bout of physical exertion would negatively affect the linguistic competence of persons with MS in four areas: expressive language, word finding, subjective confrontation naming times, and objective confrontation naming times. The hypothesis was accepted in most respects.

Fatigue is a common symptom of MS. Although extensive research has been carried out on other cognitive deficits caused by MS, previously, little research has been conducted on the communication component of verbal fluency in relation to fatigue. Kahneman’s (1973) cognitive model showed that within a fixed cognitive resource, competing stimuli must be prioritized, and for persons with MS, paired with the presence of fatigue, prioritization may be more difficult, thus resulting in a reduction in expressive language and verbal fluency. This study was designed to validate this presumption by quantifying the reduction in expressive language and verbal fluency caused by a single bout of fatigue.

Demographics Discussions

In the United States, 400,000 people have a diagnosis of MS, with an additional 10,000 diagnoses being added each year (NMSS, n.d). The prevalence of MS is 2 to 3 times higher for women, compared to rates for men (Cook, 2006). The chosen sample of 24 ($n = 17$ in the intervention group and $n = 7$ in the control group) reflected the gender composition of MS patients in the intervention group but not in the control group (70.6% were female in the intervention group, compared to 28.6% in the control group). The intervention group was also
strongly representative of White Caucasian heritage (64.7% for the intervention group; 42.9% for the control group). The intervention group contained no respondents of Asian or Hispanic heritage; however, the control group included one person from each category. Thus, the lower sample size indicated a higher proportion of the whole. Overall, the sample size was representative of the distribution and trajectory of the condition within the United States (NMSS, n.d), ensuring validity of the sample.

Some differences were present between ethnicity and ambulatory status. African American participants scored on average at a higher disability level of 6.5, compared to the Caucasian participants, who scored at a lower disability level of 5.0, which is defined as being ambulatory without rest for 200 meters. The differences in condition status by ethnicity were greater than differences in terms of gender or diagnostic years. The intervention group contained no members of Asian or Hispanic heritage, only members of Caucasian and African American heritage. Although the investigation of condition status and ethnicity was not a part of the study, and reliable statistical evidence was absent, further investigation into the relationship between condition status, ethnic heritage and verbal fluency could be of value.

The mean age of both groups was similar, 51.41 years for the intervention group and 48.15 for the control group. The two groups had a broadly similar age range: 32 to 65 and 31 to 64, respectively. For the intervention group, the time interval post diagnosis was very wide, from 1 to 37 years with a mean of 12.82 years. Of the intervention group, 5 participants had been diagnosed with primary-progressive (PP) MS and 12 with the relapsing-remitting (RR) type. This distribution within the sample conformed to the national distribution of MS disease types (National MS Society, n.d.) and therefore validated the composition of the sample.
The findings are discussed in relation to the following research questions:

1. Does a single bout of physical exertion cause a decline in expressive language skills in persons with MS?
2. Does a single bout of physical exertion cause a decline in word-finding skills in persons with MS?
3. Does a single bout of physical exertion increase the duration of time needed to complete confrontation naming performance measures?
4. Do subjective patient ratings of fatigue (VAS-F) and objective EDSS scores correlate with test performance on the FAS task (verbal fluency)?

The results in their entirety were presented in Chapter 3. In the following discussion, the evaluative devices are explained in relation to each test.

The Expanded Disability Status Scale (EDSS) was used by a trained examiner to determine the extent of the respondents’ ambulatory disability. The scale scores ranged from 7.5 for three participants unable to take more than a few steps, who were thus designated wheelchair dependent, to 3.0 for those having moderate disability with full ambulatory ability. The mean score for the 17 intervention participants was 5.50 ($SD = 1.36$), which is equivalent to being ambulatory without rest for 100 meters but with disability sufficient to preclude full participation in daily living activities.

The research questions focused on the effects of a single bout of physical activity on linguistic competence. The test was consistently structured to deliver the same effect outcome to each participant by increasing the VAS-F value 50% from the baseline. Therefore, despite the differences in values demonstrated through the EDSS, each participant undertook the language
testing with the same perceived increase in the amount of fatigue. Research Questions 1 through 3 focused on three objective semantic tests of verbal fluency: (a) expressive language, (b) word finding, and (c) confrontation naming. The fourth research question correlated the participants’ subjective evaluation of their fatigue ratings (VAS-F) with their objective EDSS scores and their verbal fluency performance scores.

This study was intended to investigate impaired expressive language and verbal fluency as part of the process of broadening the research into the impact of MS on language function. The findings that persons with MS perform more poorly than controls on linguistic tasks provide insight into the relationship between fatigue from physical exertion and its effects on verbal fluency, which is imperative in day-to-day communication and social interactions. Using the same methodology as Thornton and Raz (1997), and Henry and Beattie (2006), this research study utilized a testing process that included primary-progressive (PP) and relapsing-remitting (RR) MS. The disease severity, measured on the EDSS scale, was combined with an extensive set of language test scores to deliver a consistent measurement.

According to Henry and Beattie (2006), a meta-analysis of 35 studies comprising a total of 3,673 participants showed this field has previously been under-researched. A direct association between the type of MS and deficits in phonetic and semantic fluency was found, with a higher deficit observed for primary-progressive MS (Henry & Beattie, 2006). This dissertation expands upon the research literature by specifically investigating the relationship between fatigue from physical exertion and its effects on verbal fluency in persons with various forms of MS.

Research into the impact of cognitive activities indicated that for the controls, cognitive activity increases verbal fluency and conceptual planning; however, MS patients experience the
reverse (Krupp & Elkins, 2000). Their findings indicate that cognitive fatigue reduces verbal fluency and the speed of cognitive processing for persons with MS. In this dissertation study, the influence on verbal fluency of physical activity as a source of fatigue was investigated in MS patients and controls. The study design was justified by research conducted by Karpatkin et al. (2013), which showed that physical fatigue affects physical attributes such as gait and balance. In addition, Holtzer and Foley (2009) found that physical fatigue reduces cognitive functioning and therefore affects verbal fluency and semantic recall.

**Discussion of Research Questions**

**Research Question 1**

Research Question 1 was, “Does a single bout of physical exertion cause a decline in expressive language skills?” The value of this research over previous studies lies in its use of real-time testing of communication competence. Unlike other studies that used subjective reports from respondents (e.g., Beukelman et al., 1985), this current study used objective communication measures to assess language performance and its relationship to a single bout of physical fatigue. Beukelman et al.’s research approach facilitated greater accuracy of performance measures captured during the actual bout of physical fatigue, compared to previous research approaches.

Beukelman et al. (1985) reported a reduced capability in verbal fluency; however, the results were achieved through the administration of a questionnaire encompassing several aspects of MS, one section of which focused on communication. Difficulties in communication were not specified but included the ability to converse with strangers; hence, the findings included comprehension of participants’ speech by others (Beukelman et al., 1985). This dissertation focuses on utilizing objective language testing to measure the direct impact of fatigue upon linguistic competence in persons with MS. This is an enhancement upon the work
of Beukelman et al. (1985) who utilized questionnaire for their data collection which is highly subjective in nature.

In the current study, the focus was to examine verbal expression capabilities among two groups. The Intervention Fatigue Group demonstrated significantly more naming errors than did the Control Fatigue Group, indicating the impact of MS upon expressive language skills through a single bout of physical exertion. No further significant differences were found between the Intervention Rest or Control Rest Groups. The reduced expressive language found by Beatty (2002) and reduced verbal fluency (Friend et al., 1999) was confirmed by these data; however, the data also showed anomalies and indicators that could be investigated further.

One of the complicating factors when testing expressive language is accounting for the influence of a research participants’ native language(s) morphological and phonological differences. In a study of letter fluency, Beatty (2002) found that language structure such as syllable numbers contributed to verbal fluency when it was used to name body parts or animals; thus, some languages are structured in such a way that performance deficits attributable to fatigue may be reduced because of features inherent in that language. To minimize this confounding factor, in the current study all respondents were native English speakers. Further investigation is warranted into the impact of additional linguistic competence variables in persons with MS.

Friend et al. (1999) found both primary-progressive and relapsing-remitting MS patients had reduced linguistic capabilities, compared to controls. However, Friend et al. questioned how tests could be administered without precipitating fatigue, rather than attempting to quantify the effects of that fatigue upon the linguistic competence of persons with MS. The current study addressed the implications of fatigue by utilizing the VAS-F to quantify the participants fatigue.
level. The investigation of the relationship between fatigue and expressive language function contributes new knowledge to the field of study.

**Research Question 2**

Research Question 2 was, “Does a single bout of physical exertion cause a decline in word-finding skills in individuals with MS?” Word-finding deficiencies have been found in as many as 40% of MS patients (Lacour et al., 2004). The word-finding aspect of this study was not designed to investigate the incidence of aphasia, because aphasia is a condition normally associated with the grey matter of the brain (Achiron et al., 1992; Friedman, Brem & Mayeux, 1983; Cook, 2005). Of relevance to this study was the white matter, or neural links, considered important in understanding the pathology of MS. Therefore, the incidence of aphasia was not directly relevant to this current research and thus was not a part of the study design. Instead, the focus of the investigation involved the period of time required by MS patients and controls to complete tasks of word retrieval once they underwent a single bout of physical exertion.

The implication of this study’s findings is that even relatively small amounts of exertion caused fatigue, and this fatigue delayed response times in day-to-day word finding and verbal interactions for participants with MS. These delayed response times potentially could affect their social lives, their work lives, and their employment progression. In terms of therapeutic relevance, it could be surmised that some patients with MS may benefit from having short breaks built into their therapy sessions, allowing them to recover from highly demanding cognitive linguistic tasks.

In the FAS (MCLA) test, a respondent’s capability to generate words beginning with a given letter of the alphabet is measured. In the current study, the Intervention Fatigue Group presented with significantly lower scores and fewer words generated in the allotted time,
compared to the Control Fatigue Group and the Intervention Rest Group. The Intervention Fatigue Group also had a significantly lower DSIM score than did all other groups, showing that these respondents elicited fewer items within an abstract category, for instance, naming items that can be closed. Therefore, physical fatigue negatively affected the word-finding capabilities of MS and non-MS participants but did so differentially between the groups.

For the Picture Description task, only one of the four variables was statistically significant, and the groups differed on the recoded RISDM task. The test indicated that both the Intervention Fatigue Group and the Intervention Rest Group had significantly lower scores than the Control groups in both testing conditions. This finding shows that the MS participants had reduced narrative production skills, compared to Controls. This study is consistent with those of Wallace and Holmes (1993) and Beukelman et al. (1985). Previous researchers have found that MS patients provide fewer words per utterances within a given time frame than do individuals without MS. However, Wallace and Holmes’s (1993) use of the Arizona Battery for Communication Disorders (ABCD) test was limited to a total of only four female MS respondents, which highlights the importance of sample size and demographics. The current study included a total of 17 persons with MS, 12 female and five male which is representative of the distribution of individuals living with MS in the United States (National MS Society, n.d.).

In a trial of 59 research participants, Krupp and Elkins (2000) found that the MS respondents declined in verbal memory and conceptual planning scores after undertaking a challenging computer-based mental arithmetic task; the scores of the control group improved. Krupp and Elkins’s research approach differed from the current study’s approach, which used physical rather than cognitive fatigue as the variable for both groups. Physical fatigue negatively
affected both groups. The quantitative survey used a questionnaire to collect the subjective perceptions of MS participants (Krupp & Elkins, 2000).

The type of fatigue-inducing activity selected may be a valuable research avenue to explore. In the current study, physical fatigue affected both groups, but the MS participants experienced a greater effect, compared to the controls. Karpatkin (2012) found that whether the exercise element was continuous or consisted of episodes of shorter duration interspersed with periods of rest, the exercise affected respondents’ perceptions of their level of the fatigue. This finding is relevant to this research and to possible extensions of it. Although in the current study, only a single bout of exercise was used, by varying the duration of the activity or numbers of bouts, differences in scores could be generated. Closely examining variables such as the type of physical exertion, the length of time between bouts, and the total time of physical exertion could be fruitful areas for further investigation and quantification.

The findings of this study are consistent with the findings of Lacour et al. (2004), Beukelman et al. (1985), and Friend et al. (1999), even though their work derived from subjectively quantified data. The studies focused on MS patients complaints about the difficulties they encountered in word finding. Fatigue is largely subjective and open to personal interpretation but it can also be graded according to the Fatigue Severity Scale (FSS) in accordance with the subject’s own experience (Krupp, LaRocca, Muier-Nash, & Steinberg, 1989). The value of this dissertation study lies in the use of multiple scales, both objective (e.g., EDSS) and subjective (e.g., VAS-F). Holtzer and Foley (2009) found the presence of MS intensified fatigue; thus, fatigue was directly linked to a decline in cognitive and executive functions. The findings of this study confirmed this decline in cognitive and executive functions, including word-finding abilities. The ability to “find words,” as both self-expression and as
social participation, is limited by MS fatigue and could lead to the increased likelihood of consequential reactive depression (Bakshi et al., 2000). In linking MS with neurological disability and depression, Bakshi et al. (2000) offered a model of an attenuation of linguistic and semantic functioning diminution as a consequence of MS fatigue. Language is required for executive functioning (Holtzer & Foley, 2009); any limitations in language associated with neurological disability have a strong likelihood of being linked with reactive depression (Bakshi et al., 2000).

**Research Question 3**

Research Question 3 was, “Does a single bout of physical exertion increase the duration of time needed to complete confrontation naming performance measures?” The results show that the Intervention Fatigue Group required more time to complete test stimuli in comparison to the Control Fatigue and Rest Groups, illustrating the need for people with MS to receive extended time when completing naming tasks. This finding is important for contexts such as schools, colleges, and work programs in which speed of performance is important. Further, time management accommodations, including taking breaks during testing when time is not part of the competence being tested, would allow individuals with MS to manage their fatigue symptoms and facilitate the best possible test performance.

A similar finding occurred for the rapid object naming (C9TT) test in comparison with the Control Fatigue and Rest Groups. In contrast, the time required for the Intervention Rest Group to complete C9TT was only slightly faster than the times for the Intervention Fatigue Group, indicating that regardless of fatigue status, the MS participants always required additional time to complete the rapid object naming compared to controls. This finding shows the impact of MS on linguistic-based tasks and activities.
The Visual Naming Test developed by Benton and Hamsher (1978) was the first to indicate the existence of naming impairments for both PP and RR MS subjects, and for PP subjects more so than for RR subjects. From this finding, Benton and Hamsher surmised that individuals with PP MS have more difficulty and are slower in visual naming tasks than those with RR MS. This aspect requires further investigation not only in terms of the outcome of a single bout of physical exertion between the two forms of the disease, but also because the two forms differ in the impact they have on language competence.

Corpus callosum (CC) lesions are also associated with deficits in visual naming tasks because these tasks require both physiological (sight) and cognitive (memory and recall) capabilities within a single context (Pozzilli et al., 1991). Pozzilli et al. (1991) conducted one of the early studies on the impact of lesions in cognitive impairment in persons with MS. Investigation into the site and lesion load associated with MS was beyond the scope of this dissertation, however is an interesting area for further investigation.

**Research Question 4**

Research Question 4 was, “Do subjective patient ratings of fatigue (VAS-F) and objective EDSS scores correlate with test performance on the FAS task (verbal fluency)?” The question was intended to reconcile the subjective (VAS-F) with the objective EDSS scores and the FAS test performances of verbal fluency. The VAS-F fatigue rating assessment was taken at baseline, at 3 minutes, and at the end of exercising. The VAS-F change score was computed as the difference between the baseline score and the end of exercise score. Of these scores, the one with greatest significance was the FAS (MCLA) variable. The FAS (MCLA) was negatively correlated with the Intervention Fatigue Group and others, but not with the Control Fatigue Group.
The Intervention Fatigue Group scores differed little from the Control Rest Group scores, indicating that a single bout of physical fatigue compromised verbal fluency for people with MS. Tasks requiring high linguistic demands were more vulnerable to fatigue among MS patients, compared to non-MS individuals. This finding was consistent with the findings by Parmentier et al. (2003) and Karpatkin (2013), but contrasts the findings of Krupp and Elkins (2000), who determined that cognitive (rather than physical) exercise benefited the non-MS participants but did not benefit individuals with MS. In the current study, physical exercise diminished the scores for both controls and MS respondents, but more severely for the MS intervention group than for the controls. Parmentier et al. (2003) drew attention to a further variable that could not be incorporated within the tests: the fact that across any given day, people with MS experience different levels of fatigue commensurate with the disease itself and with fluctuating fatigue. Changes in language performance influenced by fluctuations in MS fatigue over the course of a day are an additional area of interest for future research.

Limitations of the Study

Limitations of this dissertation were predominantly associated with the nonrandom small sample size ($n = 17$ intervention, $n = 7$ control), although the demographic balance of the intervention group was commensurate with the national profile (NMSS, n.d.). A linear mixed-effects model would have been valuable in mitigating the nonhomogeneity of variance. Some of the data could not be analyzed and were therefore rendered redundant. Nevertheless, the findings contribute to the field of study and build upon preexisting research.

Another limitation of the current study was the fact that the sample did not include subjects younger than 30 years of age or adults older than 64. MS can affect individuals from
childhood through adulthood; an area for future research could involve using a more representative sample that includes younger adults and adults over 64.

Although this dissertation’s sample included individuals with MS of varying EDSS scores, a limitation of the study was that linguistic performance was not stratified by disease severity. This could be an interesting area for further investigation as currently there is little known association between the severity of physical symptoms and the severity of cognitive deficits in persons with MS (Rao et al., 1985; Rao, 1995; Sliwa & Cohen, 1998).

Another limitation of the current study is the difficulty in differentiating between the effects of cognitive fatigue versus physical fatigue on linguistic performance. Overwhelming, a majority of studies have failed to show that an individual’s perceived level of cognitive fatigue has a predictable effect on performance of cognitive measures, meaning that as a subject’s self-reported level of cognitive fatigue increases, their behavioral performance worsen (Beatty, Goretti, Siracusa, Zipoli, Portaccio, et al., 2003; Jennekens-Schinkel, Sanders, Lanser, Van der Velde, 1988; Johnson, Lange, DeLuca, Korn, Natelson, 1997). To date, there is no known objective measure or validated scale allowing researchers to reliably differentiate between an individual’s perceived cognitive fatigue versus their perceived physical fatigue. Should such a measurement exist, it could validate that the changes in linguistic performance seen in this dissertation were exclusively due to the physical fatigue induced by a single bout of physical excursion.

Lastly, in the research literature an increase in core body temperature as an objective measure has been used to signify that research participants have demonstrated physical exertion (Gonzalez-Alonso et al., 1999, Sumowski & Leavitt, 2014, White et al., 2000). Changes in core body temperature may be an underlying mechanism that results in fatigue. In this study, changes
in core body temperature measured at the tympanic membrane were not significant and may not accurately represent the respondents’ true core body temperature. Authors including White et al. (2000) measured rectal temperature by inserting a thermistor 10 cm past the anal sphincter and found an increase in core body temperature after a short period (2 minutes) of physical exercise. Accurate measurement of core body temperature requires a procedure too invasive (rectal temperature or gastrointestinal temperature) for the participants of this dissertation. The purpose of this study was not to determine the physiologic basis for fatigue in persons with MS but rather to investigate the effects of MS fatigue on expressive language skills. If feasible, future studies could include a requirement for capturing core body temperature as a possible indicator of physical exertion.

**Summary and Conclusion**

The findings from the current study confirm that relatively light physical exertion reduces performance in selected language tests for people with MS. The findings show the impact of fatigue resultant from a single bout of exercise upon the outcome of linguistic assessments. The findings of this research have value specifically in cognitive-linguistic rehabilitation for people with MS.

The assessments used in this dissertation were similar to the evaluation test batteries frequently performed by speech-language pathologists and neuropsychologists as a part of MS care. The VAS-F device was valuable for determining patients’ preexisting perceived fatigue level. The findings may motivate evaluators of MS to divide test batteries into smaller testing units and provide adequate rest between test intervals.

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3 A Spearman’s rho analysis was run between the participants’ baseline and end of exercise core body temperature. The correlation was not significant $r_s = .314, p > .05$. 
The study as a whole therefore confirms the hypothesis that even a single bout of physical activity can impair language function in individuals with MS. Lower scores may be anticipated, compared to the scores of the Control (non-MS) Fatigue Group, even for the Intervention Rest Group. MS negatively affects language performance, and linguistic abilities are worsened when the individual is fatigued. In clinical terms, attention must be paid to the precondition of language intervention to ensure that the MS patient is in an optimal state of rest when assessments are made or interventions are carried out. Further, future researchers should investigate variables such as EDSS ratings, possible links with ethnicity, lesion load, and the type of exercise performed, because these variables may all strongly influence linguistic performance for individuals with MS.

Because fatigue is a common symptom of MS (Claros-Salinas et al., 2013; Schwid et al., 2002), fatigue is likely propagated increased by physical or cognitive activity, thus limiting MS patients’ verbal fluency capacities. Fatigue impairs the executive control required in the verbalization and semantic recall processes (Foong et al., 1997; Matotek, Saling, Gates, & Sedal, 2001; Schwid et al., 2002). Language is a higher order cognitive function requiring greater attention and focus (Parmentier et al., 2003), and therefore, language is vulnerable to a single bout of fatigue induced by physical activity.
### Table 1
*Profile of Cognitive Deficits in Multiple Sclerosis*

<table>
<thead>
<tr>
<th>Cognitive Function</th>
<th>Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention and distractibility</td>
<td>Attention for simple tasks is generally preserved. With increased task difficulty and complexity, deficits with attention and concentration are likely to occur. Problems arise when individuals with MS are asked to attend to more than one thing at a time (such as office or household environments). Specifically, individuals with MS have difficulty attending to tasks in noise. Distractibility is problematic. Often these individuals work best in quiet, distraction-free environments.</td>
</tr>
<tr>
<td>Processing speed</td>
<td>Many people with MS experience a reduction in the rate of information processing. Some individuals describe a lag in time between when they recognize the need to say or do something and when their body physically reacts.</td>
</tr>
<tr>
<td>Memory</td>
<td>Individual with MS typically have difficulty with procedural memory as well as semantic memory.</td>
</tr>
</tbody>
</table>

### Table 2
*Description of Language Performance Measures*

<table>
<thead>
<tr>
<th>Name of Measure</th>
<th>Sample</th>
<th>Number of stimuli</th>
<th>Time</th>
<th>Skill(s) Measured</th>
<th>Data Collection Tool(s)</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid Naming Subtest (CTOPP)</strong></td>
<td>Normed on a sample of 1,900 individuals ages 4-65 including individuals classified with exceptionality status.</td>
<td>144 total items (Test Form A or B)</td>
<td>10 minutes</td>
<td>Confrontation &amp; rapid naming (Letters, numbers, colors, objects)</td>
<td>Digit recording</td>
<td>Response Time (% correct)</td>
</tr>
<tr>
<td><strong>EVT-2</strong></td>
<td>Normed on a sample of 1,451 examinees from 2 years and 6 months through 61 years old. Twenty percent of the sample had a special-education classification or a neurological disorder.</td>
<td>190 total items (Test Form A or B)</td>
<td>25 minutes</td>
<td>Expressive vocabulary in 20 content areas (e.g., actions, vegetables, tools), parts of speech (nouns, verbs, attributes), and the community</td>
<td>Digit Recording</td>
<td>Response Time (% correct)</td>
</tr>
<tr>
<td><strong>FAS (MCLA)</strong></td>
<td>Normed using a sample size of 204 people ranging in age from 16-77. Half of respondents had a head injury or neurologic involvement.</td>
<td>3 items</td>
<td>3 minutes</td>
<td>Verbal fluency (phonemic, categorical, divergent)</td>
<td>Digit recording</td>
<td>% correct</td>
</tr>
<tr>
<td><strong>Picture Description (BDAE and MCLA)</strong></td>
<td>BDAE-Normative sample of 242 patients, 50% with aphasic symptoms. MCLA-Normed using a sample size of 204 people ranging in age from 16-77. Half of respondents had a head injury or neurologic involvement.</td>
<td>Cookie Theft (BDAE)</td>
<td>2 minutes</td>
<td>Narrative composition</td>
<td>Digit recording</td>
<td>Response DRS</td>
</tr>
<tr>
<td>Office Scene (MCLA)</td>
<td></td>
<td></td>
<td></td>
<td>Syntax</td>
<td>Scoring form</td>
<td></td>
</tr>
<tr>
<td><strong>Total testing time</strong></td>
<td></td>
<td></td>
<td></td>
<td>Digit recording</td>
<td>Scoring form</td>
<td></td>
</tr>
</tbody>
</table>

30 total minutes
Table 3
*Phase 1: The Fatigue Condition—Counterbalanced Methodology*

<table>
<thead>
<tr>
<th>Condition A</th>
<th>Condition B</th>
<th>Condition C</th>
<th>Condition D</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVT-2 (Form A)</td>
<td>Picture Description (Office Scene)</td>
<td>Rapid Naming Subtest (CTOPP) (Form A)</td>
<td>FAS (MCLA) (phonemic, categorical, divergent)</td>
</tr>
<tr>
<td>Rapid Naming Subtest (CTOPP) (Form A)</td>
<td>FAS (MCLA) (phonemic, categorical, divergent)</td>
<td>Picture Description (Office Scene)</td>
<td>EVT-2 (Form A)</td>
</tr>
<tr>
<td>FAS (MCLA) (phonemic, categorical, divergent)</td>
<td>Rapid Naming Subtest (CTOPP) (Form A)</td>
<td>EVT-2 (Form A)</td>
<td>Picture Description (Office Scene)</td>
</tr>
<tr>
<td>Picture Description (Office Scene)</td>
<td>EVT-2 (Form A)</td>
<td>FAS (MCLA) (phonemic, categorical, divergent)</td>
<td>Rapid Naming Subtest (CTOPP) (Form A)</td>
</tr>
<tr>
<td>Participants 1, 5, 9, 13, 17, 21</td>
<td>Participants 2, 6, 10, 14, 18, 22</td>
<td>Participants 3, 7, 11, 15, 19, 23</td>
<td>Participants 4, 8, 12, 16, 20, 24</td>
</tr>
</tbody>
</table>
Table 4
*Phase 2: The Rest Condition—Counterbalanced Methodology*

<table>
<thead>
<tr>
<th>Condition A</th>
<th>Condition B</th>
<th>Condition C</th>
<th>Condition D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Picture Description (Cookie Theft)</td>
<td>EVT-2 (Form B)</td>
<td>FAS (MCLA) (categorical, divergent, phonemic)</td>
<td>Rapid Naming Subtest (CTOPP-2) (Form B)</td>
</tr>
<tr>
<td>FAS (MCLA) (categorical, divergent, phonemic)</td>
<td>Rapid Naming Subtest</td>
<td>EVT-2 (Form B)</td>
<td>Picture Description (Cookie Theft)</td>
</tr>
<tr>
<td></td>
<td>(CTOPP-2) (Form B)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid Naming Subtest (CTOPP-2) (Form B)</td>
<td>FAS (MCLA) (categorical, divergent, phonemic)</td>
<td>Picture Description (Cookie Theft)</td>
<td>EVT-2 (Form B)</td>
</tr>
<tr>
<td>EVP-2 (Form B)</td>
<td>Picture Description</td>
<td>Rapid Naming Subtest (CTOPP-2) (Form B)</td>
<td>FAS (MCLA) (categorical, divergent, phonemic)</td>
</tr>
<tr>
<td></td>
<td>(Cookie Theft)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants 1, 5, 9, 13, 17, 21</td>
<td>Participants 2, 6, 10, 14, 18, 22</td>
<td>Participants 3, 7, 11, 15, 19, 23</td>
<td>Participants 4, 8, 12, 16, 20, 24</td>
</tr>
</tbody>
</table>
Table 5
*Descriptive Statistics: Type of Multiple Sclerosis (MS) for Intervention Group*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of MS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary-progressive (PP)</td>
<td>5</td>
<td>29.4</td>
</tr>
<tr>
<td>Relapsing-remitting (RR)</td>
<td>12</td>
<td>70.6</td>
</tr>
</tbody>
</table>
Table 6
*Descriptive Statistics: Gender and Ethnicity of Intervention and Control Group*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention (n = 17)</th>
<th>Control (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>Percentage</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>29.4</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>70.6</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White/Caucasian</td>
<td>11</td>
<td>64.7</td>
</tr>
<tr>
<td>Black/African American</td>
<td>6</td>
<td>35.3</td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

(N = 24)
Table 7
*Descriptive Statistics: Age & Education of Intervention and Control Group*

<table>
<thead>
<tr>
<th>Variable</th>
<th>$n$</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention Group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in years)</td>
<td>17</td>
<td>51.41</td>
<td>9.57</td>
<td>32.00</td>
<td>65.00</td>
</tr>
<tr>
<td>Education (in years)</td>
<td>17</td>
<td>15.59</td>
<td>1.94</td>
<td>9.00</td>
<td>17.00</td>
</tr>
<tr>
<td><strong>Control Group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in years)</td>
<td>7</td>
<td>48.15</td>
<td>12.00</td>
<td>31.00</td>
<td>64.00</td>
</tr>
<tr>
<td>Education (in years)</td>
<td>7</td>
<td>14.71</td>
<td>2.06</td>
<td>12.00</td>
<td>17.00</td>
</tr>
</tbody>
</table>

(N = 24)
Table 8

Descriptive Statistics: Expanded Disability Status Scale (EDSS) of Intervention Group (N = 17)

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>M</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Zsk</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDSS</td>
<td>17</td>
<td>5.50</td>
<td>1.36</td>
<td>3.00</td>
<td>7.50</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*Note. Zsk = Z skewness score, calculated by dividing skewness by skewness standard error. See Addendum A for EDSS score interruptions*
Table 9
Descriptive Statistics: FAS (MCLA) Study Variables

<table>
<thead>
<tr>
<th>Variables - Description</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Z_{sk}</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FAS (MCLA)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal Fluency - Phonemic Category Naming Total (PS1T)</td>
<td>48.00</td>
<td>24.32</td>
<td>21.00</td>
<td>156.00</td>
<td>7.71</td>
</tr>
<tr>
<td>Verbal Fluency - Phonemic Category Naming Errors (PS1E)</td>
<td>4.08</td>
<td>3.72</td>
<td>0.00</td>
<td>15.00</td>
<td>3.19</td>
</tr>
<tr>
<td>Verbal Fluency - Phonemic Category Naming Total Correct (PSTC)</td>
<td>44.96</td>
<td>23.80</td>
<td>20.00</td>
<td>146.00</td>
<td>7.06</td>
</tr>
<tr>
<td>Verbal Fluency - Phonemic Category Naming Mean Comparison Score (PS1M)</td>
<td>0.69</td>
<td>0.47</td>
<td>0.00</td>
<td>1.00</td>
<td>N/A</td>
</tr>
<tr>
<td>Verbal Fluency - Rapid Country Naming Total (CS1T)</td>
<td>20.44</td>
<td>9.82</td>
<td>4.00</td>
<td>46.00</td>
<td>1.52</td>
</tr>
<tr>
<td>Verbal Fluency - Rapid Country Naming Errors (CS1E)</td>
<td>2.21</td>
<td>1.95</td>
<td>0.00</td>
<td>7.00</td>
<td>2.90</td>
</tr>
<tr>
<td>Verbal Fluency - Rapid Country Naming Total Correct (CS1TC)</td>
<td>18.23</td>
<td>10.26</td>
<td>1.00</td>
<td>43.00</td>
<td>1.01</td>
</tr>
<tr>
<td>Verbal Fluency - Rapid Country Naming Mean Comparison Score (CS1M)</td>
<td>0.56</td>
<td>0.50</td>
<td>0.00</td>
<td>1.00</td>
<td>N/A</td>
</tr>
<tr>
<td>Verbal Fluency - Divergent Naming Total (DS1T)</td>
<td>12.06</td>
<td>4.79</td>
<td>5.00</td>
<td>24.00</td>
<td>2.01</td>
</tr>
<tr>
<td>Verbal Fluency - Divergent Naming Error (DS1E)</td>
<td>1.88</td>
<td>2.34</td>
<td>0.00</td>
<td>11.00</td>
<td>5.34</td>
</tr>
<tr>
<td>Verbal Fluency - Divergent Naming Total Correct (DS1TC)</td>
<td>10.00</td>
<td>4.41</td>
<td>0.00</td>
<td>23.00</td>
<td>2.53</td>
</tr>
<tr>
<td>Verbal Fluency - Divergent Naming Mean Comparison Score (DS1M)</td>
<td>0.67</td>
<td>0.48</td>
<td>0.00</td>
<td>1.00</td>
<td>N/A</td>
</tr>
<tr>
<td>Verbal Fluency - Phonemic Category Naming Manual Mean (PS1MEAN)</td>
<td>47.79</td>
<td>5.72</td>
<td>33.00</td>
<td>61.0</td>
<td>0.59</td>
</tr>
<tr>
<td>Verbal Fluency - Phonemic Category Naming Manual SD (PS1SD)</td>
<td>12.48</td>
<td>3.33</td>
<td>2.50</td>
<td>19.00</td>
<td>-2.53</td>
</tr>
<tr>
<td>Verbal Fluency - Phonemic Category Participant SD from Manual Mean (PS1SDM)</td>
<td>0.042</td>
<td>2.14</td>
<td>-2.63</td>
<td>6.80</td>
<td>5.45</td>
</tr>
<tr>
<td>Variables - Description</td>
<td>Mean</td>
<td>SD</td>
<td>Minimum</td>
<td>Maximum</td>
<td>Zsk</td>
</tr>
<tr>
<td>--------------------------------------------------------------</td>
<td>------</td>
<td>------</td>
<td>---------</td>
<td>---------</td>
<td>-----</td>
</tr>
<tr>
<td><strong>FAS (MCLA)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal Fluency - Rapid Country Naming Manual Mean (CS1MEAN)</td>
<td>22.92</td>
<td>3.67</td>
<td>19.00</td>
<td>30.00</td>
<td>2.24</td>
</tr>
<tr>
<td>Verbal Fluency- Country Naming Manual SD (CS1SD)</td>
<td>6.77</td>
<td>1.69</td>
<td>4.00</td>
<td>10.00</td>
<td>0.57</td>
</tr>
<tr>
<td>Verbal Fluency- Country Naming Participant SD from Manual Mean (CS1SDM)</td>
<td>-4.06</td>
<td>24.69</td>
<td>-171.00</td>
<td>6.00</td>
<td>-20.12</td>
</tr>
<tr>
<td>Verbal Fluency- Divergent Naming Manual Mean (DS1MEAN)</td>
<td>11.00</td>
<td>1.69</td>
<td>8.00</td>
<td>15.00</td>
<td>1.66</td>
</tr>
<tr>
<td>Verbal Fluency- Divergent Naming Manual SD (DS1SD)</td>
<td>3.66</td>
<td>1.59</td>
<td>0.00</td>
<td>5.90</td>
<td>-2.71</td>
</tr>
<tr>
<td>Verbal Fluency- Divergent Naming Participant SD from Manual Mean (DS1SDM)</td>
<td>-0.091</td>
<td>1.49</td>
<td>-2.10</td>
<td>6.63</td>
<td>6.94</td>
</tr>
</tbody>
</table>

(N =24)

*Note.* $Z_{sk}$ = $Z$ skewness score were calculated by dividing skewness by skewness standard error. Bold and italicized scales were used for hypothesis testing. N/A: dichotomous variable, skewness not relevant.
Table 10

Descriptive Statistics: EVT-2 Study Variables

<table>
<thead>
<tr>
<th>EVT-2 Form- EVT2 Error (ES100)</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Zsk</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVT-2 Form- EVT2 Error (ES100)</td>
<td>38.44</td>
<td>16.48</td>
<td>12.00</td>
<td>89.00</td>
<td>2.24</td>
</tr>
<tr>
<td>EVT-2 Form- Total Time (in Seconds)</td>
<td>1322.57</td>
<td>228.32</td>
<td>900.10</td>
<td>1984.00</td>
<td>2.54</td>
</tr>
</tbody>
</table>

(N =24)

Note. Zsk = Z skewness score were calculated by dividing skewness by skewness standard error. Bold and italicized scales were used for hypothesis testing. N/A: dichotomous variable, skewness not relevant.
Table 11
Descriptive Statistics: CTOPP-2 Study Variables

<table>
<thead>
<tr>
<th>CTOPP-2</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Zsk</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTOPP-2- Rapid Digit Naming</td>
<td>16.84</td>
<td>6.45</td>
<td>1.30</td>
<td>46.02</td>
<td>6.40</td>
</tr>
<tr>
<td>Total Time (C4TT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CTOPP-2 C4TT Recoded</strong></td>
<td>4.44</td>
<td>1.76</td>
<td>1.00</td>
<td>7.00</td>
<td>0.01</td>
</tr>
<tr>
<td>CTOPP-2 Rapid Letter Naming</td>
<td>18.93</td>
<td>8.08</td>
<td>10.00</td>
<td>55.82</td>
<td>8.53</td>
</tr>
<tr>
<td>Total Time (C6TT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTOPP-2 C6TT Recoded</td>
<td>4.65</td>
<td>1.86</td>
<td>1.00</td>
<td>7.00</td>
<td>0.01</td>
</tr>
<tr>
<td>CTOPP-2 – Rapid Color Naming</td>
<td>27.21</td>
<td>7.03</td>
<td>18.42</td>
<td>55.00</td>
<td>4.93</td>
</tr>
<tr>
<td>Total Time (C7TT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CTOPP-2 C7TT Recoded</strong></td>
<td>4.46</td>
<td>1.68</td>
<td>1.00</td>
<td>7.00</td>
<td>-0.93</td>
</tr>
<tr>
<td>CTOPP-2 – Rapid Object Naming</td>
<td>29.67</td>
<td>7.77</td>
<td>18.94</td>
<td>55.22</td>
<td>3.18</td>
</tr>
<tr>
<td>Total Time (C9TT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CTOPP-2 C9TT Recoded</strong></td>
<td>4.19</td>
<td>1.68</td>
<td>1.00</td>
<td>7.00</td>
<td>0.16</td>
</tr>
</tbody>
</table>

(N =24)

CTOPP C4TT recoding: 1.30-10.77: 1; 11.07-12.10: 2; 13.08-13.94: 3; 14.00-16.00: 4; 16.23-17.82: 5; 18.05-19.90: 6; 20.42-46.02: 7; CTOPP C6TT Recoding: 10.00-11.19: 1; 12.00-12.95: 2; 13.80-14.60: 3; 15.00-16.67: 4; 17.00-18.71: 5; 19.17-20.84: 6; 21.17-55.82: 7; CTOPP C7TT Recoding: 18.42-18.69: 1; 19.11-19.50: 2; 21.33-22.76: 3; 23.00-25.95: 4; 26.14-27.99: 5; 28.00-34.00: 6; 37.22-55.00: 7; CTOPP C9TT Recoding: 18.94-19.30: 1; 20.31-21.81: 2; 22.36-25.71: 3; 26.67-29.64: 4; 30.00-33.70: 5; 34.48-36.95: 6; 41.00-55.22: 7. Picture RS1SD Recoding: .0: 1; .4-1.1: 2, dichotomous coding was 1 & 2 as 0 existed in data; RS1SDM Recoding .45-.20: 1; .16-.10: 2; .09-.20: 3; 0: 4; .90: 5.

Note. Zsk = Z skewness score were calculated by dividing skewness by skewness standard error. Bold and italicized scales were used for hypothesis testing. N/A: dichotomous variable, skewness not relevant.
Table 12
**Descriptive Statistics: Picture Description Study Variables**

<table>
<thead>
<tr>
<th>Picture Description</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Z(_{sk})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Picture Des. – Discourse Rating Scale Manual Mean (RS1Mean)</td>
<td>15.32</td>
<td>35.36</td>
<td>0.60</td>
<td>100.00</td>
<td>6.04</td>
</tr>
<tr>
<td>Picture Des. RS1Mean Recoded</td>
<td>44.83</td>
<td>0.38</td>
<td>44.00</td>
<td>45.00</td>
<td>N/A</td>
</tr>
<tr>
<td>Picture Des. – Discourse Rating Scale SD from Manual (RS1SD)</td>
<td>0.41</td>
<td>0.43</td>
<td>0.00</td>
<td>1.10</td>
<td>1.10</td>
</tr>
<tr>
<td>Picture Des. RS1SD Recoded</td>
<td>1.54</td>
<td>0.50</td>
<td>1.00</td>
<td>2.00</td>
<td>N/A</td>
</tr>
<tr>
<td>Picture Des. – Discourse Rating Scale Participant SD from Manual (RS1 SDM)</td>
<td>−6.47</td>
<td>9.62</td>
<td>−45.00</td>
<td>0.90</td>
<td>−6.32</td>
</tr>
<tr>
<td>Picture Des. RS1SDM Recoded</td>
<td>3.02</td>
<td>1.02</td>
<td>1.00</td>
<td>5.00</td>
<td>1.22</td>
</tr>
</tbody>
</table>

(N =24)

*Note. Z\(_{sk}\) = Z skewness score were by dividing skewness by skewness standard error. Bold and italicized scales were used for hypothesis testing. N/A: dichotomous variable, skewness not relevant.*

Table 13
**Descriptive Statistics: VAS-F Study Variables**

<table>
<thead>
<tr>
<th>VAS-F</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Z(_{sk})</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS-F- Fatigue Rating at 3 Min (3 Minute Score)</td>
<td>31.67</td>
<td>25.65</td>
<td>0.00</td>
<td>77.00</td>
<td>0.89</td>
</tr>
<tr>
<td>VAS-F- Total Time of Exercise (Time in Minutes Score)</td>
<td>5.16</td>
<td>2.60</td>
<td>3.04</td>
<td>8.43</td>
<td>1.72</td>
</tr>
<tr>
<td>VAS-F-Baseline vs End (Change Score)</td>
<td>13.85</td>
<td>21.55</td>
<td>−28.00</td>
<td>55.00</td>
<td>0.89</td>
</tr>
</tbody>
</table>

(N =24)

*Note. Z\(_{sk}\) = Z skewness score were calculated by dividing skewness by skewness standard error. Bold and italicized scales were used for hypothesis testing. N/A: dichotomous variable, skewness not relevant.*
Table 14
*Pearson Bivariate Correlation Coefficients: Multicollinearity Between FAS (MCLA) Verbal Fluency Variables*

<table>
<thead>
<tr>
<th>Variable 1</th>
<th>Variable 2</th>
<th>$r$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS1T</td>
<td>PSTC</td>
<td>.94*</td>
</tr>
<tr>
<td>PS1T</td>
<td>PS1M</td>
<td>.82*</td>
</tr>
<tr>
<td>PS1T</td>
<td>PS1SDM</td>
<td>.80*</td>
</tr>
<tr>
<td>PSTC</td>
<td>PS1M</td>
<td>.80*</td>
</tr>
<tr>
<td>PSTC</td>
<td>PS1SDM</td>
<td>.85*</td>
</tr>
<tr>
<td>PS1M</td>
<td>PS1SDM</td>
<td>.81*</td>
</tr>
<tr>
<td>CS1T</td>
<td>CS1TC</td>
<td>.98*</td>
</tr>
<tr>
<td>CS1E</td>
<td>CS1SDM</td>
<td>.99*</td>
</tr>
<tr>
<td>DS1T</td>
<td>DS1E</td>
<td>.81*</td>
</tr>
<tr>
<td>DS1T</td>
<td>DS1TC</td>
<td>.82*</td>
</tr>
<tr>
<td>DS1TC</td>
<td>DS1M</td>
<td>.81*</td>
</tr>
<tr>
<td>DS1TC</td>
<td>DS1SDM</td>
<td>.81*</td>
</tr>
<tr>
<td>PS1Mean</td>
<td>CS1Mean</td>
<td>.86*</td>
</tr>
<tr>
<td>CS1SD</td>
<td>DS1Mean</td>
<td>.93*</td>
</tr>
<tr>
<td>CS1SD</td>
<td>DS1SD</td>
<td>.83*</td>
</tr>
<tr>
<td>DS1Mean</td>
<td>DS1SD</td>
<td>.84*</td>
</tr>
</tbody>
</table>

(N = 24)

*p < .001
Table 15
One-way MANOVA: Group Differences on EVT-2 Variables

<table>
<thead>
<tr>
<th>Source</th>
<th>Dependent Variable</th>
<th>F</th>
<th>df</th>
<th>p</th>
<th>$\eta^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>EVT-2</td>
<td>4.97*</td>
<td>3, 44</td>
<td>.005</td>
<td>.253</td>
</tr>
<tr>
<td></td>
<td>EVT-2 time (in seconds)</td>
<td>1.74</td>
<td>3, 44</td>
<td>.173</td>
<td>.106</td>
</tr>
</tbody>
</table>

(N = 24)
Note. *illustrates significant results.

Table 16
One-way MANOVA: Group Differences on FAS (MCLA) Variables

<table>
<thead>
<tr>
<th>Source</th>
<th>Dependent Variable</th>
<th>F</th>
<th>df</th>
<th>p</th>
<th>$\eta^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>PS1M</td>
<td>3.44*</td>
<td>3, 44</td>
<td>.025</td>
<td>.190</td>
</tr>
<tr>
<td></td>
<td>CS1E</td>
<td>1.18</td>
<td>3, 44</td>
<td>.330</td>
<td>.074</td>
</tr>
<tr>
<td></td>
<td>CS1TC</td>
<td>1.19</td>
<td>3, 44</td>
<td>.324</td>
<td>.075</td>
</tr>
<tr>
<td></td>
<td>CS1M</td>
<td>0.88</td>
<td>3, 44</td>
<td>.458</td>
<td>.057</td>
</tr>
<tr>
<td></td>
<td>DS1T</td>
<td>2.58</td>
<td>3, 44</td>
<td>.066</td>
<td>.149</td>
</tr>
<tr>
<td></td>
<td>DS1M</td>
<td>6.44*</td>
<td>3, 44</td>
<td>.001</td>
<td>.305</td>
</tr>
<tr>
<td></td>
<td>PS1Mean</td>
<td>1.46</td>
<td>3, 44</td>
<td>.240</td>
<td>.090</td>
</tr>
<tr>
<td></td>
<td>PS1SD</td>
<td>2.08</td>
<td>3, 44</td>
<td>.117</td>
<td>.124</td>
</tr>
</tbody>
</table>

(N = 24)
* illustrates significant results.
Table 17
One-way MANOVA: Group Differences on Picture Description Variables

<table>
<thead>
<tr>
<th>Source</th>
<th>Dependent Variable</th>
<th>$F$</th>
<th>$df$</th>
<th>$p$</th>
<th>$\eta^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>RS1</td>
<td>2.71</td>
<td>3,44</td>
<td>.061</td>
<td>.161</td>
</tr>
<tr>
<td></td>
<td>RS1 Mean</td>
<td>0.03</td>
<td>3,44</td>
<td>.995</td>
<td>.002</td>
</tr>
<tr>
<td></td>
<td>RS1SD Recoded</td>
<td>0.02</td>
<td>3,44</td>
<td>.996</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>RS1SDM Recoded</td>
<td>9.86*</td>
<td>3,44</td>
<td>&lt; .001</td>
<td>.402</td>
</tr>
</tbody>
</table>

(N = 24)
* illustrates significant results.

Table 18
One-way MANOVA: Group Differences on CTOPP-2 Variables

<table>
<thead>
<tr>
<th>Source</th>
<th>Dependent Variable</th>
<th>$F$</th>
<th>$df$</th>
<th>$p$</th>
<th>$\eta^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C4TT</td>
<td>0.65</td>
<td>3,44</td>
<td>.590</td>
<td>.042</td>
</tr>
<tr>
<td></td>
<td>C7TT</td>
<td>2.97*</td>
<td>3,44</td>
<td>.042</td>
<td>.168</td>
</tr>
<tr>
<td></td>
<td>C9TT</td>
<td>3.20*</td>
<td>3,44</td>
<td>.032</td>
<td>.179</td>
</tr>
</tbody>
</table>

(N = 24)
* illustrates significant results.
### Table 19

*Pearson Bivariate Correlation for the Intervention Fatigue Group: FAS (MCLA) Variables and VAS-F and EDSS Variables*

<table>
<thead>
<tr>
<th>FAS (MCLA) Variables</th>
<th>VAS-F 3 Minutes</th>
<th>VAS-F (in Seconds)</th>
<th>VAS-F Change Score&lt;sup&gt;a&lt;/sup&gt;</th>
<th>EDSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS1M</td>
<td>-.37</td>
<td>.06</td>
<td>-.53&lt;sup&gt;*&lt;/sup&gt;</td>
<td>.05</td>
</tr>
<tr>
<td>CS1E</td>
<td>-.14</td>
<td>-.00</td>
<td>-.17</td>
<td>.34</td>
</tr>
<tr>
<td>CS1TC</td>
<td>.45</td>
<td>.36</td>
<td>.38</td>
<td>-.05</td>
</tr>
<tr>
<td>CS1M</td>
<td>-.04</td>
<td>.16</td>
<td>.00</td>
<td>.05</td>
</tr>
<tr>
<td>DS1T</td>
<td>-.25</td>
<td>-.29</td>
<td>-.13</td>
<td>-.19</td>
</tr>
<tr>
<td>DS1M</td>
<td>-.30</td>
<td>-.07</td>
<td>-.19</td>
<td>-.42</td>
</tr>
<tr>
<td>PS1Mean</td>
<td>.02</td>
<td>-.11</td>
<td>-.02</td>
<td>-.20</td>
</tr>
<tr>
<td>PS1SD</td>
<td>.32</td>
<td>.29</td>
<td>.41</td>
<td>.30</td>
</tr>
</tbody>
</table>

<sup>(N = 17)  
* p < .05.  
<sup>a</sup> VAS-F change scores were calculated by subtracting baseline VAS-F scores from VAS-F end scores.
Table 20
*Pearson Bivariate Correlations for Control Fatigue Group: FAS (MCLA) and VAS-F Variables*

<table>
<thead>
<tr>
<th>FAS (MCLA) Variables</th>
<th>VAS-F 3 Minutes</th>
<th>VAS-F (in Seconds)</th>
<th>VAS-F Change Score&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS1E</td>
<td>.56</td>
<td>.02</td>
<td>.66</td>
</tr>
<tr>
<td>CS1TC</td>
<td>.42</td>
<td>.59</td>
<td>.38</td>
</tr>
<tr>
<td>CS1M</td>
<td>.65</td>
<td>.59</td>
<td>.65</td>
</tr>
<tr>
<td>DS1T</td>
<td>.58</td>
<td>.37</td>
<td>.47</td>
</tr>
<tr>
<td>PS1Mean</td>
<td>.27</td>
<td>.09</td>
<td>.27</td>
</tr>
<tr>
<td>PS1SD</td>
<td>.69</td>
<td>.46</td>
<td>.64</td>
</tr>
</tbody>
</table>

<sup>(N = 7)</sup>

*<sup>p</sup> < .05.

<sup>a</sup> VASF change scores were calculated by subtracting baseline VAS-F scores from VAS-F end scores.
Table 21
*Pearson Bivariate Correlations for the Intervention Rest Group: FAS (MCLA) and VAS-F Variables*

<table>
<thead>
<tr>
<th>FAS (MCLA) Variables</th>
<th>VAS-F 3 Minutes</th>
<th>VAS-F (in Seconds)</th>
<th>VAS-F Change Score&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS1M</td>
<td>.17</td>
<td>.37</td>
<td>-.27</td>
</tr>
<tr>
<td>CS1E</td>
<td>-.01</td>
<td>.12</td>
<td>.12</td>
</tr>
<tr>
<td>CS1TC</td>
<td>-.00</td>
<td>.11</td>
<td>-.63**</td>
</tr>
<tr>
<td>CS1M</td>
<td>-.04</td>
<td>-.01</td>
<td>-.31</td>
</tr>
<tr>
<td>DS1T</td>
<td>-.31</td>
<td>.00</td>
<td>-.32</td>
</tr>
<tr>
<td>DS1M</td>
<td>-.21</td>
<td>-.15</td>
<td>-.02</td>
</tr>
<tr>
<td>PS1Mean</td>
<td>-.19</td>
<td>-.11</td>
<td>-.58*</td>
</tr>
<tr>
<td>PS1SD</td>
<td>.13</td>
<td>.26</td>
<td>.03</td>
</tr>
</tbody>
</table>

<sup>a</sup>VASF change scores were calculated by subtracting baseline VAS-F scores from VAS-F end scores.

(N = 17)
*<sup>p</sup> < .05, **<sup>p</sup> < .01.

* <sup>a</sup>VASF change scores were calculated by subtracting baseline VAS-F scores from VAS-F end scores.
Table 22
*Pearson Bivariate Correlation for the Control Rest Group: FAS (MCLA) and VAS-F Variables*

<table>
<thead>
<tr>
<th>FAS (MCLA) Variables</th>
<th>VAS-F 3 Minutes</th>
<th>VAS-F (in Seconds)</th>
<th>VAS-F Change Score&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS1E</td>
<td>-.12</td>
<td>-.47</td>
<td>.14</td>
</tr>
<tr>
<td>CS1TC</td>
<td>.04</td>
<td>.47</td>
<td>-.60</td>
</tr>
<tr>
<td>CS1M</td>
<td>-.03</td>
<td>.36</td>
<td>-.71</td>
</tr>
<tr>
<td>DS1T</td>
<td>.79*</td>
<td>.42</td>
<td>.02</td>
</tr>
<tr>
<td>PS1Mean</td>
<td>-.22</td>
<td>.09</td>
<td>-.93**</td>
</tr>
<tr>
<td>PS1SD</td>
<td>-.11</td>
<td>.46</td>
<td>-.85*</td>
</tr>
</tbody>
</table>

(N = 7)
* p < .05, ** p < .01.

<sup>a</sup> VASF change scores were calculated by subtracting baseline VAS-F scores from VAS-F end scores.

Table 23
*Pearson Bivariate Correlations: Significant Correlations by Groups*

<table>
<thead>
<tr>
<th>Group</th>
<th>Significant Correlations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention Fatigue</td>
<td>PS1M and VASF change score, $r(17) = .53, p = .031$</td>
</tr>
<tr>
<td>Control Fatigue</td>
<td>None</td>
</tr>
</tbody>
</table>
| Intervention Rest   | CS1TC and VASF change score, $r(17) = .63, p = .007$  
|                     | PS1Mean and VASF change score, $r(17) = .58, p = .014$ |
| Control Rest        | DS1T and VASF 3 minute score, $r(17) = .79, p = .035$  
|                     | PS1Mean and VASF change score, $r(17) = .93, p = .002$  
|                     | PS1SD and VASF change score, $r(17) = .85, p = .014$  |

(N = 24)
<table>
<thead>
<tr>
<th>Source</th>
<th>Dependent Variable</th>
<th>F</th>
<th>df</th>
<th>p</th>
<th>η²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>VAS-F 3 minute score</td>
<td>2.68</td>
<td>3,44</td>
<td>.059</td>
<td>.154</td>
</tr>
<tr>
<td></td>
<td>VAS-F time (in seconds)</td>
<td>0.07</td>
<td>3,44</td>
<td>.974</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>VAS-F change score</td>
<td>14.87*</td>
<td>3,44</td>
<td>&lt; .001</td>
<td>.503</td>
</tr>
</tbody>
</table>

(N = 24)
* illustrates significant results
APPENDIX A:

VISUAL LOG FATIGUE SCALE

Directions: Please make a cross through the point on the line below which best represents your fatigue at this moment.

Less Fatigue .................................................. More Fatigue

73
APPENDIX B:

BARRERA DISSERTATION CASE HISTORY FATIGUE CONDITION

**ADULT CASE HISTORY**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Date of Birth:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Address:</th>
<th>City:</th>
<th>State:</th>
<th>Zip:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Home Telephone:</th>
<th>Work or Cell Phone:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Multiple Sclerosis, date of onset, and disease type:

Current Medications including MS disease modifying therapies. Specifically, do you take any anti-fatigue medications?

Additional Medical Conditions:

Allergies (seasonal, environmental, medications):

<table>
<thead>
<tr>
<th>Race</th>
<th>Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>Less than High School Education</td>
</tr>
<tr>
<td>African American</td>
<td>High School Education</td>
</tr>
<tr>
<td>Hispanic</td>
<td>College Education</td>
</tr>
<tr>
<td>Caucasian</td>
<td>Advance Degree (Masters, PhD)</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>Other (please specify)</td>
</tr>
</tbody>
</table>
Marital Status | Family
---|---
| Single | Name of Spouse/Kin |
| Married | Number of Children |
| Separated/Divorced | Name of Home |
| Widow | Health Aide |

Occupation

Who do you currently live with?

Are you mono-lingual? Yes or no? If so, what other languages do you speak?

**Medical History:**

Please describe any recent hospitalizations, accidents, surgeries or serious injuries?

Please describe any recent hospitalizations due to MS?

How many exacerbations have you have experienced over your disease courses?
When were these exacerbations?

Have you participated in PT, OT, SLP? If so when?
Is there a personal history of any of the following?

<table>
<thead>
<tr>
<th>Hearing Loss:</th>
<th>Swallowing Disorder:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speech Problem:</td>
<td>Seizure Disorder:</td>
</tr>
<tr>
<td>Learning Disability:</td>
<td>Mental Illness:</td>
</tr>
<tr>
<td>Neurological Condition:</td>
<td>Alcoholism/Drug Use:</td>
</tr>
<tr>
<td>High Blood Pressure:</td>
<td>Stroke/Heart Attack:</td>
</tr>
</tbody>
</table>

Please describe any respiratory/breathing problems you may have.

Who is your neurologist?

When is the last time you saw your neurologist?

Please explain any additional information that we may feel is important to your participation in the study?
APPENDIX C:

BARRERA DISSERTATION CASE HISTORY REST CONDITION

ADULT CASE HISTORY

Name: ________________________ Date of Birth: ________________________

Multiple Sclerosis, has there been any complications since the last session?

Since the last session have you been diagnosed with any additional medical conditions?

Since the last session has there been any changes to your medications including MS disease modifying therapies (or anti-fatigue medications):

Since the last session have you experienced any allergies (seasonal, environmental, medications):

Social Information

Have there been any changes in your occupation since the last session?

Since the last session has there been any changes in your living situation?
Medical History:

Since the last session have you had any hospitalizations, accidents, surgeries or serious injuries?

Since the last session have you had any hospitalizations due to MS?

Have you experienced any exacerbations since the last session?

Since the last session have you started or changed your PT, OT, SLP services?

Since the last session have your experienced any respiratory/breathing.

Since the last session have your seen your neurologist? Have they recommended any changes to your plan of care?

Please explain any additional information that we may feel is important to your participation in the study?
APPENDIX D:

KURTZKE FUNCTIONAL SYSTEMS SCORES (FSS)

Pyramidal Functions

0 - Normal
1 - Abnormal signs without disability
2 - Minimal disability
3 - Mild to moderate paraparesis or hemiparesis (detectable weakness but most function sustained for short periods, fatigue a problem); severe monoparesis (almost no function)
4 - Marked paraparesis or hemiparesis (function is difficult), moderate quadriparesis (function is decreased but can be sustained for short periods); or monoplegia
5 - Paraplegia, hemiplegia, or marked quadriparesis
6 - Quadriplegia
9 - (Unknown)

Cerebellar Functions

0 - Normal
1 - Abnormal signs without disability
2 - Mild ataxia (tremor or clumsy movements easily seen, minor interference with function)
3 - Moderate truncal or limb ataxia (tremor or clumsy movements interfere with function in all spheres)
4 - Severe ataxia in all limbs (most function is very difficult)
5 - Unable to perform coordinated movements due to ataxia
9 - (Unknown)

Record #1 in small box when weakness (grade 3 or worse on pyramidal) interferes with testing.

Brainstem Functions

0 - Normal
1 - Signs only
2 - Moderate nystagmus or other mild disability
3 - Severe nystagmus, marked extraocular weakness, or moderate disability of other cranial nerves
4 - Marked dysarthria or other marked disability
5 - Inability to swallow or speak
9 - (Unknown)
Sensory Function

0 - Normal
1 - Vibration or figure-writing decrease only in one or two limbs
2 - Mild decrease in touch or pain or position sense, and/or moderate decrease in vibration in one or two limbs; or vibratory (c/s figure writing) decrease alone in three or four limbs
3 - Moderate decrease in touch or pain or position sense, and/or essentially lost vibration in one or two limbs; or mild decrease in touch or pain and/or moderate decrease in all proprioceptive tests in three or four limbs
4 - Marked decrease in touch or pain or loss of proprioception, alone or combined, in one or two limbs; or moderate decrease in touch or pain and/or severe proprioceptive decrease in more than two limbs
5 - Loss (essentially) of sensation in one or two limbs; or moderate decrease in touch or pain and/or loss of proprioception for most of the body below the head
6 - Sensation essentially lost below the head
9 - (Unknown)

Bowel and Bladder Function

(Rate on the basis of the worse function, either bowel or bladder)
0 - Normal
1 - Mild urinary hesitance, urgency, or retention
2 - Moderate hesitance, urgency, retention of bowel or bladder, or rare urinary incontinence (intermittent self-catheterization, manual compression to evacuate bladder, or finger evacuation of stool)
3 - Frequent urinary incontinence
4 - In need of almost constant catheterization (constant use of measures to evacuate stool)
5 - Loss of bladder function
6 - Loss of bowel and bladder function
9 - (Unknown)

Visual Function

0 - Normal
1 - Scotoma with visual acuity (corrected) better than 20/30
2 - Worse eye with scotoma with maximal visual acuity (corrected) of 20/30.20/59
3 - Worse eye with large scotoma, or moderate decrease in fields, but with maximal visual acuity (corrected) of 20/60.20/99
4 - Worse eye with marked decrease of fields and maximal visual acuity (corrected) of 20/100.20/200; grade 3 plus maximal acuity of better eye of 20/60 or less
5 - Worse eye with maximal visual acuity (corrected) less than 20/200; grade 4 plus maximal acuity of better eye of 20/60 or less
6 - Grade 5 plus maximal visual acuity of better eye of 20/60 or less
9 - (Unknown)
Record #1 in small box for presence of temporal pallor

Cerebral (or Mental) Functions

0 - Normal
1 - Mood alteration only (does not affect EDSS score)
2 - Mild decrease in mentation
3 - Moderate decrease in mentation
4 - Marked decrease in mentation (chronic brain syndrome, moderate)
5 - Dementia or chronic brain syndrome, severe or incompetent
9 - (Unknown)

APPENDIX E:

KURTZKE EXPANDED DISABILITY STATUS SCALE (EDSS)

- 0.0 - Normal neurological exam (all grade 0 in all Functional System (FS) scores*).
- 1.0 - No disability, minimal signs in one FS* (i.e., grade 1).
- 1.5 - No disability, minimal signs in more than one FS* (more than 1 FS grade 1).
- 2.0 - Minimal disability in one FS (one FS grade 2, others 0 or 1).
- 2.5 - Minimal disability in two FS (two FS grade 2, others 0 or 1).
- 3.0 - Moderate disability in one FS (one FS grade 3, others 0 or 1) or mild disability in three or four FS (three or four FS grade 2, others 0 or 1) though fully ambulatory.
- 3.5 - Fully ambulatory but with moderate disability in one FS (one grade 3) and one or two FS grade 2; or two FS grade 3 (others 0 or 1) or five grade 2 (others 0 or 1).
- 4.0 - Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability consisting of one FS grade 4 (others 0 or 1), or combination of lesser grades exceeding limits of previous steps; able to walk without aid or rest some 500 meters.
- 4.5 - Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability usually consisting of one FS grade 4 (others or 1) or combinations of lesser grades exceeding limits of previous steps; able to walk without aid or rest some 300 meters.
5.0 - Ambulatory without aid or rest for about 200 meters; disability severe enough to impair full daily activities (e.g., to work a full day without special provisions); (Usual FS equivalents are one grade 5 alone, others 0 or 1; or combinations of lesser grades usually exceeding specifications for step 4.0).

5.5 - Ambulatory without aid for about 100 meters; disability severe enough to preclude full daily activities; (Usual FS equivalents are one grade 5 alone, others 0 or 1; or combination of lesser grades usually exceeding those for step 4.0).

6.0 - Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk about 100 meters with or without resting; (Usual FS equivalents are combinations with more than two FS grade 3+).

6.5 - Constant bilateral assistance (canes, crutches, braces) required to walk about 20 meters without resting; (Usual FS equivalents are combinations with more than two FS grade 3+).

7.0 - Unable to walk beyond approximately 5 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; (Usual FS equivalents are combinations with more than one FS grade 4+; very rarely pyramidal grade 5 alone).

7.5 - 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; (Usual FS equivalents are combinations with more than one FS grade 4+).

8.0 - 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; (Usual FS equivalents are combinations, generally grade 4+ in several systems).

8.5 - Essentially restricted to bed much of day; has some effective use of arm(s); retains some self-care functions; (Usual FS equivalents are combinations, generally 4+ in several systems).
- 9.0 - Helpless bed patient; can communicate and eat; (Usual FS equivalents are combinations, mostly grade 4+).

- 9.5 - Totally helpless bed patient; unable to communicate effectively or eat/swallow; (Usual FS equivalents are combinations, almost all grade 4+).

- 10.0 - Death due to MS.

*Excludes cerebral function grade 1.

EDSS Score Interpretations

EDDS values are 1.0-1.5: No disability; 2.0-2.5: Minimal disability; 3.0-3.5: Moderate Disability; 4.0-4.5: Fully ambulatory; 5.0-5.5: Ambulatory without aid; 6.0: Intermittent or unilateral constant assistance; 6.5: Intermittent or unilateral constant assistance; 7.0: Unable to walk beyond 5 meters even with aid; 7.5: Unable to take more than a few steps; 8.0: Restricted to bed or chair; 8.5: Restricted to bed much of day; 9.0: Helpless bed patient; 9.5: Totally helpless bed patient; 10.0: Death due to MS

Note 1: EDSS steps 1.0 to 4.5 refer to patients who are fully ambulatory and the precise step number is defined by the Functional System score(s). EDSS steps 5.0 to 9.5 are defined by the impairment to ambulation and usual equivalents in Functional Systems scores are provided.

Note 2: EDSS should not change by 1.0 step unless there is a change in the same direction of at least one step in at least one FS.

APPENDIX F:
RESEARCH PROCEDURE FLOWCHART

Assessed for eligibility N=24

Recruited from the New York City Chapter of the National Multiple Sclerosis Society via flyers posted in MS centers.

Exclusion Criteria
- known cardiac condition
- additional neurological conditions
- orthopedic condition that could affect physical performance
- recent course of Solu-Medrol for the treatment of an exacerbation within 2 weeks of study participation
- failing one or both of the minimum performance measures (Snellen and physical performance)

Intervention Group n=17

Phase 1. Fatigue Condition
- Investigator facilitated interview
- Baseline VAS-F and core body temperature collected
- Exercise at 25% resistance on nu-step
- At 3 minutes of exercise VAS-F collected
- VAS-F collected every 30 seconds after 3 minutes
- Exercise discontinued when VAS-F increased 50% from baseline.
- Core body temperature re-collected
- Participant moved from nu-step to arm chair in quiet room for language testing completed.
- Language measures administered in a counterbalanced fashion.

Healthy Controls n=7

Phase 2. Rest Condition
- Investigator facilitated interview
- Baseline VAS-F and core body temperature collected
- Participants sat quietly in an arm chair for the total time it took them to reach fatigue in the Phase 1.
- At 3 minutes, VAS-F collected.
- VAS-F collected every 30 seconds after 3 minutes until total time was reached.
- Core body temperature re-collected
- Language measures administered in a counterbalanced fashion.

EDSS rating assessed

Nonrandom, matched-subject, mixed-factor design with covariates N=24
REFERENCES


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Krupp, L. (2006). Fatigue is intrinsic to multiple sclerosis (MS) and is the most commonly reported symptom of the disease. *Multiple Sclerosis, 12*(4), 367–368.


