IMPROVING FUNCTIONAL INDEPENDENCE IN PEOPLE WITH INCOMPLETE SPINAL CORD INJURY THROUGH ECCENTRIC RESISTANCE TRAINING

by:

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A Dissertation Submitted in Partial Fulfillment
of the Requirements for the Degree of
Doctor of Philosophy in Human Performance

Middle Tennessee State University
August 2017

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I would like to dedicate my dissertation to two groups of individuals, former faculty mentors and family that passed too soon. My time with each of you was short, but the impact you made in my life was profound. Each of you encouraged me to see beyond my self-perception, gave me the courage to reach beyond my comfort, and drove me to pursue more than I could have expected for myself. It is difficult to not share this time with you, but please know that I am eternally grateful.

ACKNOWLEDGEMENTS

I am humbled by the grace and support provided by my immediate family, Lisa Stone, Jamie Stone, and Lindsy Rhoten. Each of you found it within yourself to serve as a sound board for my troubles, voice of reason when I was in need of guidance, and were unwavering when I was tumbling through this graduate school process. I think of each of you when I have the opportunity to share my experiences, work, and success brought on by my postsecondary education. I also extend this gratitude to my close friends and loved ones. You were not deterred when I isolated myself with my work, rather, you graciously stood fast in our relationship. You have seen me at my best and worst, and continue to love me none the less. I am unable to describe my gratefulness.

The individuals who participated in both my research practicum and dissertation deserve this moment of acknowledgment. Each of you were a small piece of this dissertation’s success. This project could not have been completed without your willingness and courage to try new things and comply with my requests. You taught me what it means to treat each day as a gift and to view the world as a place where “everything is snow.”

This page would not be complete without acknowledging the commitment of my committee. Dr. Fuller, you have always been more than patient in my efforts to understand the meaning of my research data. Dr. Stevens and Dr. Caputo, you have each served as more than committee members, rather, your mentorship enabled me to become the professional I am today. Both of your doors were always open to my ideas, troubles, and concerns. I cannot thank you enough for your guidance and friendship.

ABSTRACT

Individuals with an incomplete spinal cord injury (iSCI) experience physical and functional challenges from decreased metabolic efficiency and maximal oxygen consumption and musculoskeletal wasting. To minimize the impact of these changes, individuals with iSCI are encouraged to participate in physical activities to promote overall health and skeletal muscle development. Eccentric resistance training (ERT) is a promising modality for individuals with iSCI due to its inherently low metabolic cost and potential to stimulate musculoskeletal hypertrophy. To investigate the benefits of this training modality in this population, participants with iSCI to the cervical (n = 6), thoracic (n = 4), or lumbar (n = 1) region were included in the current sample. In the first study, changes in muscular strength (eccentric and isometric) and daily step physical activity (PA) were assessed following twice weekly sessions of ERT for 12 weeks. Secondly, data were evaluated to assess improved walking function following the ERT intervention. Participants completed a 10 meter walk test (10MWT; walking speed), timed up and go (TUG; mobility), Walking Index for Spinal Cord Injury (WISCI; walking independence), and Spinal Cord Independence Measure (SCIM; at home function) at baseline, after week 6 of training, and following the training program.

Following the ERT intervention, eccentric strength (p = .009; d = .473) and isometric strength (p = .005; d = .689) improved, but there was no change in daily step PA (p = .092; d = .256). Relative to function, participants improved walking speed (p = .005, d = .23), TUG mobility (p = .034, d = .62), and WISCI performance (p = .004, d = .73) as a result of the ERT. However, SCIM outcomes did not change (p = .20, d = .18).

Further, 10MWT (r = .735, p = .01), TUG (r = -.708, p = .015), and WISCI (r = .829, p = .002) outcomes correlated with daily step PA, respectively, after 6 weeks of ERT. Correlations with daily step PA continued for TUG (r = -.689, p = .019) and 10MWT (r = .694, p = .018), respectively, post-test.

Overall, ERT improved measures of strength, walking speed, mobility, and independence in individuals with an iSCI. This information may help clinicians justify the implementation of ERT when seeking to improve strength and walking function in individuals with neurological disorders. Further, these improvements can be produced with low therapist and client burden. Future investigations seeking to determine the effectiveness of ERT on at home function may consider a measurement tool more sensitive than the SCIM.

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CHAPTER I

DISSERTATION INTRODUCTION

Spinal cord injuries (SCI) affect approximately 39 people in every one million Americans (Cripps et al., 2011). The majority of injuries occur in young, White males following motor vehicle accidents or falls (Chen, Tang, Vogel, & DeVivo, 2013). Traumatic SCI affect the spinal cord by laceration, contusion, or dislocation followed by a dangerous inflammatory, ischemic, and/or apoptotic response (Sekhon & Fehlings, 2001). Within the first several days following SCI, a neurological and functional classification assessment is performed to determine the severity of injury (Kirshblum et al., 2011). The American Spinal Injury Association's (ASIA) Impairment Scale (AIS; Kirshblum et al., 2011; Maynard et al., 1997) is used to evaluate the sensory response, motor control preservation, and completeness of injury. These assessments are repeated one-year post SCI after neurological stability is established (Jacobs & Nash, 2004).

Reduced physical activity (PA) following SCI exposes individuals to musculoskeletal disorders, metabolic dysfunction, and cardiovascular disease risk factors. Denervation following SCI results in negative adaptations to muscle structure, force production capacity, metabolism, and neurological function. Muscle fibers transform from smaller, slow twitch fibers to larger, fast twitch fibers, while concurrently atrophying (Burnham et al., 1997; Castro, Apple, Staron, Campos, & Dudley, 1999). The fast twitch dominant muscles rely heavily on anaerobic metabolism because capillaries and oxidative enzymes are limited (Chilibeck, Jeon, Weiss, Bell, & Burnham, 1999). In addition to being less resistant to fatigue, the atrophied muscle fibers have graded paralysis because of interrupted signaling from higher brain centers (Riley, Burns, Carrion-Jones, & Dillingham, 2011). This disuse of skeletal muscle leads to overuse injuries and pain, even when performing daily tasks, potentially explaining the lowered quality of life (QOL) after SCI (Pentland & Twomey, 1994b).

Bone demineralization is also a cause for concern in individuals aging with SCI. Skeletal under loading and loss or lowered hormone levels elevate risk for bone fractures (Elefteriou et al., 2005; Field-Foote, 2009). After SCI, individuals also have increased risk of atherogenic risk factors such as low high-density lipoproteins, elevated low-density lipoproteins, insulinemia, and higher blood glucose levels (Bauman & Spungen, 1994). Additionally, after SCI, individuals are prone to glucose intolerance and insulin insensitivity (Warram, Martin, Krolewski, Soeldner, & Kahn, 1990). Together, these deleterious repercussions of incomplete SCI (iSCI) result in attenuated exercise capacity and greater risk of hypokinetic diseases.

As such, those with SCI need to participate in activities that will reverse this hypokinesis. Initially post-injury, patients participate in rehabilitation aimed at improving gait and learning to complete tasks of daily living. Popular gait training methods after SCI are robotics and functional electrical stimulation (FES). Both training modalities provide the environment for physical improvement after SCI. Much like in the able-bodied population, it is recommended that individuals with SCI be physically active most days of the week, performing cardiorespiratory and resistance training activities (Ginis et al., 2011; Jacobs & Nash, 2004; Pescatello, 2014). Not only will increased PA be beneficial to the preservation of physical function and independence, evidence also illustrates improvements in QOL with regular PA (Anneken, Hanssen-Doose, Hirschfeld, & Thietje, 2010; Manns & Chad, 1999). Examples of exercise options for individuals with SCI are arm and leg cycling (with and without FES), aquatic treadmill walking, traditional weight lifting (with and without electrical stimulation), and circuit resistance training (CRT) modified for those in wheelchairs. All of these training modalities provide adaptations specific to the training style and have been shown to be beneficial to individuals with SCI.

Activities that can improve muscle force production with low metabolic costs may be especially beneficial to those with a SCI who have a low functional capacity. Eccentric resistance training (ERT), or resistance-training focused only on the eccentric portion of a repetition, has a low oxygen demand and increases muscle strength, muscle volume, fascicle length, and muscle pennation which could inevitably translate to greater force output (Seynnes, de Boer, & Narici, 2007). Added benefits from focused eccentric training include increasing electrical activity of the prime mover, decreasing antagonist coactivation, and recruiting lower threshold fibers to perform the work (Enoka, 1996; Hortobagyi et al., 1996; Pensini, Martin, & Maffiuletti, 2002). Eccentric resistance training is not only safe in able-bodied individuals, the efficacy and practicality is also evident in those with neurological deficiencies and muscle weakness, such as those with incomplete spinal cord injury (iSCI; Dibble et al., 2006; Leszczak, Olson, Stafford, & Di Brezzo, 2013). Further, those with iSCI may be able to perform more total work with the lower extremity because of the lower metabolic cost of ERT (LaStayo, Reich, Urquhart, Hoppeler, & Lindstedt, 1999). Together, the increased neural adaptations, muscle architectural changes, and low metabolic cost leading to higher total work capacity points to ERT as an ideal physical activity for those living with iSCI.

Overall Purpose

This dissertation includes two studies of ERT. The first study was designed to quantify eccentric and isometric strength adaptations and changes in PA as measured in steps following a 12-week ERT program in those with iSCI. It was hypothesized that the ERT would improve eccentric and isometric strength of the legs and increase daily step count from pre- to post-ERT. The second study was designed to evaluate the effects of the same ERT program on walking speed, walking mobility, walking independence, and at home function. It was hypothesized that walking speed, walking mobility, and at home function would improve, and there would be less dependence on assistive devices during ambulation. It was further hypothesized walking speed, mobility, and independence while walking would be predictors of daily step PA.

Significance of Studies

Individuals with SCI have several physiological maladaptations that predispose this population to hypokinetic diseases, diminished physical function, and reduced QOL. As such, it is even more important to implement safe and effective exercise training programs that will improve the health of men and women aging with SCI. However, individuals with SCI have reduced functional capacity compared to an able-bodied population, so exercises that require little oxygen uptake, but provide muscular overload, may prove optimal in this group of individuals. Eccentric style weight training may be a preferential modality of exercise after iSCI because of the lower aerobic function and muscle strength in these individuals, but there is a brevity of evidence evaluating the outcomes of ERT following iSCI. Also, little is known on how well lower body ERT translates to ambulation and daily PA. If ERT provides practical value and sizable physical gains or simply deters losses, this training mode can potentially be added to rehabilitation techniques to mitigate the dramatic loss of strength after injury.

CHAPTER II

REVIEW OF THE LITERATURE

The literature review begins with an overview of the etiology, pathophysiology, and epidemiology of SCI and how practitioners evaluate injuries to determine an individual's motor and sensory capacity. Next, an evaluation of the functional and physiological consequences to the muscular system and cardiorespiratory system following SCI is presented. Succeeding sections include the impact of SCI on bone, metabolism, thermoregulation, pain, QOL, and functional independence. An examination of traditional modalities of rehabilitation are then presented followed by descriptions of current rehabilitation modalities. A review of the muscular and neuromuscular adaptations to ERT and how ERT is tolerated and effective in special populations follows. This sections ends with a presentation of how little is known about lower body resistance training, specifically ERT, in those with iSCI.

Statistics and Epidemiology

The yearly incidence rate of SCI in the United States (US) is approximately 39 injuries per one million people (Cripps et al., 2011). In 2015, the National SCI Database (NSCID) estimated an incidence rate of 12,500 SCI per year and currently, an estimated 276,000 persons in the United States are living with SCI (NSCID Facts and Figures at a Glance, 2015). These incidence and prevalence estimations do not include individuals who died before arriving at the hospital. Level of SCI is a strong predictor of prognosis, where injuries to cervical vertebrae 1-3 increase mortality rate over 6 fold compared to non-cervical injuries (Sekhon & Fehlings, 2001). According to an analysis of the NSCID and National Shriners SCI Database, between 2005 and 2011, the majority of SCI were attributed to motor vehicle accidents (31.5%), falls (25.3%), and gunshot wounds (10.4%; Chen et al., 2013). In those younger than 45 years of age, motor vehicle accidents were the most common cause of SCI and in those over 45 years of age, falls were the most prevalent cause (Chen et al., 2013).

When further considering factors associated with SCI, close to 65% of injuries occur in those younger than 45 years old and only 21.5% in those between 46 and 60 years of age (Chen et al., 2013). Between 2005 and 2011, 78.3% of SCI occurred in males (Chen et al., 2013) and in 2015, 80% occurred in males (NSCID Facts and Figures at a Glance, 2015). Race/ethnicity is also related to the incidence of SCI, with 66.8% of cases occurring in White individuals, 20.7% in Black individuals, and 9.2% in Hispanic individuals (Chen et al., 2013).

Etiology and Pathophysiology of SCI

Rarely are SCI the outcome of a singular event. The initial injury, or primary mechanism, is often a traumatic impact, compression, dislocation, or laceration that subsequently initiates a cascade of acute, destructive events termed secondary mechanisms of injury (Sekhon & Fehlings, 2001). Secondary mechanisms of SCI may include, systemic effects on blood pressure, hypoxia, vascular deformities, electrolyte imbalances, edema, and apoptosis (Sekhon & Fehlings, 2001; Tator & Fehlings, 1991). The inflammatory response following SCI also often leads to compression of the spinal cord paired with ischemia and infarction (Field-Fote, 2009; Sekhon & Fehlings, 2001; Tator & Koyanagi, 1997). Somatosensory and motor recovery potential improves up to 85% if decompression occurs within hours of injury compared to below 30% if decompression occurs beyond 6 hours (Delamarter, Sherman, & Carr, 1995). When left untreated, ischemia has a direct linear response to severity of injury and axonal dysfunction within hours of the primary SCI (Tator & Fehlings, 1991).

Programmed cell death, or apoptosis, is another potential mechanism of secondary injury following traumatic SCI. Opposed to the passive nature of necrosis, apoptosis is an active response to cell death wherein phagocytes consume and retain cellular content without initiating an inflammatory response (Sekhon & Fehlings, 2001). Although apoptosis is well documented following SCI, the mechanisms behind this degradation, outside of embryonic development, are unclear. Apoptosis is responsible for axonal demyelination, likely secondary to ischemia, modifications to the cellular environment, and trauma (Sekhon & Fehlings, 2001).

The initial mechanism for injury is followed by debilitating secondary mechanisms such as inflammation, ischemia, and apoptosis. As a result, it is critical to conduct physical evaluations throughout the recovery period in order to identify specific levels of function and recovery and to monitor progression of the injury.

Defining and evaluating SCI lesion levels.

The International Standards for Neurological and Functional Classification of SCI were developed as a means to objectively categorize the severity of a SCI (Kirshblum et al., 2011; Maynard et al., 1997). The standards require professionals to assess the degree to which sensory and motor neuron activity remain intact. Sensory examinations are completed by testing the responsiveness to a pinprick and light touch of a cotton swab at 28 dermatomes on the right and left sides of the body. Graded on a 3-point scale, each dermatome can score a sensory response of absent, impaired, or normal. The sensory scores from the right and left sides are summed together to create an overall score for the pinprick and light touch assessments.

Motor control is quantified on a 6-point scale ranging from total paralysis, palpable or visual contraction, movement with and without the effects of gravity, ability to move against an added resistance, or normal. Ten sets of paired myotomes are assessed across the right and left sides of the body. It is recommended that this testing series be completed one year after the SCI for optimal neurological stability (Jacobs & Nash, 2004). Acknowledging that damage to the spinal cord may result in a variety of sensory-motor dysfunctions, defining the level of the SCI based off a single score may be too elementary. As such, in standards presented by Kirshblum et al. (2011), motor level impairment is defined by the lowest set of myotomes scoring at least a 3 (active movement against gravity) provided that the next most superior set of myotomes scored a 5 (normal or intact). The motor scores may be summed, similar to the sensory scores. Combining information regarding sensory and motor retention, individuals post-SCI are often categorized as either tetraplegic, referrring to an injury in the cervical vertebra, whereas an individual with an SCI to the thoracic or lumbosacral regions is referred to as paraplegic.

Testing for the completeness of the SCI is accomplished using the ASIA AIS, which objectively assesses the severity of the lesion (Field-Fote, 2009; Kirshblum et al., 2011; Maynard et al., 1997). Ranked on a scale from A (complete) to E (normal), individuals are scaled based off sensory and motor preservation at the sacral 4-5 level and/or motor function below the SCI. Complete injuries (A) present with neither sensory nor motor function at the sacral level 4-5, whereas those with iSCI rated as B have preserved sensory function at this sacral segment. Those with an iSCI ranking of C demonstrate motor function below the lesion, but over half of tested muscle groups score less than 3 on the motor assessment. Individuals who have incomplete injuries where at least half of the tested myotomes below the lesion score at least a 3 are ranked as an incomplete D. If there are no sensory or motor dysfunctions, the individual is classified as normal or E.

Many variables must be taken into consideration when describing an individual's function after an SCI including lesion location and loss of sensory and motor function. The classification of the SCI allows professionals to predict subsequent musculoskeletal, neurological, and contractile function.

Functional and Physiological Consequences of SCI on the Muscular System

Muscular adaptations to SCI are more severe than the negative consequences of weightlessness, immobilization, and bed rest (Fits, Riley, & Widrick, 2000; Ohira, 1989; Veldhuizen, Verstappen, Vroemen, Kuipers, & Greep, 1993). Denervation results in changes to muscle architecture, contractile capacity, cellular metabolism, and neuronal function.

Muscle biopsies have shown acute myofibril changes occur as early as four to six weeks post SCI (Burnham et al., 1997; Mohr et al., 1997). Slow twitch muscle fibers below the injury level begin transforming towards glycolytic fibers through co-expression of TIIa and TIIx myosin heavy chain isoforms (Burnham et al., 1997). During the early transitional phases, approximately 11-24 weeks post SCI, muscle fibers express hybrid transitional fibers composed of both TIIa and TIIx phenotypes (Castro et al., 1999). Individuals assessed beyond a year post SCI have shown a complete transformation towards glycolytic myofibers, nearly void of TI isoforms (Chilibeck et al., 1999).

In as little as 8 months after a SCI, individuals undergo significant muscle atrophy where whole muscles are as small as 1/3rd that of able-bodied controls (Castro et al., 1999) and there is significant decrease in muscular force and velocity capacity. Preferential atrophy begins to target TIIa fibers beyond 24 weeks post SCI, potentially due to the higher ratio of TII fibers relative to TI fibers (Castro et al., 1999). This concept of preferential atrophy may be supported by the heightened activity of the cellular metabolism regulator peroxisome proliferator-activated receptor-γ coactivator (PGC-1α) after SCI (Higashino et al., 2013). Rats exposed to SCI demonstrated accelerated release of PGC-1α which served as a protective mechanism for TI fibers, promoting fiber retention and fighting local muscle wasting by down regulating atrophic genes (Higashino et al., 2013). The protection provided from PGC-1α does not seem to translate to TII isoforms, predominate in those with SCI (Higashino et al., 2013). As a result of these architectural adaptations, metabolic and contractile characteristics concomitantly decline.

Individuals with SCI demonstrate 40% lower metabolic function compared to able-bodied individuals (Castro et al., 1999). There is a greater reliance on anaerobic metabolism confirmed by attenuated oxidative enzymatic activity and diminished capillary density (Chilibeck et al., 1999). The fibers composing whole muscle in those with SCI are less resistant to fatigue (Gerrits et al., 1999; Krieger, Pierotti, & Coast, 2005). Additionally, it is important to note that investigations evaluating muscular response to SCI have documented great variability, showing that not all muscles below the spinal cord lesion respond similarly to the injury (Krieger et al., 2005). As such, it is important to prescribe exercise relative to the individual characteristics of each participant.

Spinal cord injuries cause interrupted signaling from the cortex to motor neurons below the injury, resulting in attenuated force capacity and graded paralysis (Riley et al., 2011). Adaptations may include the loss of presynaptic axons, postsynaptic acetylcholine receptors, reduced membrane potential at rest, and neuronal fibrillation (Ollivier-Lanvin, Lemay, Tessler, & Burns, 2009; Riley et al., 2011). The fibrillations and anatomical deformities are indicative of decreased communication at the neuromuscular junction (Ollivier-Lanvin et al., 2009; Riley et al., 2011). These changes to nervous system physiology likely contribute to the greater fatigue in those with SCI, similar to reduced calcium removal dexterity and fiber conversion (Ollivier-Lanvin et al., 2009).

In sum, disruption in the spinal cord following injury inherently interrupts signaling from higher brain activity to motor units in the skeletal muscles. This often leads to a greater expression of fast twitch muscle fibers, reduced muscular force generation and velocity, muscle atrophy, and deteriorated neuromuscular junction physiology. These precursory changes also affect muscle metabolism and exercise capacity. Comprehensively, these changes reduce exercise capacity in those with a SCI, leaving them at greater risk of hypokinetic diseases.

Functional and Physiological Consequences of SCI on the Cardiorespiratory System

Cardiovascular (CV) and respiratory control originates in the brain, specifically from the hypothalamus. The hypothalamus coordinates responses of the autonomic nervous system (ANS) resulting in the release of either stimulatory efferents via the sympathetic nervous system (SNS) or inhibitory efferents through the parasympathetic nervous system (PNS). The dorsomedial hypothalamus, ventorlateral medulla, raphe pallidus, and paraventricular nucleus receive afferent messages and coordinate CV responses (Furlan & Fehlings, 2008; Horiuchi et al., 2004; Horiuchi, McDowall, & Dampney, 2006). Excitatory input from the SNS results in more rapid depolarization of the sinoatrial (SA) node, elevating HR. This cardiac acceleration is traced back to the raphe pallidus and paraventricular nucleus (Horiuchi et al., 2006; Yang, Wheatley, & Coote, 2002). Sympathetic nervous system input also increases myocardial contractility, influences vasomotor pathways in the periphery to maintain blood pressure (BP), and assists with venous return (Garstang & Miller-Smith, 2007; Horiuchi et al., 2006). Afferent feedback is received through cranial nerves IX (glossopharyngeal) and X (vagus) where it is transferred to the medulla oblongata for processing, and then efferent signals are sent to the periphery (Garstang & Miller-Smith, 2007).

The innervation sites for the SNS are located throughout the spinal cord while the vagus nerve (PNS) does not travel through the spinal column. As such, SCI impacts SNS input to the heart while not effecting PNS input. Following injury, individuals may experience excessive vagal tone, without matched SNS stimulation, resulting in lower resting HR and oxygen consumption (VO_2), decreased cardiac acceleration, ventricular contractility, and local metabolic responses during exercise, ultimately resulting in impaired aerobic capacity (Schmid et al., 1998a; 1998b).

The level and severity of a SCI affect the extent of CV dysfunction (Furlan, Fehlings, Shannon, Norenberg, & Krassioukov, 2003; Furlan & Fehlings, 2008; McKinley, Jackson, & Cardenas, 1999; Schmid et al., 1998a). Cervical SCI (tetraplegia) interrupts supraspinal signals from the medullary command center, resulting in the loss of regulatory control over HR, myocardial blood flow, and left ventricular contractility (Garstang, 2007). Without this stimulatory input, continuous PNS tone will cause lower resting and exercise HRs and abnormal atrial and ventricular contraction synchrony because of delayed atrioventricular conduction, thus leading to impairments in end diastolic volume and stroke volume (Garstang, 2007). Detectable CV consequences to tetraplegia may include arrhythmias such as bradycardia (HR < 60 beats/minute), atrioventricular block, and atrial fibrillation (Garstang, 2007). Additionally, individuals with cervical SCI have lower resting epinephrine and norepinephrine plasma levels compared to individuals without injury, indicating decreased catecholamine secretion from the adrenal medulla and the SNS (Schmid et al., 1998a).

Peak aerobic capacity also has a strong negative correlation with the level of SCI (Hjeltnes, 1986). During peak exercise testing, minute ventilation (VE) is related to the level of injury, wherein those with anatomically higher SCI increase VE by accelerating breathing frequency rather than increasing tidal volume (Hjeltnes, 1986). Venous return is decreased following SCI due to the resulting hypotension (Claydon, Hol, Eng, & Krassioukov, 2006; Ditor et al., 2005; Hjeltnes, 1986) and lower resting and exercising HRs (Claydon et al., 2006; Ditor et al., 2005). Cardiac output is also decreased due to the deconditioned myocardial and skeletal muscle from under loading and a smaller left ventricular chamber and wall size (Kessler et al., 1986). Denervation to the heart and respiratory musculature may also explain the lower VO_2 and stroke volume at matched work rates in those with cervical SCI, so exercise performance and adaptations are likely due to peripheral adjustments in local muscular VO_2 and breathing frequency (Hjeltnes, 1986; Schmid et al., 1998a).

Similar to cervical SCI, thoracic (T) lesions (T6 and above) result in reduced CV functionality from interrupted supraspinal signaling (Furlan et al., 2003; Furlan & Fehlings, 2008). Preganglionic sympathetic neurons innervating the myocardium and intrinsic conduction units leave the spinal cord between the cervical vertebrae and T6 (Bonica, 1968). Individuals with injuries superior to T6 are prone to orthostatic hypotension (systolic BP < 90 mmHg; Cariga, Ahmed, Mathias, & Gardner, 2002) and autonomic dysreflexia (systolic BP reaching 300 mmHg; Teasell, Arnold, Krassioukov, & Delaney, 2000). At rest, those with high thoracic lesions (HLpara) have lower resting HR and exercise VO_2, stroke volume, catecholamine release, and maximal work rate compared to individuals with injuries below T4 (Schmid et al., 1998a). Individuals with HLpara appear to have the highest HR relative to VO_2 when exercising, suggesting compensatory mechanisms to achieve similar cardiac output with depressed SNS input (Schmid et al., 1998a).

Lower level paraplegia (LLpara; at or below T5) affects CV function differently from tetraplegia and HLpara because SNS tone to the heart should be unaffected by the SCI. Typical resting HR for those with LLpara is higher than in those without SCI due to lower stroke volume from decreased venous return and left ventricular atrophy (Jacobs & Nash, 2004). Individuals with LLpara have adrenal medulla hyperactivity resulting in elevated resting and exercise plasma catecholamine levels compared to those with tetraplegia, HLpara, and able-bodied individuals (Schmid et al., 1998a; 1998b). Those with LLpara show similar levels of maximal VO_2 as those without SCI, but it is achieved by higher adrenergic activity and maximal HR to compensate for lower venous return and subsequently reduced stroke volume (Jacobs & Nash, 2004; Schmid et al., 1998a). Individuals with injuries below this level of sympathetic innervation should experience relatively normal CV responses to stimuli, with injuries to the lumbosacral portion resulting in minimal ANS dysfunction (Garstang, 2007).

Cardiorespiratory function and response will be compromised according to the level of SCI. Injuries superior to T6 result in significantly lower sympathetic innervation to cardiac and diaphragmatic tissue compared to injuries at T6 and below. Therefore, one should expect lower cardiac output from concurrently lowered stroke volume and HR, reduced venous return, and in-proper blood redistribution with exercise, with exaggerated breathing frequency and oxygen consumption at any absolute work intensity for those with SCI above T6.

Physiological Consequences of SCI on Bone, Metabolism, and Thermoregulation

Bone demineralization

A major health concern following SCI is bone demineralization. Approximately 2% of individuals with SCI experience a bone fracture annually (Vestergaard, Krogh, Rejnmark, & Mosekilde, 1998) with the initial fracture occurring within nine years post injury (Zehnder et al., 2004). Individuals who maintain some level of muscle tone through spasticity have greater retention of bone mineral density than those with flaccid paralysis (Demirel, Yilmax, Paker, & Onel, 1998). Chronic bone loss can be accredited to dramatic mechanical unloading and disuse (Field-Foote, 2009), in addition to a disruption in hormonal activity, especially with males.

Disruption in SNS response due to bone and skeletal muscle unloading may trigger an imbalance between osteoblast and osteoclast cell activity. This inequality causes disproportionate bone resorption without proper bone reformation (Field-Fote, 2009). The SNS promotes osteoclast activity via sympathetic β2-adrenergic receptors while osteoblast differentiation is down regulated by neuropeptides (Elefteriou et al., 2005). Communication between these neuropeptides and hormones, including testosterone, may play a key role in bone remodeling (Elefteriou et al., 2005; Ferlin, Selice, Carraro, & Foresta, 2013).

Lesions to the spinal cord affect neural activity to endocrine glands. Following SCI, males experience hypogonadism from altered testicular innervation, leading to low secretion of testosterone and Leydig cell dysfunction (Ferlin et al., 2013). Interruption of Leydig cells diminishes the secretion of the hormone insulin-like 3, which is responsible for osteoblast activity (Ferlin et al., 2013). It is unclear whether central (hypothalamic or pituitary glands) or peripheral function is responsible for the hypogonadism in men (Bauman & Spungen, 2000; Gaspar, Brandao, & Lazaretti-Castro, 2014).

Testosterone regulates bone composition similar to protein synthesis (Bauman & Spungen, 2000). In males, there appears to be a neural pathway between the brain and reproductive organs that maintains testosterone levels (Lee, Miselis, & Rivier, 2002). As such, disruption in this pathway via SCI results in a negative bone mineral flux and muscle wasting due to inappropriate concentrations of gonadotrophins, vitamin D, and testosterone (Gaspar et al., 2014; Yarrow et al., 2014). In addition to low bone density, those with SCI have disproportionately high fat mass relative to low lean body mass (LBM) when compared to able-bodied individuals (Kocina, 1997). High doses of testosterone post-SCI, limits bone mineral loss and muscular atrophy in male rats, with lower doses demonstrating less benefit (Gregory, Vandenborn, Huang, Ottenweller, & Dudley, 2003; Yarrow et al., 2014). Testosterone replacement therapy also improves LBM and fat mass in uninjured, older males and females (Borst et al., 2014; Villareal, Holloszy, & Kohrt, 2000), but data are not available demonstrating this effect in female rats or humans with SCI.

In summary, individuals after SCI are at greater risk for imbalanced bone formation because of altered SNS and hormonal activity. Although mechanisms are currently unclear, testosterone replacement therapy improves bone density and LBM in male rats with SCI and uninjured older adults. Further evidence is needed to determine the efficacy of hormone therapy in humans after SCI.

Metabolism

Individuals with SCI have a higher incidence of hyperglycemia, glucose intolerance, and insulin resistance when compared to those without SCI (Bauman & Spungen, 2000; Duckworth et al., 1980). Inactivity and increased adiposity lead to depressed high-density lipoprotein with elevated low-density lipoprotein, triglycerides, and plasma insulin (Bauman & Spungen, 1994). This atherogenic profile occurs earlier in those with SCI compared to those without SCI, along with development of metabolic syndrome (Bauman & Spungen, 1994; 2000). Carbohydrate metabolism dysfunction is positively correlated with neurological lesion level (Bauman, Adkins, Spungen, & Waters, 1999). Further, time since SCI and adiposity were positively associated with glucose intolerance in those with SCI (Duckworth et al., 1980). Bauman and Spungen (2000) postulated that heredity exerts the greatest influence on insulin sensitivity and glucose metabolism following SCI, beyond chronic inactivity. However, the chronic inactivity paired with a genetic predisposition leads to higher rates of impaired metabolism in those with SCI compared to individuals without SCI.

Augmenting the impaired carbohydrate metabolism, denervation of skeletal muscle is often associated with insulin resistance (Buse & Buse, 1958; Warram et al., 1990). Insulin insensitivity may also be attributed to muscle fiber transition towards fibers with lower capillary density, potentially blunting insulin dependent and independent glucose transport (Bauman & Spungen, 2000). Duckworth et al. (1980)

suggested that the degradation of glucose transport is not due to attenuated insulin secretion, but to post-receptor resistance. Although the post-receptor mechanism was not elucidated in their work, the investigators found that glucose intolerance, despite elevated serum insulin levels, was not rectified by exogenous insulin injection (Duckworth et al., 1980).

Incidence and prevalence of altered glucose metabolism and insulin regulation are higher in a population with SCI compared to able-bodied individuals. This discrepancy may originate from the central denervation of skeletal muscle, chronic inactivity, and post-insulin receptor kinetics.

Thermoregulation

Individuals with SCI display disruption in autonomic thermoregulatory patterns due to loss of hypothalamic innervation, vasomotor tone, and altered shivering and sweating patterns (Downey, Miller, & Darlin, 1969; Khan, Plummer, Martinez-Arizala, & Banovac, 2007). These physiological breakdowns manifest as an inability to thermoregulate in cold and hot conditions. Following SCI, individuals are two times more likely to exhibit subnormal body temperature (< 97.7°F; Khan et al., 2007) at ambient temperatures ranging from 72°F-74°F and require lower skin and core temperatures to elicit a negative feedback thermoregulatory response (Downey et al., 1969). Temperature regulation following SCI appears to be most closely related to level of lesion rather than age or time since injury (Khan et al., 2007). Those with injuries above T6 experience greater difficulty responding to cold and heat stress because of a loss of input from peripheral skin receptors (Downey et al., 1969; Song, Won, Park, Ko, & Seo, 2015).

However, those with injuries below T6 have approximately 50% of skin sensation intact, resulting in a greater ability to respond to thermoregulatory stress through central thermoregulatory mechanisms, shivering, and vasomotor responses (Downey et al., 1969).

As with rest, individuals with SCI do not possess the same capacity to thermoregulate when exercising as individuals without SCI. Those with SCI have blunted temperature regulation at all absolute intensities of exercise due to reliance on dry heat exchange because of impaired vasomotor and sudomotor control below the lesion (Sawka, Latzka, & Pandolf, 1989; Theisen, Vanlandewijk, Sturbois, & Francaux, 2000). Additionally, those with high thoracic injuries demonstrate greater core and skin temperature during graded exercise than those with low thoracic or lumbar SCIs (Griggs, Leicht, Price, & Goosey-Tolfrey, 2015; Price & Campbell, 2003; Theisen et al., 2000). Skin blood flow increases to non-exercising limbs, despite the level of SCI, indicating a lack of sympathetic inflow and vasoconstriction in all individuals with spinal lesions (Theisen et al., 2000). The difference in core temperature without differences in skin blood flow indicates variability in heat loss mechanisms between those with high and low level spinal lesions (Griggs et al., 2015; Price & Campbell, 2003). Griggs et al. (2015) claimed this disparity lies in the amount of tissue available for sweating and subsequent heat loss above the lesion (Griggs et al., 2015).

Vasomotor and sudomotor inhibition may explain the loss of thermoregulatory control following SCI. Those with higher levels of injury experience greater loss of temperature control. Evaporative heat loss mechanisms are attenuated below the level of lesion, resulting in higher core and skin temperature in those with tetraplegia versus paraplegia when exercising.

Physiological function below the level of SCI has an effect on bone mineralization, metabolism of macronutrients, and regulation of body temperature during exercise. Muscle and bone wasting after denervation can be attributed to mechanical unloading and decreased anabolic hormone action. Additionally, those with SCI are predisposed to hyperglycemia due to malfunctioning glucose transport mechanisms and glucose utilization in the cell. Despite exogenous insulin therapy, individuals with SCI experience hyperinsulinemia, hyperglycemia, and risk for Diabetes Mellitus. During exercise, individuals with a SCI face higher core temperatures at all absolute workloads because of altered thermoregulatory mechanisms. All of the above physiological and functional consequences of SCI can lead to pain, which can directly impact QOL and level of independence.

Impact of SCI on Pain, Functional Independence, and Quality of Life

Those with SCI are exposed to two types of pain, nociceptive and neuropathic. Nociceptive pain can be dull or sharp in nature and is experienced by those with and those without SCI. Neuropathic pain is specific to SCI and is characterized by sharp, burning, stabbing, or electrical sensations (Field-Foote, 2009). Neuropathic pain is the result of disturbed afferent signaling and is labeled based on the region and description of pain (Field-Foote, 2009). Investigators of pain in people with SCI often fail to distinguish between types of pain; so further discussion will combine nociceptive and neuropathic pain into the generalized term of pain. In those with SCI, 48% to 80% of sampled individuals report experiencing pain, with 25% rating pain as severe to extreme (Nepomuceno et al., 1979; Pentland & Twomey, 1994b; Richards, Meredith, Nepomuceno, Fine, & Bennett, 1980). Approximately 31-40% of those using wheelchairs report pain in the upper extremity (Pentland & Twomey, 1994a), and roughly half report that it interferes with daily tasks (Nepomuceno et al., 1979). Although 60%, 58%, and 60% of mobility, self-care, and general tasks, respectively, elicit pain in individuals with paraplegia, only 35% modify activities of daily living (ADLs) to alleviate the pain and even fewer seek help when performing ADLs (Pentland & Twomey, 1994a).

Regardless of the mechanism of injury, older age is most often associated with increased pain following SCI (Richards et al., 1980). There is a greater prevalence of pain in individuals with higher intelligence, anxiety, and distress (Richards et al., 1980). The first 4 years after SCI are marked with variability in psychosocial and mood disturbances which stabilize following this time period (Lundqvist, Siosteen, Blomstrand, Lind, & Sullivan, 1991). Further analyses of patient histories reveal that diminished QOL, physical and psychosocial function, and mood are associated with severe pain following SCI (Lundqvist et al., 1991). Data are not uniform in the effect PA has on pain following SCI. An analysis by Anneken et al., (2010) found no decline in pain following PA, whereas Hicks et al. (2003) reported reductions in pain, depression, and stress following a 9-month aerobic arm ergometry and resistance training exercise regimen in those with SCI.

Approximately 60% of pain in the upper extremity is experienced during work or school activities, driving, and outdoor wheelchair propulsion (Pentland & Twomey, 1994b). In a pattern similar to those who are not impaired, musculoskeletal deterioration following SCI increases with age (Pentland & Twomey, 1994b). This decline in contractile tissue likely leads to overuse injuries and is positively correlated with upper extremity pain (Pentland & Twomey, 1994a; 1994b). Over time, this upper extremity pain may preclude an individual from wheeling, completing ADLs (Pentland & Twomey, 1994b), and/or participating in social endeavors. However, ADLs requiring moderate to heavy intensity PA (subjectively reported) after injury were associated with lower pain, fatigue, and depression (Tawashy, Eng, Lin, Tang, & Hung, 2009). It should be considered that those with lower pain, fatigue, and depression may be more willing to participate in PA. Noting these data, preventative and rehabilitative measures need to be practiced to facilitate functional independence, prevent overuse injuries, and promote QOL in those aging with SCI (Pentland & Twomey, 1994a).

A widely used and validated measure of functional independence is SCIM III (Catz et al., 2001; Itzkovich et al., 2007), which provides a broader functional view than the more commonly used Functional Independence Measure (Itzkovich et al., 2007). Quantification of baseline and changes in functional independence may be completed using the SCIM III rubric.

There are also several measures available to quantify physical function, specifically walking, after a SCI. An evaluation of the 6MWT, 10MWT, TUG, and the WISCI II found all timed tests valid and reliable across 3 testing sessions performed within seven days in males and females with long term cervical, thoracic, lumbar, or sacral complete or iSCI (van Hedel, Wirz, & Dietz, 2005). The walking tests were highly correlated with one another (r > .88), but only moderately correlated to the WISCI II (r > .60; van Hedel et al., 2005). The combination of several walking measures with functional independence indexes may be preferable when describing physical functioning in those with iSCI (Ditunno, Burns, & Marino, 2005). With this, investigators may pair multiple walking measures (6MWT, TUG, or 10MWT) with physical functionality indexes (SCIM III and WISCI-II) to gather the most holistic view of an individual's gait and level of function following a SCI.

Quantification of daily PA level in those with impaired gait is often difficult to attain because algorithms utilized in activity monitors are designed for populations without physical impairment. To date, the most accurate accelerometer to quantify stepping in those with SCI is the Step Activity Monitor (SAM). The SAM counted steps with 97% accuracy when compared with human tallied counts during the 6MWT and the 10MWT performed by adult males and females with long duration iSCI, level of injury was not provided (Bowden & Behrmann, 2007). However, the SAM is designed to be worn on the ankle, so any wheeling activities would be omitted from activity counts. Other monitors, such as SenseWear and RT3 activity monitors, have fallen short on accuracy with estimation errors ranging from 22 to 126% when individuals with longstanding iSCI below T1 wheeled in chairs or on arm crank ergometers (Hiremath & Ding, 2011). However, accelerometry with the Actigraph GT3x has shown to provide a valid estimate VO_2 (r = .86) for those with long standing, motor complete SCI below T2 and above L5, when adjusting algorithms for wheelchair use through adapted regression models (Garcia-Masso et al., 2013). Unfortunately, there are little data available to evaluate the step count accuracy with this accelerometer when gait is impaired. With these data, investigators wishing to evaluate step PA outside the laboratory setting may consider using the SAM accelerometer on the ankle and the Actigraph GT3x on the wrist to quantify both walking and wheeling activities.

Despite lacking a universally accepted definition of QOL, investigators measure objective and subjective constructs to evaluate an individual's level of life satisfaction. A reliable and valid measure of QOL following SCI is the Spinal Cord Injury-Quality of Life (SCI-QOL) measurement system (Tulsky et al., 2015). The SCI-QOL branches across physical, social, and emotional constructs to give a quantitative overview of an individual's QOL following SCI (Tulsky et al., 2015). The SCI-QOL is one of the first QOL assessments specifically designed for individuals with SCI (Tulsky et al., 2015). In general, those with SCI report lower QOL than those without SCI (Kreuter, Sullivan, Dahllof, & Siosteen, 1998; Westgren & Levi, 1998). General predictors of diminished QOL following SCI are reduced PA and both perceived and quantified loss of physical and social function (Anneken et al., 2010; Dijkers, 1997; Kreuter et al., 1998; Stevens, Caputo, Fuller, & Morgan, 2008).

The data are conflicting regarding the influence that level of SCI has on QOL. Two meta-analyses found an association between level of injury and QOL, where higher and more complete injuries resulted in lower QOL (Dijkers, 1997; Evans et al., 1994). However, in later work evaluating original research, investigations reported no relationship between QOL and level of injury (Kreuter et al., 1998; Manns & Chad, 1999; Tate, Kalpakjian, & Forchheimer, 2002; Westgren & Levi, 1998). Another disputed predictor of QOL is time since injury. Investigators show that QOL improves positively in relation to time since injury (Westgren & Levi, 1998), remains relatively constant if measured six months post-injury (Kennedy & Rogers, 2000, McColl, 1999), or declines each decade as one ages with SCI (McColl, 1999). McColl (1999) attributed this waning QOL to fear of injury, institutionalization, and loss of independence.

Physical activity plays an important role in the psychosocial QOL framework of an individual with SCI (Anneken et al., 2010). Data demonstrate positive effects of chronic PA on physical, social, and psychological contexts in those who are generally active versus those who are inactive following SCI (Anneken et al., 2010). Physical activity, rather than fitness, may be a more sensitive measure of life satisfaction because improvements in QOL are independent of improvements in physical fitness (Manns & Chad, 1999).

In summary, the incidence of pain in those with SCI is influenced by psychosocial factors and increases with age. If not prevented, pain may inhibit ADLs and function in those aging with SCI. However, individuals who safely participate in ADLs requiring moderate to high intensity PA may benefit through reductions in pain, fatigue, and depression. Further investigation is needed to determine the relationship between different exercise modalities and chronic pain following SCI. Preventative and rehabilitative techniques should focus on reducing pain and building muscle to avoid loss of physical function. Measured both objectively and subjectively, QOL appears to be lower in those with SCI compared to those without SCI. The data are not clear on the influence level or time since injury has on QOL. However, PA appears to have a direct positive relationship with QOL and physical functioning, and an inverse relationship with pain in those with SCI. Individuals often participate in various rehabilitation modalities (robotics and electrical stimulation) in efforts to offset the diminished QOL, functional independence, and pain following SCI.

Contemporary Gait Training Interventions Following SCI

Robotics

Robotic exoskeletons support the body weight of an individual after SCI, allowing for the attainment of an upright, semi-weight bearing posture. Traditionally, physiotherapists assist in gait restoration by manually moving the limbs through stepping patterns while an overhead harness supports the person's body weight. Affixed to the lower limbs and trunk, robotic devices assist in forward movement by providing sagittal and lateral stabilization without the assistance of a therapist. Robotic exoskeletons promote stepping through several means, such as participant controlled buttons embedded on a walker, the participant shifting weight to change center of mass to stimulate stepping, or stepping movements initiated remotely by the therapist (Kressler et al., 2014). Like harnesses and electrical stimulation, individuals post SCI may use robotics to potentially progress from wheelchair dependence to functional ambulation in therapeutic and community settings (Louie et al., 2015).

The external stabilization provided by robotics reduces the muscular activity needed to remain upright, therefore, energy consumption is lower for robotic training compared to physiotherapist assisted training (Israel, Campbell, Kahn, & Hornby, 2006). It is advantageous to progressively decrease the support of the exoskeleton to facilitate regeneration of intrinsic muscle activity patterns (Israel et al., 2006). However, few investigators have reported the percentage of body weight supported or the external guidance provided from the robotics (how much lateral deviation allowed before correction), leading to difficulty when comparing and developing training protocols. In general, there is little clinical evidence to support robotic training over traditional physiotherapist assisted training when evaluating walking function (Swinnen, Deurinck, Baeyens, Meeusen, & Kerckhof, 2010), but use of robotics does help individuals with SCI experience improvements in walking speed and endurance.

Improvements following robotic training in walking speed and endurance have been documented when measured by the 10MWT, 6MWT, and TUG (Fleerkotte et al., 2014; Louie et al., 2015; Wirz et al., 2005). In a sample of slow and fast walkers with SCI, those walking between 0.02-0.09 m/s increased their walking speed by 57% and those walking between 0.12-0.16 m/s lost walking speed by 19% after 12 weeks of robotic training (Field-Fote, Lindley, & Sherman, 2005). Despite the loss in walking speed in the faster group, the combined sample of individuals training with robotics increased step symmetry by 24% (Field-Fote et al., 2005). On average, those who gait train with robotics reach a walking speed of 0.26 m/s (range of 0.12 – 0.50 m/s; Louie et al., 2015), which is slower than that deemed necessary to ambulate in the community (Forrest et al., 2014). As such, robotics may serve as a therapeutic stepping-stone to community ambulation, but not a full solution.

With respect to stride length, individuals training with robotics may lose 1-22% of step length, but gain in bilateral leg strength symmetry (Field-Fote et al., 2005).

However, other authors have noted improvements in gait speed follow developments in step length and hip range of motion (Fleerkotte et al., 2014). Differential findings between these investigations may be due to variability in training duration and frequency. Despite the discrepancies in findings regarding step length, Fleerkotte et al. (2014) and Field-Fote et al. (2005) agreed that the initially weaker leg undergoes greater improvements than the stronger limb with robotic therapy.

As with most forms of therapy, the greatest improvements from robotic training are noted in those with the greatest initial impairment (Field-Fote, 2005). Early in rehabilitation, powered exoskeletons can be used to allow the transition from a wheelchair to standing in those who lack the strength to weight bare and produce the kinetics necessary to ambulate (Louie et al., 2015). Robotic exoskeleton gait training may also be a viable therapeutic modality for those with pronounced muscle wasting after SCI. By providing stepping guidance and body weight support, robotic exoskeletons allow individuals to obtain upright posture and reciprocal stepping without physical human assistance. More needs to be known on optimal training progression so that those using robotics continue to provoke neuromuscular improvements, rather than become reliant on the exoskeleton for ambulation. Another traditional mode of rehabilitation following SCI is FES.

Functional electrical stimulation

Functional electrical stimulation is the technique of applying coordinated stimulation to neural circuitry to elicit muscular contraction (Karimi, 2013; Peckham & Knutson, 2005). Muscles targeted for FES exercise are often the quadriceps, hamstrings, vastus lateralis, and gluteus maximus (Deley, Denuziller, & Babault, 2015; Peckham & Knutson, 2005). Evidence supports the efficacy of FES to promote hypertrophy and prevent atrophy (Gorgey, Mather, Cupp, & Gater, 2012), improve exercise VO_2 (Deley et al., 2015), and improve walking speed (Field-Fote, 2001; Field-Fote et al., 2005), and cardiovascular endurance (Field-Fote, 2001; Ryan, Erickson, Young, & McCully, 2013) in those with chronic SCI.

Walking speed is often the gait parameter that individuals with SCI struggle the most to improve (Gallien et al., 1995). Those with the slowest initial walking speeds typically have better results in training on treadmills supplemented with FES when compared to robotics, over ground training, and treadmill (TM) training alone (Field-Fote et al., 2005). After training for three months with TM FES, individuals with iSCI improved gait speed from 0.12 m/s to 0.21 m/s over ground and 0.23 m/s to 0.49 m/s on a TM (Field-Fote, 2001). Although walking speed improved over 100% after TM FES, indices of gait pathology, or bilateral step symmetry, did not (Field-Fote et al., 2005). This asymmetry between limbs derives from differences in limb strength, stride length, and ground reaction forces from each foot (Sadeghi, Allard, Prince, & Labelle, 2000). Uncorrected asymmetry may lead to limb dominance and compensatory gait mechanisms, potentially undermining physical function and increasing instability (Yogev, Plotnik, Peretz, Giladi, & Haudsdorff, 2006).

In a longer study, males and females with chronic cervical, thoracic, or lumbar iSCI trained for 12 weeks on either a TM, over ground with FES, on a TM with therapist assistance, or locomotor robotic training on a TM (Nooijen, ter Hoeve, & Field-Fote, 2009). Those with iSCI training with FES experienced increases in walking speed (adding four to five steps per minute), step length (0.06-0.10 meter improvement), and stride length (0.07-0.16 meter improvement), with concomitant gains in coordination and knee extension timing (Nooijen et al., 2009). Step length was defined as the distance between heel strike of one foot to the subsequent heel strike of the contralateral foot, whereas stride length was the total distance travelled between heel strike of one foot to the fifth heel strike of the same foot (Nooijen et al., 2009). Nooijen et al (2009) summed the individual gait variables to create a total gait quality score, wherein improvements in quality were higher following both training modalities involving FES compared to robotic intervention or therapist assistance (Nooijen et al., 2009). The group training with FES over ground improved similarly in walking speed when compared to those who trained with FES over ground in the Field-Fote et al. (2005) study. However, no over ground walking speeds approached those measured when speeds were assessed on a TM (Field-Fote et al., 2005; Nooijen et al., 2009).

On average, individuals with SCI support one-third to nearly one-half of their body weight with their arms when ambulating with a walker (Bobet, Chong, Rolf, & Stein, 2013). To address this, researchers have developed hybrid orthotics incorporating FES in order to aid in body weight support and stabilization (Bobet et al., 2013). Field-Fote (2001) reported increased walking distance on a TM from 93 $\pm$ 84 meters (m) to 243 $\pm$ 139 m following three months of FES TM training in those with chronic iSCI. The researchers surmised the improvement in walking distance was due to increased step length and improved lower extremity motor control (according to ASIA standards).

Increasing lower extremity movement through FES appears to benefit blood flow and venous return during exercise in those with SCI (Phillips, Burkett, Munro, Davis, & Pomeroy, 1995). This improved blood flow may explain why Ryan, Erickson, et al. (2013) found a three-fold increase in mitochondrial capacity, most of which occurred within the first 12 weeks of FES endurance training. This in vivo finding demonstrates the effect FES has on cellular adaptations, in addition to kinematic changes.

In summary, gait training following SCI often involves body weight support through harnesses, orthotics, and robotics. Robotics may help individuals with greatest impairments following SCI, but should be used sparingly and phased out as the individual improves, as to not develop dependence. Functional electrical stimulation may serve as the next intervening modality for improving gait based on its ability to lengthen stride and steps, stimulate hypertrophy, and promote aerobic capacity through improved muscle blood flow and mitochondrial content. Gait function gained after training with FES appear to outweigh those recorded following robotic therapy. Because therapy is often dependent on insurance funding, individuals with SCI may consider building on and improving functional gains from therapy by participating in various exercise modalities. Although limited compared to what is available for an able-bodied population, those with SCI may participate in cycling, underwater treadmill walking, and resistance training.

Exercise Modalities Used in Rehabilitation after SCI

Physical activity guidelines for individuals with SCI

Much like PA guidelines for individuals without disability, it is recommended that those with SCI participate in PA most days of the week (Pescatello, 2014) including 20-

60 minutes of activities aimed at improving cardiorespiratory endurance on two to three days (Ginis et al., 2011; Hicks et al., 2011; Jacobs & Nash, 2004). Individuals can participate in wheeling, arm and leg cycling, body weight supported TM training, and water exercises at intensities ranging from 50-80% maximal aerobic or heart rate capacity to improve their cardiovascular fitness (Ginis et al., 2011; Jacobs & Nash, 2004). To offset musculoskeletal weakness, individuals with SCI should also include strengthening activities such as free weights, elastic bands, or weight machines two days per week (Ginis et al., 2011; Jacobs & Nash, 2004). Strengthening guidelines include three sets of 8 to 12 repetitions at moderate to high intensity (Ginis et al., 2011; Jacobs & Nash, 2004).

Arm and leg cycling

Arm and leg cycling are two common aerobic exercise modalities for individuals after SCI. In general, those with injuries at C5 or below should have the capacity for hand cycling, whereas injuries above C5 may require FES (Valent et al., 2010). Most interventions incorporating leg cycling involve inducing contractions in paralytic muscles via FES (Hasnan et al., 2012; Krause, Szesci, & Straube, 2008; Sadowsky et al., 2013). Whether working on an arm ergometer or recumbent cycle, individuals with insufficient grip strength or lower extremity control are often strapped to the ergometer’s pedals to ensure complete range of motion. Incorporating arm and/or leg cycling into rehabilitation and daily living may improve physical function, musculoskeletal strength, and aerobic performance in those with complete and iSCI.

Following three months of FES lower extremity cycle (LEC) training, adult men and women with varying levels of chronic complete and iSCI obtained gains in motor and sensory function (Sadowsky et al., 2013). Training 45-60 minutes a day, three days a week resulted in an average improvement of 8.1 motor points and 5.8 sensory points on the 325-point ASIA impairment scale. Physical function, assessed using the Functional Independence Measure (FIM), also improved following this FES+LEC program (Sadowsky et al., 2013). Some individuals after SCI experience dramatic spasticity, which limits range of motion and physical functioning. A single bout of FES+LEC for 60 minutes reduced spasticity by 68% in adult men and women with chronic thoracic level complete SCI (Krause et al., 2008). Additionally, those with complete and iSCI who participated in a three month FES+LEC program took significantly fewer anti-spasticity medications compared to control participants (Sadowsky et al., 2013). Passive cycling (without FES) promoted reduced spasticity, but not to the same extent as FES+LEC (Krause et al., 2008). Passive leg cycling did not, however, elicit greater arterial blood flow to the lower extremities when compared to rest in those with complete SCI (Ter Woerds, De Groot, van Kuppevelt, & Hopman, 2006). Cycling with FES increased lower extremity blood flow five-fold in those with chronic complete paraplegia (Olive, Slade, Dudley, & McCully, 2003). This increase in blood flow and reduced spasticity should improve physical function and capacity following SCI.

After injury, individuals may choose to exercise on arm crank ergometers (ACE) or combine ACE with FES induced lower extremity isometric contractions (ACE+ISO). Both adults with chronic complete and incomplete paraplegia participating in ACE exercise improved power output by an average of 42% (16 watts) and VO_2 by 21% (0.21 liters/minute more than control participants; Valent et al., 2008). These improvements were not supported in a sample with tetraplegia (Valent et al., 2008). The improvements reported in the group with tetraplegia were much smaller than those of individuals with paraplegia (Valent et al., 2008). According to Valent et al. (2008), the small effect size of training, heterogeneity of participants, and small sample size (*n* = 4) left the analysis underpowered to identify any differences that might have been present in those with tetraplegia.

Combining upper and lower body activity via ACE+ISO allows for approximately 14-18% higher VO_2 compared to ACE alone, likely attributable to the greater muscle mass involved in the exercise (Hasnan et al., 2012). Because of the higher VO_2, ACE+ISO may provide greater cardiovascular overload and potential for exercise progression in those with SCI (Hasnan et al., 2012). There are no added benefits in VO_2 when comparing ACE paired with FES+LEC to ACE+ISO in those with complete SCI above T6 (Brurok et al., 2013). Although isometric contractions are known to inhibit stroke volume, ACE+ISO and ACE with FES+LEC appear to have equivocal cardiac output via venous return (Brurok et al., 2013).

Increased VO_2 and muscle volume are associated with improvements in physical function after SCI. Sadowsky et al. (2013) reported a 36% increase in LBM and a 44% decrease in fat mass in quadriceps following three months of FES+LEC in adult men and women with varying levels of chronic complete and iSCI. This improved ratio of LBM to fat mass was accompanied by a 30% and 35% increase in hamstring and quadriceps strength, respectively, when measured on an isokinetic dynamometer (Sadowsky et al., 2013). A longitudinal study revealed that those with paraplegia, both complete and incomplete, who performed ACE one or more time per week had greater muscle strength than those who did not participate in ACE (Valent et al., 2008). The same correlation between strength and ACE could not be said for those with tetraplegia, likely due, as noted, to the heterogeneity and small number of participants in the study (Valent et al., 2008).

Cadence for FES cycling is often set according to participant comfort (typically 50 revolutions per minute; rpm) and resistance is progressed to tolerance. An investigation by Johnston and colleagues (2016) evaluated the effect of low (20 rpm) and high (50 rpm) cadence FES cycling on muscle volume and bone mass. Participants progressed when the workload prescribed could be maintained for the full 56 minutes of training at the desired cadence. After 6 months of training three days per week, those with complete SCI between C4 and T6 improved muscle volume by 20% when training at a lower cadence compared to a 10% improvement reported at the higher cadence (Johnston et al., 2016). The greater muscle volume adaptations in the low cadence group may be explained by the substantially greater torque experienced by the participants, however, there was no statistically significant effect on bone mass (Johnston et al., 2016). Yet, the low cadence group did have a 34% lower bone resorption rate after training, which is a clinically meaningful change (Johnston et al., 2016). With this, individuals with similar demographics may consider training at lower repetition frequencies to improve muscle composition and force production.

Individuals with SCI should participate in aerobic exercise on two to three days per week, ranging from moderate to vigorous intensity. Persons with SCI should also engage in resistance exercises two days each week. Lower extremity FES cycling improves VO_2 and reduces spasticity. Oxygen consumption improves further when FES+LEC is paired with ACE. Arm cranking with LEC+FES is a potent stimulus for hypertrophy and may chronically reduce bone loss after SCI. Greater gains in muscle volume may be observed if FES+LEC is performed at a cadence of 20 rpm compared to a cadence of 50 rpm. Considering the available data, individuals with SCI may experience improvements in muscle function and composition when supplementing training with FES. Electrical stimulation may be used as an aid to resistance training much like aerobic cycling. Individuals with SCI may also consider aquatic TM walking to benefit musculoskeletal health. Further, exercise modalities may involve both the upper and lower body, despite SCI. Combining resistance training and cardiovascular activities into a single session may be an ideal mode of exercise for those with diminished metabolic reservoirs.

Underwater treadmill training

Underwater treadmill training (UTT) incorporates the kinematics required for ambulation on a traditional TM in an aquatic setting. As the belt moves, individuals participating in UTT ambulate forward or backward against the innate water resistance or supplemental hydro jets. Water level is typically even with the participant's xyphoid process and passively provides partial body weight support. Progression in intensity for UTT may involve lowering the water level, increasing the speed of the belt, and/or increasing the duration of training (Stevens, Caputo, Fuller, & Morgan, 2015). Training on an underwater TM may be more beneficial than using an over ground harness for those with severe physical impairments. Harnesses simply support upper body weight, leaving leg weight unchanged. Exercising in the water provides buoyancy for the legs thereby making the appendages easier to move for individuals with high levels of impairment, while concurrently training balance (Stevens & Morgan, 2010; Stevens et al., 2015).

Those with iSCI who choose to perform UTT may experience improvements in leg strength, muscle activity, gait, walking speed, dynamic balance, daily step activity, cardiovascular performance, and reduced pain (Stevens & Morgan, 2010; 2015; Stevens et al., 2015). Underwater TM training may provide more functional benefits than over ground training after iSCI. In a group of adult males and females with chronic cervical, thoracic, and lumbar iSCI, Stevens et al. (2015) reported improvements in leg strength (measured by hand held dynamometry), balance (assessed using the Berg balance test), walking speed during a 10MWT, walking endurance on a 6MWT, and daily step counts measured by pedometer following a 2-month UTT program consisting of 3, 15 to 25 minute training sessions per week. Walking speed and endurance performance exceeded that reported by Wirz et al. (2005) who trained a demographically similar group of individuals three to five times each week for eight weeks using over ground robotic therapy. Hand-held dynamometry has shown to be both valid compared to the gold standard isokinetic strength testing devices (Stark, Walker, Phillips, Fejer, & Beck, 2011) and reliable in adults and children with neurological deficiencies (Berry, Giuliani, & Damiano, 2004; Riddle, Finucane, Rothstein, & Walker, 1989).

In the same sample described in Stevens et al. (2015), Stevens and Morgan (2015) also reported a decrease in mean exercise heart rate during training, measured during the last 2 minutes of each walk, despite an increase in workload across the eight week UTT intervention. Silvers, Rutledge, and Dolny (2007) reported similar VO_2, respiratory exchange ratios, blood lactate concentrations, ratings of perceived exertion (RPE), and exercise speeds and durations in healthy, young adult men who performed TM peak tests in aquatic and over ground environments. When water level is at the participant's xyphoid process and water jets are used to replicate the intensity changes brought about by TM inclination, peak testing over ground and in an aquatic TM produce similar workloads and physiological responses (Silvers et al., 2007). Together, these data indicate that UTT is an equivocally potent stimulus for cardiovascular adaptations when exercising, irrespective of functional status. As such, aquatic TM training may be supplemented for those in need of cardiovascular exercise when over ground exercise is impeded because of musculoskeletal weakness or joint pain. Future investigations may consider evaluating backwards walking in those with SCI, because backwards aquatic TM walking allowed for greater muscle activation and higher peak heart rate values in young healthy men compared to forward walking (Masumoto, Takasugi, Hotta, Fujishima, & Iwamoto, 2006).

Underwater treadmill training improves physical function after iSCI by increasing lower extremity strength, walking speed and endurance, and promoting community ambulation (Stevens et al., 2015). Another promising training modality in those with iSCI is resistance training. Stevens, Fuller, and Morgan (2013) reported leg strength as one of the greatest predictors of daily walking in those with iSCI.

Traditional resistance training

The initial resistance training option for an individual with complete SCI may be neuromuscular electrical stimulation (NMES). Much like FES, NMES targets excitable tissue to elicit a contraction. Lower extremity resistance training after complete injury involves NMES of the quadriceps muscles to elicit knee extension, often progressed though ankle weights and increasing stimulation frequency (Gorgey et al., 2012; Ryan, Brizendine, Backus, & McCully, 2013). Following a 12-week NMES resistance training program, adult males with chronic, complete SCI varying in injury location, improved muscle volume through hypertrophy, reduced visceral fat, and reduced percent intramuscular fat (Gorgey et al., 2012). The participants trained two times per week, completing four sets of 10 repetitions, progressing in ankle weight as needed. In addition to resistance training, Gorgey et al. (2012) also had participants consume a diet balanced with 45% carbohydrates, 30% fats, and 25% proteins. This diet regimen may explain why similarly designed 16-week NMES training study conducted by Ryan and colleagues (2013) reported hypertrophy, but no differences in intramuscular fat in a demographically similar population.

Resistance training can be performed with the upper body without need for NMES following complete SCI below C7 (Maynard et al., 1997). Improving upper extremity strength has positive effects on aerobic performance in adults, despite the completeness and level of SCI (Zoeller et al., 2005). Progressive upper body resistance training three days per week for eight weeks significantly improved isokinetic and isometric strength measured with an isokinetic ergometer, increased arm fat free mass and decreased arm fat mass assessed using dual energy x-ray absorptiometry (DEXA), increased upper limb functional according to the Disabilities of the Arm, Shoulder, and Hand questionnaire (Hudak, Amadio, Bombardier, & the Upper Extremity Collaborative Group, 1996), and decreased pain, evaluated by the wheelchair users shoulder pain index (WUSPI) in adult males with chronic, complete thoracic level SCI (Serra-Ano et al., 2012). The training involved three sets of 12 repetitions performed on eight upper body movements that were designed to target shoulder rotators. Intensity was gradually increased, while maintaining an RPE of 7 or 8 out of 10 (Serra-Ano et al., 2012). In another investigation, Jacobs (2009) progressed resistive workload based on a percent of the estimated one repetition maximum (1RM) for horizontal press and row, overhead press and pull, dips, and biceps curls. Participants completed three sets of 10 repetitions of each movement. The participants were adults with chronic, complete thoracic SCI who trained for 12 weeks, divided into three cycles where workload progressed for each exercise from 60-70% 1RM throughout each 4 week cycle (Jacobs, 2009). Resistance training was associated with a 15.1% increase in arm cranking VO_2 peak, isotonic upper body muscular strength improved by 45.8% on average across six movements, and a 15.6% increase in upper body power improved, assessed using the Wingate anaerobic test (Jacobs, 2009). Progression based on RPE in a group with SCI may be too conservative, because a protocol based on percent 1RM improved isoinertial strength on average of

45.8% across muscle groups (Jacobs, 2009) compared to an average of 11% when workload was prescribed subjectively (Serra-Ano et al., 2012).

Maximal intensity resistance training was compared to traditional resistance training in a small sample of adult males with chronic, cervical or thoracic iSCI (Jayaraman, Thompson, Rymer, & Hornby, 2013). Half the sample participated in traditionally progressed resistance training consisting of one to three sets of 12 repetitions targeting the knee extensors, knee flexors, ankle dorsiflexors, and plantarflexors. Workload was increased by 5-10% 1RM as tolerated. Other participants were involved in maximal intensity training on a Biodex isokinetic ergometer, training the same muscle groups as the traditional group, however, performing three sets of 10, 5-second maximal isometric contractions (Jayaraman et al., 2013). After four weeks of training, the maximal intensity group improved 12.19m on the 6MWT and 4 points on the Berg balance test, respectively, without concurrent improvements in the traditional group (Jayaraman et al., 2013). These short-term improvements following maximal intensity training represent an individual’s ability to acutely adapt to exercise after SCI, however, isokinetic training is not readily available in the community and maximal isometric contractions may be contraindicated in some individuals with SCI.

Plyometrics, or jumping style exercises where muscles exert maximal force in brief intervals, are often paired with resistance training for athletic improvement. A 12-week resistance training program incorporating plyometric exercise two to three times per week was conducted with chronic, highly functioning males (ages 22, 61, and 58 years old) with varying levels of iSCI (Gregory et al., 2007). Participants completed lower body resistance training that targeted knee flexors and extensors, hip flexors and extensors, and ankle plantar flexors on traditional resistance training apparatus. Plyometrics were performed on a machine resembling a supine hip sled, where participants explosively pushed away from the platform with the lower body (Gregory et al., 2007). The men performed two to three sets of 6 to 12 repetitions ranging from 70-85% estimated 1RM for traditional training and the plyometric exercises progressed by increasing the resistance worked against and the number of touches (Gregory et al., 2007). Lower extremity peak torque improved and time to peak torque decreased as assessed on a Biodex isokinetic machine, and walking speed during a 10MWT increased (Gregory et al., 2007). These results indicate the efficacy and safety of lower body resistance and plyometric training after iSCI. However, participants recruited from this study were highly functioning (baseline walking speed of 1.08 m/s), so comparison of outcome variables to previous literature incorporating different rehabilitative exercise modalities is difficult.

Resistance training for those with SCI can be tailored to the individual’s exercise capacity by including NMES, upper body strength training, lower body strength training, and/or plyometrics. Individuals performing NMES may consider maintaining a balanced diet to optimize lean body mass and reduce intramuscular adipose tissue. Although not specific to the training, strengthening exercises are important for individuals with SCI when improving walking function. Exercise progression for upper body resistance training should utilize programmed increases based on 1RM rather than subjective RPE values to maximize outcomes. Few long term, lower extremity resistance training interventions with a variety of SCI levels and completeness are available.

Circuit resistance training

Circuit resistance training is a modality of resistance training where resistance exercises are performed with little rest between exercises in sequence and between sets (Haff & Triplett, 2016). The goal of CRT is to maintain an elevated heart rate in effort to promote CV and muscular adaptations simultaneously. To accomplish CRT in those with SCI, individuals complete traditional upper body isoinertial resistance maneuvers with intermittent arm cranking between resistance movements to prevent HR from returning to baseline. Circuit resistance training can be safely and effectively implemented with isoinertial exercise stations or with elastic bands varying in resistance in men and women with complete SCI (Nash et al., 2002).

Jacobs, Nash, and Rusinowski (2001) conducted a 12-week CRT intervention in adult men with chronic, complete paraplegia between T5 and L1, where SCI lesion level was chosen specifically to control for sympathetic cardiovascular innervation among participants. The participants trained three times a week and performed one set of 10 repetitions on six isoinertial resistance maneuvers (shoulder overhead and horizontal press, horizontal row, arm curls, shoulder pulls, and dips; Jacobs et al., 2001). The men completed one set of two resistance maneuvers and then cycled on an arm ergometer at a fast speed, but low resistance. This progression continued until all six resistance exercises were complete (Jacobs et al., 2001). Workloads ranged from 50-60% of the estimated 1RM for each movement (Jacobs et al., 2001). After training, peak VO_2 increased by an average of 30% and time to fatigue increased as evaluated during arm ergometer graded exercise test. Isokinetic power and isoinertial strength also increased. On average, the participants completing CRT (Jacobs et al., 2001) had better strength outcomes, averaging 21.1% improvement, when intensity was progressed based on 1RM rather than traditional resistance training prescribed based on RPE (11%; Serro-Ano et al., 2012), but did not achieve the same magnitude of improvement as resistance training alone (45.8% average improvement; Jacobs, 2009).

The CRT program developed by Jacobs and colleagues (2001) was repeated in a group of adult males and females with chronic complete and incomplete tetraplegia by Kressler, Burns, Betancourt, and Nash (2014) with the addition of protein supplementation. The sample in this study was split into participants who received whey protein supplementation before and after training or into a group that received whey protein 24 hours post exercise (Kressler et al., 2014). Following six months of CRT training three times a week, individuals with complete and iSCI improved 1RM by an average of 8-11%, irrespective of group (Kressler et al., 2014). Aerobic performance (arm ergometer graded exercise test) and anaerobic performance (Wingate anaerobic test) only improved in the group that received protein supplementation immediately before and after CRT (Kressler et al., 2014). For those with complete or incomplete tetraplegia, CRT may be optimized if whey protein is supplemented immediately before and after training, opposed to delaying ingestion by 24 hours.

Also replicating the CRT program by Jacobs et al. (2001), Nash, van den Ven, van Elk, and Johnson (2007) trained adult men with chronic, complete thoracic SCI with confirmed shoulder pain. After four months of CRT three times a week, pain rated on the WUSPI decreased from 31.9 points (out of 150) to 5.7 points. This near resolution of pain exceeded that reported after resistance training, where few participants included in the study even reported pain at baseline (Serro-Ano et al., 2012).

Circuit resistance training is effective at evoking muscular adaptations specific to training, but also improves anaerobic power, isokinetic strength, and aerobic performance. Additionally, CRT may be instrumental in alleviating pain in some individuals with SCI. Despite the fitness improvements reported after CRT, it is important to consider integrating lower extremity exercise either as the aerobic or isoinertial part of training in future research. Incorporating lower body training may assist in improving hemodynamic responses by decreasing blood pooling and promoting venous return. Additionally, little has been reported on the efficacy and safety of eccentrically based resistance training programs or CRT with individuals following SCI.

Eccentric resistance training

Muscular adaptations to ERT.

Eccentric resistance training is a strength training modality involving only eccentric muscle actions. In a traditional resistance training repetition, the muscle lengthens eccentrically to lower a weight followed by the muscle shortening concentrically to return the weight to the initial position. With ERT, participants only work during the eccentric portion of a repetition. Microscopically, ERT requires the creation of tensile forces as the sarcomere lengthens, often promoting damage to the cell.

While ERT programs elicit hypertrophic muscular adaptations at a fraction of the oxygen cost required for concentric work, ERT also more readily results in delayed onset of muscle soreness (DOMS). The cellular damage after ERT that leads to DOMS and prolonged muscular fatigue may be preceded by damage to neuromuscular excitatory mechanisms such as deformation of transverse tubules or cellular structures like titin, desmin, and z-lines (Proske & Morgan, 2001; Warren, Hayes, Lowe, & Armstrong, 1993). However, this cellular damage, most often measured as plasma creatine kinase (CK), is often avoided after repeated exposure to ERT, termed the repeated bout effect.

The repeated bout effect was demonstrated in a study conducted by McHugh and Tetro (2003) who evaluated knee extension isometric strength at varying joint angles before and after ERT. Adult males and females completed two bouts requiring six sets of 10 eccentric actions at 90% peak isometric strength, separated by 14 days. These individuals reported pain and displayed significant losses in isometric strength following the first training bout. However, no pain or loss of strength were reported after the second training day, in fact, isometric strength improved 13.6% when assessed at 110° knee flexion (McHugh & Tetro, 2003). Although not measured by the investigators, this improvement in torque production at a longer muscle length is indicative of the addition of sarcomeres longitudinally, thus limiting the strain of ERT (McHugh & Tetro, 2003; Seynnes et al., 2007). Additionally, more sarcomeres in series may optimize myofilament overlap, potentially explaining the acute improvement in torque production (McHugh & Tetro, 2003).

In order to substantiate the claims by McHugh and Tetro (2003) that sarcomeres are added to muscle fibers after being exposed to ERT, Seynnes et al. (2007) assessed isometric strength, muscle cross sectional area (CSA), fascicle length, and pennation angle of the vastus lateralus muscle after 10 days and 35 days of ERT. Young, healthy males and females completed quadriceps ERT three days per week on an eccentrically driven flywheel. Participants eccentrically resisted the lever arm by contracting the quadriceps as it moved their legs into knee flexion for four sets of seven maximal attempts. Only isometric strength (measured on an isokinetic dynamometer) and fascicle length was increased after 10 days of training. After 35 days of ERT, isometric strength improved 38.9%, CSA increased 7%, fascicles lengthened by 9.9%, and pennation angle increased 7.7% (Seynnes et al., 2007). This finding of lengthened fascicles after ERT supports the theory proposed by McHugh and Tetro (2003) that repeated exposure to ERT stimulates the addition of sarcomeres in length to attenuate strain damage following eccentric muscle actions (Seynnes et al., 2007). Further, this rapid hypertrophic response to ERT suggests that neural adaptations (34.8% increase in electromyography activity; EMG) were supported by architectural modifications (pennation angle and fascicle length) to promote isometric strength improvement. Based on these data, cellular adaptations such as adding sarcomeres to myofibers occur within 10 days following exposure to ERT. Continued ERT may also promote hypertrophy in the trained muscles.

The velocity of eccentric muscle actions may exert influence on the degree of muscle damage following ERT. In a cross-sectional study design, young males and females completed fast (210°/second) and slow (30°/second) isokinetic ERT using the elbow flexors (Chapman, Newton, Sacco, & Nasaka, 2006). Training time (120 seconds) was held constant between conditions to control for time under tension. As such, the slow velocity training consisted of five sets of six repetitions (30 muscle actions) and the fast velocity training consisted of 35 sets of six repetitions (210 muscle actions) with 90 seconds rest between each set, in each condition (Chapman et al., 2006). While both protocols resulted in loss of isometric strength and dynamic torque (measured on the isokinetic device) across seven days of recovery, the fast velocity ERT evoked greater muscle soreness (measured by a visual analog scale; VAS), 4.5 times higher plasma CK, and slower recovery of elbow range of motion (Chapman et al., 2006). These data would imply greater muscle damage, soreness, and reduction in function following fast ERT compared to slow ERT.

In a similar investigation evaluating fast and slow velocities of ERT, Shepstone et al. (2005) reported higher protein remodeling factors after fast ERT, suggesting greater potential for hypertrophy with greater velocity eccentric action in young, adult males. In the same investigation, the researchers then tested this speculation when 12 young men completed eight weeks of ERT (Shepstone et al., 2005). Participants trained one arm at a fast velocity (3.6 radians/second) and the contralateral arm at a slow velocity (0.35 radians/second), three days per week. After training, greater hypertrophic gains were evident in the arm that completed fast ERT compared to the arm that completed slow ERT (Shepstone et al., 2005). These data indicate that fast velocity ERT elicits greater muscle microstructure disruption, which in this study, was associated with greater hypertrophy.

It has been well documented that ERT promotes hypertrophy and strength gains more than concentric-based training (LaStayo et al., 1999). However, the cellular damage and pain associated with ERT may deter individuals from participating in ERT. As such, Flann, LaStayo, McClain, Hazel, & Lindstedt (2011) implemented a gradually progressed ERT program designed to avoid apparent muscle damage and soreness in young adults. University aged male and female students were divided into either a pre-trained group or naïve group. Both groups completed three days a week of 20-minute ERT sessions for eight weeks on an eccentrically driven recumbent stair stepper, the Eccentron. Exercise intensity progression was based on participants working at an RPE of 13 (scale ranged from 6 to 20). The pre-trained group was exposed to gradual increases in intensity and duration of ERT for three weeks prior to the eight-week training period. This ramping phase negated excess muscle damage (measured by CK levels) and pain (assessed by a 15cm VAS). During the eight weeks of ERT, participants in both groups completed similar work, but the naïve group experienced 5 times higher CK levels and significantly more muscle soreness than the pre-trained group (Flann et al., 2011). Despite vast differences in muscle damage markers, post-training assessments revealed similar increases in CSA, isometric strength, and muscle growth factors (insulin like growth factor 1). These findings indicate that extensive muscle soreness is not necessary to stimulate muscle growth and strength improvements following ERT.

An eight-week ERT program was designed to resemble traditional resistance training with sets and repetitions rather than endurance focused ERT (Weir, Housh, Housh, & Weir, 1995). Young men trained their non-dominant leg on a leg extension device for three to five sets of six repetitions at 80% of their eccentrically tested 1RM (Weir et al., 1995). Repetitions were timed and described as participant controlled lowering of the weight by flexing the knee for 1 to 2 seconds, at which time the weight was returned to its original position by the investigator. The ERT improved isometric strength by 13.5% (assessed on an isokinetic dynamometer) and eccentric strength by 29% (assessed on the training device; Weir et al., 1995). Resistance style ERT improves eccentric and isometric strength, but little is known about how this method translates to walking performance in those with impaired gait.

Eccentric resistance training is associated with greater pain and cellular deformation because of the high workloads and tensile forces. These negative consequences to ERT are pronounced if the negative work is completed at a fast work rate rather than a slow work rate. Excess muscle damage and pain may be avoided by repeated exposure to ERT or by cautiously increasing ERT intensity and duration to mitigate any acute deleterious effects. Further, data are available to support the positive hypertrophic adaptations uncoupled from stereotypical ERT consequences, such as pain or muscle fiber damage. With this, exercise professionals seeking to implement ERT with a novice trainee should gradually expose the individual to eccentric muscle actions at slow work rates in order to obtain gains in strength and muscle volume without negative consequences. Neuromuscular responses to training precede adaptations to musculoskeletal architecture. Neuromuscular responses to training may vary from traditional resistance training when exercise is based on eccentric muscle actions

Neuromuscular adaptations to ERT.

Neuromuscular adaptations are responsible for early accommodations to resistance training. Increases in strength within the first 20 weeks of training are most often associated with improved coordination of motor unit firing and decreased antagonist coactivation. Neuromuscular adaptations (increased EMG and cross-education) are greater following ERT compared to traditional resistance training (Hortobagyi et al., 1996). Even during maximal force production, eccentric muscle actions have lower levels of activation, likely due to a lower, but broader recruitment of fibers across a muscle or recruitment of only a subset of fibers to produce the necessary force (Enoka, 1996). A greater mechanical efficiency may explain why eccentric muscle actions provoke lower cardiovascular responses when total work is matched concentrically (HR, mean arterial pressure, and RPE; Hortobagyi & DeVita, 2000).

It is well documented that eccentric training may bring about muscle fatigue and damage. Following a bout of eccentrically lowering 40% of a young male's or female's maximum voluntary contraction (MVC) of the biceps in sets of 10 until fatigue, force capacity was hindered for more than 24 hours (loss of approximately 29%; Dartnall, Rogasch, Nordstrom, & Semmler, 2009). Further, after one week, the same task lead to greater motor unit discharge synchronization (Dartnall, Nordstrom, & Semmler, 2011). Because of muscle damage after the acute bout of ERT, the second exposure to eccentric actions lead to a lower threshold for muscle firing (occurring around 3.36% of MVC) when compared to before training (occurring around 8.4% MVC; Dartnall et al., 2009). This reduced threshold implies the recruitment of lower threshold motor units (Type I) rather than relying on fast twitch motor units (Dartnall et al., 2009). An additional protective adaptation after ERT was an increase of 11% in the motor unit discharge rate (Dartnall et al., 2009). These data may help explain the repeated bout phenomenon. Specifically, following an acute eccentric exercise bout, there are neuromuscular adaptations that prevent further muscular damage by decreasing the force necessary to bring about muscle action, speeding up motor unit discharge, and increasing motor unit synchronization. These modifications decrease the strain on the muscle fibers that are recruited to produce the eccentric force (Dartnall et al., 2011) and/or result in the recruitment of more slow motor units to withstand the load (Guilhem, Comu, & Guevel, 2010).

Eccentric resistance training may lead to greater agonist activation and reduced antagonist activation termed coactivation (Krentz & Farthing, 2010; Pensini et al., 2002). Maximal ERT on an isokinetic dynamometer for 20 days was sufficient to increase agonist activation (biceps) and decrease antagonist (triceps) coactivation in young men and women (Krentz & Farthing, 2010). However, this program of maximal efforts for six sets of eight repetitions every other day for 20 days lead to decreases in muscle strength and increased joint pain (Krentz & Farthing, 2010). A longer study (four weeks) brought about similar increases in agonist (gastrocnemius and soleus) activation and decreases in coactivation (-22%; tibialis anterior) without the decreases in strength and muscle damage (Pensini et al., 2002). In the Pensini et al. (2002) study, young males completed six sets of six, 3 second eccentric contractions at 120% concentric 1RM four times a week. Although muscle girth measurements were not measured, Pensini and colleagues

(2002) attributed the 46% increase in strength to neuromuscular adaptations rather than architectural hypertrophy. Although positive neural adaptations can be quantified within 20 days of ERT, preventing decreased strength is an important justification to train longer, at a less than maximum intensity, with longer recovery between bouts.

Neuromuscular training responses are evident in both younger (Lepley & Palmieri-Smith, 2014; Seger & Thorstensson, 2004) and older adults (Hortobagyi et al., 1996). The group of young individuals that lowered a maximal resistance isokinetically with the quadriceps three times a week for eight weeks improved strength and neural adaptations (measured by EMG) more than a group that performed the same exercise concentrically (Lepley & Palmieri-Smith, 2014). Further, the group that trained eccentrically displayed a crossover effect of increased EMG activity and strength in the unexercised limb (Lepley & Palmieri-Smith, 2014). This evidence of crossover was evident after 10 weeks of maximal isokinetic quadriceps ERT three days a week (Seger & Thorstensson, 2004). In healthy, adult men, four sets of 10 maximal efforts resulted in greater strength and EMG activation in the untrained limb following ERT (Seger & Thorstensson, 2004). This improved neural activity in the trained and untrained limbs may be valuable in rehabilitation settings where clinicians are seeking to develop leg strength in patients (Lepley & Palmieri-Smith, 2014).

Eccentric resistance training can lead to protective neuromuscular adaptations such as recruiting lower threshold motor units and increasing the rate of motor unit discharge. These neural adaptations occur in the prime mover and the inactive limb due to a crossover effect. There is also a decrease in coactivation following ERT. The transfer of neural improvements and the decrease in coactivation may be especially beneficial to those with bilateral deficiencies due to neurological disease or damage, similar to those reported after SCI (Kirshblum et al., 2011). With this, it would be beneficial to understand how special populations including those with SCI respond to ERT.

***Eccentric resistance training in special populations*.**

The potential for high force generation at low metabolic costs may prove optimal for individuals with diminished functional capacity. For example, there are two studies that document the efficacy of ERT in individuals with Parkinson's disease. Males and females with long term Parkinson's disease completed 12 weeks of training where ERT bouts progressively lengthened from three to five minutes to 15 to 30 minutes and intensity increased from 7 to 13 on an RPE scale ranging from 6 to 20 (Dibble et al., 2006; Dibble, Hale, Marcus, Gerber, & LaStayo, 2009). Eccentric resistance training three days a week on a recumbent stepper resulted in improved muscle force potential in the more affected limb (18-29%) and less affected limb (13-19%), the TUG improved (17%), QOL improved (15.6%), and the 6MWT improved (17%; Dibble et al., 2006; 2009). These data represent the potential for ERT to stimulate muscular adaptations and functional outcomes despite neurological deficits. Because strength, walking parameters, and QOL improved in those with disease originated neurological deficiencies (Parkinson's disease), it may be presumed that those with iSCI would reap similar gait, QOL, and strength benefits after completing ERT.

Older adults are known to have diminished aerobic capacity, muscular strength, and balance (Hortobagyi et al., 1995; LaStayo, Ewy, Pierotti, Johns, & Lindstedt, 2003). In one study of older adults, participants completed eight weeks of ERT on leg curl, extension, and press machines where the concentric portion of the lift was accomplished by the trainer lifting the weight and then the participant eccentrically lowering the weight for three to five seconds, three sets of eight to 12 repetitions, at 75% 1RM (Lezczak et al., 2013). Males and females (average age = 75.6 years) improved walking speed, the eight-foot TUG test, number of completed chair stands in 30 seconds, and isotonic strength (Lezczak et al., 2013). In a longer study (14 weeks) with older adults, fascicle length and knee extensor torque (measured on an isokinetic dynamometer) increased after participants trained the quadriceps eccentrically by lowering a weight for two sets of 10 repetitions at 80% estimated 1RM (Reeves, Maganaris, Longo, & Narici, 2009). As with individuals who have Parkinson's disease, these data highlight the benefit of using ERT to improve muscular and functional adaptations in those with lower exercise tolerance, similar to that reported in men and women living with iSCI. However, data are not available to assess the efficacy and tolerance of ERT in a population with iSCI.

Eccentric resistance training can be used to improve balance, strength, and physical functional parameters in those with neurological disorders and older adults. Data show that ERT programs can be completed at low intensity based on RPE or high intensity based on percent 1RM. Further investigation is needed to understand the efficacy of ERT in those with non-disease related spinal cord disorders. The low metabolic cost and high force potential associated with ERT may prove useful for those who have diminished functional capacity and muscle strength, like those with iSCI. Increasing muscular strength of the lower extremity should improve walking ability and dynamic balance when erect in those with SCI. An interesting ERT machine, the Eccentron, resembles a recumbent cycle ergometer, but where cycle pedals would be, stair stepping pedals reside. Isokinetic in nature, this ergometer incorporates eccentric muscle actions of the hamstrings and gluteal muscles as the participant resists the upward movement of the pedal as the knees and hips move into flexion. This machine provides accuracy values, which are usually unavailable with other isokinetic dynamometers, and additionally provides a platform to prescribe exercise based on eccentric multiple RM values. Unlike cyclical isokinetic dynamometers, this stair stepping machine replicates the motion and targets the muscles used during the stance and swing phases of gait. Further, the alternating pattern between legs allows participants to train both legs concurrently, much like gait training, a feature not available with other dynamometers.

Further, as the pedals of the Eccentron apply pressure to the bottom of the foot like a treadmill belt, an autonomic reflex of pushing is initiated independent of higher-level brain signaling (Stevens & Morgan, 2010). This reflexive force production is possible despite interrupted higher-level brain signaling following iSCI. This alternating, reflexive, high force muscle activity may translate to muscle gains specific to eccentric contractions, potentially translating to isometric and concentric muscle strength, and theoretically to walking function. If ERT on the Eccentron can improve muscle strength that translates to walking function, individuals with SCI may train, even if reflexive in nature only, to improve functional independence.

Conclusions

In sum, the consequences to SCI can affect an individual physically, physiologically, and psychologically. However, PA has shown to have a multifaceted positive impact on an individual recovering from SCI. As rehabilitation funding wanes, individuals with SCI need exercise modalities that can allow them to continue to gain function and maintain independence. Special consideration is needed when prescribing exercise to those with SCI because the loss of muscle innervation and size often leads to low aerobic capacities. As such, practitioners need to implement exercises that improve neurological function and muscle strength while keeping metabolic costs low. Eccentric resistance training allows for a high volume of work to be accomplished with a low oxygen requirement. Working eccentrically improves muscle architecture by adding sarcomeres and developing more forceful pennation angles, and improves neurological function by increasing agonist activation, decreasing antagonist coactivation, and transferring muscle excitability in untrained bilateral limbs. The applicability of ERT in other special populations is evident, however, this training practice has yet to be implemented in those with iSCI.

CHAPTER III

STRENGTH AND STEP ACTIVITY AFTER ECCENTRIC RESISTANCE TRAINING IN THOSE WITH INCOMPLETE SPINAL CORD INJURIES

Introduction

Incomplete spinal cord injury (iSCI) can interrupt or completely sever communication between higher-level brain centers and distal organs, sensory-motor neurons, and skeletal muscle (Kirshblum et al., 2011). Individuals with an incomplete SCI (iSCI) often experience diminished neurological and muscle function below the lesion (Riley, Burns, Carrion-Jones, & Dillingham, 2011). Following denervation, skeletal muscle transitions to a predominantly anaerobic, or glycolytic, fiber arrangement, further degrading oxidative function (Castro, Apple, Staron, Campos, & Dudley, 1999). With peak aerobic capacity averaging below the fifth percentile of individuals without SCI (Janssen, Dallmeijer, Veeger, & van der Woude, 2002; Pescatello, 2014), focused efforts are necessary to offset the spiraling effects of an often-sedentary lifestyle following iSCI. Much like in the able-bodied population, it is recommended that individuals with iSCI participate in regular physical activity (PA) throughout the week, including activities that will improve cardiorespiratory and musculoskeletal health (Pescatello, 2014).

Improving muscle strength after iSCI is an important emphasis of PA based on the strong positive correlation between walking performance and strength of hip flexors, extensors, and abductors, respectively (Kim, Eng, & Whittaker, 2004). Eccentric resistance training (ERT) is weight training that involves muscle actions only during the lowering, or eccentric, portion of a repetition. When compared to concentric muscle work, eccentric muscle actions have a lower metabolic demand, allow for greater force production, and lead to greater improvements in neural activation and strength (Hortobagyi et al., 1996; LaStayo, Reich, Urquhart, Hoppeler, & Lindstedt, 1999). There are four known modalities for ERT: (1) the participant eccentrically lowers a weight and a bystander performs the concentric portion of the repetition by returning the load back to position, (2) motor driven cycle ergometers where the participant eccentrically resists the pedals spinning backwards, (3) unilateral training on an isokinetic dynamometer, or (4) motor driven, recumbent stair steppers where the participant resists the upward motion of the pedals.

In a population with similar muscle strength characteristics as those with iSCI, older adults have improved balance, neurological function, coordination, and muscle architecture following ERT programs (LaStayo, Ewy, Pierotti, Johns, & Lindstedt, 2003; Mueller et al., 2009; Reeves, Maganaris, Longo, & Narici, 2009). Although all ERT modalities have been shown to benefit muscular strength, the recumbent stepper most closely resembles the reciprocal stepping pattern of ambulation. Further, training on a recumbent stair stepper may increase neurological adaptations because of the alternating neural activation necessary to perform ERT. Presently, there is no literature describing a relationship between ERT and walking activity, despite the correlation between muscle strength and step PA after iSCI.

Given the lack of information detailing the efficacy and safety of implementing lower body resistance training after iSCI, the purpose of this study was to quantify changes in lower body eccentric and isometric strength following a 12-week ERT on a recumbent stair stepping device. It was hypothesized that ERT for individuals with iSCI would increase eccentric strength and isometric strength. We also hypothesized that step PA would increase following ERT.

Methodology

Participants

Apparently healthy males and females (*N* = 11) who were a minimum of one year post iSCI completed the ERT. These individuals had cervical (*n* = 6), thoracic (*n* = 4), or lumbar (*n* = 1) iSCI for an average of 9.5 $\pm$ 4.7 years and an average age of 39.1 $\pm$ 15.9 years. Exclusion criteria included musculoskeletal injury within one year of training or during training and other participation in structured resistance training for the lower extremities. Further, participants were not permitted to begin any new lower body resistance training program during the study. Participant characteristics are presented in Tables 1 and 2. This study was approved by the university Institutional Review Board and participants signed a written consent form prior to pre-testing.

Table 1

Participant Descriptive Statistics (*N* = 11)

Variable	*M*	*SD*
Height (inches)	65.6	48.2
Weight (pounds)	167.2	48.2
Baseline walking speed (m/s)	0.34	0.42
Baseline WISCI	8	7

Note. Data are presented as means (*M*) and standard deviations (*SD*). M/s = meters per second during baseline 10 Meter Walk Test. WISCI = Walking index for spinal cord injury.

Table 2

Individual Descriptive Characteristics of Study Participants

Participant	Level of lesion	Years post-injury	Mode of locomotion	WISCI
1	C5-6	10.3	Ambulation	9
2	T12-L1	8.6	Wheel Chair	6
3	C3-7 & L4-5	5.2	Ambulation	19
4	T9-10	8.3	Wheel Chair	6
5	T5-6	4.9	Wheel Chair	2
6	T6	9.1	Wheel Chair	9
7	C1-L5	4.9	Ambulation	10
8	C6-7	8.8	Wheel Chair	2
9	C4-T3	8.9	Wheel Chair	2
10	C5-6	20.5	Ambulation	20
11	L2	15.0	Wheel Chair	2

Note. C = cervical, T = thoracic, L = lumbar. WISCI = score on baseline Walking Index for Spinal Cord Injury.

Instrumentation

Anthropometric measurement and pain.

Body mass was measured in gym clothing with shoes removed to nearest tenth of a kilogram (Health O' Meter 753KL, IL, USA, or Seca 674, Hamburg, Germay). General lower extremity pain or soreness was assessed at the beginning of each testing or training day. Individuals marked a vertical line representing lower extremity pain or soreness on a 10-centimeter visual analog scale (VAS) where the left end of the scale equaled zero (denoted by the words "no pain") and the right end of the scale equaled 10 (denoted by the words "pain as bad as it could possibly be (Flann, LaStayo, McClain, Hazel, & Hoppeler, 2004). Initial pain measures on day one and day two were averaged to establish a baseline for comparisons throughout the ERT. In the instance that pain or soreness increased more than three centimeters from baseline or exceeded a total of nine centimeters, the participant could request to postpone training or any increase in training load was delayed until the next training session.

Isometric strength.

Isometric strength was assessed using a hand-held, digital dynamometer (JTech Commander PowerTrack II, Midvale, UT, USA). The validity (R^2 = .66 to .76) and reliability (r = .81 to .93) of this dynamometer have been confirmed (Roy et al., 2009) and the use of hand-held dynamometry is highly correlated with the gold standard isokinetic testing in both able-bodied individuals (Stark et al., 2011) and those with neurological impairments (Berry, Giuliani, & Damiano, 2004; Riddle, Finucane, Rothstein, & Walker, 1989). Isometric strength was measured on both pretesting days, midway through the ERT, and after the ERT.

For hip extensor strength, the participant was supine on a cushioned table with one leg fully extended and the other flexed to 90° at the hip and knee joints. The investigators assisted the participant in holding this leg position to prevent muscular fatigue. Once hip and knee angles were established based on goniometry validation, the investigator placed the dynamometer's sensor immediately proximal to the knee. When ready, the participant used his or her hamstrings and gluteal muscles to press against the sensor in the investigator's hand for approximately four seconds, establishing a maximal voluntary contraction (MVC) for hip extension. After resting, the participant repeated this procedure until there was no improvement. The testing procedure was then repeated on the other limb. While in this position, the investigator moved the sensor to the anterior portion of the thigh, proximal to the knee to capture forces exerted during hip flexion. The participant was asked to continue with hip flexion until there was no improvement on either leg. Next, the participant sat upright with both legs off the table, again, with the hips and knees at 90°. One at a time, the participant attempted to extend the shank with the quadriceps to obtain a knee extension MVC. Data were recorded by the sensor in the investigator's hand located directly above the ankle on the anterior portion of the shin. Testing was repeated until there was no improvement and then completed on the contralateral leg. To assess knee flexion, the sensor was moved to the posterior portion of the shank directly above the calcaneus tendon. Testing was repeated with four second MVCs to performance plateau. The sensor was then moved to the bottom of the foot and the participant was asked to repeat the MVC procedures while attempting to plantarflex. Participants were exposed to MVC testing on the first day for familiarization and MVC assessments were repeated and recorded on the second visit to the laboratory to account for learning effects. A summed isometric strength score was composed of the best recordings on day two for each movement on each leg. Isometric strength was summed to a single score to match the data derived from the eccentric ergometer. The total score was converted to a value in newtons and relative to the participant's mass (N/kg) to allow for the direct comparison of other training modalities previously reported in the literature.

Eccentric strength.

Eccentric strength testing was completed on a recumbent, motor driven stepper (Eccentron, BTETech, Hanover, MD, USA). The participant was seated in a chair that was adjusted so that when both feet were on the pedals and one leg was extended, the knee angle of the extended leg was no less than 45° and no more than 55° and the flexed knee was approximately 90°. After familiarization and a one minute warm up, participants were asked to allow the pedals to move through several repetitions without exerting force. This allowed the investigators to evaluate resting lower extremity tone. After familiarization with the function of the machine and an eccentric warm up, the participant completed two bilateral, three repetition maximum (RM) attempts (left leg, then the right leg, and so on; Jacobs, 2009). After dosing, a 1RM for eccentric strength was calculated for subsequent exercise prescription (Brzycki, 1993). All dosing tests were performed before training sessions to avoid muscle fatigue. The highest average peak force of 1RM attempts (or dose) on day two was used to set the initial training intensity. Revolutions per minute (rpm) during 3RM testing was set at 12 rpm (see Table 3).

Daily step physical activity.

Daily step PA was captured by a Step Activity Monitor (SAM). The SAM is reliable (97-98% accuracy) and valid for measuring step activity in those with SCI (Bowden & Behrmann, 2007). Calibration for expected gait characteristics followed procedures outlined by Stevens, Caputo, Fuller, and Morgan (2015). After calibration on day two, the participant affixed the SAM with a Velcro strap around the less-impaired leg (Bowden & Behrmann, 2007). Daily step counts began the day after the participant received the SAM and continued for three consecutive weekdays and one weekend day (excluding bathing activities and scheduled training session). Data were collected in 1-minute epochs.

Procedures

Participants were instructed not to engage in strenuous exercise for two days prior to pre-, mid-, and post-testing. When entering the laboratory on day one, participants completed the VAS, isometric strength, and eccentric strength testing protocols for familiarization. On day two, the participants repeated the procedures and measures and for pre-test data were recorded. Additionally, care and a wearing schedule for the SAM were discussed with the participant before leaving the laboratory on day two. On the third visit, participants began training on the eccentric stepping ergometer. Participants trained two times a week for 12 weeks with a minimum of 48 hours between training sessions. During the first two weeks, training intensity was based off of the pre-test eccentric assessment. After two weeks, the participants re-dosed on the eccentric stepper to establish workload 2 which was used to calculate training intensity until participants re-dosed again at the end of week 6 (see Table 3). Muscle strength measures and step PA were repeated at the end of week 6 as a mid-point assessment. The ERT was designed to target muscular strength and hypertrophy according to guidelines presented by the National Strength and Conditioning Association (Haff & Triplett, 2016). If, however, the calculated training workload outlined in Table 3 was less than the previously evaluated tone, the same intensity progression was followed and added to the tone value serving as the training workload (ex. tone + 35% and tone + 17%). When participants could complete two additional repetitions in the last two sets of a training day, exercise intensity was increased in accordance to the training guidelines presented in Table 3. However, if participants were unable to reach target workloads for more than 30% of efforts, the intensity was reduced to allow for successful and accurate repetitions. Following training, participants returned to the laboratory to repeat the assessments. Efforts were made to ensure that testing and training occurred at approximately the same time of day.

Statistical analyses

An a priori power computation indicated that the analyses would be powered at 80% when 10 participants completed the ERT (G*Power, Version 3.1). IBM Statistics for Windows, Version 23.0 (Aramonk, NY: IBM Corp) was used to analyze data. Three one-way repeated measures analysis of variances (ANOVAs) were used to evaluate the

Table 3

Eccentric Resistance Training Program

Week	Day	Resistance	Sets	Reps	RPM	Rest (min)
1	1	Familiarization			12	
	2	Familiarization			12	
2	1	Familiarization			12	
	2	**3RM Assessment for Workload 2				
3	1	≥85	2 - 6	≤ 6	12	3.0
	2	67 - 75	3 - 6	6-10	12	1.5
4	1	≥85	3 - 6	≤ 6	12	3.0
	2	67 - 75	3 - 6	6 -10	12	1.5
5	1	≥85	4 - 6	≤ 6	12	3.0
	2	70 - 80	4 - 6	8-12	12	1.5
6	1	≥85	5 - 6	≤ 6	12	3 - 5
	2	**3RM Assessment for Workload 3 and Mid-Test Outcome				
7	1	≥85	2 - 6	≤ 6	12	3 - 5
	2	67 - 75	3 - 6	6-10	12	1.5
8	1	≥85	3 - 6	≤ 6	12	3.0
	2	67 - 75	3 - 6	6 -10	12	1.5
9	1	≥85	4 - 6	≤ 6	12	3.0
	2	67 - 75	4 - 6	8-12	12	1.5
10	1	≥85	5 - 6	≤ 6	12	3.0
	2	70 - 80	5 - 6	8-12	12	1.5
11	1	≥85	5 - 6	≤ 6	12	3 - 5
	2	70 - 80	5 - 6	10 -12	12	1.5
12	1	≥85	5 - 6	≤ 6	12	3 - 5
	2	75 - 85	5 - 6	10 - 12	12	1.5

Note. Reps = repetitions; RPM = repetitions per minute; min = minutes; Day 1 = muscular strength; Day 2 = muscular hypertrophy; Resistance = percent of peak mean force of the weaker leg during respective 3RM. Rest = time between sets; Familiarization = self-selected training duration and intensity, approximately 2 x 8 at 50% of Workload 1 at 12 rpm.

impact of ERT (baseline, mid-training, and post-training) on isometric strength, eccentric strength, and average daily step PA. Effect sizes also were calculated (*d* = difference in means/baseline *SD*) to compare the mid- and post-training scores to the baseline scores. An a priori familywise alpha of $p < .05$ was used.

Results

Statistics describing the participants are provided in Tables 1 and 2. The study included 14 individuals, however, 3 discontinued participation, for personal reasons, prior to completing the familiarization period. Analyses included 11 individuals who finished the ERT, completing an average of 98% of training sessions (see Table 2). Step PA data were lost for one participant due to a monitor clearing error. As such, all analyses involving step PA included 10 individuals. Average daily step PA did not differ following ERT (F (2.00, 18.00) = 2.73, *MSE* = 216,836.78, H-F $p = .092$). Significant improvements were documented for eccentric strength (F (1.27, 12.71) = 8.42, *MSE* = 1738.35, H-F $p = .009$) and isometric strength (F (1.97, 19.77) = 7.10, *MSE* = 11.29, H-F $p = .005$). Post hoc comparisons with Sidak corrections indicated that eccentric strength improved from pre-test to mid-test ($p = .034$) and from pre-test to post-test ($p = .038$). No change was noted between mid-test and post-test ($p = .15$). Differences in isometric strength only occurred when comparing pre-test to post-test data ($p = .031$). See Table 4 for means and standard deviations of study variables.

Table 4

Eccentric Strength, Isometric Strength, and Average Daily Step Activity

Variable	*M*	*SD*
Eccentric strength (lbs)		
Baseline	152.8	122.2
Mid-assessment	187.5*	149.9
Post-assessment	210.6*	175.6
Isometric strength (N/kg)		
Baseline	8.2	7.4
Mid-assessment	11.3	11.8
Post-assessment	13.5*	12.5
Average daily step activity (steps)		
Baseline	1514	1898
Mid-assessment	1731	1903
Post-assessment	2000	2189

Note. Eccentric strength is sum of the right and left legs during dosing procedure. Isometric strength is sum of the highest trial for the right and left legs from each assessment. Average daily step activity is step activity of less impaired limb during 3 week days and 1 weekend day. * = Significantly different from pre-test (p < .05).

Discussion

The current investigation was designed to determine how ERT effected eccentric strength, isometric strength, and daily step PA for those with chronic iSCI. Eccentric strength improved as a result of the ERT (~34%), with most improvements occurring during the initial six weeks of training (~26%). Isometric strength improved an average of 120% across the 12-week ERT. While not statistically significant, on average, step PA increased by 32% across the study.

In support of previous work (Stone, Stevens, Fuller, & Caputo, 2017), data from the current study support the contention that individuals with iSCI have the capacity to improve neuromuscular function of the affected limbs similarly to unimpaired individuals. Our participants with iSCI showed similar improvements as young, healthy men who completed 35 ERT training sessions on a knee extension machine (~39%; Seynnes, de Boer, & Narici, 2007) and neurologically intact men who completed eight weeks of unilateral ERT targeting the knee extensors (~29%; Weir, Housh, Housh, & Weir, 1995). These investigations varied in ERT design in regard to training intensity, sets, repetitions, and total volume. Seynnes et al. (2007) designed the ERT so that participants completed four sets of seven maximal eccentric muscle actions. Weir and colleagues (1995) allowed for a familiarization period, similar to the current study, wherein participants increased from three to five sets across the first three weeks with the final five weeks consisting of six sets of six repetitions at 80% 1RM.

In comparison to other data drawn from people with other neurological impairments, the current participants demonstrated greater improvements in lower extremity eccentric strength. A sample of individuals with Parkinson's disease showed improvements ranging from 13-29% after 12 weeks of ERT on a recumbent, eccentrically driven cycle ergometer (Dibble et al., 2006). These individuals progressed from three to five minutes per session to 15 to 20 minutes per session while mediating intensity through ratings of perceived exertion (Dibble et al., 2006). The more dramatic improvements observed in the current study may be due to the higher intensities and the overall program design.

Previously, Stone et al. (2017) utilized the same training ergometer in a similar sample of individuals with iSCI who would be described as daily ambulators (one cervical and two thoracic iSCIs) and reported improvements in eccentric strength averaging 79% following an 8-week ERT. These participants completed three training sessions per week where the first four weeks emphasized muscular endurance and the second four weeks targeted muscular strength and hypertrophy. The eccentric strength improvements might be higher than in the current study because of the variability in iSCI severity (i.e. the inclusion of wheelchair users) and differences in overall training volume. Similarly, the effect size for eccentric strength for the current ERT is smaller (n^2 = .05) than the previously published ERT ($n_p{}^2$ = .68; Stone et al., 2017). Data are not available to determine if the variance between these two ERT protocols derives from neurological or architectural origins. Future investigations may consider directly comparing the available ERT programs to determine the value of each design relative to local muscular adaptations.

As with eccentric strength, the summed lower extremity isometric strength improved from pre-ERT to post-ERT. It is likely that the nearly 72% improvement from pre-test to mid-test and 29% change from mid-mid to post-testing failed to reach statistical significant because of the variance in inter-participant performance. For example, if one participant improved from 100 N/kg to 150 N/kg, this individual response would equate to a 50% improvement. Similarly, another participant who improved from 1 N/kg to 3 N/kg would improve by 300%. Future investigations may consider separating samples into groups of those who are primarily wheelchair users and community ambulators to achieve a more refined statistic. Despite this, the effect of the ERT was large enough to improve isometric strength from pre-ERT to post-ERT in the hip and knee flexors and extensors as well as ankle plantar flexors in those with chronic iSCI.

The improvements in bilateral leg strength in those with iSCI following the current ERT intervention are like those shown following other gait training modalities. Stevens et al. (2015) noted a 57% improvement in isometric leg strength following 8 weeks of underwater treadmill training in individuals with chronic iSCI. These individuals were older (average of 47.7 years old) and closer in duration to their iSCI (average of 4.8 years) compared to the current sample (average of 9.5 years post-iSCI and 39.1 years old). Weir and colleagues (1995) noted a 13.5% improvement in isometric strength in healthy men following an 8-week ERT. The current ERT program may have elicited a greater percent change than previously reported protocols for various reasons: (1) the ERT was performed by individuals with lower levels of baseline function allowing for a greater ability to respond to the training and (2) the current study had an additional four weeks of training compared to these comparison studies. Knowing that eccentric strength training can also improve isometric strength in those with iSCI has clinical implications. Eccentric training, may allow improvements in gait mechanics such as stride length and stance support time, with lower metabolic demand for patients.

While speculative, the improvements observed for eccentric and isometric strength in those with iSCI may be derivative of both neural and architectural adaptations. Short duration, high intensity ERT has resulted in increased cross sectional area, fascicular length, pennation angle, and muscular activity in healthy adults (McHugh & Tetro, 2003; Seynnes et al., 2007). Despite the short term training duration, it is reasonable that participants in the current study experienced neuromuscular and architectural changes in the lower extremities. Evidence is available to support that sarcomeres are added longitudinally to myofibrils in as little as 10 days following repeated exposure to ERT (McHugh & Tetro et al., 2003). Others have shown that short term (approximately one month) ERT is sufficient to increase agonist activation and attenuate antagonist coactivation (Krentz & Farthing, 2010; Pensini, Martin, & Maffiuletti, 2001).

Eccentric and isometric strength are valuable musculoskeletal fitness components of gait training after neurological disorders. The potential for neurogenesis and regeneration of muscle microarchitecture following ERT sets the stage for individuals with iSCI to regain neuromotor control and strengthen skeletal muscles below the injury to the spinal column. Focused training of the muscles involved with standing and ambulation on the recumbent stepper may serve as a starting point for those with iSCI seeking to regain ambulatory capacity. In a different sample, it was shown that people with Cerebral Palsy, strengthening of the knee flexors (r = .60) and extensors (r = .68) highly correlate with walking skills (Damiano, Martellotta, Sullivan, Granata, & Abel, 2000). Damiano et al. (2000) identified weakness in the quadriceps and lower muscle activity tied to depreciated walking function in Cerebral Palsy. Specific to the ankle, gait parameters such as speed (r = .58) and single leg support time (r = -.25) are correlated with plantar flexor strength (Lin, Yang, Cheng, & Wang, 2006). In the current study, plantar flexor strength improved by 124% across the 12-week ERT. Although not specifically defined in a population with iSCI, it is postulated that lower extremity strength is highly correlated with physical function. Future investigations are needed to solidify this theory and to identify the relationship between hip strength and walking function after iSCI.

There we no significant changes in step activity as a result of the ERT. On average, daily step PA improved by an average of 32% from pre-test to post-testing with an effect size of $n^2 = 0.02$. This percent improvement and effect are smaller than that seen with iSCI after aquatic gait training (120% and $n_p^2 = 0.51$; Stevens et al., 2015). Unsolicited participant remarks indicated that perceived walking self-efficacy improved as a result of the ERT. However, if there were not sufficient means for the participant to walk at home (walker, braces, physical assistance, etc.), the individual could not translate the improvements in leg strength to home or community walking activity. As such, future investigations seeking to identify the relationship between ERT and daily step PA should limit participation to individuals with the means to perform gait activities at home. Additionally, follow-up analyses evaluating the relationship between eccentric leg strength and daily step PA could provide support to data demonstrating a linear relationship between isometric strength and daily step PA in individuals with chronic iSCI (Stevens et al., 2015). The documented change in step activity should be valued because any improvement in PA in a population as sedentary as those with iSCI is worthwhile. However, this method of exercise training is likely not the most effective in eliciting the greatest ambulatory PA changes.

In conclusion, ERT can serve as a potent stimulus in the development of eccentric and isometric strength. Although not studied in the current investigation, it may be speculated that the attained isometric and eccentric strength could translate to specific gait mechanics and walking function and is a valuable avenue for future research.

CHAPTER III REFERENCES

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APPENDIX FOR STUDY I

APPENDIX A

IRB Approval Letter

MIDDLE TENNESSEE STATE UNIVERSITY

IRB
INSTITUTIONAL REVIEW BOARD
Office of Research Compliance,
010A Sam Ingram Building,
2269 Middle Tennessee Blvd
Murfreesboro, TN 37129

EXPEDITED PROTOCOL APPROVAL NOTICE

8/3/2015

Investigator(s): Whitley Stone (PI), Jenn Caputo, Sandra Stevens and Dana Fuller
Investigator(s) Email: wjs3c@mtmail.mtsu.edu; jenn.caputo@mtsu.edu; and sandra.stevens@mtsu.edu

Department: Health and Human Performance

Protocol Title: "Eccentric resistance training in those with spinal cord injuries and able bodied adults "

Protocol ID: 15-340

Dear Investigator(s),
The MTSU Institutional Review Board (IRB), or its' representative, has reviewed the research proposal identified above. The MTSU IRB or its representative has determined that the study poses minimal risk to participants and qualifies for an **EXPEDITED** review under 45 CFR 46.110 and 21 CFR 56.110 within the category *(4) Collection of data through noninvasive procedures.* This approval is valid for one year from the date of this letter **for 10 (TEN) participants** and it expires on **8/4/2016**.

Any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615) 494-8918 within 48 hours of the incident. Any change(s) to this protocol must be approved by the IRB. The MTSU HRP defines a "researcher" as someone who works with data or has contact with participants. Anyone meeting this definition needs to be listed on the protocol and needs to complete the required training. New researchers can be amended to this protocol by submitting an Addendum request researchers to the Office of Compliance before they begin to work on the project.

Completion of this protocol MUST be notified to the Office of Compliance. A "completed research" refers to a protocol in which no further data collection or analysis is carried out. This protocol can be continued up to THREE years by submitting annual Progress Reports prior to expiration. Failure to request for continuation will automatically result in cancellation of this protocol and you will not be able to collect or use any new data.

All research materials must be retained by the PI or the faculty advisor (if the PI is a student) for at least three (3) years after study completion. Subsequently, the researcher may destroy the data in a manner that maintains confidentiality and anonymity. IRB reserves the right to modify, change or cancel the terms of this letter without prior notice. Be advised that IRB also reserves the right to inspect or audit your records if needed.

Sincerely,
Institutional Review Board
Middle Tennessee State University

8/31/2015

Investigator(s): Whitley Stone (PI), Jenn Caputo, Sandra Stevens and Dana Fuller

Department: Health and Human Performance

Protocol Title: Eccentric resistance training in those with spinal cord injuries and able-bodied adults

Protocol Number: #15-340

Dear Investigator(s):
We have reviewed your research proposal identified above and your requested changes. The following changes have been approved:

(1) New investigators Samantha Johnson and Layci Watts-Harrison are approved to be included in this protocol;
(2) The number of participants are approved to be increased from 10 to 40.

Please note that any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615)494-8918 or compliance@mtsu.edu. Any change to the protocol must be submitted to the IRB before implementing this change.

You will need to submit an end-of-project report to the Office of Compliance upon completion of your research. Complete research means that you have finished collecting data and are ready to submit your thesis and/or publish your findings. Should you not finish your research within the one (1) year period, you must submit a Progress Report and request a continuation ***prior*** to the expiration date on your approval letter. Please allow time for review and request revisions.

According to MTSU Policy, a researcher is defined as anyone who works with data or has contact with participants. Anyone meeting this definition needs to be listed on the protocol and needs to complete the online training. If you add researchers to an approved project, please forward an updated list of researchers to the Office of Compliance ***before*** they begin to work on the project.

Please note: **all research materials must be retained by the PI or a faculty advisor** (if the PI is a student) for at least **three (3) years after study completion**. Should you have any questions or need additional information, please do not hesitate to contact our office.

Sincerely,

Office of Compliance
Institutional Review Board Member
Middle Tennessee State University Office of Compliance

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Middle Tennessee State University
1301 E. Main St. Murfreesboro, TN 37129

IRB
INSTITUTIONAL REVIEW BOARD
Office of Research Compliance,
010A Sam Ingram Building,
2269 Middle Tennessee Blvd
Murfreesboro, TN 37129

IRBN001 - EXPEDITED PROTOCOL APPROVAL NOTICE

Friday, May 27, 2016

Investigator(s): Whitley Stone (Student PI), Sandra Stevens, Dana Fuller and Jennifer Caputo
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Department: Health and Human Performance

Study Title: ***Eccentric resistance training in those with spinal cord injuries and able-bodied adults***
Protocol ID: **15-340**

Dear Investigator(s),

The above identified research proposal has been reviewed by the MTSU Institutional Review Board (IRB) through the **EXPEDITED** mechanism under 45 CFR 46.110 and 21 CFR 56.110 within the category *(4) Collection of data through noninvasive procedures* A summary of the IRB action and other particulars in regard to this protocol application is tabulated as shown below:

IRB Action	APPROVED for one year	
Date of expiration	**8/4/2017**	
Sample Size	10 (TEN)	
Participant Pool	**Adults with spinal cord injury**	
Exceptions	NONE	
Restrictions	**Inclusion/exclussion criteria (on file) must be adhered through IRB approved screening procedure**	
Comments	ACSM Risk Stratification allowed	
Amendments	**Date**	**Post-approval Amendments**
	8/27/2015	Appoved to include Samantha Johnson and Layci Watts-Harrison to the protocol
	8/31/2015	Approved to increase sample size from 10 to 40 (FORTY)
	5/5/2016	1. Samantha Johnson & Layci Harrison are removed from the protocol 2. Only individuals with spinal cord injury will be recruited 3. Request to increase the training period from 8 weeks to 10 weeks is granted - However, the number of training sessions per week has been reduced from 3 to 2 times a week 4. The requested procedural amendment measure walking speed after each session has been approved 5. The "Quality of Life Spinal Cord Injury III and Spinal Cord Injury Independence Measure" questionaire has been approved to be administered to the participating individuals 6. Use of pedometer is permitted - No identifiable information or

	5/5/2016	other types of tracking can be used in the pedometer study. 7. A revised informed consent form to reflect all the changes in this amendment has been reviewed and approved
	5/27/2016	1. New investigator Core Gray added to help data collection, testing and exercise training 2. Two additional isometric measurements have been approved: (a) Measurement of hip flexion stated in the addendum; AND (b) knee extension 3. Requested additional VAS scale has been approved 4. Informed consent document reflecting these amendments has also been approved

This protocol can be continued for up to THREE years (**8/4/2018**) by obtaining a continuation approval prior to **8/4/2017**. Refer to the following schedule to plan your annual project reports and be aware that you may not receive a separate reminder to complete your continuing reviews. Failure in obtaining an approval for continuation will automatically result in cancellation of this protocol. Moreover, the completion of this study MUST be notified to the Office of Compliance by filing a final report in order to close-out the protocol.

Continuing Review Schedule:

Reporting Period	Requisition Deadline	IRB Comments
First year report	7/4/2016	5/5/2016 - Continuing review was conducted on this protocol. It has been approved for an additional year in accordance with Expedited Category 8 "Continuing Review of Previously Approved Protocol"
Second year report	7/4/2017	INCOMPLETE
Final report	7/4/2018	INCOMPLETE

The investigator(s) indicated in this notification should read and abide by all of the post-approval conditions imposed with this approval. Refer to the post-approval guidelines posted in the MTSU IRB's website. Any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615) 494-8918 within 48 hours of the incident. Amendments to this protocol must be approved by the IRB. Inclusion of new researchers must also be approved by the Office of Compliance before they begin to work on the project.

All of the research-related records, which include signed consent forms, investigator information and other documents related to the study, must be retained by the PI or the faculty advisor (if the PI is a student) at the secure location mentioned in the protocol application. The data storage must be maintained for at least three (3) years after study completion. Subsequently, the researcher may destroy the data in a manner that maintains confidentiality and anonymity. IRB reserves the right to modify, change or cancel the terms of this letter without prior notice. Be advised that IRB also reserves the right to inspect or audit your records if needed.

Sincerely,

Institutional Review Board

CHAPTER IV

AMBULATION AND PHYSICAL FUNCTION AFTER ECCENTRIC RESISTANCE TRAINING IN ADULTS WITH INCOMPLETE SPINAL CORD INJURY

Introduction

Interrupted nervous system signaling to the periphery following spinal cord injury (SCI) often leads to impaired gait, decreased muscular strength, and altered metabolic function (Chilibeck, Jeon, Weiss, Bell, & Burham, 1999; Maynard et al. 1997). As such, those with SCI are often deconditioned and experience hypokinetic diseases (Jacobs & Nash, 2004). Like those without disability, to combat the deleterious effects of a sedentary life style, it is recommended that individuals with SCI participate in cardiovascular activities most days of the week supplemented with muscular strengthening exercises (Ginis et al., 2011; Jacobs & Nash, 2004). Common modes of physical activity (PA) after SCI include arm and leg cycling, aquatic walking, and upper body resistance training. There is limited evidence available on the efficacy of lower body resistance training following SCI, likely because of the high metabolic demand and neural activation.

Although speculative, active lower body resistance training may improve ambulatory capacity in individuals after incomplete spinal cord injury (iSCI). Electrically stimulated resistance training of the quadriceps improves mitochondrial capacity (Ryan, Erickson, Young, & McCully, 2013) and leg muscular strength is positively correlated with walking performance (Kim, Eng, & Whittaker, 2004). However, the attenuated muscular force capacity following iSCI (Jacobs & Nash, 2004) may be insufficient to stimulate muscular adaptations necessary for ambulation. As such, eccentric resistance training (ERT) may be an optimal training regimen for those with iSCI seeking increases in muscular strength without external neuromuscular electrical stimulation. Compared to concentric contractions, eccentric muscle actions require fewer neurons to fire to generate any absolute force, metabolic demand is lower for a given workload, and maximal force production is higher (Enoka, 1996). Further, muscular adaptations in fiber area, fiber length, and pennation angle (Seynnes, de Boar, & Narici, 2007) may be greater after ERT compared to traditional resistance training (LaStayo, Reich, Urquhart, Hoppeler, & Lindstedt, 1999). With this, ERT may serve as an ideal lower body training modality in those with iSCI, who have significant skeletal muscle atrophy, impaired force production, and limited functional capacity.

Eccentric resistance training after iSCI may be performed on several exercise devices. Initially, a recumbent stair stepper may be the best option. Training on a motor driven eccentric stepper (Eccentron; BTETech, Hanover, MD, USA) differs from other exercise devices by allowing the individual with iSCI to train the limbs bilaterally and visually track the accuracy of force production during repetitions. Further, the upward driving force of the pedals may stimulate reflexive muscle activation of the lower extremities, despite interrupted signaling from higher-brain centers. The Eccentron may assist in concurrently improving lower extremity muscle strength and reciprocal limb activation, both of which may improve ambulatory function.

Although muscular strength is correlated with walking capacity, little is known on the efficacy of ERT on improving walking speed (10MWT), mobility (TUG), assistance needed during walking tasks (WISCI), at home daily physical function (SCIM), and daily step PA. Therefore, the purpose of this study was to evaluate ambulatory measures, physical function, and daily step PA before, after 6-weeks, and after 12-weeks of ERT on the Eccentron. It was hypothesized that time on the TUG and 10MWT would decrease and scores on the SCIM and WISCI tests would increase. Further, it was hypothesized that the TUG, 10MWT, WISCI, and SCIM would be predictors of daily step PA.

Methodology

Participants

The sample included 7 males and 4 females, 6 of whom had a cervical iSCI, 4 had a thoracic iSCI, and 1 had a lumbar iSCI. The average age of the participants was 39.0 years ($\pm$15.9 years) and participants were an average of 9.5 years ($\pm$ 4.7) post-iSCI. Individual participant characteristics are provided in Table 1. Participants were excluded if they had experienced musculoskeletal injury within the past year or were currently participating in a structured lower body resistance-training program. The study was approved by the university Institutional Review Board and participants signed an informed consent.

Instrumentation

Anthropometric measure and pain.

Body mass was measured to the nearest 0.01 kilogram on a standing scale (Health O' Meter 753KL, IL, USA) or wheelchair scale (Seca 674, Hamburg, Germany). Upon

Table 1

Individual Participant Characteristics (*N* = 11)

Sex	Injury level	Chronicity (years)	Walking speed (m/s)	WISCI	SCIM	Primary mode of locomotion
F	C5-6	10.3	0.60	9	77	Rolling walker
M	T12-L1	8.6	0.21	6	75	M. wheel chair
M	C3-7, L5-6	5.2	0.84	19	94	Forearm crutch
M	T9-10	8.3	0.09	6	70	M. wheel chair
M	T5-6	4.9	0.03	2	66	M. wheel chair
M	T6	9.1	0.19	9	86	M. wheel chair
F	C1-L5	4.9	0.40	10	77	Cane + AFO
M	C6-7	8.8	0.02	2	57	M. wheel chair
F	C4-T3	8.9	0.01	2	27	P. wheel chair
F	C5-6	20.5	1.30	20	89	Ambulation
M	L2	15.0	0.02	2	75	M. wheel chair

Note. Injury level; C = cervical; T = thoracic; L = lumbar. Walking speed = baseline 10 meter walk test. WISCI = Walking Index for Spinal Cord Injury. SCIM = baseline Spinal Cord Independence Measure. Primary modes of locomotion included three wheeled (rolling) walkers, manual wheel chairs (M. wheel chair), powered wheel chairs (P. wheel chair), forearm crutches, canes with ankle foot orthotics (AFO), and ambulation (with no assistive devices).

arriving to the laboratory for training each day, participants made a vertical line on a 10-centimeter visual analog scale (VAS) to represent lower extremity pain or soreness associated with the training protocol. Scores ranged from 0 “no pain” to 10 “pain as bad as it can be.” Pain was assessed on the first two laboratory visits to establish an average baseline of lower body discomfort. Scores beyond 9 centimeters on the VAS or deviations from baseline beyond 3 centimeters on subsequent training days resulted in the delay of any increase in training intensity until the next scheduled training time or the participant was given the option to postpone training to another day.

Functional independence.

The ability of the participants to complete daily tasks associated with independent living was assessed with the SCI Independence Measure (SCIM). The SCIM allows an individual to earn up to 20 points on self-care, 40 points for respiration and sphincter management, and 40 points for mobility, with a possible total score of 100. Participants completed the SCIM after visit one, at mid-assessments, and post-ERT.

Resting tone, eccentric testing, and training.

Training took place on an Eccentron. This motor driven eccentric ergometer drives the pedals towards the seated individual who is eccentrically resisting the movement. The Eccentron targets the gluteal, hamstring, and quadriceps muscles. Participants were familiarized with eccentric strength testing on the first laboratory visit and tested again on the second laboratory visit to establish a baseline for data collection. Positioning for testing and training was adjusted so that when the left foot was on the pedal and the leg was fully extended, the knee angle was no less than 45° and no more than 55°. While in this position, the contralateral knee was flexed at approximately 90°. After familiarization, but prior to three repetition maximum (3RM) testing, the participant was asked to maintain the starting position and allow the Eccentron pedals to move for 1 minute. By doing so, the investigators determined the average force exerted by the legs and underlying muscular tone when the legs were passively moving throughout the range of motion. The participant was given time for familiarization and an eccentric warm up prior to testing.

Bilateral eccentric strength was determined after performing a 3RM test on the Eccentron (Jacobs, 2009). Testing repetitions per minute (rpm) were set at 12 rpm. Taking the better of 2 trials on day two, the peak force of the more impaired leg during the 3RM was converted to a 1RM and used for the initial exercise prescription (Brzycki, 1993). This dosing procedure was repeated at the beginning of week three to obtain workload two, week six to establish workload three (midpoint assessment), and after completing the ERT (see Table 2). All dosing tests were performed immediately before training to prevent the effects of muscular fatigue.

Mobility.

The timed up and go (TUG) is an ambulatory test designed to assess walking performance and mobility. As quickly and safely as possible, the participant stood from a chair, walked 3 meters, turned, and returned to a seated position in the chair. The participant used the least amount of assistance (physical or device) needed to safely complete the task. Any assistive device(s) used during pre-testing was also used at

Table 2

Eccentric Resistance Training Program

Week(s)	Training load %	Sets	Reps	Rest (min)
1-2	Familiarization			
	**Week 2 Day 2: 3RM Assessment for workload 2			
3-5	Day 1: ≥ 85	2-6	≤ 6	3.0
	Day 2: 67-80	3-6	6 - 10	1.5
6	Day 1: ≥ 85	5-6	≤ 6	3.0
	**Week 6 Day 2: 3RM Assessment for workload 3 & mid-test data			
7-9	Day 1: ≥ 85	2-6	≤ 6	3.0
	Day 2: 67-75	3-6	6 - 10	1.5
10-12	Day 1: ≥ 85	5-6	≤ 6	3.0
	Day 2: 70-84	5-6	10 - 12	1.5

Note. Reps = repetitions; min = minutes; Day 1 = muscular strength; Day 2 = muscular hypertrophy. Resistance = percent of the peak mean force of the weaker leg during the respective 3RM. Rest = time between sets. Weeks 1 and 2 were a familiarization period where participants chose training duration and intensity, but were advised to work around 2 x 8 at 40% of Workload 1 at 12 rpm.

midpoint and post-testing. Time to complete the TUG was recorded in seconds from the moment the participant left the chair to the moment the participant returned to the chair in a seated position. Each participant completed up to 3 trials and the fastest attempt was recorded for data analyses.

Walking speed.

The 10 meter walk test (10MWT) is a measure of mobility and walking speed. Starting in a standing position, 2 meters behind a timing device (Brower TC Timing System, Draper, Utah), the participant walked as fast and as safely possible for 14 meters. The time to complete the intermediate 10 meters was used to calculate walking speed (reported in meters per second; m/s). Pre-, mid-, and post-testing 10MWT performed with the same level of assistance.

Walking independence.

The level of assistance used during pre-testing 10MWT attempts was categorized using the Walking Index for Spinal Cord Injury (WISCI II) index. Before training occurred on the visit to the lab following mid-assessment or when returning study equipment after post-assessment, participants completed an untimed 10MWT with less assistance compared to pre-test or mid-test, if possible. If less assistance was used, it was denoted on the WISCI II scale. The untimed 10MWTs were analyzed to evaluate the effect of ERT on WISCI II performance.

Daily step physical activity.

Daily step PA was assessed on four consecutive days (three weekdays and one weekend day) with a Step Activity Monitor (SAM). Data were not collected during any water activities and study training sessions. The SAM is valid and reliable in those with iSCI (Bowden & Behrmann, 2007). Participants affixed the SAM with a Velcro strap on their less-impaired leg after the investigator completed calibration procedures outline by Stevens, Caputo, Fuller, and Morgan (2015). The SAM was set to record data in 1-minute epochs throughout the wear time. Step PA data collection started the day after receiving the SAM at pre-, mid-, and post-testing time points.

Procedures

When arriving to the laboratory for the first time, participants signed the consent form and body mass was measured. To avoid potential for muscular fatigue, participants had been advised to avoid heavy physical activity 48 hours before this first visit. After anthropometric measured, participants filled out the VAS, and then did the TUG and 10MWT for familiarization. At the end of the visit, participants were introduced to the Eccentron and practiced the eccentric strength test protocol. Before leaving, participants were given the SCI Independence Measure (SCIM) to complete. Participants returned to the lab no sooner than 48 hours later for a second visit to repeat the TUG, 10MWT, then eccentric strength tests, this time for baseline data collection. The eccentric strength measurement from the second visit was used to calculate the initial training intensity. At the end of the second visit, participants were fitted with a SAM, briefed on care, application, and the schedule for wearing the device.

The ERT began with a two-week familiarization period to avoid undue muscle soreness. During this time, participants started training at 50% of 1RM for two to three sets of eight at 12 rpm. Participants trained two times a week for 12 weeks. Eccentric strength was reassessed to ensure proper exercise progression at weeks three and six (see Table 2 for training program). The ERT was designed to target both muscular strength and endurance as outlined by the National Strength and Conditioning Association (Haff & Triplett, 2016). Exercise prescription was modified if the aforementioned training percentages were less than the participant's resting tone. In this instance, the same intensity change was added to the tone value and served as the new training workload (ex. tone + 35% and tone + 17%). Intensity increased when the participant was able to accurately complete two additional repetitions in the last two sets on any given training day. However, if participants were unable to successfully generate the force needed and were inaccurate more than 30% of the training session, intensity was reduced to the previously successful intensity. Participants returned to the lab after completing 12-weeks of ERT to repeat all assessments. Participants trained and tested at approximately the same time of day each week.

Statistical analyses

Data were analyzed with Version 23.0 of IBM SPSS Statistics for Windows (Armonk, NY: IBM Corp). Descriptive statistics are provided for participant demographics (see Table 1) and calculated for study variables (see Table 3). One-way repeated measures analysis of variances (ANOVAs) were used to determine the effects of ERT on the TUG, 10MWT, SCIM, and WISCI. Bivariate correlational analyses were conducted to determine the relationship between daily step PA and the TUG, 10MWT, SCIM, and WISCI, respectively at pre-, mid, and post-test. Additional correlations were conducted to determine if the pre-test to post-test change in the TUG, 10MWT, SCIM,

Table 3

Means and Standard Deviations of Outcome Variables Across the 12-week ERT

	Pre-ERT		Mid-ERT		Post-ERT	
Measure	*M*	*SD*	*M*	*SD*	*M*	*SD*
TUG (secs)	158.36	165.84	89.48	82.38	56.31	42.42
10 MWT (m/s)	0.34	0.42	0.39	0.44	0.43	0.50
WISCI	8	7	10	7	13	7
SCIM	22	10	23	10	24	10

Note. ERT = eccentric resistance training; TUG = Timed Up and Go; 10 MWT = 10 meter walk test; WISCI = Walking Index for Spinal Cord Injury II; SCIM = Spinal Cord Independence Measure.

and WISCI scores, respectively, correlated with the change observed in daily step PA (see Table 4). A familywise alpha of .05 determined statistical significance. Measures of effect were calculated for study variables (*d* = difference in means/baseline standard deviation) to evaluate mid-test and post-test values to pre-test.

Results

Initially, there were 14 participants, of which 11 completed the full ERT intervention. For personal reasons, 3 participants withdrew from the study prior to completing the two-week familiarization period. Additionally, pre-step PA data were lost for one participant as the result of a programming error. Therefore, analyses for step PA had a sample size of 10 and analyses for ERT had a sample size of 11. On average, the participants completed 98% of ERT sessions.

The one-way repeated measures ANOVAs indicated significant ERT effects on TUG performance (F (1.40, 13.95) = 4.93, MSE = 8664.94, H-F p = .034) and 10MWT speed (F (1.74, 17.36) = 7.92, MSE = 0.004, H-F p = .005). Post hoc analyses, corrected using the Sidak procedure, failed to determine where the change occurred regarding TUG performance, but the pairwise comparisons did elucidate that change in 10MWT speed occurred from pre-test to post-testing (p = .027). Participants also improved in WISCI scores from pre-test to post-test (F (1.80, 18.00) = 8.22, MSE = 8.38, H-F p = .004), but not in SCIM scores (F (1.22, 12.20) = 0.87, MSE = 33.14, p = .20). Additionally, the ERT did not have an effect on questions specific to mobility on the SCIM questionnaire, (F (1.66, 16.56) = 2.75, p = .10 MSE = 1.96).

Table 4

Pearson's Correlation Coefficients of Step PA to TUG, 10MWT, WISCI, and SCIM

	Step activity		
Variable	Pre-test	Mid-test	Post-test
Pre-TUG	-.608		
Pre-10MWT	.554		
Pre-WISCI	.609		
Pre-SCIM	.441		
Mid-TUG		-.708*	
Mid-10MWT		.735*	
Mid-WISCI		.829**	
Mid-SCIM		.494	
Post-TUG			-.689*
Post-10MWT			.694*
Post-WISCI			-.613
Post-SCIM			.417
			Change in step activity
Change in TUG			.002
Change in 10MWT			.649*
Change in WISCI			-.613
Change in SCIM			-.470

Note. Change represents difference from baseline to post-test. TUG = Timed Up and Go; 10MWT = 10 meter walk test; WISCI = Walking Index for Spinal Cord Injury; SCIM = Spinal Cord Independence Measure. Significance is denoted as * = $p < .05$ *and* ** = $p < .01$.

Correlational data are presented in Table 4. No variables were correlated with step PA at pre-test, but after 6 weeks of training (mid-point), TUG performance (r = -.708, p = .015), 10MWT (r = .735, p = .01), and WISCI (r = .829, p = .002), respectively, correlated with mid-step PA. At post-test, TUG (r = -.689, p = .019) and 10MWT (r = .694, p = .018) were correlated with daily step PA. The improvement in 10MWT performance across the ERT was positively correlated with the change identified in daily step PA (r = .649, p = .04; see Figure 1).

Discussion

The ERT program was successful in improving performance on the TUG, 10MWT, and WISCI tests in those with chronic iSCI. Observed changes in 10MWT and WISCI were significantly different at post-ERT compared to pre-ERT. Alternatively, the ERT had no effect on function as measured by the SCIM. Correlational analyses were unable to identify relationships between the study variables and daily step PA before training. However, after implementing lower extremity strength there was a significant relationship between step PA and TUG, 10MWT, and/or WISCI values, respectively, at mid-test and post-test. Further, the improvement in 10MWT walking speed positively correlated with the improvement noted in daily step PA. The SCIM failed to correlate with step PA in any analysis.

Although post hoc analyses were unable to determine where the change occurred, main effect outcomes indicated that TUG performance in those with iSCI moderately improved as a result of the ERT. Improvement from pre-test to post-test (~45%) appeared to occur linearly from pre-test to mid-test (~25%) and from mid-test to post-test (~23%).

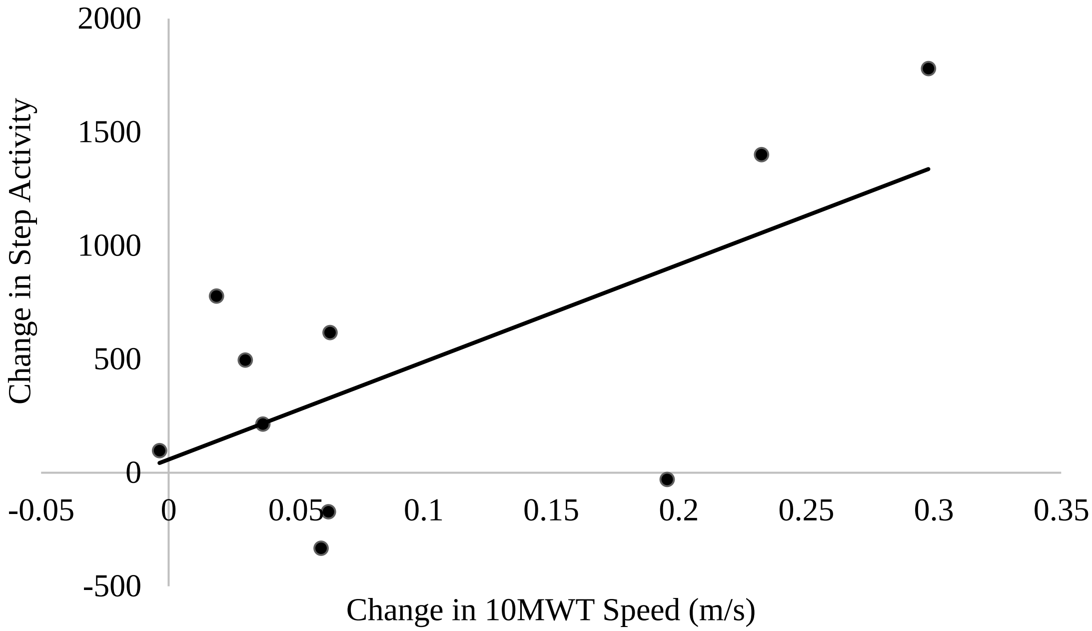

Figure 1. Change scores are different in performance from baseline to post testing. Step activity represents steps taken across 3 week days and 1 weekend day by less impaired limb. 10MWT = 10 meter walk test. Correlation of *r* = .649 significant at *p* = .04.

Lam, Noonan, Eng, and the SCIRE Research Team (2008) defined a meaningful change on the TUG by individuals with iSCI as a minimum of 10.8 seconds or 30%. Not only did participants in this investigation improve more than 30%, the average change in TUG performance from pre-test to post-test was 102 seconds. These data should be considered in light that the test was slightly modified to accommodate the participants' abilities. As described in the procedures, the test did not begin until the participant's buttocks left the seat, rather than the count off method ending in "go".

Other resistance training programs have elicited improvements in TUG performance in populations with chronic pain and neurological dysfunction, similar to iSCI. In a sample with chronic pain, participants with rheumatoid arthritis completed a 14 session concentric only resistance training program targeting the hamstrings and quadriceps (McMeekan, Stillman, Story, Kent, & Smith, 1999). This isokinetic training consisted of four sets of five maximal effort repetitions at a speed determined during a sit-to-stand test (70% max speed). These participants improved on the TUG by 12.5% with a concurrent 80% drop in pain (measured via VAS). Although not statistically analyzed, individuals in the current sample also reported lower levels of daily pain/discomfort (as measured by VAS) over the course of the ERT. Future investigations may be designed specifically to elucidate this potential connection between resistance training and reductions in pain, specifically, looking into neuropathic pain experienced after iSCI.

In comparison to training outcomes in a sample with Parkinson's disease, participants in the current sample showed greater improved in TUG performance. Dibble, Hale, Marcus, Gerber, and LaStayo, 2009 trained individuals with Parkinson's disease an average of 30-45 minutes per day, three days a week, where intensity was regulated by ratings of perceived exertion. Their participants improved an average of 14% on the TUG following the 12-week ERT. The 45% mobility improvement in the current sample of participants with iSCI may overshadow improvements in other populations (12.5-14%) because of the lower baseline mobility capacity after iSCI and sensitivity for training adaptations imposed by the ERT.

Performance on the TUG test in the current study was more linear than that noted after body weight supported treadmill training (BWSTT). Wirz et al. (2005) noted that improvements in walking performance, as measured by the TUG, plateaued after the first 4 weeks of BWSTT in those with similar ages, injury levels, and duration post-iSCI to the current sample. The average improvement across 8 weeks of BWSTT was 25 $\pm$ 30 seconds, with the initial 4 weeks accounting for 20 $\pm$ 26 seconds (Wirz et al., 2005). Not only did the current ERT program prompt greater improvements in TUG performance compared to other eccentric, concentric, and robotic programs, individuals with iSCI in the current sample continued improving beyond the initial phase of training. This superior progress in TUG performance may have resulted from the development of lower extremity strength and explosiveness (McMeeken et al., 1999). The ability to propel out of a seated position and subsequently perform gait mechanics may be derivatives of both neural and architectural adaptations to the local musculature. Unfortunately, this investigation did not evaluate these variables, leaving this theory unsubstantiated. It is important to note that participants in the current study had lower baseline performance on the TUG compared to other studied groups (Dibble et al., 2009; Wirz et al., 2005). As such, post hoc analyses may be needed to better compare individuals of similar baseline TUG performance to further understand the efficacy of ERT in samples that include individuals with iSCI.

Walking speed on the 10MWT improved from 0.34 m/s at pre-test to 0.39 m/s at mid-test, to 0.43 m/s at post-test, resulting in a significant improvement from pre-test to post-test (~26.5%, respectively). Researchers postulate that a minimum change of 0.13-0.17 m/s or 39% is needed to be considered meaningful for those with iSCI (Lam, Noonan, Eng, & the SCIRE Research Team, 2008; Musselman & Yang, 2014). It is important to note that these standards were developed in individuals post-iSCI with faster initial walking speeds (average speed = 0.81 ± 0.34 m/s; Lemay & Nadeau, 2010). Despite falling short of the predetermined benchmarks for meaningful change in gait speed, individuals in the current sample improved walking speed following a 12-week ERT, without formal gait training.

Stevens et al. (2015) noted that freely chosen walking speed during a 10MWT was associated with daily step PA in those with longstanding cervical, thoracic, or lumbar iSCI. Through their work, 0.42 m/s was identified as a walking speed threshold for the start of a curvilinear increase in daily step PA with minor improvements in gait speed. The current ERT stimulated dramatic improvements in gait speed, bringing the sample average to 0.43 m/s (0.01-1.3 m/s). While not studied, a longer duration of ERT may bring about faster walking speeds and subsequently higher volumes of PA at home and in the community.

The current ERT was a sufficient catalyst to bring about observable changes in gait speed in the absence of formal gait training. The improvement noted in the current investigation appears to fall within the range of progress for those with iSCI following other gait training modalities. Following 3 months of BWSTT with functional electrical stimulation for an hour and a half 3 days a week, individuals with chronic iSCI (tetraplegia and paraplegia) improved from 0.23 m/s to 0.49 m/s (d = .33; Field-Fote, 2001). Robot assisted BWSTT for 8 weeks, 3 to 5 days per week, averaged an improvement of 0.11 m/s (~56%) in those with chronic iSCI (Wirz et al., 2005). In a sample of individuals with similar gait abilities at baseline as the current sample, training 5 days per week for 12 weeks on a treadmill resulted in no difference between groups that received functional electrical stimulation or robotic assistance (Field-Fote & Roach, 2011). The average effect size for walking speed after the 12-week gait training interventions was d = .33 (Field-Fote & Roach, 2011). The lower therapist and patient time investment accompanied by similar gait improvements (TUG d = .62 and 10MWT d = .23) following ERT supports its implementation in the therapeutic realm.

On average, individuals in the current sample improved 5 points on the WISCI scale after the 12-week ERT (d = .73). This average recovery of 5 points on the walking independence measure is considered substantial. Burns, Delparte, Patrick, Marino, and Ditunno (2011) determined that a change of 1 point is a meaningful difference in mostly ambulatory individuals with acute and chronic iSCI. There is a wide range of responsiveness on the WISCI scale following exercise and therapy interventions. Robotic BWSTT for 4 weeks improved WISCI scores an average of 7 points in three individuals with varying severities of chronic iSCI, with an additional average of 2.7 points increase following 4 weeks of therapist assisted gait training (Hornby, Zemon, & Campbell, 2005). Alternatively, 20 individuals with longstanding cervical, thoracic, or lumbar iSCI failed to see improvement in WISCI scores following 3 to 5 days per week for 8 weeks of robotic assisted BWSTT (Wirz et al., 2005). More studies should be evaluated to determine which modality of training or therapy provides the greatest improvement in gait independence, correcting for baseline walking ability, walking speed, and duration and severity of injury.

In the current sample, there was an average improvement of 4.5% on the SCIM questionnaire. This improvement bears little weight because it failed to reach statistical significance and the minimum difference to determine meaningful change has yet to be resolved. To combat this lack of information, Corallo et al. (2017) asked 12 individuals with iSCI ranging from complete tetraplegia to thoracic level iSCIs to subjectively identify a personal, meaningful change in SCIM ratings. These individuals noted meaningful changes ranging from 1 to 7 points (approximately 2.5-18.2 %) on the mobility portion of the measure. This range of points and percentages may serve as potential benchmarks for clinically meaningful changes on the SCIM questionnaire (Corallo et al., 2017). Although the SCIM has been deemed more sensitive than the more widely used Functional Independence Measure (Field-Fote, 2009), the SCIM may not have been sensitive enough to detect changes realized as a result of the ERT.

Outcomes on TUG, 10MWT, WISCI, and SCIM did not correlate with daily step PA at pre-test. After engaging in the ERT, however, scores on the TUG, 10MWT, and

WISCI were highly correlated with daily step PA midway through training with correlations remaining for post-test TUG and 10MWT scores. The lack of correlations at pre-test may be due the variability in participants' daily steps (1514 $\pm$ 1898 steps) and general lower extremity weakness (summed eccentric strength averaged 152.8 $\pm$ 122.2 lbs and summed isometric strength averaged 8.2 $\pm$ 7.7 N/kg). Potentially, the lack of lower extremity strength at baseline might have brought about a floor effect on daily step PA. However, as participants began to train and build lower extremity strength as a result of the ERT (compared to pre-test, mid-eccentric strength improved = 22.7% and 37.8% at post, respectively), they responded similarly, thus increasing the ability to detect correlations between walking measures and daily step PA. From these data, there appears to be no relationship between TUG, 10MWT, and WISCI scores to daily step PA, respectively, prior to an exercise intervention. Noting that there is a relationship between walking function (WISCI and TUG) and speed (10MWT) to step PA after ERT, future investigations are needed to determine the direction of the relationship and prediction capacity of the TUG, 10MWT, and WISCI to daily step PA as lower extremity strength improves in those with iSCI.

Correlational results from the current study support data presented by Stevens et al. (2015) where improved walking speed correlated with higher daily step PA in a similar sample with iSCI. This novel approach of using laboratory measurement tools (WISCI, TUG, and 10MWT) to identify relationships with daily step PA differs from previous literature. Typically, investigations have determined relationships between measurement tools themselves, i.e. 10MWT to TUG or TUG to WISCI, etc. Rather, this new approach determines the ability to predict daily step PA from laboratory-based gait assessments. Future studies are needed to elaborate why daily step PA correlates with the 10MWT, TUG, and WISCI tests after exercise training, but not before training. Additionally, researchers may consider evaluating correlations between change in lower extremity leg strength after ERT to performance on 10MWT, TUG, WISCI, and daily step PA assessments.

Conclusion

The 12 weeks of ERT served as a sufficient stimulus to improve measures of walking speed and independence without formal gait training. Individuals with chronic iSCI significantly improved mobility an average of 45% (TUG), walking speed by 39% (10MWT), and walking independence by 134% (WISCI). These individuals improved at home function by an insignificant average of 4% (SCIM). Daily step PA was not correlated with 10MWT, TUG, WISCI, and SCIM measures prior to lower extremity exercise training. However, correlations were significant after the implementation of ERT. These data support the implementation of ERT, as an adjunct to formal gait training, in therapeutic regimens seeking to improve walking capacity in those with iSCI.

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APPENDIX FOR STUDY II

APPENDIX A

IRB Approval Letter

MIDDLE TENNESSEE STATE UNIVERSITY

IRB
INSTITUTIONAL REVIEW BOARD
Office of Research Compliance,
010A Sam Ingram Building,
2269 Middle Tennessee Blvd
Murfreesboro, TN 37129

EXPEDITED PROTOCOL APPROVAL NOTICE

8/3/2015

Investigator(s): Whitley Stone (PI), Jenn Caputo, Sandra Stevens and Dana Fuller
Investigator(s) Email: wjs3c@mtmail.mtsu.edu; jenn.caputo@mtsu.edu; and sandra.stevens@mtsu.edu

Department: Health and Human Performance

Protocol Title: "Eccentric resistance training in those with spinal cord injuries and able bodied adults "

Protocol ID: 15-340

Dear Investigator(s),
The MTSU Institutional Review Board (IRB), or its' representative, has reviewed the research proposal identified above. The MTSU IRB or its representative has determined that the study poses minimal risk to participants and qualifies for an **EXPEDITED** review under 45 CFR 46.110 and 21 CFR 56.110 within the category *(4) Collection of data through noninvasive procedures.* This approval is valid for one year from the date of this letter **for 10 (TEN) participants** and it expires on **8/4/2016**.

Any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615) 494-8918 within 48 hours of the incident. Any change(s) to this protocol must be approved by the IRB. The MTSU HRP defines a "researcher" as someone who works with data or has contact with participants. Anyone meeting this definition needs to be listed on the protocol and needs to complete the required training. New researchers can be amended to this protocol by submitting an Addendum request researchers to the Office of Compliance before they begin to work on the project.

Completion of this protocol MUST be notified to the Office of Compliance. A "completed research" refers to a protocol in which no further data collection or analysis is carried out. This protocol can be continued up to THREE years by submitting annual Progress Reports prior to expiration. Failure to request for continuation will automatically result in cancellation of this protocol and you will not be able to collect or use any new data.

All research materials must be retained by the PI or the faculty advisor (if the PI is a student) for at least three (3) years after study completion. Subsequently, the researcher may destroy the data in a manner that maintains confidentiality and anonymity. IRB reserves the right to modify, change or cancel the terms of this letter without prior notice. Be advised that IRB also reserves the right to inspect or audit your records if needed.

Sincerely,
Institutional Review Board
Middle Tennessee State University

8/31/2015

Investigator(s): Whitley Stone (PI), Jenn Caputo, Sandra Stevens and Dana Fuller

Department: Health and Human Performance

Protocol Title: Eccentric resistance training in those with spinal cord injuries and able-bodied adults

Protocol Number: #15-340

Dear Investigator(s):
We have reviewed your research proposal identified above and your requested changes. The following changes have been approved:

(1) New investigators Samantha Johnson and Layci Watts-Harrison are approved to be included in this protocol;
(2) The number of participants are approved to be increased from 10 to 40.

Please note that any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615)494-8918 or compliance@mtsu.edu. Any change to the protocol must be submitted to the IRB before implementing this change.

You will need to submit an end-of-project report to the Office of Compliance upon completion of your research. Complete research means that you have finished collecting data and are ready to submit your thesis and/or publish your findings. Should you not finish your research within the one (1) year period, you must submit a Progress Report and request a continuation ***prior*** to the expiration date on your approval letter. Please allow time for review and request revisions.

According to MTSU Policy, a researcher is defined as anyone who works with data or has contact with participants. Anyone meeting this definition needs to be listed on the protocol and needs to complete the online training. If you add researchers to an approved project, please forward an updated list of researchers to the Office of Compliance ***before*** they begin to work on the project.

Please note: **all research materials must be retained by the PI or a faculty advisor** (if the PI is a student) for at least **three (3) years after study completion**. Should you have any questions or need additional information, please do not hesitate to contact our office.

Sincerely,

Office of Compliance
Institutional Review Board Member
Middle Tennessee State University Office of Compliance

010A Sam Ingram Bldg.
Middle Tennessee State University
1301 E. Main St. Murfreesboro, TN 37129

IRB
INSTITUTIONAL REVIEW BOARD
Office of Research Compliance,
010A Sam Ingram Building,
2269 Middle Tennessee Blvd
Murfreesboro, TN 37129

IRBN001 - EXPEDITED PROTOCOL APPROVAL NOTICE

Friday, May 27, 2016

Investigator(s):	Whitley Stone (Student PI), Sandra Stevens, Dana Fuller and Jennifer Caputo
Investigator(s') Email(s):	*wjs3c@mtmail.mtsu.edu; jenn.caputo@mtsu.edu and sandra.stephens@mtsu.edu*
Department:	Health and Human Performance
Study Title:	***Eccentric resistance training in those with spinal cord injuries and able-bodied adults***
Protocol ID:	**15-340**

Dear Investigator(s),

The above identified research proposal has been reviewed by the MTSU Institutional Review Board (IRB) through the **EXPEDITED** mechanism under 45 CFR 46.110 and 21 CFR 56.110 within the category *(4) Collection of data through noninvasive procedures* A summary of the IRB action and other particulars in regard to this protocol application is tabulated as shown below:

IRB Action	APPROVED for one year	
Date of expiration	8/4/2017	
Sample Size	10 (TEN)	
Participant Pool	**Adults with spinal cord injury**	
Exceptions	NONE	
Restrictions	**Inclusion/exclussion criteria (on file) must be adhered through IRB approved screening procedure**	
Comments	ACSM Risk Stratification allowed	
Amendments	**Date**	**Post-approval Amendments**
	8/27/2015	Appoved to include Samantha Johnson and Layci Watts-Harrison to the protocol
	8/31/2015	Approved to increase sample size from 10 to 40 (FORTY)
	5/5/2016	1. Samantha Johnson & Layci Harrison are removed from the protocol 2. Only individuals with spinal cord injury will be recruited 3. Request to increase the training period from 8 weeks to 10 weeks is granted - However, the number of training sessions per week has been reduced from 3 to 2 times a week 4. The requested procedural amendment measure walking speed after each session has been approved 5. The "Quality of Life Spinal Cord Injury III and Spinal Cord Injury Independence Measure" questionaire has been approved to be administered to the participating individuals 6. Use of pedometer is permitted - No identifiable information or

	5/5/2016	other types of tracking can be used in the pedometer study. 7. A revised informed consent form to reflect all the changes in this amendment has been reviewed and approved
	5/27/2016	1. New investigator Core Gray added to help data collection, testing and exercise training 2. Two additional isometric measurements have been approved: (a) Measurement of hip flexion stated in the addendum; AND (b) knee extension 3. Requested additional VAS scale has been approved 4. Informed consent document reflecting these amendments has also been approved

This protocol can be continued for up to THREE years (**8/4/2018**) by obtaining a continuation approval prior to **8/4/2017**. Refer to the following schedule to plan your annual project reports and be aware that you may not receive a separate reminder to complete your continuing reviews. Failure in obtaining an approval for continuation will automatically result in cancellation of this protocol. Moreover, the completion of this study MUST be notified to the Office of Compliance by filing a final report in order to close-out the protocol.

Continuing Review Schedule:

Reporting Period	Requisition Deadline	IRB Comments
First year report	7/4/2016	5/5/2016 - Continuing review was conducted on this protocol. It has been approved for an additional year in accordance with Expedited Category 8 "Continuing Review of Previously Approved Protocol"
Second year report	7/4/2017	INCOMPLETE
Final report	7/4/2018	INCOMPLETE

The investigator(s) indicated in this notification should read and abide by all of the post-approval conditions imposed with this approval. Refer to the post-approval guidelines posted in the MTSU IRB's website. Any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615) 494-8918 within 48 hours of the incident. Amendments to this protocol must be approved by the IRB. Inclusion of new researchers must also be approved by the Office of Compliance before they begin to work on the project.

All of the research-related records, which include signed consent forms, investigator information and other documents related to the study, must be retained by the PI or the faculty advisor (if the PI is a student) at the secure location mentioned in the protocol application. The data storage must be maintained for at least three (3) years after study completion. Subsequently, the researcher may destroy the data in a manner that maintains confidentiality and anonymity. IRB reserves the right to modify, change or cancel the terms of this letter without prior notice. Be advised that IRB also reserves the right to inspect or audit your records if needed.

Sincerely,

Institutional Review Board

CHAPTER V

OVERALL CONCLUSIONS

The goal of this dissertation was to determine the safety and efficacy of ERT in individuals with iSCI. Eccentric muscle actions are generated when muscle fibers generate force as the fiber lengthens. Eccentrically-based exercise requires lower neural activation, results in greater hypertrophic responses, and potentiates greater force at lower oxygen demands than concentric muscle actions. These features bode well in conjunction with the lower metabolic capacity, reduced neural drive, and atrophied muscle fibers characteristic following iSCI.

In Study 1, the potency of ERT in improving eccentric muscular strength, isometric muscular strength, and daily step activity in neurologically stable individuals with iSCI was tested. Participants (N = 11) completed 12 weeks of ERT on a recumbent, eccentrically driven, step ergometer. The two training sessions per week emphasized either muscular strength or muscular endurance and hypertrophy according to the intensity prescription guidelines provided by the National Strength and Conditioning Association (Haff & Triplett, 2016). The ERT program was safe and lead to increases in eccentric strength and isometric strength, but not daily step activity in those with iSCI.

These improvements in lower extremity strength are in agreement with previous studies that have evaluated eccentric and isometric strength changes following ERT in healthy (LaStayo et al., 1999) and special populations (Stone, Stevens, Fuller, & Caputo, 2017). The current study was unique in that daily step activity was assessed following an ERT program and individuals with iSCI varied in lesion level and primary mode of locomotion. When considering current findings, it may be extrapolated that ERT is a safe and effective modality of exercise in those with neurological impairments. However, ERT alone may not elicit changes in daily step activity. In future investigations, it would be valuable to compare the effect of ERT on strength and step activity between groups of primarily ambulators and wheel-chair users with iSCI to see if the outcome differed. Although speculative, the changes in eccentric and isometric strength may have derived from both neural and musculoskeletal architectural adaptations. Additionally, the results from the first study did not elucidate if ERT impacted gait quality (walking speed, mobility, and independence) and at home independence. Thus, the second study of this dissertation was conducted to evaluate the effect the ERT on measures of gait and at home independence.

The same sample of individuals with iSCI completed a walking (10MWT), mobility (TUG), walking independence (WISCI), and at home functional independence assessments (SCIM) at baseline, at 6 weeks, and after 12 weeks of ERT. The outcomes from these assessments were also analyzed to determine the relationship to daily step activity.

Participants who completed the ERT attained an average improvement of 27% in walking speed (10MWT), 45% improvement in mobility (TUG), a 5-point improvement on the 20-point walking independence scale (WISCI), and an insignificant 4.5% increase in at home functional independence (SCIM). These changes were either equal to or better than those seen following other resistance training regimens or traditional physical therapy modalities in older adults and individuals with iSCI (Field-Fote, 2001; Kressler et al., 2014; LaStayo et al., 2003). Overall, results from Study 2 indicate that individuals with iSCI can improve walking mechanics following an exercise training program void of formal gait training. It is unclear if the improved walking speed, mobility, and independence were accomplished by improving stride length, single leg stance ability, or other gait mechanisms. It would be valuable to evaluate specific walking characteristics in future investigations to determine the gait mechanisms affected by the ERT. Additionally, investigators may consider utilizing a questionnaire that is more sensitive to changes in lower extremity mobility and at home function than the SCIM.

In addition to improving in walking function, mobility, and independence, the WISCI, 10MWT, and/or TUG were correlated with daily step activity at week 6 and 12 of the ERT. These correlations did not hold true at baseline or for the SCIM assessment. The current study is the first to analyze the relationship between laboratory assessments and daily step PA in those with iSCI. Increasing the sample size in future research in order to evaluate the ability of the WISCI, 10MWT, and TUG to predict daily step activity after iSCI is warranted. This information would allow for therapists to create PA prognoses post-iSCI according to individual ambulatory capacity. These predictions may allow for clinicians to develop performance benchmarks within the WISCI, 10MWT, and TUG that indicate risk for hypokinetic diseases following iSCI.

In conclusion, the results from Study 1 and 2 support the efficacy of ERT interventions within a population with iSCI. It can be speculated that improvements in strength (eccentric and isometric) may have brought about the changes observed in walking speed, mobility, and independence. The studies in this dissertation documented that ERT is a potent intervention in individuals with impaired neurological function, eliciting musculoskeletal adaptations and walking performance without formal gait training. Knowing the potential to improve walking ability, clinicians can now take this information and implement ERT programs to build strength in those with iSCI and improve ambulatory function while keeping client and therapist burden low.

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