

A 4-WEEK NEUROMUSCULAR STIMULATION INTERVENTION
ON SKELETAL MUSCLE FATIGUE IN OLDER ADULTS

by

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LIST OF ABBREVIATIONS

Abbreviation	Description
NMES	Neuromuscular Electrical Stimulation
MVC	Maximal Voluntary Contraction
sEMG	Surface Electromyography
RMS	Root Mean Square
MPF	Median Power Frequency
6MWT	6-Minute Walk Test

1. INTRODUCTION

Introduction

Older Adult Population

As aging occurs, the muscles experience what is known as age related loss of skeletal muscle mass and strength, or sarcopenia. This then leads to a decrease in muscle size and often a simultaneous increase in fat and connective tissue content within the skeletal muscle tissue.¹ Other noted changes may include reductions in strength,² decreased muscle activation,³ decreased overall muscle fiber count,⁴ reductions in the size of the motor neuron pool,⁵ reductions in functioning motor units,⁶ decreased muscle cross sectional area,⁷ reduction in Type II muscle fiber type size,⁸ and alterations in the contractile characteristics of the muscle such as reductions in size of the mitochondria or increased contraction time.⁹ This leads to changes in muscle function causing decreases in muscular endurance and strength. Research has shown that after analyzing walking speed during a 4 m and 400m walking task, there was an increase in completion time from the 20-25 age bracket to the 65-70 age bracket ultimately showing declines in mobility starting from ages 20-25.¹⁰ Other important changes occurring within the motor system include increases in tendon compliance as the muscles become thinner¹¹ as well as the slowing and decreased precision in physical movements.⁷ Muscular endurance, also known as the muscles' resistance to fatigue, is vital for certain activities of daily living such as climbing stairs, standing ability, and walking.³ The necessity of these activities in everyday tasks leads to the importance in improving muscular endurance in order to help older adults maintain independence and high quality of life.^{3,7} With this in mind,

alternative treatment options that aid in improving muscular endurance to reduce the rate of muscular fatigue in the older adult population are needed.

The beneficial effects of repeated muscle contraction as may occur with muscular endurance training is applicable to not only younger adults but is essential for the elderly as well. Older adults have the ability to gradually improve performance throughout common activities requiring muscular endurance.³ As a result of muscular endurance training, muscles of commonly used limbs perform more efficiently during sustained muscular activity, and thus, have greater resistance to fatigue.¹² Endurance exercises typical within the older adult population include walking with required endurance needed when changing pace or direction,¹²⁻¹⁴ stair climbing, or cycling.¹⁵ Ultimately, studies have shown that older adults have the ability to gain physical function benefits from training due to the adaptability of the muscles trained.¹⁶

Skeletal Muscle Fatigue

The physiological definition of muscular fatigue is the failure to maintain a required or expected force output.¹⁷ Essentially, as fatigue begins to set in, a gradual decrease in maximal force production occurs.¹⁸ When stimulated, muscles undergoing fatigue demonstrate slower and lower amplitude twitches, lower maximal force capacity, and a decreased maximal rate of tension development and decline.¹⁹ This decrease in maximal force output could be attributed to mechanisms involving motor unit recruitment as the muscle begins to fatigue.

Fatigue may occur as a result of central or peripheral elements of the motor system. Aspects of peripheral muscle fatigue, may occur due to mechanisms such as neurotransmitter depletion,²⁰ excitation-contraction coupling failure,²¹ postsynaptic

membrane failure, and failure to propagate the action potential into axonal branches.²⁰

Central fatigue is defined as the elements in the central nervous system that may affect fatigue such as emotions and other psychological factors involved in an individual's sense of effort as well as at the various descending motor pathways and the interneurons and motoneurons in the brainstem and spinal cord.²²

As all motor units have been recruited at the level of fatigue, the inability to recruit additional motor units to assist in maintaining force output leads to the decrement in maximal force production.²³ Fatigue is also characterized by an increased effort needed to maintain a submaximal contractile force when force level remains the same and when the effort required to maintain a constant submaximal task gradually increases. This is resulting from the central nervous system's attempt to maintain force output ultimately delaying fatigue.²⁰ The rate of fatigue generally depends on an array of factors including the muscles employed, the relative intensity of the exercise, and whether the contractions performed are continuous or intermittent.²⁴

Intermittent contractions refer to rest periods applied during a fatigue task versus a constant (continuous) contraction fatigue task that does not allow rest time and continues to keep the muscle activated for a given amount of time. Determination of the effects of intermittent or continuous contractions on voluntary EMG activation revealed no changes between the two types of contractions during a fatigue task.²⁵ However, Bilodeau²⁶ found that time to fatigue was increased during a 3-minute fatigue task with intermittent contractions versus a 3-minute fatigue task with continuous contractions in which showed decreases in time to fatigue. Ultimately, this shows that fatigue is affected when considering intermittent versus a continuous contraction fatiguing tasks.²⁶ This

decrease in contractile response will then be compensated by an increase in motor unit recruitment, motor unit firing rate, or both. This delay in fatigue could result from a quick decline in motor unit firing rate with a gradual increase later in the fatiguing task, or when nearing the fatigued state, as seen after muscular endurance training.²⁷⁻³¹ This occurs as a result of the central nervous system increasing excitation of the motor neuron pool, and thereby increasing the motor unit firing rates, to compensate for decreases in motor unit force twitch amplitude and maintain a given force output during a fatiguing task.^{28,30,32,33}

Increases in functional movement impairment have been associated with increased muscle fatigability within the elderly population. This fatigability is characterized by accelerated decreases in relative muscle power while performing dynamic or static exercises. Essentially, this would result in decreased force production and slower shortening velocity of the muscle.³⁴ With progressive exercise, changes may occur in the nervous system that could play a role in improving the pattern of motor activation in order to maintain a specific force output.

Neuromuscular Electrical Stimulation

Neuromuscular electrical stimulation (NMES) is typically used as a physical rehabilitative modality to improve skeletal muscle strength and endurance for therapeutic, training, or functional means such as walking, standing, and upper limb movements such as reaching and grasping.^{35,36} NMES is the therapeutic application of a sequence of electrical stimulation pulses that elicit skeletal muscle contraction in hopes of mimicking a voluntary skeletal muscle contraction.³⁷ NMES has been shown to activate paretic or paralyzed muscles that assist in improving functional limb movements such as standing

and walking in individuals with stroke, hemiplegia, paraplegia, and other neuromuscular disorders^{35,38,39} and to induce anabolic processes in hemiplegic and neurologically intact skeletal muscle of older adults.⁴⁰ NMES induces involuntary muscle contraction by sending an electrical current directly in the muscle. Current administered during NMES influences the muscle by synchronously recruiting all motor units within the electrode pickup area. As the stimulation is delivered, the electrical current produces an action potential on the sarcolemma and, thereby, activates the muscle fibers resulting in an physical involuntary muscle contraction.³⁶ Involuntary skeletal muscle contractions differ from voluntary muscle contractions in that they lack the motor unit size-order recruitment, also known as the Henneman Size Principle present within a voluntary contraction,⁴¹ by having muscle fibers recruited in a non-selective, fixed recruitment pattern with no obvious sequencing pattern.⁴² Motor units in an involuntary muscle contraction are activated in a maximal and synchronous manner, and the motor unit firing rates occur at a quicker rate than those recruited during voluntary contractions.^{42,37} Due to the inability to control motor unit recruitment order and the lack of control over the motor unit firing frequency, it has been stated that involuntary skeletal muscle contractions make the muscle stimulated more vulnerable to a quicker rate to fatigue.³⁷ However, this poses as an advantage in that faster muscle fibers that are needed for voluntary contractions can be recruited at a low stimulation intensity, which would be beneficial for populations that cannot physically perform muscle contractions at higher force levels.^{37,43} Alternatively, voluntary muscle contractions depend on the amount of motor units that activate as well as the rate at which they are activated in order to reach a desired force output. Therefore, the increase in force output or force maintenance needed

requires an increase in the amount of motor units recruited and a faster rate of activation.⁴⁴ When applied to skeletal muscle fatigue, voluntary skeletal muscle contractions result in a decreased motor unit firing rate in which is compensated with an increase in the amount of motor units recruited to maintain the required force output.⁴⁴⁻⁴⁷

Using NMES allows motor unit recruitment patterns to heighten metabolic demands with one of the goals being to maintain tension within the muscle. It is possible that NMES may ultimately be used within rehabilitation settings that aim to achieve therapeutic goals related to muscular endurance.^{36,38} NMES has been considered an effective alternative to exercise training for various patient populations including those diagnosed with Chronic Obstructive Pulmonary Disease (COPD), those requiring respiratory therapy, and those with severely deconditioned muscles to name a few.^{48,49} It has been commonly found that NMES can produce up to 20-30% increases in quadriceps strength as compared to a control group.⁴⁹ NMES can improve exercise capabilities during activities such as walking^{50,51} and cycling⁵² and endurance amongst other activities of daily living.⁴⁹

Evidence has showed improvements in the 6-Minute Walk Test (6MWT) pre-post treatment in the experimental group of NMES and pulmonary rehabilitation combined as compared to just pulmonary rehabilitation alone. This ultimately showed an increase in exercise tolerance applying to aerobic and muscular endurance with NMES incorporation.⁴⁸

NMES has also been shown to lead to significant improvements in various functional outcomes. Enhancement of force output and preservation are results presented as a result of NMES. NMES stimulation sessions were studied during three separate

sessions separated by at least 48 hours, and on these days, the participants would complete 1 of 3 stimulation patterns. The first stimulation pattern included a 3-min pattern of 20 Hz stimulation, the second consisted of a 3-min pattern of 90 seconds of 20 Hz followed by 90 seconds of a gradual increase from 20 to 40 Hz, and the third included a 3-min pattern of 90 seconds of 20 Hz followed by 90 s of 20 Hz doublet stimulation. The aim was to find the effects of variable stimulation patterns of NMES in the thenar muscles of younger and older adults, and results revealed enhanced force production pre- to post-NMES intervention.⁵³ Furthermore, another study comparing the effects of a low and high frequency stimulation on torque output parameters of the quadriceps muscle found that low-frequency NMES results in increased preservation of torque output during a stimulation protocol.⁴⁰

With repeated application, NMES may improve voluntary muscular endurance. NMES interventions have shown to produce significant functional improvements such as evidence showing the influence of 2 different 6-week NMES interventions with 3 sessions per week protocols (narrow [50Hz] and wide-pulse NMES [100Hz]) on the triceps surae muscle and mobility of healthy older adults. The findings show significant improvements in walking endurance, maximal walking speed, chair-rise time, rapid-step speed, and plantar flexor strength.⁵⁴ Other functional improvements have been seen within the healthy older adult population including balance,^{55,56} time to complete the Timed Up and Go Test (TUG), gait velocity, 5 x chair rise,⁵⁷ short physical performance battery testing for the lower extremity, 10-meter walk test (habitual and fastest walking speed),⁵⁷ 12 flight stair test,⁵⁷ vertical jump performance,⁵⁵ and 10-meter walking speed.⁵⁷ Evidence has also shown functional improvements as a result of NMES within older

adults with knee osteoarthritis including 5 x chair rise, 12 flight stair test,^{58,59} and 6MWT.⁵⁸ Continually, NMES interventions have also been performed in older adults with existing comorbidities such as results revealing improvements in the 12 flight stair test within older adults whom have undergone knee arthroplasty⁶⁰ and results reporting improvements in gait speed, walking endurance, dorsiflexor/plantarflexor muscle strength and force control in older adults diagnosed with Multiple Sclerosis.⁶¹ Furthermore, improvements in functional outcomes have been found including improvements in Maximal Voluntary Contractions (MVC) and standing postural control within the pre-frail elderly,⁶² improvements in balance and 6MWT distance in older adults living in a geriatric nursing home,⁶³ and increases in 6MWT distance within older adults diagnosed with Chronic Heart Failure.⁶⁴ Of these findings, NMES interventions typically consist of stimulation frequencies of 4Hz,⁶⁴ 20Hz,⁵⁵ 50Hz,^{54,58-61,63} 60Hz,⁵⁷ 70Hz,⁵⁶ and 100Hz.^{54,61,62} Furthermore, most of the evidence on effects of NMES on functional outcomes consists of 3,^{54,57,59,61,62} 4,^{55,56} or 5^{58,60,64} NMES training sessions per week for 4,^{56,62} 6,^{54,55,57,58,60,61} 8,⁶⁴ 12,⁵⁹ and 16⁶³ week intervention lengths.

Electromyography and Fatigue

Surface electromyography (sEMG) is used as a means of measuring skeletal muscle activation. This technique has versatility as it measures muscle activity at rest or during muscular activities.^{38,65} Muscular activation level as well as muscular fatigue are typical outcome measures of sEMG and they are quantified as a means of reflecting these parameters. In order to quantify the EMG data, specific measures can be used such as frequency spectrum parameters known as median power frequency (MPF) as well as root mean square (RMS) to name the most commonly used.^{66,67} RMS is typically used to

quantify changes in muscular activation level because it reflects the physiologic activity in the muscle's activation via motor unit depolarization/repolarization during the contraction.⁶⁷

In order to get the most accurate EMG results, isometric contractions are typically utilized to maintain stability of the electrodes. Other factors could interfere with the sEMG signal including the use of appropriate electrode size or type according to the activity assessed, location of electrode placement in relation to the muscle fibers of the muscle examined, the position of sEMG electrodes to each other, muscle fiber characteristics (diameter), tissue filtering (skinfold thickness and blood flow), muscle length, data acquisition, and filtering complications (filter selection, and electrode, skin, or wire movement).⁶⁸

When comparing EMG signals across test subjects, it is typical to use maximal voluntary contractions as a way to normalize data to reflect the degree of muscle activity during the muscle contraction.^{67,69} One way in which to assess peripheral fatigue is by analysis of the M-wave which is an EMG response to a single action potential at the level of the axon of the peripheral nerve or directly from application to the muscle as is the case with NMES. Changes in the M-wave signify possible changes in muscular fatigue. These changes will demonstrate an increase in the M-wave amplitude throughout the first few stages of fatigue with a decrease nearing true fatigue, or the inability to maintain the required force output.⁷⁰⁻⁷² When completing sustained submaximal contractions until fatigue, the surface EMG of the muscle begins to increase gradually as more motor units are recruited to maintain the force output.^{22,73-78} When the submaximal target force can no longer be maintained, muscle activation levels, also known as EMG, begin to

decrease.^{74,76,79} Multiple mechanisms may be working in conjunction that contribute to this decrease in muscle activation associated with fatigue. These could include decreased excitability of the motor neuron, decreased excitatory influence from peripheral sources, increased inhibitory influences on motoneurons, decreased force from individual cross bridges, and decreased excitation of motoneurons.^{70,80-82}

Firing frequencies of motor units begin to decrease when analyzing EMG.⁸¹ Typically, motoneuron firing rate gradually decreases during sustained contractions and increases late in the fatigue process.²⁷ The change occurs within the EMG activity due to the resulting decrease in the frequency of firing of the recruited motor units. Further, this decrease in muscle activation is shown as a result of the decreasing firing frequency of motor units during rhythmic or sustained effort.⁸³ Many contributors to muscular fatigue can be determined by examination of the M-wave presented by surface electromyography.

Multiple studies have shown improvements with training in muscular fatigue through median power frequency (MPF) as well as RMS parameters of sEMG. Bedrest on quadriceps fatigue found an increase in rate of increase of maximal RMS EMG amplitude and increased rate of decrease in EMG MPF throughout a fatiguing task pre- to post-bed rest ultimately showing an increase in muscular fatigue or a decrease in the time to fatigue.⁸⁴ Bed rest on EMG RMS and EMG MPF as compared to resistive vibration exercise (RVE) found decreases in MPF with bed rest and significant increases in RMS as a result of the RVE after repeated submaximal contractions. Ultimately, the increase in RMS shows there was more muscle activation, possibly motor unit firing rates, within the tested quadriceps femoris muscle after resistive vibration training pre- to post-bed rest

allowing for improved muscular fatigue or maintenance of force output. Alternatively, the decrease in MPF post-bed rest shows decreases in muscle activation and therefore decline in the ability to maintain a given force.⁸⁵ Umehara et al.⁸² found a significant decrease in MPF during an acute fatigue task of the serratus anterior muscle.⁸² The medial hamstring muscle showed similar decreases in MPF as a result of muscular fatigue as well as an increase in RMS EMG after a fatigue protocol in the medial hamstring and vastus lateralis muscles.⁸⁶

Study Rationale

There has been limited research on the effects of NMES training and how it may influence voluntary muscle fatigue specifically within the older adult population. Some studies on older adults have noted increases of muscular endurance by ways of various functional tests ranging from the 6-min walk test^{48,64,87} to the Timed Up and Go Test^{57,87} amongst others.^{49,54,57,88} Conversely, there is evidence that shows no changes in skeletal muscle endurance pre-post NMES intervention.⁸⁹ Evidence on EMG parameters have been measured during voluntary contractions and compared pre-post NMES training programs^{38,90} with few exploring the effects of NMES on EMG parameters as well as endurance times to muscular fatigue. However, evidence have also presented no significant differences^{38,49,89,91-93} or decreases^{38,91} in skeletal muscle endurance along with no significant differences in EMG parameters⁹⁴ pre-post NMES intervention. The effectiveness of combination therapy with NMES has been explored⁴⁸ along with various intervention lengths,^{24,49,64,95} and various subject populations such as athletes,⁹⁶⁻¹⁰⁰ those living in a nursing home lifestyle,⁸⁷ and older adults with confounding conditions.^{48,49,60,64,95,101-104} There has been limited evidence covering the effects of

NMES on the highly used quadriceps muscle^{49,60,87,88,101} specifically for functional independence with many exploring NMES effects on varying muscles ranging from the triceps surae⁵⁴ to the digital finger flexor muscles⁸⁸ amongst others.⁴⁹ In patient populations, often the goal is to reduce the decline to maintain function, rather than to improve function. Limited information has been found looking at the effects of a 4-week NMES stimulation intervention on quadriceps skeletal muscle fatigue by ways of a submaximal fatiguing task and sEMG in healthy older adults.

Operational Definitions

1. Older Adults: Adults 60 and older.
2. Neuromuscular Electrical Stimulation Training: The protocol consists of a 4-week, 3 times a week stimulation session consisting of a 40 minute stimulation administered to both legs with a duty cycle of 10 seconds on and 15 seconds off at a frequency of 60 Hz with a pulse duration of 200 μ s at an intensity (mA) that produces a torque at 15% of subject's MVC.
3. NMES Group: Participants receiving the millicurrent treatment whereby they will experience a buzzing sensation and visible muscle contraction.
4. Sham Group: Participants will be told they are receiving a microcurrent treatment whereby they are not expected to feel anything. However, they will not be receiving any stimulation treatment.
5. Muscular Endurance: Distance covered throughout the 6MWT and time to completion during the submaximal isometric fatigue task.
6. Muscular Fatigue: Failure to maintain a force output above 47% MVC for 2 consecutive seconds.

Limitations

1. Only those within the 60 and older age bracket were included. This limits the generalizability of the study data to the general population.
2. The specific NMES protocol used may not generalize to all NMES intervention protocols.
3. Alternative activities and exercises (Zumba, Yoga, Hiking, Pickleball, etc.) allowed other resistance exercises throughout the length of the study. This could allow data to be potentially affected by skeletal muscle adaptations from the subject's respective exercise regimen and not the NMES intervention alone.
4. Inclusion of only generally healthy older adults limits the populations that the data can be applied to such as those with alternative comorbidities.

Abbreviation List

NMES: Neuromuscular Electrical Stimulation

MVC: Maximal Voluntary Contraction

sEMG: Surface Electromyography

RMS: Root Mean Square

MPF: Median Power Frequency

6MWT: 6-Minute Walk Test

Purpose

The primary purpose of this study was to determine the effects of a 4-week NMES intervention on voluntary muscular fatigue of the quadriceps and changes in neuromuscular activation patterns during voluntary fatiguing muscle contractions in older adults. The secondary purpose was to determine the degree of neuromuscular activation

during submaximal voluntary contractions and MVC, MVC (strength), and 6-min walk performance pre-post 4 weeks of NMES in older adults.

Hypotheses

The following hypotheses will address the primary and secondary purposes of the study:

1. Muscle endurance time of the intermittent involuntary fatigue task performed by the quadriceps muscles will increase after 4 weeks of NMES training. Muscle endurance of the Sham group will not change pre-post NMES intervention.
2. The rate of decrease in median frequency EMG during the muscle fatigue task will be slower post- 4 weeks of NMES compared to pre-NMES. There will be no change in the Sham group pre-post NMES intervention.
3. The rate of the increase in RMS EMG, or level of muscle activation, during the voluntary muscle fatigue task will be higher after the NMES training intervention compared to before training. There will be no change in the Sham group pre-post NMES intervention.
4. Muscle activation, as measured by RMS EMG, will be higher during each of the isometric submaximal voluntary contractions (20%, 30%, 40%, 60%, 80% MVC) following 4 weeks of NMES training compared to pre-training. No change will occur for the Sham group pre-post NMES intervention.
5. Maximal voluntary contraction (MVC) will increase in the NMES group after 4 weeks of NMES training compared to pre-training. MVC will not change pre-post intervention in the Sham group.
6. Distance completed during the 6-Minute Walk Test will increase in the NMES group and will not change in the Sham group pre-post 4-weeks of NMES intervention.

2. MANUSCRIPT

Introduction

Older Adult Population

As aging occurs, the muscles experience what is known as age related loss of skeletal muscle mass and strength, or sarcopenia. This then leads to a decrease in muscle size and often a simultaneous increase in fat and connective tissue content within the skeletal muscle tissue.¹ Other noted changes may include reductions in strength,² decreased muscle activation,³ decreased overall muscle fiber count,⁴ reductions in the size of the motor neuron pool,⁵ reductions in functioning motor units,⁶ decreased muscle cross sectional area,⁷ reduction in Type II muscle fiber type size,⁸ and alterations in the contractile characteristics of the muscle such as reductions in size of the mitochondria or increased contraction time.⁹ This leads to changes in muscle function causing decreases in muscular endurance and strength. Research has shown that after analyzing walking speed during a 4 m and 400m walking task, there was an increase in completion time from the 20-25 age bracket to the 65-70 age bracket ultimately showing declines in mobility starting from ages 20-25.¹⁰ Other important changes occurring within the motor system include increases in tendon compliance as the muscles become thinner¹¹ as well as the slowing and decreased precision in physical movements.⁷ Muscular endurance, also known as the muscles' resistance to fatigue, is vital for certain activities of daily living such as climbing stairs, standing ability, and walking.³ The necessity of these activities in everyday tasks leads to the importance in improving muscular endurance in order to help older adults maintain independence and high quality of life.^{3,7} With this in mind,

alternative treatment options that aid in improving muscular endurance to reduce the rate of muscular fatigue in the older adult population are needed.

The beneficial effects of repeated muscle contraction as may occur with muscular endurance training is applicable to not only younger adults but is essential for the elderly as well. Older adults have the ability to gradually improve performance throughout common activities requiring muscular endurance.³ As a result of muscular endurance training, muscles of commonly used limbs perform more efficiently during sustained muscular activity, and thus, have greater resistance to fatigue.¹² Endurance exercises typical within the older adult population include walking with required endurance needed when changing pace or direction,¹²⁻¹⁴ stair climbing, or cycling.¹⁵ Ultimately, studies have shown that older adults have the ability to gain physical function benefits from training due to the adaptability of the muscles trained.¹⁶

Skeletal Muscle Fatigue

The physiological definition of muscular fatigue is the failure to maintain a required or expected force output.¹⁷ Essentially, as fatigue begins to set in, a gradual decrease in maximal force production occurs.¹⁸ When stimulated, muscles undergoing fatigue demonstrate slower and lower amplitude twitches, lower maximal force capacity, and a decreased maximal rate of tension development and decline.¹⁹ This decrease in maximal force output could be attributed to mechanisms involving motor unit recruitment as the muscle begins to fatigue.

Fatigue may occur as a result of central or peripheral elements of the motor system. Aspects of peripheral muscle fatigue, may occur due to mechanisms such as neurotransmitter depletion,²⁰ excitation-contraction coupling failure,²¹ postsynaptic

membrane failure, and failure to propagate the action potential into axonal branches.²⁰

Central fatigue is defined as the elements in the central nervous system that may affect fatigue such as emotions and other psychological factors involved in an individual's sense of effort as well as at the various descending motor pathways and the interneurons and motoneurons in the brainstem and spinal cord.²²

As all motor units have been recruited at the level of fatigue, the inability to recruit additional motor units to assist in maintaining force output leads to the decrement in maximal force production.²³ Fatigue is also characterized by an increased effort needed to maintain a submaximal contractile force when force level remains the same and when the effort required to maintain a constant submaximal task gradually increases. This is resulting from the central nervous system's attempt to maintain force output ultimately delaying fatigue.²⁰ The rate of fatigue generally depends on an array of factors including the muscles employed, the relative intensity of the exercise, and whether the contractions performed are continuous or intermittent.²⁴

Intermittent contractions refer to rest periods applied during a fatigue task versus a constant (continuous) contraction fatigue task that does not allow rest time and continues to keep the muscle activated for a given amount of time. Determination of the effects of intermittent or continuous contractions on voluntary EMG activation revealed no changes between the two types of contractions during a fatigue task.²⁵ However, Bilodeau²⁶ found that time to fatigue was increased during a 3-minute fatigue task with intermittent contractions versus a 3-minute fatigue task with continuous contractions in which showed decreases in time to fatigue. Ultimately, this shows that fatigue is affected when considering intermittent versus a continuous contraction fatiguing tasks.²⁶ This

decrease in contractile response will then be compensated by an increase in motor unit recruitment, motor unit firing rate, or both. This delay in fatigue could result from a quick decline in motor unit firing rate with a gradual increase later in the fatiguing task, or when nearing the fatigued state, as seen after muscular endurance training.²⁷⁻³¹ This occurs as a result of the central nervous system increasing excitation of the motor neuron pool, and thereby increasing the motor unit firing rates, to compensate for decreases in motor unit force twitch amplitude and maintain a given force output during a fatiguing task.^{28,30,32,33}

Increases in functional movement impairment have been associated with increased muscle fatigability within the elderly population. This fatigability is characterized by accelerated decreases in relative muscle power while performing dynamic or static exercises. Essentially, this would result in decreased force production and slower shortening velocity of the muscle.³⁴ With progressive exercise, changes may occur in the nervous system that could play a role in improving the pattern of motor activation in order to maintain a specific force output.

Neuromuscular Electrical Stimulation

Neuromuscular electrical stimulation (NMES) is typically used as a physical rehabilitative modality to improve skeletal muscle strength and endurance for therapeutic, training, or functional means such as walking, standing, and upper limb movements such as reaching and grasping.^{35,36} NMES is the therapeutic application of a sequence of electrical stimulation pulses that elicit skeletal muscle contraction in hopes of mimicking a voluntary skeletal muscle contraction.³⁷ NMES has been shown to activate paretic or paralyzed muscles that assist in improving functional limb movements such as standing

and walking in individuals with stroke, hemiplegia, paraplegia, and other neuromuscular disorders^{35,38,39} and to induce anabolic processes in hemiplegic and neurologically intact skeletal muscle of older adults.⁴⁰ NMES induces involuntary muscle contraction by sending an electrical current directly in the muscle. Current administered during NMES influences the muscle by synchronously recruiting all motor units within the electrode pickup area. As the stimulation is delivered, the electrical current produces an action potential on the sarcolemma and, thereby, activates the muscle fibers resulting in an physical involuntary muscle contraction.³⁶ Involuntary skeletal muscle contractions differ from voluntary muscle contractions in that they lack the motor unit size-order recruitment, also known as the Henneman Size Principal present within a voluntary contraction,⁴¹ by having muscle fibers recruited in a non-selective, fixed recruitment pattern with no obvious sequencing pattern.⁴² Motor units in an involuntary muscle contraction are activated in a maximal and synchronous manner, and the motor unit firing rates occur at a quicker rate than those recruited during voluntary contractions.^{42,37} Due to the inability to control motor unit recruitment order and the lack of control over the motor unit firing frequency, it has been stated that involuntary skeletal muscle contractions make the muscle stimulated more vulnerable to a quicker rate to fatigue.³⁷ However, this poses as an advantage in that faster muscle fibers that are needed for voluntary contractions can be recruited at low stimulation levels, which would be beneficial for populations that cannot physically perform muscle contractions at higher force levels.^{37,43} Alternatively, voluntary muscle contractions depend on the amount of motor units that activate as well as the rate at which they are activated in order to reach a desired force output. Therefore, the increase in force output or force maintenance needed

requires an increase in the amount of motor units recruited and a faster rate of activation.⁴⁴ When applied to skeletal muscle fatigue, voluntary skeletal muscle contractions result in a decreased motor unit firing rate in which is compensated with an increase in the amount of motor units recruited to maintain the required force output.⁴⁴⁻⁴⁷

Using NMES allows motor unit recruitment patterns to heighten metabolic demands with one of the goals being to maintain tension within the muscle. It is possible that NMES may ultimately be used within rehabilitation settings that aim to achieve therapeutic goals related to muscular endurance.^{36,38} NMES has been considered an effective alternative to exercise training for various patient populations including those diagnosed with Chronic Obstructive Pulmonary Disease (COPD), those requiring respiratory therapy, and those with severely deconditioned muscles to name a few.^{48,49} It has been commonly found that NMES can produce up to 20-30% increases in quadriceps strength as compared to a control group.⁴⁹ NMES can improve exercise capabilities during activities such as walking^{50,51} and cycling⁵² and endurance amongst other activities of daily living.⁴⁹

Evidence has showed improvements in the 6-Minute Walk Test (6MWT) pre-post treatment in the experimental group of NMES and pulmonary rehabilitation combined as compared to just pulmonary rehabilitation alone. This ultimately showed an increase in exercise tolerance applying to aerobic and muscular endurance with NMES incorporation.⁴⁸

NMES has also been shown to lead to significant improvements in various functional outcomes. Enhancement of force output and preservation are results presented as a result of NMES. NMES stimulation sessions were studied during three separate

sessions separated by at least 48 hours, and on these days, the participants would complete 1 of 3 stimulation patterns. The first stimulation pattern included a 3-min pattern of 20 Hz stimulation, the second consisted of a 3-min pattern of 90 seconds of 20 Hz followed by 90 seconds of a gradual increase from 20 to 40 Hz, and the third included a 3-min pattern of 90 seconds of 20 Hz followed by 90 s of 20 Hz doublet stimulation. The aim was to find the effects of variable stimulation patterns of NMES in the thenar muscles of younger and older adults, and results revealed enhanced force production pre- to post-NMES intervention.⁵³ Furthermore, another study comparing the effects of a low and high frequency stimulation on torque output parameters of the quadriceps muscle found that low-frequency NMES results in increased preservation of torque output during a stimulation protocol.⁴⁰

With repeated application, NMES may improve voluntary muscular endurance. NMES interventions have shown to produce significant functional improvements such as evidence showing the influence of 2 different 6-week NMES interventions with 3 sessions per week protocols (narrow [50Hz] and wide-pulse NMES [100Hz]) on the triceps surae muscle and mobility of healthy older adults. These findings reported significant improvements in walking endurance, maximal walking speed, chair-rise time, rapid-step speed, and plantar flexor strength.⁵⁴ Other functional improvements have been seen within the healthy older adult population including balance,^{55,56} time to complete the Timed Up and Go Test (TUG), gait velocity, 5 x chair rise,⁵⁷ short physical performance battery testing for the lower extremity, 10-meter walk test (habitual and fastest walking speed),⁵⁷ 12 flight stair test,⁵⁷ vertical jump performance,⁵⁵ and 10-meter walking speed.⁵⁷ Evidence has also shown functional improvements as a result of NMES within older

adults with knee osteoarthritis including 5 x chair rise, 12 flight stair test,^{58,59} and 6MWT.⁵⁸ Continually, NMES interventions have also been performed in older adults with existing comorbidities such as results revealing improvements in the 12 flight stair test within older adults whom have undergone knee arthroplasty⁶⁰ and results reporting improvements in gait speed, walking endurance, dorsiflexor/plantarflexor muscle strength and force control in older adults diagnosed with Multiple Sclerosis.⁶¹ Furthermore, improvements in functional outcomes have been found including improvements in Maximal Voluntary Contractions (MVC) and standing postural control within the pre-frail elderly,⁶² improvements in balance and 6MWT distance in older adults living in a geriatric nursing home,⁶³ and increases in 6MWT distance within older adults diagnosed with Chronic Heart Failure.⁶⁴ Of these findings, NMES interventions typically consist of stimulation frequencies of 4Hz,⁶⁴ 20Hz,⁵⁵ 50Hz,^{54,58-61,63} 60Hz,⁵⁷ 70Hz,⁵⁶ and 100Hz.^{54,61,62} Furthermore, most of the evidence on effects of NMES on functional outcomes consists of 3,^{54,57,59,61,62} 4,^{55,56} or 5^{58,60,64} NMES training sessions per week for 4,^{56,62} 6,^{54,55,57,58,60,61} 8,⁶⁴ 12,⁵⁹ and 16⁶³ week intervention lengths.

Electromyography and Fatigue

Surface electromyography (sEMG) is used as a means of measuring skeletal muscle activation. This technique has versatility as it measures muscle activity at rest or during muscular activities.^{38,65} Muscular activation level as well as muscular fatigue are typical outcome measures of sEMG and they are quantified as a means of reflecting these parameters. In order to quantify the EMG data, specific measures can be used such as frequency spectrum parameters known as median power frequency (MPF) as well as root mean square (RMS) to name the most commonly used.^{66,67} RMS is typically used to

quantify changes in muscular activation level because it reflects the physiologic activity in the muscle's activation via motor unit depolarization/repolarization during the contraction.⁶⁷

In order to get the most accurate EMG results, isometric contractions are typically utilized to maintain stability of the electrodes. Other factors could interfere with the sEMG signal including the use of appropriate electrode size or type according to the activity assessed, location of electrode placement in relation to the muscle fibers of the muscle examined, the position of sEMG electrodes to each other, muscle fiber characteristics (diameter), tissue filtering (skinfold thickness and blood flow), muscle length, data acquisition, and filtering complications (filter selection, and electrode, skin, or wire movement).⁶⁸

When comparing EMG signals across test subjects, it is typical to use maximal voluntary contractions as a way to normalize data to reflect the degree of muscle activity during the muscle contraction.^{67,69} One way in which to assess peripheral fatigue is by analysis of the M-wave which is an EMG response to a single action potential at the level of the axon of the peripheral nerve or directly from application to the muscle as is the case with NMES. Changes in the M-wave signify possible changes in muscular fatigue. These changes will demonstrate an increase in the M-wave amplitude throughout the first few stages of fatigue with a decrease nearing true fatigue, or the inability to maintain the required force output.⁷⁰⁻⁷² When completing sustained submaximal contractions until fatigue, the surface EMG of the muscle begins to increase gradually as more motor units are recruited to maintain the force output.^{22,73-78} When the submaximal target force can no longer be maintained, muscle activation levels, also known as EMG, begin to

decrease.^{74,76,79} Multiple mechanisms may be working in conjunction that contribute to this decrease in muscle activation associated with fatigue. These could include decreased excitability of the motor neuron, decreased excitatory influence from peripheral sources, increased inhibitory influences on motoneurons, decreased force from individual cross bridges, and decreased excitation of motoneurons.^{70,80-82}

Firing frequencies of motor units begin to decrease when analyzing EMG.⁸¹ Typically, motoneuron firing rate gradually decreases during sustained contractions and increases late in the fatigue process.²⁷ The change occurs within the EMG activity due to the resulting decrease in the frequency of firing of the recruited motor units. Further, this decrease in muscle activation is shown as a result of the decreasing firing frequency of motor units during rhythmic or sustained effort.⁸³ Many contributors to muscular fatigue can be determined by examination of the M-wave presented by surface electromyography.

Multiple studies have shown improvements with training in muscular fatigue through median power frequency (MPF) as well as RMS parameters of sEMG. Bedrest on quadriceps fatigue found an increase in rate of increase of maximal RMS EMG amplitude and increased rate of decrease in EMG MPF throughout a fatiguing task pre- to post-bed rest ultimately showing an increase in muscular fatigue or a decrease in the time to fatigue.⁸⁴ Bed rest on EMG RMS and EMG MPF as compared to resistive vibration exercise (RVE) found decreases in MPF with bed rest and significant increases in RMS as a result of the RVE after repeated submaximal contractions. Ultimately, the increase in RMS shows there was more muscle activation, possibly motor unit firing rates, within the tested quadriceps femoris muscle after resistive vibration training pre- to post-bed rest

allowing for improved muscular fatigue or maintenance of force output. Alternatively, the decrease in MPF post-bed rest shows decreases in muscle activation and therefore decline in the ability to maintain a given force.⁸⁵ Umehara et al.⁸² found a significant decrease in MPF during an acute fatigue task of the serratus anterior muscle.⁸² The medial hamstring muscle showed similar decreases in MPF as a result of muscular fatigue as well as an increase in RMS EMG after a fatigue protocol in the medial hamstring and vastus lateralis muscles.⁸⁶

Study Rationale

There has been limited research on the effects of NMES training and how it may influence voluntary muscle fatigue specifically within the older adult population. Some studies on older adults have noted increases of muscular endurance by ways of various functional tests ranging from the 6-min walk test^{48,64,87} to the Timed Up and Go Test^{57,87} amongst others.^{49,54,57,88} Conversely, there is evidence that shows no changes in skeletal muscle endurance pre-post NMES intervention.⁸⁹ Evidence on EMG parameters have been measured during voluntary contractions and compared pre-post NMES training programs^{38,90} with few exploring the effects of NMES on EMG parameters as well as endurance times to muscular fatigue. However, evidence have also presented no significant differences^{38,49,89,91-93} or decreases^{38,91} in skeletal muscle endurance along with no significant differences in EMG parameters⁹⁴ pre-post NMES intervention. The effectiveness of combination therapy with NMES has been explored⁴⁸ along with various intervention lengths,^{24,49,64,95} and various subject populations such as athletes,⁹⁶⁻¹⁰⁰ those living in a nursing home lifestyle,⁸⁷ and older adults with confounding conditions.^{48,49,60,64,95,101-104} There has been limited evidence covering the effects of

NMES on the highly used quadriceps muscle^{49,60,87,88,101} specifically for functional independence with many exploring NMES effects on varying muscles ranging from the triceps surae⁵⁴ to the digital finger flexor muscles⁸⁸ amongst others.⁴⁹ In patient populations, often the goal is to reduce the decline to maintain function, rather than to improve function. Limited information has been found looking at the effects of a 4-week NMES stimulation intervention on quadriceps skeletal muscle fatigue by ways of a submaximal fatiguing task and sEMG in healthy older adults.

Purpose

The primary purpose of this study was to determine the effects of a 4-week NMES intervention on voluntary muscular fatigue of the quadriceps and changes in neuromuscular activation patterns during voluntary fatiguing muscle contractions in older adults. The secondary purpose was to determine the degree of neuromuscular activation during submaximal voluntary contractions and MVC, MVC (strength), and 6-min walk performance pre-post 4 weeks of NMES in older adults.

Methods

Participants

Data were collected and analyzed for 17 healthy, older adults aged 60 or older (11 females; 6 males; 68.8 ± 1.8 years old). Subject age was 68.8 ± 1.8 (NMES: 67.9 ± 1.9 ; SHAM: 70.8 ± 3.9). NMES group consisted of 6 males and 6 females (67.9 ± 1.9 years old) and the SHAM group consisted of 5 females (70.8 ± 3.9 years old) with participants randomly placed in one of two groups 1) NMES group or 2) Sham group who received no treatment. Participants were recruited via flyer distribution in the San Marcos/Austin, Texas area. Inclusion criteria included generally healthy participants ages 60 and older. Exclusion criteria were participation in regular resistance training exercise or physical rehabilitation

of the lower extremity within 2 months of the study, presentation of contraindicating conditions for electrical stimulation (i.e., swollen, infected or inflamed areas including open wounds, or painful areas on the lower limbs, implanted electronics including pacemakers, electronic infusion pumps, implanted stimulators, or surgical hardware in the lower limbs), having current knee pain or knee injury, currently diagnosed with a neuromuscular disease, currently taking insulin for diabetes regulation, and a history of seizures. Participants completed a health history phone screening to obtain information regarding inclusion and exclusion criteria prior to study enrollment. All procedures have been approved by the Texas State University Institutional Review Board. All eligible and interested participants signed the informed consent form prior to participation in the study.

Procedures

All procedures were completed in the Translational Neuromuscular Physiology Laboratory at Texas State University as well as other facilities located within Jowers Center at Texas State University. This clinical trial used a pre-test post-test randomized experimental design.

Neuromuscular Electrical Stimulation

Subjects were seated on an isokinetic dynamometer (Biodex, Systems-4, Shirley, NY) used to measure force output. Data were collected with the knee fixed at 60 degrees of knee flexion and the hip placed at 85 degrees of flexion. (Figure 1) The same positioning was used during Pre-Post Test Day 1 procedures including MVC, isometric submaximal contractions, fatigue task, and sEMG. (Figure 1) Both legs received the NMES intervention. The first leg stimulated was randomized for all subjects for each

training session. Stimulation electrodes (carbon cloth electrodes, 3x5 in; Axelgaard, LTD, Fallbrook, CA) were used in administering the NMES treatment. Prior to placing the stimulating electrodes, participants were asked to shave the anterior aspect of each leg from the knee up, and each leg was cleaned with isopropyl alcohol. Four stimulating electrodes were then placed at the proximal and distal ends of the vastus lateralis and vastus medialis muscles. (Figure 1) Participants were randomized into the NMES (millicurrent) group receiving stimulation or the Sham group receiving no stimulation. Participants assigned to the millicurrent group were told the stimulation will produce a buzzing sensation that will create a muscle contraction and movement in the leg. Participants assigned to the Sham group were told that they would receive microcurrent stimulation and were told the treatment would not result in muscle contraction or sensations in the leg and that the treatment induces cellular processes.

All participants completed 3 training sessions a week for 4 weeks (12 total sessions). Each session included NMES applied for 40 minutes to each leg. (Figure 2) A constant current stimulator (Digitimer DS7A, Garden City, England) was used to administer the electrical stimulation. The NMES was administered using a stimulation frequency of 60Hz, a pulse width of 200 μ s, and cycled on for 10 seconds and off for 15 seconds for the duration of the 40-minute treatment. The stimulation intensity was initially adjusted to meet the 15% target torque, as measured during pre-testing, and then was adjusted every 5 minutes to meet the 15% target torque if the participant's torque output no longer met the target. The stimulation intensity was recorded every 5 minutes. All procedures were consistent for both experimental groups, except no stimulation was delivered to the Sham group participants.

Pre-Post Test Day 1:

Body composition, muscular strength, muscular endurance, and sEMG testing were completed on Pre and Post Test Day 1. (Figure 2) Both legs were tested in random order for all participants. These tests were completed prior to the start of NMES training sessions and at least 2 days following the last training session.

Body Size and Composition Testing

First, height and weight were measured using a digital scale (Health-O-Meter Professional 500KL, Alsip, IL) and these measurements were also used to calculate Body Mass Index ($BMI = kg/m^2$). Bioelectrical impedance analysis (BIA) (Omron Healthcare, Lake Forest, IL) was used to determine body fat percentage. Body size and composition testing were assessed for descriptive subject information. (Table 1)

Muscular Strength and Endurance Testing

MVC Testing

Electromyography (EMG) recording electrodes (Differential EMG Sensors, Trigno Wireless EMG System; Delsys, Inc., Boston, MA) were used to obtain electromyographic data in order to measure changes in muscle activation patterns during MVC, non-fatiguing submaximal isometric contractions, and the fatigue task. Electromyography data was collected using a data acquisition system (PowerLab 16/35, ADInstruments, Colorado Springs, CO) and LabChart software (Version 8.1.13, Bella Vista, Australia). Prior to testing, EMG electrodes were placed on the belly of the vastus medialis and vastus lateralis muscles. Prior to placing the electrodes, participants were asked to shave the front of each leg from the knee up, and each leg was cleaned with

isopropyl alcohol. Data collection commenced with MVCs for knee extension. Visual feedback of torque output was provided on a computer monitor placed in front of the participant for all Pre-Post Test Day 1 and Day 7 MVC testing. Surface EMG of the vastus lateralis and vastus medialis was recorded for all Pre-Post Day 1 testing. Torque output was also assessed during all Pre-Post Day 1 during MVC, non-fatiguing submaximal isometric contractions, voluntary submaximal isometric fatigue task, and Day 7 MVC testing. These tests were completed prior to the start of NMES training sessions and at least 2 days following the last training session. The participant was told to kick out as fast and as forcefully as possible, and 2 MVCs were performed. Each repetition was held for 4 seconds with 6 seconds of rest between, and verbal encouragement was given throughout the testing. Additional MVCs were completed if the peak torque increased from the first to the second MVC. The MVC with the highest torque output was used as a measure of strength (MVC) and to calculate for target torque for the non-fatiguing submaximal contractions, the fatigue task, and the NMES training sessions. A rest interval of fifteen minutes was given following quadriceps MVC testing prior to the next test.

Non-Fatiguing Isometric Submaximal Contractions

Next, non-fatiguing voluntary isometric submaximal contractions at 20, 30, 40, 60, and 80 percent of knee extension MVC were performed in random order. Visual feedback of torque output was provided on a computer monitor placed in front of the participant for all Pre-Post Test Day 1 testing. Surface EMG of the vastus lateralis and vastus medialis was recorded for all Pre-Post Day 1 testing. Torque output was also assessed during all submaximal contractions. Each participant was asked to match a

target line indicating force output of a specific contraction intensity (percent MVC). Subjects were then asked to continue matching the line while keeping force output as steady as possible on that target line. Participants were told “your line on top of the target line is perfect, just do your best” for both the non-fatiguing submaximal and fatigue task testing. For 20 and 30 percent MVC, the participants maintained the target torque for 7 seconds. Submaximal contractions at these intensities were performed once and were given a 1-minute rest prior to starting the next contraction. For the contractions at 40, 60, and 80 percent of MVC, the target torque was maintained for 5 seconds. These were also performed one time, and participants were given 2 minutes of rest prior to completing the next contraction. EMG was determined to analyze for degree of muscle activation at each level of contraction pre-post NMES intervention. On completion of the submaximal contractions, a 10-minute rest was provided before beginning the fatigue task.

Isometric Submaximal Voluntary Fatigue Task

For the voluntary, intermittent, submaximal fatigue task, visual feedback of torque output was provided on a computer monitor placed in front of the participant for all Pre-Post Test Day 1 testing. The task was a knee extension contraction and surface EMG of the vastus lateralis and vastus medialis were recorded for all Pre-Post Day 1 testing. Torque output was also assessed during all procedures. These tests were completed prior to the start of NMES training sessions and at least 2 days following the last training session. Participants were instructed to kick out to meet a target torque of 50% MVC. Subjects were told to match the target torque, and to maintain torque output to match the target torque line for 20 seconds. Following the 20 seconds, the subjects were given 2 seconds of rest. This process was repeated until the participant failed to

maintain a force output of above 47% MVC for at least 2.5 consecutive seconds. This indicated endurance time and the end of the fatigue task. To determine the level of fatigue, 3 MVCS were performed immediately following the fatigue task and held for approximately 3 seconds each with 1 second rest in between. Pre-fatigue MVCs and post-fatigue MVCs were compared and expressed as a percent change pre- to post-fatigue task as a measure of the degree of muscular fatigue achieved by the end of the fatigue task. Verbal encouragement was provided throughout the fatigue task. EMG was measured to determine changes in muscle activation (RMS EMG, integrated EMG) and fatigue parameters (median frequency EMG) pre-post NMES intervention. Prior to strength and endurance testing, a practice session was completed to familiarize the participants to the instrumentation and protocols. During this practice session, each participant completed a series of maximal and submaximal isometric contractions for knee extension. A 10-minute rest period was provided between the practice session and the testing.

Pre-Post Test Day 2

The 6-Minute Walk Test (6MWT) to assess endurance during a physical function test was completed on Pre-Post Test Day 2. This test was completed at least 1 week following Pre-Test Day 1 and at least 2 days prior to the start of NMES training sessions and for post-testing, 2 days following Post Test Day 1. (Figure 2) Participants were told to walk as fast as they can without running for 6 minutes. A designated path was provided with guidance on the first lap. Participants were told they can rest or slow down if needed. Distance completed pre- and post-NMES was recorded in yards to the nearest inch and used for statistical analysis.

Data Analysis

MVC

Torque analysis was performed using LabChart software (Version 8.1.13, Bella Vista, Australia) to assess MVC torque output changes pre, to Day 7, to post-NMES intervention. Maximal torque was measured for each MVC. The MVC with the highest torque output was used for statistical analysis. EMG (RMS, MPF, and peak) were measured 0.5 seconds on each side of the peak torque output during the MVC pre, Day 7, and post-NMES intervention (Mulder et al., 2007). EMG RMS and peak EMG were normalized to respective variable values during the pre-training MVC and are presented as a percentage of MVC (post-training MVC EMG value/pre-training MVC EMG x 100). Normalized EMG values of the mean of both legs were used for statistical analysis.

Non-Fatiguing Isometric Submaximal Voluntary Contractions

LabChart (ADInstruments, Colorado Springs, CO) software was used to measure average torque output and levels of muscle activation (RMS EMG) pre- and post-NMES intervention. For the following contraction intensities, 20%, 30%, 40%, 60%, and 80%, data were analyzed to measure the average torque and RMS EMG during each contraction. For each submaximal contraction, EMG (RMS and MPF) was measured during a 2-second window in which torque fluctuations were minimal and most closely matched the target line (Mulder et al., 2009). EMG RMS was normalized to respective variable value obtained during the pre-training MVC and were presented as a percentage of MVC (post-training MVC EMG value/pre-training MVC EMG x 100). Normalized EMG values of the mean of both legs were used for statistical analysis.

Isometric Submaximal Voluntary Fatigue Task

Electromyography and torque data during the fatigue task protocol of each leg were analyzed using LabChart software (Version 8.1.13, Bella Vista, Australia). EMG was analyzed for RMS EMG, MPF EMG, EMG integral, and average torque of each contraction were measured. The middle 12 seconds of each 20-second contraction (excluding first and last 4 seconds of each contraction to avoid ramping up and down phases) was measured. Percent rate of change was calculated for normalized EMG (RMS and Integral) and MPF EMG ($(EMG_{\text{Final contraction}} - EMG_{\text{Initial contraction}} / EMG_{\text{Initial contraction}}) \times 100 / \text{Endurance Time}_{\text{min}}$). Muscular endurance was measured as the contraction time to the end of the fatigue task (when torque was below 47% MVC for a consecutive 2.5s) and was recorded in seconds. All variables were compared pre-post intervention.

EMG Data Analysis

All EMG data were full-wave rectified and then all submaximal EMG were normalized to MVC EMG obtained during the pre-testing for respective measures (RMS, peak, integral) and were expressed as a percentage of pre-training EMG during MVC ($EMG_{\text{Measured Contraction}} / EMG_{\text{MVCpre}}$). Normalized EMG values of the mean of both legs were used for statistical analysis.

Statistical Analysis

Data were analyzed using SPSS software (Version 21, IBM). Data analysis for MVC included independent variables of group (NMES and Sham) and time (pre-NMES, to Day 7, to post-NMES). Independent variables for the non-fatiguing isometric submaximal contractions, voluntary isometric submaximal fatigue task, and 6MWT

included group (NMES and Sham) and time (pre-NMES to post-NMES) while dependent variables included MVC, muscular endurance time, 6-Minute Walk Test (6MWT) distance, submaximal contraction RMS EMG, MPF, and average torque (20%, 30%, 40%, 60%, 80%), and RMS EMG, integrated EMG, and MPF EMG for the fatigue task. Repeated measures ANOVA were used to determine differences for group (NMES, Sham) and time (pre-NMES, post-NMES) and the group x time interaction for the following variables: muscular endurance time, 6MWT, MVC peak torque, MVC EMG (RMS, MPF, Peak), EMG (RMS and MPF) during submaximal contractions, and EMG (RMS, MPF, and integrated EMG) for the fatigue task. Cohen's d was determined for MVC peak torque pre-post training, EMG (RMS, MPF, and Peak) during MVC for the vastus lateralis muscle, RMS EMG during each respective submaximal contraction, EMG (RMS and MPF) during the non-fatiguing isometric submaximal contractions, 6MWT distance, endurance time, and rate of change of EMG (RMS, MPF, and integral) during the isometric submaximal fatigue task $((\text{Mean}_{\text{post}} - \text{Mean}_{\text{pre}}) / ((\text{SD}_{\text{pre}} + \text{SD}_{\text{post}}) / 2))$. Data are reported as mean \pm SE and statistical significance was set at $p < 0.05$.

Results

Subject Characteristics

There was 100% compliance for completing training sessions from all participants.

Maximal Voluntary Contraction (MVC)

Peak Torque

Peak torque during MVC showed a small increase pre-training to post-training for the NMES group (small effect size, Cohen's $d = 0.31$), however, was not statistically

significant (main effect for time: $p = 0.174$). (Table 2; Table 3) The main effect for group ($p = 0.142$) and the time x group interaction for peak torque were not significant ($p = 0.391$). Additionally, MVC increased 8.9% pre-training to post-training for the NMES group exceeding the established minimal clinically important difference score (MCID) of 4% change in isometric muscle strength showing that our 4-week NMES treatment resulted in a clinically meaningful improvement in functional muscle strength.¹⁰⁵ (Table 3) MVC peak torque data are in Figure 3. Similar findings were found by O-Reilly and colleagues¹⁰⁶ assessing the effectiveness in a 6 month strength training home exercise program on knee pain and disability in men and women aged 40 to 80 years old with osteoarthritis of the knee. They found an increase in quadriceps strength as measured by a modified tornvall chair that measured muscle strength during knee extension and found a 4.7% increase in the exercise group as compared to non-exercise control group. Although this was seen as a modest increase, they indicated that it was considered a clinically meaningful improvement in isometric quadriceps muscle strength within the assessed population.¹⁰⁶

EMG during MVC

Although not a statistically significant change, RMS EMG did increase 86.83% in the vastus lateralis pre-post 12 weeks of NMES in the NMES group with a large effect size (Cohen's $d = 0.83$). (Table 2) The time main effect for RMS EMG for the vastus lateralis was not significant ($p = 0.628$). The main effect for group ($p = 0.292$) and time x group interaction for RMS EMG were not statistically significant ($p = 0.403$). (Figure 4a) Data were analyzed based on 15 subjects with 2 participants excluded due to technical problems with the data collection. EMG RMS for the vastus medialis showed no change

(main effect for time: $p = 0.295$). RMS EMG for the vastus medialis muscle showed a 6.36% increase pre-post NMES with a small effect size (Cohen's $d = 0.29$). (Table 2) The main effect for group ($p = 0.364$) and the time x group interaction for RMS EMG were not significant ($p = 0.279$) (Figure 4b).

Vastus lateralis MPF EMG data are presented in Figure 5a. The time main effect for MPF EMG was not significant ($p = 0.452$). The main effect for group ($p = 0.895$) and the time x group interaction for MPF EMG were also not significant ($p = 0.350$). For vastus medialis MPF EMG during MVC pre-training, DAY 7, and post-training are presented in Figure 5b. The main effect for time and main effect for group ($p = 0.360$) for MPF EMG were not significant ($p = 0.389$) and the time x group interaction was also not significant for EMG MPF ($p = 0.153$)

The time main effect for peak EMG values for the vastus lateralis was not significant ($p = 0.655$). However, there was a large effect size showing an increase pre-post change in the NMES group (Cohen's $d = 0.88$). (Table 2) The main effect for group ($p = 0.267$) and the time x group interaction for EMG peak were not significant ($p = 0.383$). (Figure 6a) The time main effect for peak EMG for the vastus medialis was not significant ($p = 0.219$). The main effect for group in peak EMG production ($p = 0.714$) and the time x group interaction for peak EMG production were also not significant ($p = 0.326$). (Figure 6b)

Non-Fatiguing Isometric Submaximal Voluntary Contractions

Mean Torque

The average torque production at each targeted relative contraction intensity showed no change between pre-training and post-training (main effect for time: $p =$

0.646). There was no main effect for group in ability to produce target torque for each of the submaximal contraction intensities ($p = 0.523$). However, the target torque intensity levels were significantly different from each other with significant increases from 20% to 30% ($p < 0.0001$), 30% to 40% ($p < 0.0001$), 40% to 60% ($p < 0.0001$), and 60% to 80% ($p < 0.0001$). Mean torque values for the isometric submaximal contractions can be found in Figure 7.

EMG during Non-fatiguing Submaximal Isometric Contractions

When all contraction intensities were compared with a RM ANOVA, the time main effect for RMS EMG of the vastus lateralis was not significant ($p = 0.511$) and there was no main effect for group ($p = 0.358$). There was a significant main effect for contraction intensity ($p = 0.002$), pairwise comparisons show that as contraction intensity increased the RMS EMG was significantly higher from 20% to 30% ($p = 0.011$), 30% to 40% ($p = 0.002$), and 40% to 60% MVC ($p = 0.006$); however, 60% and 80% were not significantly different from each other ($p = 0.104$). The interactions were not significant ($p > 0.05$). A follow-up RM ANOVA was performed for each contraction intensity to determine training effects. For each contraction intensity, the time main effect was not significant for 20%, 30%, 40%, 60%, and 80% MVC ($p = 0.532, 0.544, 0.516, 0.522,$ and 0.481 , respectively). The main effect for group for each of the contraction intensities ($p > 0.05$), and time x group interaction were not significant for any of the contraction intensities ($p > 0.05$). For each contraction intensity, Cohen's d effect sizes were also calculated pre-post NMES training for the NMES group showing an increase in RMS EMG pre-post training across all intensities for the NMES group: 20% MVC (medium effect, Cohen's $d = 0.56$), 30% MVC (small effect, Cohen's $d = 0.49$), 40% MVC

(medium effect, Cohen's $d = 0.52$), 60% MVC (small effect, Cohen's $d = 0.48$), and 80% MVC (small effect, Cohen's $d = 0.41$). Data are presented in Figure 8a. (Table 2)

Time main effect for RMS EMG for the vastus medialis was not significant ($p = 0.152$). The main effect for group ($p = 0.507$), and the time x group interaction for RMS EMG during submaximal contractions were not significant ($p = 0.292$). However, RMS EMG increased significantly from 20% to 30% ($p < 0.001$), 30% to 40% ($p < 0.000$), 40% to 60% ($p < 0.000$), and 60% to 80% ($p < 0.001$). (Figure 8b)

The time main effect for vastus lateralis MPF EMG was not significant ($p = 0.879$). The main effect for group ($p = 0.221$) and the time x group interaction for MPF EMG were not significant ($p = 0.734$). (Figure 9a) The time main effect for training for vastus medialis MPF EMG production was not significant ($p = 0.501$). The main effect for group ($p = 0.723$) and the time x group interaction for MPF EMG were also not significant ($p = 0.734$). (Figure 9b)

Six Minute Walk Test

For 6MWT, the distance walked increased presenting a small effect size for pre-post change in the NMES group (Cohen's $d = 0.22$). (Table 2; Table 3) The main effect for time was not significant ($p = 0.512$). There was a group main effect for 6MWT distance with the NMES group walking farther than the SHAM group ($p = 0.035$). The time x group interaction was not significant ($p = 0.313$). (Figure 10)

Submaximal Isometric Voluntary Fatigue Task

Our data show that ability to maintain the target torque (50% MVC) during the fatigue task was consistent between test days and between groups (NMES Pre: $48.89 \pm 0.28\%$; NMES Post: $49.36 \pm 0.19\%$; SHAM Pre: $48.76 \pm 0.44\%$; SHAM Post: $49.04 \pm$

0.47%; time main effect: $p = 0.070$). There was no main effect group ($p = 0.609$) and the time x group interaction was not significant ($p = 0.623$).

Compared to MVC (non-fatigued), there was a reduction in MVC after the pre-training fatigue task and post-training fatigue task in the NMES group indicating that the fatigue task induced muscular fatigued by the end of the fatigue task (NMES Pre: $-30.47 \pm 4.39\%$; NMES Post: $-34.84 \pm 3.24\%$; SHAM Pre: $-33.73 \pm 2.99\%$; SHAM Post: $-27.47 \pm 5.60\%$). The main effect for time ($p = 0.995$) and main effect for group ($p = 0.789$) were not significant.

Endurance Time

Muscle endurance time did not change pre-post NMES training (time main effect: $p = 0.061$). The main effect for group ($p = 0.067$) and the time x group interaction were also not significant ($p = 0.445$) (Figure 11; Table 3).

EMG during the Isometric Submaximal Fatigue Task

For RMS EMG rate of change per min for the vastus lateralis during the fatigue task, the main effect for time was not significant ($p = 0.930$). The main effect for group ($p = 0.252$) and the time x group interaction were also not significant ($p = 0.087$). There was no effect for RMS rate of change as assessed by Cohen's d (Cohen's $d = 0.09$). (Table 2) Normalized RMS EMG rate of change data during the fatigue task are presented in Figure 12a. Representative data from one subject displaying RMS EMG for each 20s contraction of the fatigue task pre and post 12 weeks of NMES are presented in Figure 13a. For vastus medialis RMS EMG rate of change during the fatigue task are presented in Figure 12b. The main effect for time for rate of change in RMS EMG during the

fatigue task was not significant ($p = 0.423$). The main effect for group ($p = 0.112$) and the time x group interaction were not significant ($p = 0.288$).

There was a medium effect size for the rate of change in vastus lateralis MPF EMG during the fatigue task pre-post NMES training for the NMES group with lower rate of change post-training (Cohen's $d = 0.53$). (Table 2) The main effect for time was not significant ($p = 0.549$) and there was no main effect for group ($p = 0.737$). The time x group interaction was also not significant ($p = 0.565$). (Figure 14a). Representative data from one subject displaying MPF EMG for each contraction of the fatigue task pre and post 12 weeks of NMES are presented in Figure 13b. The main effect for time for the vastus medialis for MPF EMG rate of change during the fatigue task was not significant ($p = 0.219$). However, there was a medium effect size for pre-post change in the NMES group (Cohen's $d = 0.53$). (Table 2) The main effect for group ($p = 0.127$) and the time x group interaction were also not significant ($p = 0.583$). Vastus medialis MPF EMG rate of change during the fatigue task for both groups pre to post intervention are presented in Figure 14b.

The main effect for time for EMG integral rate of change during the fatigue task for the vastus lateralis was not significant ($p = 0.930$). The main effect for group ($p = 0.252$) and the time x group interaction were not significant ($p = 0.715$). (Figure 15a) Vastus medialis EMG integral rate of change during the fatigue task are presented in Figure 15b. The main effect for training for EMG integral rate of change for the vastus medialis was not significant ($p = 0.423$). The main effect for group ($p = 0.112$) and the time x group interaction were also not significant ($p = 0.288$).

Discussion

The findings of the present study suggest that a 4-week NMES intervention has the potential to improve skeletal muscle fatigue via improvement in quadriceps muscle activation and muscle strength in healthy older adults. MVC peak torque presented a clinically meaningful increase of 8.9% from pre to post NMES intervention indicating a practical meaningful improvement in quadriceps muscle strength as a result of 4 weeks of NMES. EMG RMS also presented as an increase in muscle activation pre-post NMES training with a large effect size, and therefore a large magnitude of improvement, in the vastus lateralis. Lastly, during muscle fatigue, the rate of change of the electromyographic RMS measure trended toward an increase in and MPF EMG had a slower rate of decrease, with small and medium effect sizes, respectively following 4 weeks of NMES training indicating that these changes in muscle activation may be beneficial for prolonging muscular endurance in the healthy, older adult population.

Maximal Voluntary Contraction (MVC)

The present study found that there was no significant increase in MVC peak torque pre to post NMES intervention; MVC increased 8.93% pre-training to post-training for the NMES group exceeding the established minimal clinically important difference score (MCID) of 4% change in isometric muscle strength showing that the change found in MVC in the present study reflects a clinically meaningful and practical improvement in muscle function. The MCID value was established by Ruhdorf and colleagues¹¹⁶ after assessing knee extensor strength by way of MVC in participants aged 45 to 79 at high risk for knee osteoarthritis. They ultimately found that a change in 4% knee extensor strength was associated with the MCID as recorded by self-assessment of

functional disability showing that this change is able to adequately reflect lower limb function within the assessed population.¹¹⁶ MVC in the present study also showed a small magnitude increase pre-training to post-training for the NMES group (small effect size, Cohen's $d = 0.31$). Ultimately, this demonstrates that our 4-week NMES intervention in older adults improved quadriceps muscle strength.

These findings are consistent with a assessing MVC peak torque pre-post NMES intervention in older adults scheduled to undergo a total knee replacement for end stage knee osteoarthritis.⁶⁰ The training parameters included application to the vastus medialis and vastus lateralis muscles of both the involved and uninvolved limb with a stimulation frequency of 50 Hz, duration of 20 minutes per session, training frequency of 5 times a week for 6 weeks. Post NMES intervention, they found that peak torque production during MVC in the uninvolved limb increased, but this increase was not statistically significant. They found similar results in the involved limb post NMES training.⁶⁰ Similar findings were also reported by study that assessed the effects of an NMES intervention on muscle strength in older adult participants that were hospitalized for COPD.¹⁰¹ They assessed the differences between a 35 Hz and a 50 Hz stimulation frequency for a session duration of 30 minutes daily for the length of their hospital stay with a mean of 8 days for the 35 Hz group and 9.5 days for the 50 Hz group and found that MVC peak torque increases were only significant in the group undergoing the 35 Hz stimulation frequency.¹⁰¹ Although the study did have a shorter intervention duration of 8-12 days, participants performed NMES training sessions daily, which could have contributed to the results being statistically significant. It is possible that the present study

could have benefited from more NMES training sessions each week as it may have induced a larger and statistically significant increases in MVC peak torque.¹⁰¹

It has been observed that the level of neuromuscular activation as measured by RMS EMG is a contributing factor to muscle strength as measured during MVC pre to post NMES intervention.¹⁰⁷ Present study findings for RMS EMG found no significant increases pre to post NMES intervention although they did present a large magnitude increase with a large effect size reflecting a large practical improvement in RMS EMG (Cohen's $d = 0.83$) likely meaning that possible sample size could have contributed to the lack of statistical significance in the MVC peak torque increases found in the present study. Findings of the present study were inconsistent with other studies finding increases in peak torque during MVC post NMES training as compared to pre training.^{59,108} However, these studies utilized stimulation intensities higher than that used in the present study throughout the NMES training sessions. Talbot and colleagues⁵⁹ assessed the effects of NMES on muscle strength in older adults with osteoarthritis of the knee over a 12-week NMES intervention with sessions 3 times a week with stimulation intensity of 50 Hz with stimulation intensity of a percentage of MVC increased by approximately 10% MVC with each progressive week of the intervention. Caggiano and colleagues¹⁰⁸ examined the effects of NMES on older adult, nondisabled men over a 4-week intervention with 3 sessions per week at a stimulation intensity of 40% MVC. It is possible that using a stimulation intensity target of a larger percentage of MVC could result in a larger increase in MVC peak torque pre to post NMES training.^{59,108}

A study by Kern and colleagues⁵⁷ assessed the effects of electrical stimulation of the quadriceps on muscle function in healthy older adults. Electrical stimulation

parameters included 3 10-minute electrical stimulation sessions at a 60 Hz stimulation frequency over a period of 9 weeks transitioning from 2-3 times a week sessions at the midpoint of the intervention period. Results of this study presented a statistically significant increase in MVC peak torque pre to post electrical stimulation intervention.⁵⁷ The findings of this study are inconsistent with those found in the present study although we did find a small effect size, indicating a small magnitude increase, and clinically meaningful improvement showing that 4-weeks of NMES was able to produce a practical meaningful improvement that can reflect in improvement in muscle function clinically. However, the expanded length of their stimulation intervention as compared to 4 weeks as in the present study may explain the statistical significance found in their results regarding MVC peak torque.

Almuklass and colleagues⁶¹ aimed to compare the effects of a 6-week narrow or wide-pulse NMES intervention on neuromuscular function in participants with relapsing-remitting Multiple Sclerosis (MS). The wide-pulse stimulation was applied at a 100Hz stimulation frequency while the narrow-pulse stimulation was applied at a 50 Hz stimulation frequency with both applied for 10 minutes on the dorsiflexor and plantarflexor muscles 3 times a week for 6 weeks. Ultimately, their findings showed a significant increase in MVC torque in the dorsiflexor muscles of the involved leg and the plantarflexor muscles of the less affected leg. However, they found no changes in dorsiflexor MVC torque of the less affected limb and the plantarflexor MVC torque of the affected leg.⁶¹ The later of their results is consistent with the findings of the present study as no significant changes were found in MVC peak torque pre to post NMES intervention. Mani and colleagues performed a similar NMES training protocol looking at

the effects of NMES on mobility. Although they assessed these effects in healthy older adults rather than those with Multiple Sclerosis as assessed in the previously mentioned study by Almklass and colleagues⁶¹. The results were statistically significant for an increase in MVC peak torque post-NMES training as compared to pre-training. It is possible that the intervention length may affect the resulting change observed. However, this study also included a patient population while the present study included healthy older adults. Although the referenced study found significant increases in MVC peak torque, their intervention duration was greater and stimulation frequency for the wide pulse NMES application was higher than the present study which could have been attributable to the statistical significance of their findings as compared to the present study.

Toth and colleagues¹⁰⁹ assessed the effects of NMES on skeletal muscle function in patients with breast cancer undergoing chemotherapy. With stimulation frequency of 50 Hz applied to the quadriceps muscle for 60 minutes 5 days per week for 8 weeks, they found a statistically significant decrease in isometric MVC torque pre to post NMES intervention.¹⁰⁹ These findings are inconsistent with the present study as we found no significant changes in MVC pre to post NMES intervention although, as mentioned previously, there was a clinically meaningful improvement pre to post training. However, the referenced study included a patient population that could have had adverse effects from chemotherapy causing deficits in muscular strength and fatigue leading to the decrease in MVC torque. It is also possible that the NMES stimulation did not provide the stimulus needed to overcome muscle wasting in the cancer population undergoing chemotherapy.

Inconsistent findings to the present study were found in a study by Almeida and colleagues¹¹⁰ that assessed the effects of NMES on muscle function in adults diagnosed with Rheumatoid Arthritis (RA). The intervention took place over 16 weeks with a stimulation frequency of 75 Hz applied for 15 total NMES elicited contractions 2-3 times per week. They found significant increases in MVC peak torque post-NMES training compared to pre-training.¹¹⁰ Although these findings are inconsistent with the present study, it is possible that the intervention length being longer and the stimulation frequency being 15 Hz more than the present study may have elicited more stimulation to the quadriceps, therefore, attributing to their statistically significant findings.

Muscle Activation during MVC

The present study found increases in RMS and peak EMG parameters recorded during MVC for the vastus lateralis muscle. However, these results were not statistically significant. These increases in EMG RMS were consistent with multiple studies finding an increase in EMG RMS during MVC pre to post NMES intervention although they found a statistically significant increase.^{91,111} Gondin and colleagues⁹¹ studied the effects of a 5-week NMES intervention on plantarflexor muscle strength, muscle activation and soleus and gastrocnemius. Findings from this study presented an increase in EMG RMS of both the gastrocnemius and soleus muscles post NMES intervention as compared to pre training.⁹¹ A similar stimulation protocol was used for a study by Maffiuletti and colleagues¹¹² with similar results to Gondin and colleagues⁹¹ study showing significant increases in RMS EMG during MVC after assessing muscle activation of the plantar flexor muscles pre and post electrostimulation training.¹¹² Similar results were found in a study assessing the effects of a 4-week electrical stimulation intervention on neural and

muscular changes of the quadriceps muscle in healthy males applied for 40 minutes per session with 4 sessions per week finding that RMS EMG increased significantly after the NMES intervention as compared to baseline. Although they found significant increases in RMS EMG, they used a stimulation frequency of 75Hz and stimulation intensity was progressively increased throughout the program according to participant tolerance.¹¹¹

A study by Arya and colleagues⁹⁴ assessed the effects of NMES on EMG analysis of the quadriceps muscle on children with spastic cerebral palsy. They assessed RMS EMG and peak EMG during a maximal voluntary contraction pre to post NMES intervention and found no statistically significant change in RMS EMG or peak EMG amplitude in the quadriceps femoris muscle. These results are consistent with those found in the present study relating to both RMS EMG and peak EMG findings as there were increases found in RMS EMG and peak EMG although they were statistically significant.⁹⁴ However, the present study did find large magnitude increases in RMS EMG and EMG peak showing practically meaningful improvements in muscle activation during MVC as a result of NMES.

Although the referenced studies had statistically significant increases in EMG parameters, they also included patient populations and a larger sample size, which could have led to larger increases in EMG values pre-post NMES intervention by adding more statistical power. NMES applied to patient populations likely means that there are increased deficits in the muscle making it weaker leaving more room for significant improvement as a result of a training regimen as supposed to healthy populations who have more conditioned musculature.

Non-Fatiguing Isometric Submaximal Voluntary Contractions

In regard to RMS EMG, the present study found increases in the NMES group pre to post NMES intervention for muscle activation during submaximal contraction with small to medium effect sizes presented for each of the isometric submaximal contraction intensities. However, these findings were not statistically significant. Limited research was found assessing the effects of a NMES intervention on EMG during isometric submaximal contractions.

Related studies looking at the effects of resistance training on EMG during submaximal isometric contractions at varying intensities have been explored and compared in this discussion. Villa-Chã and colleagues¹¹³ assessed the changes in motor output and motor unit behavior following 6 weeks of strength training with participants completing 3 sessions per week for six weeks including a combination of leg exercises performed at 60-70% of participant's 1RM and assessments completed during a MVC as well as a submaximal isometric contraction at 10% of MVC and at 30% of MVC.¹¹³ Findings from this study show increased average rectified EMG pre to post resistance training regimen as well as significant increases from 10% MVC to 30% MVC submaximal isometric contraction intensities. These findings were similar to the present study in that we found increases in RMS EMG at respective isometric submaximal intensities with small to medium effect sizes respectively.

A study assessing the effects bed rest with or without resistive vibration exercise (RVE) on neuromuscular function in healthy males. The training intervention took place over 56 days of bed rest and participants in the resistive vibration exercise group completed sessions 6 days per week and twice per day. After completing a non-fatiguing

submaximal isometric contractions at 5, 10, 15, 20, and 30% MVC, they found no changes in RMS EMG and found a significant decrease in MPF EMG in the control group post-bed rest. Significant increases in RMS EMG were found post-intervention in the resistive vibration exercise group while this group was said to counteract the significant decrease in MPF EMG found in the control group post-bed rest.⁸⁵ This study findings in pre-post resistive vibration exercise were consistent with the findings in the present study regarding RMS EMG pre to post NMES training in that we had medium effect sizes showing an improvement of a medium magnitude in RMS EMG.

Tracy and colleagues¹¹⁴ and Tracy and Enoka¹¹⁵ assessed electromyography during isometric contractions of the quadriceps muscle in older adults and found no changes in average rectified EMG throughout the isometric submaximal intensities tested (2, 5, 10, and 50% MVC) pre to post 16-week voluntary strength and steadiness training and found consistent results with the present study when comparing findings during submaximal isometric contractions. Although their analysis via surface EMG of average rectified EMG is different from the present study's use of EMG RMS, it is likely that the two EMG parameters are comparable in reflecting levels of muscle activation throughout submaximal isometric contractions.^{114,115} It is possible that the higher functional performance of healthy subjects may not reflect as much of an increase in electromyography measures as they would in patient populations.

Isometric Submaximal Voluntary Fatigue Task

Endurance Time

The present study showed no change in local muscular endurance with 4 weeks of NMES training; however, there were changes in EMG measures that suggest changes in

neuromuscular control strategies after 4 weeks of NMES that may promote improved muscular endurance ability. It is also possible that our older adult subject population had alterations or deficits in perceived effort ultimately leading to a premature end to the fatigue task before finding true fatigue. Within this particular population, perceived effort may be increased due to a decline in skeletal muscle mass and strength that occurs with age along with a decrease in activity level ultimately leading to a quicker rate to fatigue or increased exertion.

Inconsistent findings have been found in a study looking at the effects of a 6-week functional electrical stimulation (FES) on neuromuscular function in healthy, untrained men with participants completing 30 minute sessions 5 days a week at a ramp modulation stimulation frequency of 4-75-4 Hz and found that endurance time following the fatiguing task significantly increased post FES training compared to pre-training.¹¹⁶ A study by Reenen and colleagues¹¹⁷ looked at the effects of an 8-week resistance training program on muscle fatigue in healthy workers and found a significant increase in time to discomfort, or fatigue, post-training as compared to pre-training intervention.¹¹⁷ Although these findings were inconsistent with the present study, it is possible that their use of the localized musculoskeletal discomfort method of analyzing time to fatigue may have allowed for a more subjective point to fatigue at lower at a lower intensity level allowing for more variability to finding true fatigue time.

However, the present study's findings were consistent with findings presented in a study assessing central and peripheral contributions to fatigue pre to post 4-week and 8-week NMES intervention with NMES stimulation protocols including 4, 18-minute training sessions per week assessed at the 4-week and 8-week mark with a stimulation

frequency of 75 Hz.⁹¹ They found a significant decrease in endurance time post NMES training compared to pre-training. It is possible that an increase in absolute target torque may have attributed to a reduced time to fatigue ultimately decreasing the endurance time pre to post NMES intervention while also explaining why, in the present study, muscle activation improved without absent a change in endurance time.⁹¹ It is also possible that the high stimulation frequency, also used in the present study, is not optimal to improving muscular endurance as found by Doucet and colleagues³⁸ who assessed the effects of high (40 Hz) versus low (20 Hz) NMES stimulation frequencies on skeletal muscle endurance of the thenar muscles in a chronic post-stroke population. After a fatigue task consisting of a submaximal isometric contraction held at 30% MVC until fatigue, they found that low frequency stimulation produced significant increases in endurance time while high stimulation frequencies were better suited for improving muscular strength.³⁸

EMG

The present study found an increase in rate of change of RMS EMG and decrease in rate of change for MPF EMG pre to post NMES intervention in the NMES group with no change in the SHAM group. However, this increase was not statistically significant. As referenced above, Marqueste and colleagues¹¹⁶ studied the effects of FES on neuromuscular function of the rectus femoris muscle in healthy, untrained men and assessed changes in EMG RMS and EMG MPF pre-post FES intervention.¹¹⁶ EMG RMS throughout the isometric voluntary fatigue task presented a significant increase post FES training compared to pre training. This study also had a notable decrease in EMG MPF during the isometric voluntary fatigue task pre to post FES intervention. The study then concluded that these changes were signs of reduced time to neuromuscular fatigue.

Although these findings were significant, the study included a younger population as well as a strictly healthy, male subject population that could have contributed to the decreased variation in the EMG MPF values as well the marked increase in EMG RMS pre to post stimulation intervention. This study also used a higher stimulation frequency lending to the possibility of larger and more defined increases in EMG parameters.¹¹⁶

A study by Reenen and colleagues¹¹⁷, as mentioned above, found no changes in peak rectified EMG and EMG MPF pre to post voluntary resistance training regimen to signify muscle fatigue indicated after reaching a target localized musculoskeletal discomfort score after performance of simulated work tasks assessing the shoulder muscles. These findings were inconsistent with the present study as we found small effect sizes for RMS EMG and medium effect sizes for MPF EMG indicating improvements in muscle activation during a submaximal isometric fatigue task as a result of 4 weeks of NMES.

Similar findings were also found in a study assessing central and peripheral contributions to fatigue in healthy, adult males pre to post 4-week and 8-week NMES intervention with NMES stimulation protocols including 4, 18-minute training sessions per week assessed at the 4-week and 8-week mark with a stimulation frequency of 75 Hz. The fatigue task consisted of maintaining a continuous submaximal isometric contraction of 20% MVC until failure to maintain the target for 3 seconds with a MVC completed pre and immediately post-fatigue task.⁹¹ They ultimately found significant increase in EMG RMS from beginning to end of the voluntary isometric fatigue task as measured during the MVC immediately preceding and following the fatigue task. They also noted a

significant rate of increase in EMG RMS throughout the fatiguing task but found no significant changes pre to post NMES intervention at both 4 and 8 weeks.⁹¹

The present study found less change in electromyographic measures of the vastus medialis compared to those observed in the vastus lateralis. It is possible that the degree of knee flexion affects the degree to which the vastus medialis is activated in relation to the vastus lateralis muscle as seen by Rosa and colleagues¹¹⁸ assessing the effects of low (30°) versus high (100°) degrees of knee flexion on muscle activation of the vastus lateralis and vastus medialis muscles during isometric and stimulated contractions for knee extension in physically active men. They ultimately found that lower degree angles of knee flexion led to lower activation levels of the vastus medialis when compared the vastus lateralis muscles in support of the present study's difference in findings in muscle activation of the vastus lateralis and vastus medialis muscles as the degree of knee flexion 60° of knee flexion of participants was closer to a low degrees of flexion than to high degrees of knee flexion.¹¹⁸ Gondin and colleagues¹¹⁹ found similar findings after assessing the effects of an 8-week NMES intervention on neural drive and muscle architecture with stimulation administered at a 75 Hz stimulation frequency for 4, 18-minute sessions per week finding increased amounts of RMS EMG in the vastus lateralis muscle as compared to the vastus medialis muscle. They also found a significant increase in angle of pennation of the vastus lateralis muscle as they mentioned may have been one of the contributing factors to the increased levels of muscular activation found within the vastus lateralis when compared the to the vastus medialis muscle as a result of an NMES intervention.¹¹⁹

Six Minute Walk Test (6MWT)

The present study data show that distance recorded during the 6MWT, although not statistically significant, did improve pre to post NMES intervention with a small effect size showing a small practical meaningful improvement, and, therefore, does not improve endurance as measured by the 6MWT. These results are consistent with multiple studies showing increases in distance covered during the 6MWT. Kucio and colleagues⁴⁸ presented significant increases in 6MWT distance pre to post NMES intervention. However, the NMES protocols used involved an increase in frequency of 6 times a week NMES trainings as compared to 3 times a week in the present study possibly leading to their statistically significant improvements in distance covered during the 6MWT.⁴⁸

Vivodtsev and colleagues⁴⁹ found similar findings to our study in six of their patients after applying NMES.⁴⁹ Furthermore, similar findings were observed in Dal Corso and colleagues'¹¹⁷ study presenting evidence of no significant changes in 6MWT distance pre to post NMES intervention. The potential attributable factor resulting in this outcome in both the references study and the present study is the initial training level of the participants being at an already sufficient state, which could contribute to minimal amounts of potential improvement in the 6MWT distance.¹²⁰ They found similar findings to the present study in that they presented to changes in 6MWT pre-training to post-NMES training intervention. However, it is likely that their patient population could have had changes in muscle strength and central and peripheral aspects of muscular fatigue due to chemotherapy that would lead to their findings. However, it possible that their intervention protocol could produce statistically significant findings as compared to the present study as it was longer in length and training frequency per week.¹⁰⁹

This data in the present study were consistent with the results found in other studies where they found increases in 6MWT distance pre to post NMES intervention. However, these studies found statistically significant improvements but included subject populations with greater limitations at baseline that could contribute to the amount of improvement in the distance recorded such as those with ventricular systolic dysfunction¹²⁰, stable chronic heart failure⁶⁴, COPD^{48,121}, or healthy sedentary adults.¹²³

Limitations of the Study

We acknowledge that there are several limitations to this study. Limitations of the present study included the small sample size. The limited restrictions to physical activity performed by the subjects, other than participation in resistance training, could also be a limitation. This could mean that participants came into the study with already elevated muscle function possibly not allowing as much change in skeletal muscle improvements. However, since NMES is consistent with the affects seen as a result of resistance training, it is possible that other forms of physical activity would not have much influence on the assessed outcome measures such as strength. The fatigue task chosen could have also been a limiting factor as perceived effort plays a large role in the length of time to the end of the fatigue task. It is possible that another method of muscular fatigue could be utilized to better find true skeletal muscle fatigue of the quadriceps muscle such as a maximal voluntary contraction fatigue task or increasing the absolute torque held throughout the fatiguing task. Due to this study being a part of a larger research project, muscle biopsies also occurred two days prior to post-testing that could have affected the post-test results due to muscle soreness of the biopsied leg or due to possible guarding of the participant for fear of pain during the muscular strength and endurance testing.

Conclusion

In conclusion, a 4-week NMES intervention resulted in reductions in skeletal muscle fatigue in terms of EMG parameters, clinically meaningful improvements in muscle strength as seen with MVC, small practical improvement in 6MWT distance, no changes in muscular endurance time, and the potential contribution of neuromuscular activation to result in increases in muscular strength with trends of improved muscle activation patterns during non-fatiguing submaximal contractions and MVC in the healthy, older adult population. Further research must be completed to determine the optimal NMES intervention protocol to produce significant improvements in skeletal muscle fatigue measures within the older adult population. Ultimately, these findings show that a 4-week NMES training program can reduce skeletal muscle fatigue and improve strength of older adults and may aid in improving functional independence and improve quality of life.

Implications for Future Research

Future research implications could include interventions with an increase in number of weekly NMES sessions as well as increase the target stimulation intensity during each session to at least 20% MVC. This would increase the stimulation of the muscle weekly possibly allow for increased muscle strength and endurance ultimately increasing time to fatigue of the muscles. Another possible implication would be a change in the participation population to sedentary adults or a patient population such as those with diagnosed sarcopenia. Change in patient population would allow us to see if NMES could be useful in individuals that may be more likely to benefit from this modality. Longer intervention duration could allow for larger increases in muscular

endurance as the present study's intervention of 4 weeks may not be sufficient to produce significant improvements in muscular endurance parameters. Lastly, alternative assessments of muscular fatigue could be used, such as an isometric maximal voluntary intermittent or continuous contraction fatigue task, that can better control for perceived effort from participants. This would allow for a better opportunity to get muscular endurance measures as accurate as possible with the least involvement of possible extraneous variables affecting the accuracy the data such as perceived effort or environmental factors.

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3. SUMMARY AND RECOMMENDATIONS FOR FUTURE RESEARCH

Summary

The primary purpose of this study was to determine the effects of a 4-week NMES intervention on voluntary muscular fatigue of the quadriceps and changes in neuromuscular activation patterns during voluntary fatiguing muscle contractions in older adults. The secondary purpose was to determine changes in MVC (strength), and muscle activation during MVC, the degree of neuromuscular activation during submaximal unfatigued contractions and 6-min walk performance pre-post 4 weeks of NMES in older adults.

This study followed a pre-test post-test randomized controlled experimental design. Following inclusion and exclusion criteria screening, 17 men and women who were 60 and older (68.8 ± 1.8 years old) participated in the study and were randomly placed in one of two groups 1) NMES group or 2) Sham group who received a sham treatment.

The NMES intervention was completed for 3 training sessions a week for 4 weeks (12 total sessions). Each session included NMES applied for 40 minutes to each leg. The stimulation intensity was increased until the participant's torque output met the target torque of 15% of the MVC measured during the pre-testing. NMES was administered using a stimulation frequency of 60Hz, a pulse width of 200 μ s, and cycled on for 10 seconds and off for 15 seconds for the duration of the 40-minute treatment. The stimulation intensity was initially adjusted to meet the 15% target torque and then was adjusted every 5 minutes to meet the 15% target torque if the participant's torque output no longer met the target

Outcome measures assessed included MVC, EMG (RMS, MPF, and peak) during MVC, muscular endurance time, 6MWT distance, non-fatiguing isometric submaximal contraction EMG (RMS and MPF), and rate of change of EMG (RMS, MPF, and integrated EMG) during the submaximal isometric fatigue task. Outcome measures were assessed pre-training and post-training intervention (and MVC at 7 weeks). All outcome measures were analyzed using repeated measures analysis of variance (ANOVA). Effect size was also calculated using Cohen's *d*. Data are presented as a mean \pm SE with statistical significance set at $p < 0.05$.

Present study findings suggest that a 4-week NMES intervention has the potential to reduce skeletal muscle fatigue by improving quadriceps muscle activation in healthy older adults. MVC peak torque presented a clinically meaningful increase of 8.9% from pre to post NMES intervention showing clinically meaningful improvements in quadriceps muscle strength as a result of NMES. However, muscle activation in the quadriceps muscle during MVC presented improvements only in vastus lateralis EMG RMS and peak EMG both with large effect sizes. Additionally, EMG RMS during all non-fatiguing submaximal isometric contractions trended towards improvement as a result of NMES with small (30, 60, and 80% MVC) to medium effect sizes (20 and 40% MVC) respectively pre-post NMES intervention indicating that this particular intervention may improve voluntary muscle activation during submaximal isometric contraction intensities for training interventions. After 4 weeks of NMES training, 6MWT improved with a small effect size showing improvement of a small magnitude. Lastly, endurance time as measured by the fatigue task did not change as a result of NMES training. Rate of change of electromyographic measures trended towards an

increase only within RMS EMG and MPF EMG measures with small and medium effect sizes respectively as a result of NMES training indicating changes in muscle activation that may be beneficial for tasks requiring voluntary muscular endurance.

In conclusion, a 4-week NMES intervention can lead to improvements in skeletal muscle fatigue in healthy older adults with improved muscle activation patterns during non-fatiguing submaximal contractions and clinically meaningful improvements in muscle strength as seen with MVC. Further research must be completed with longer interventions to determine the NMES effects following additional weeks of treatment in older adults.

Recommendations for Future Research

Future research implications include an increase in NMES session frequency weekly as well as boost the target stimulation intensity during each session to at least 20% MVC. This will increase the stimulation of the muscle weekly possibly allowing for increased muscle strength and endurance ultimately increasing time to fatigue of the muscles.

Another possible implication would be a change in the participation population to sedentary adults or a patient population such as those with diagnosed sarcopenia. The current study focuses on healthy older adults, but they were also active which lessened the possibility for them to show large increases in the outcomes measured. Change in patient population would allow us to see if NMES could be useful in individuals that would be more likely to benefit from this modality.

Longer intervention duration could allow for larger increases in muscular endurance as the present study's intervention of 4 weeks may not be sufficient to produce

significant improvements in muscular endurance parameters. Lastly, alternative assessments of muscular fatigue could be used that can better control for perceived effort from participants. This would allow for a better opportunity to get muscular endurance measures as accurate as possible with less opportunity for confounding variables.

APPENDIX SECTION

APPENDIX A

Figures

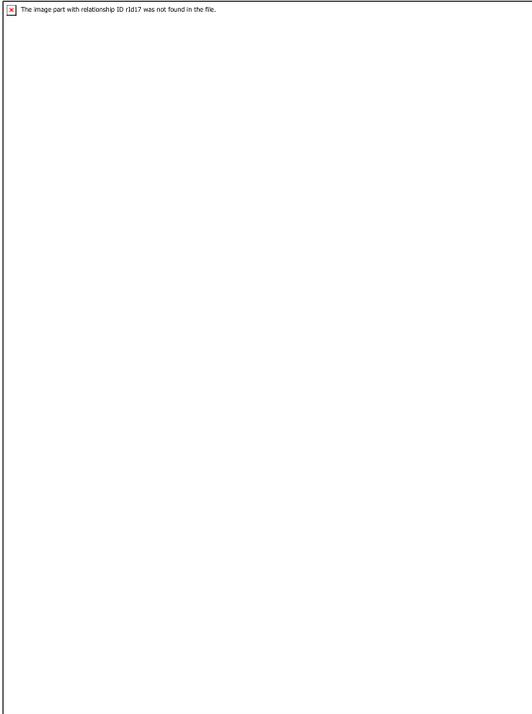


Figure 1. Subject Position for NMES Treatment and NMES electrode placement

(Permission was obtained for the use of this picture)

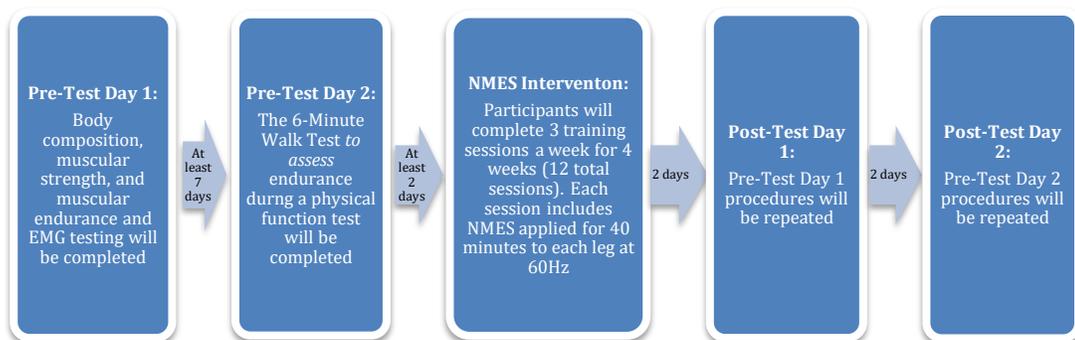


Figure 2. Study Timeline

Figure 3

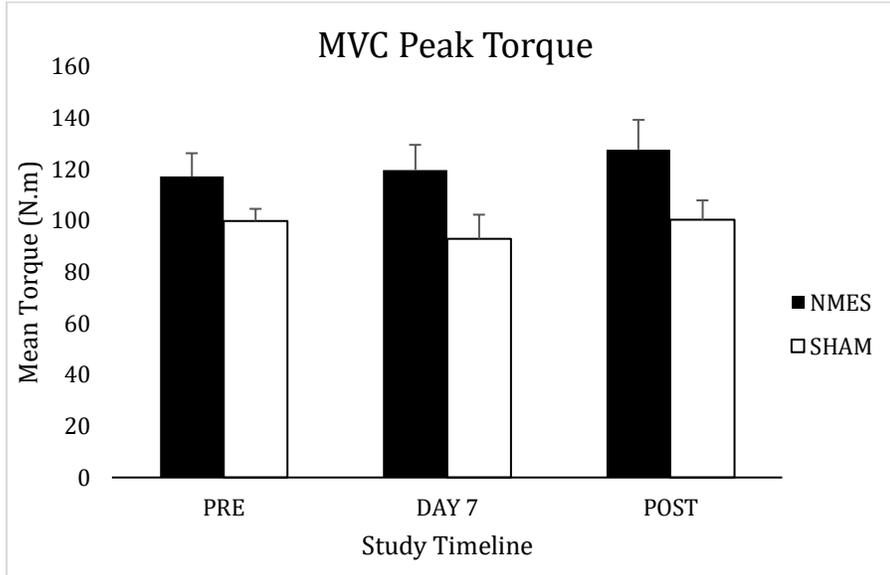


Figure 3. Maximal voluntary contraction (MVC) peak torque measured at pre-training, day 7, and post-training. No significant difference for training or between groups ($p > 0.05$). MVC increased 8.93% pre-training to post-training for the NMES group exceeding established the minimal clinically important difference score (MCID) of 4%. Data were analyzed and displayed as the average of right and left legs. Data are presented as mean \pm SE.

Figure 4

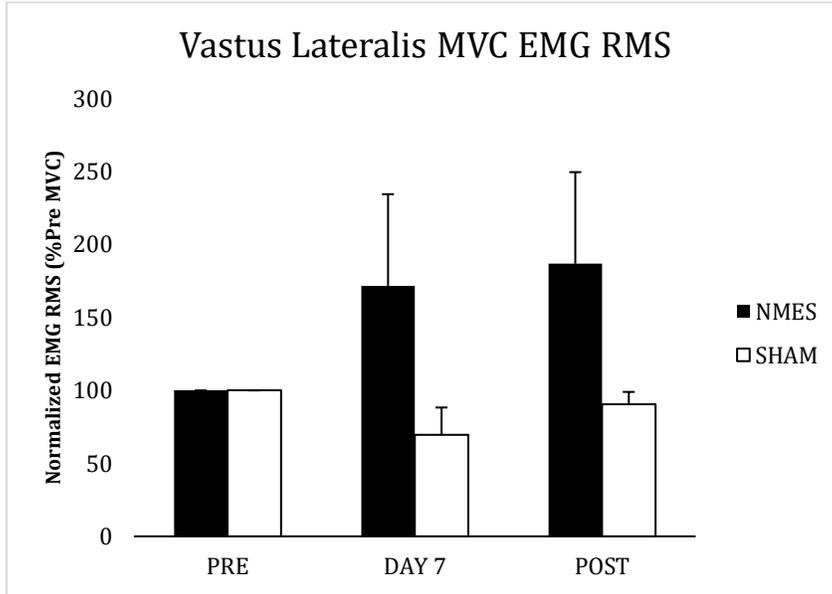


Figure 4a. Maximal voluntary contraction (MVC) electromyography (EMG) root mean square (RMS) for the vastus lateralis muscle pre-training, day 7, and post-training. No significant changes for training or between groups ($p > 0.05$). RMS EMG did increase with an 86.83% increase in the VL pre-post 12 weeks of NMES in the NMES group with a large effect size (Cohen's $d = 0.83$). Data are analyzed and displayed as an average of right and left legs. Data are normalized to pre-training MVC EMG RMS and are presented as mean \pm SE.

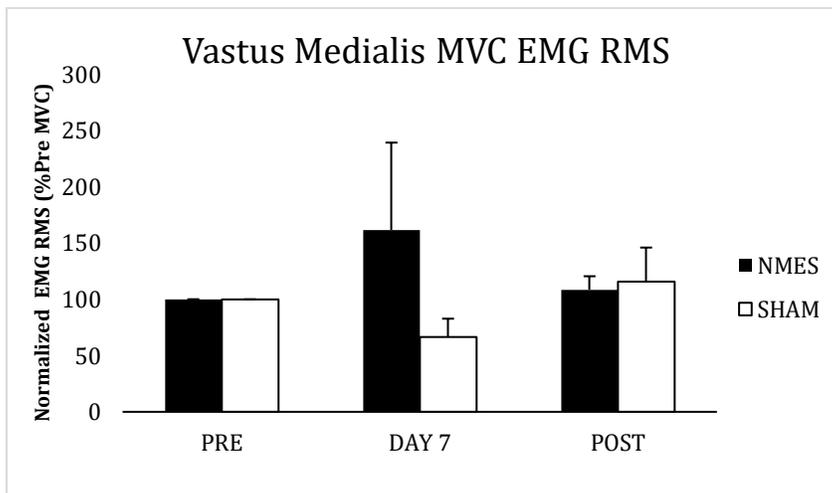


Figure 4b. Maximal voluntary contraction (MVC) electromyography (EMG) root mean square (RMS) for the vastus medialis muscle pre-training, day 7, and post-training. No significant changes for training or between groups ($p > 0.05$). Data are analyzed and displayed as an average of right and left legs. Data are normalized to pre-training MVC EMG RMS and are presented as mean \pm SE.

Figure 5

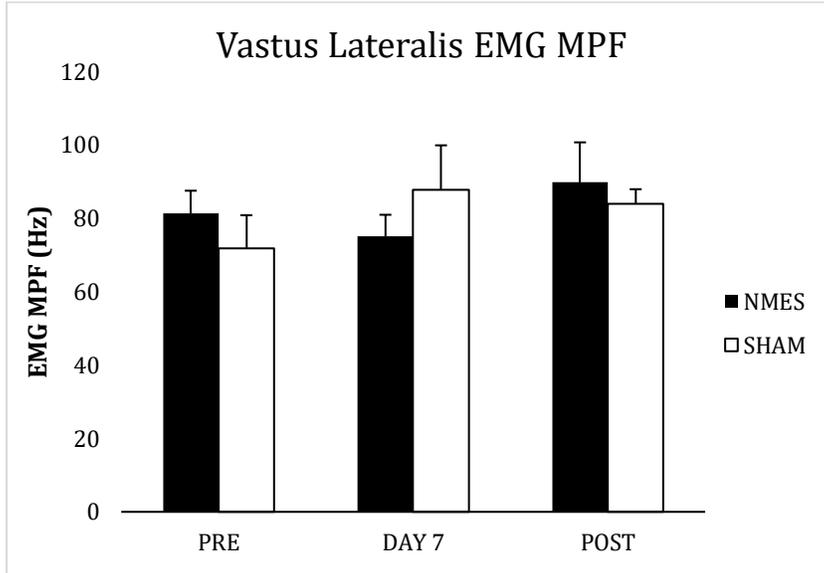


Figure 5a. Maximal voluntary contraction (MVC) median power frequency (MPF) electromyography (EMG) for the vastus lateralis muscle pre-training, day 7, and post-training. No significant changes for training or between groups ($p > 0.05$). Data were analyzed and displayed as an average of right and left legs. Data are presented as mean \pm SE.

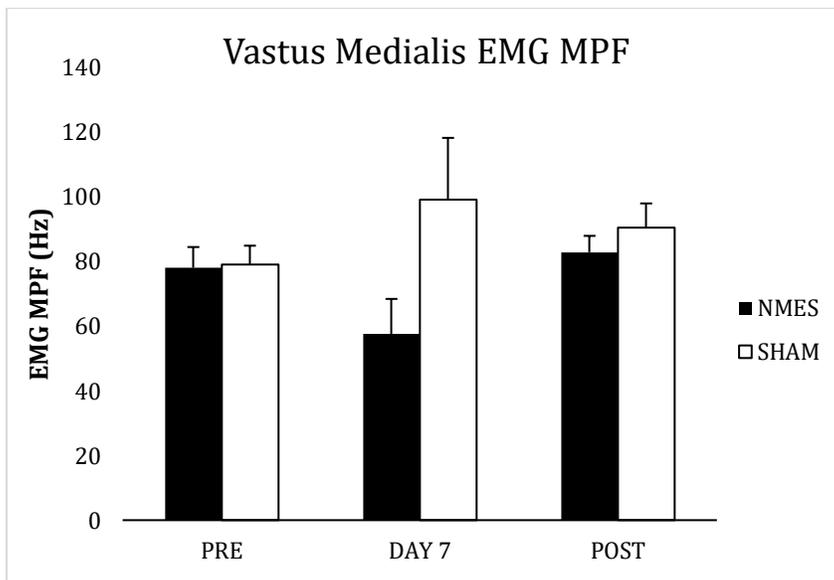


Figure 5b. Maximal voluntary contraction (MVC) median power frequency (MPF) electromyography (EMG) for the vastus medialis muscle pre-training, day 7, and post-training. No significant changes for training or between groups ($p > 0.05$). Data were analyzed and displayed as an average of right and left legs. Data are presented as mean \pm SE.

Figure 6

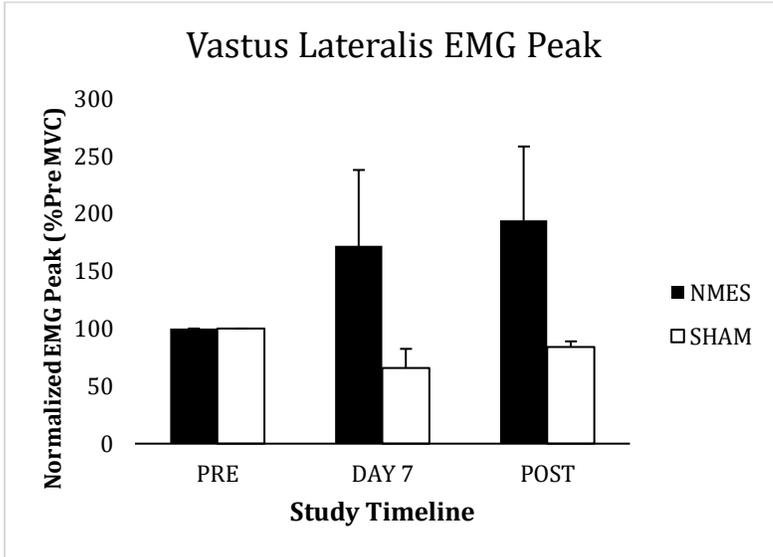


Figure 6a. Maximal voluntary contraction (MVC) electromyography (EMG) peak for the vastus lateralis muscle pre-training, day 7, and post-training. No significant changes for training or between groups ($p > 0.05$). However, there was a large effect size for pre-post change in the NMES group (Cohen's $d = 0.88$). Data are normalized to pre-training MVC EMG peak and are presented as mean \pm SE.

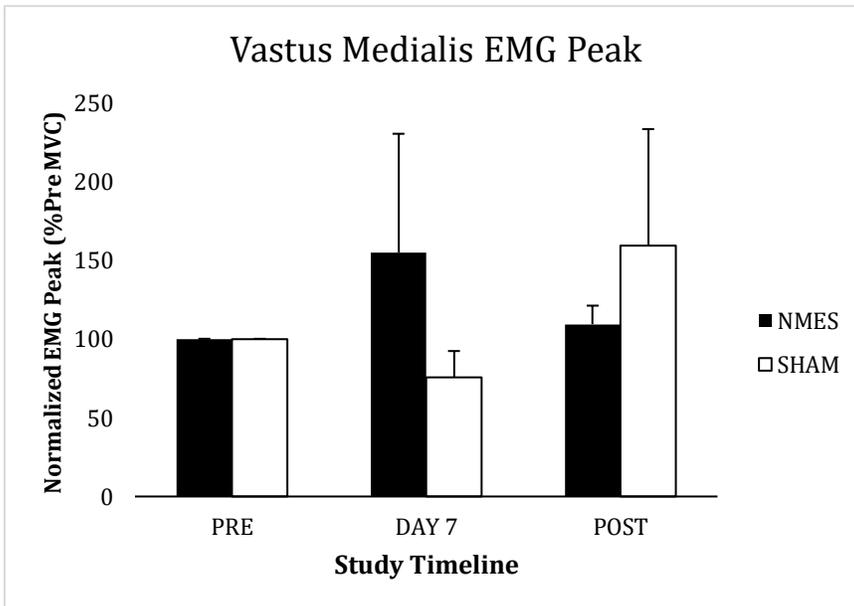


Figure 6b. Maximal voluntary contraction (MVC) electromyography (EMG) peak for the vastus medialis muscle pre-training, day 7, and post-training. No significant changes for training or between groups ($p > 0.05$). Data are analyzed and displayed as an average of right and left legs. Data are normalized to pre-training MVC EMG peak and are presented as mean \pm SE.

Figure 7

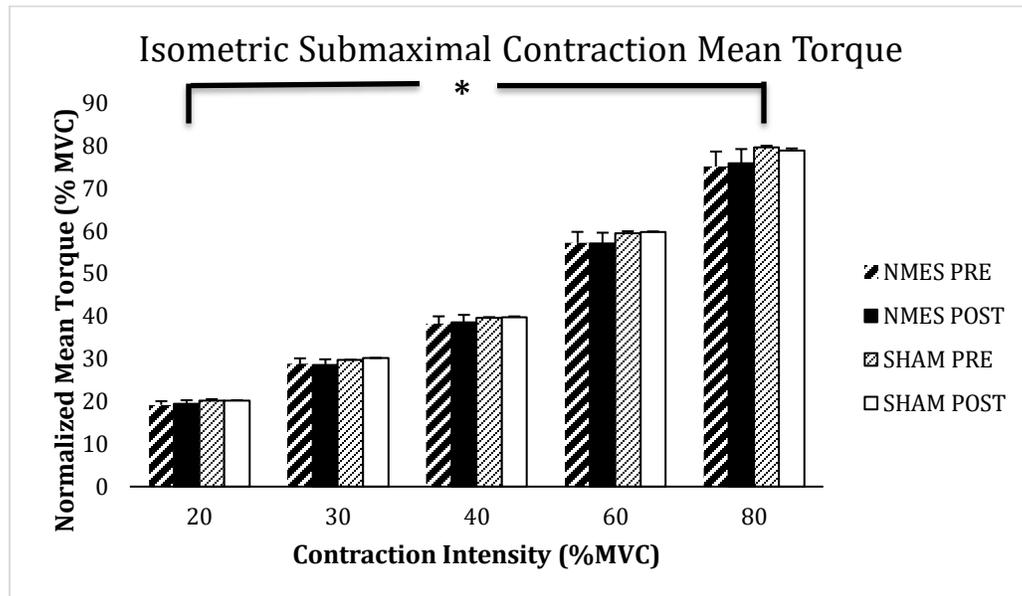


Figure 7. Isometric submaximal contraction mean torque at respective contraction intensities (20, 30, 40, 60, 80% MVC). No significant changes for training or between groups ($p > 0.05$). There was a significant increase in mean torque as the submaximal contraction intensity increased ($p < 0.0001$). Data are analyzed and displayed as an average of right and left legs. Data are normalized to pre training MVC peak torque and are presented as mean \pm SE. * Significant difference ($p > 0.05$) between contraction intensities.

Figure 8

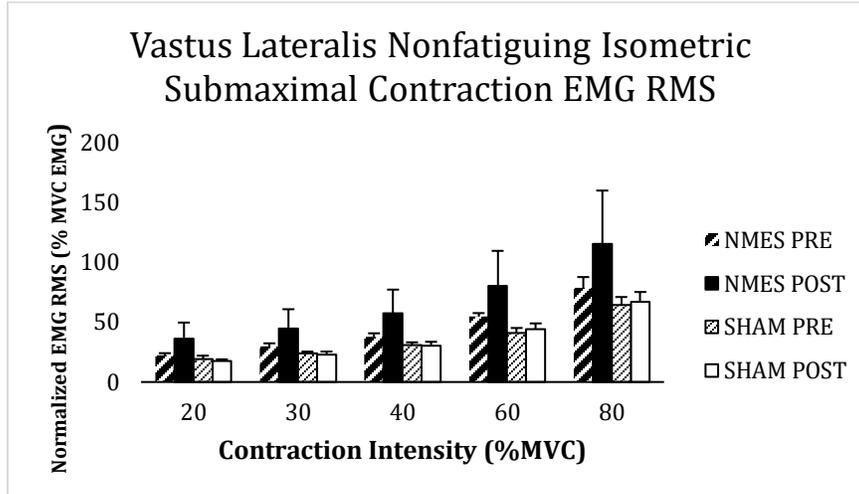


Figure 8a. Submaximal contraction electromyography (EMG) root mean square (RMS) for the vastus lateralis muscle at increasing contraction intensities (20, 30, 40, 60, 80% MVC). No significant changes for training or between groups ($p > 0.05$). Data are normalized to EMG RMS during MVC and are presented as mean \pm SE. A follow-up RM ANOVA was performed for each contraction intensity individually to determine training effects. Each respective intensity training main effect was not significant ($p > 0.05$). There were no differences between groups for each respective intensity ($p > 0.05$), and training x group interaction presenting no change for each contraction intensity ($p > 0.05$). Increases in RMS EMG are indicated as small to medium effect sizes pre-post NMES training for the NMES group (medium effect (20% and 40% MVC), small effect (30%, 60%, and 80% MVC)).

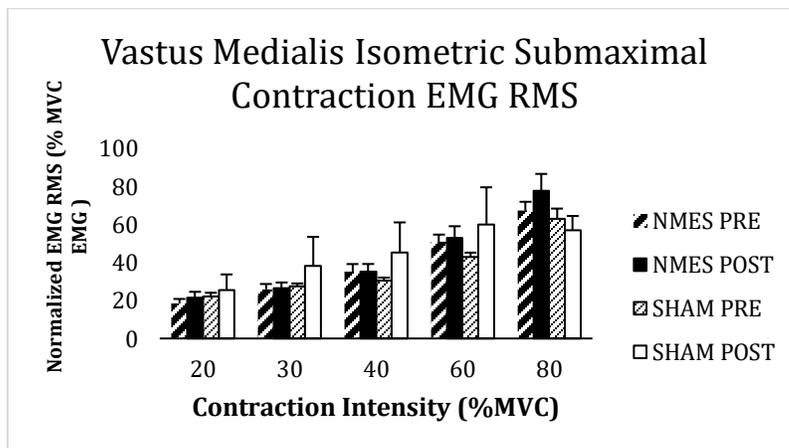


Figure 8b. Isometric submaximal contraction electromyography (EMG) root mean square (RMS) for the vastus medialis muscle at respective contraction intensities of % maximal voluntary contraction (MVC) (20, 30, 40, 60, 80). No significant changes for training or between groups ($p > 0.05$). Data are analyzed and displayed as an average of right and left legs. Data are normalized to EMG RMS during MVC and are presented as mean \pm SE.

Figure 9

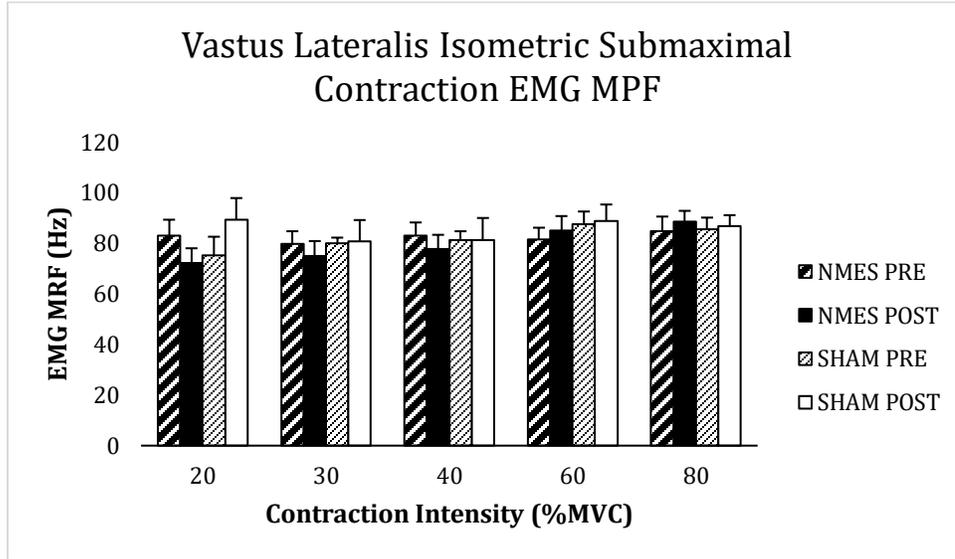


Figure 9a. Isometric submaximal contraction electromyography (EMG) median power frequency (MPF) for the vastus lateralis muscle at respective contraction intensities of % maximal voluntary contraction (MVC) (20, 30, 40, 60, 80). No significant changes for training or between groups ($p > 0.05$). Data are presented as an average of right and left legs and displayed as a mean \pm SE.

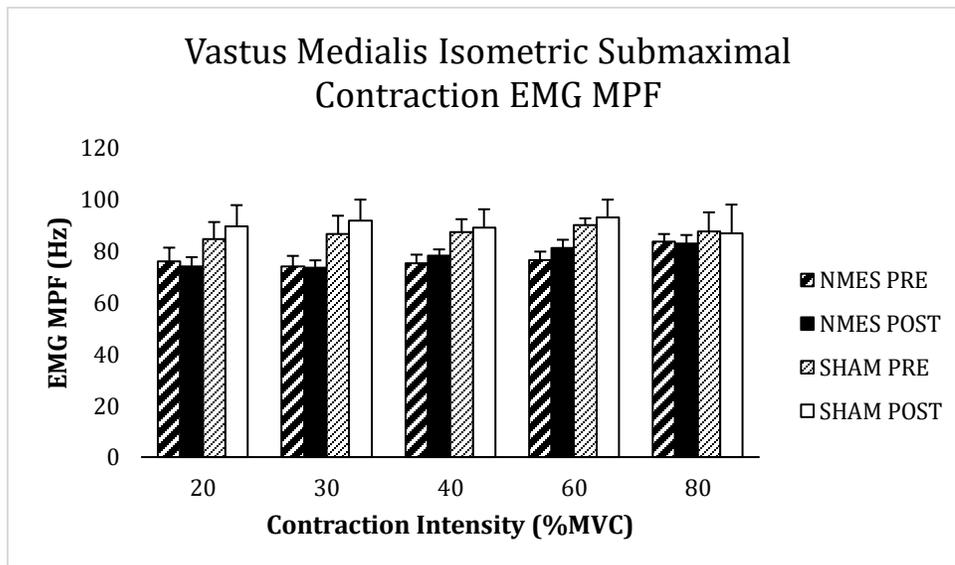


Figure 9b. Isometric submaximal contraction electromyography (EMG) median power frequency (MPF) for the vastus medialis muscle at respective contraction intensities of % maximal voluntary contraction (MVC) (20, 30, 40, 60, 80). No significant changes for training or between groups ($p > 0.05$). Data are presented as an average of right and left legs and displayed as a mean \pm SE.

Figure 10

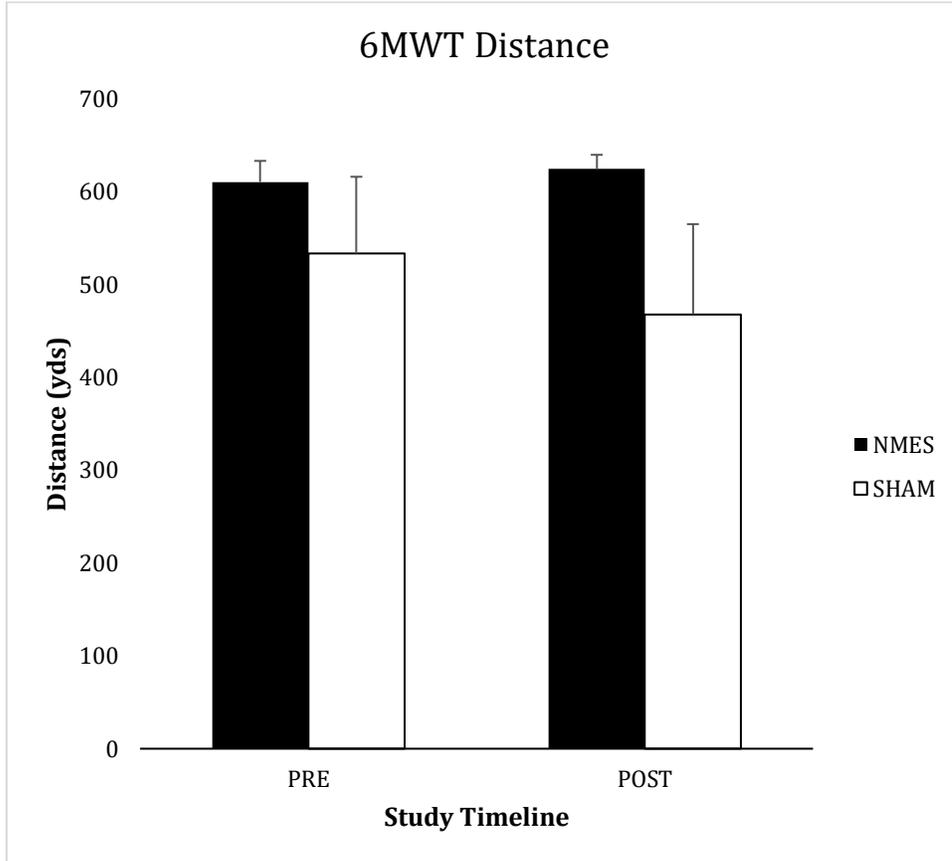


Figure 10. Six-Minute Walk Test (6MWT) distance in yards. No significant changes pre- to post-training with a significant difference between groups ($p < 0.05$). However, there was a small effect size for pre-post change in the NMES group (Cohen's $d = 0.22$). Data are presented as mean \pm SE.

Figure 11

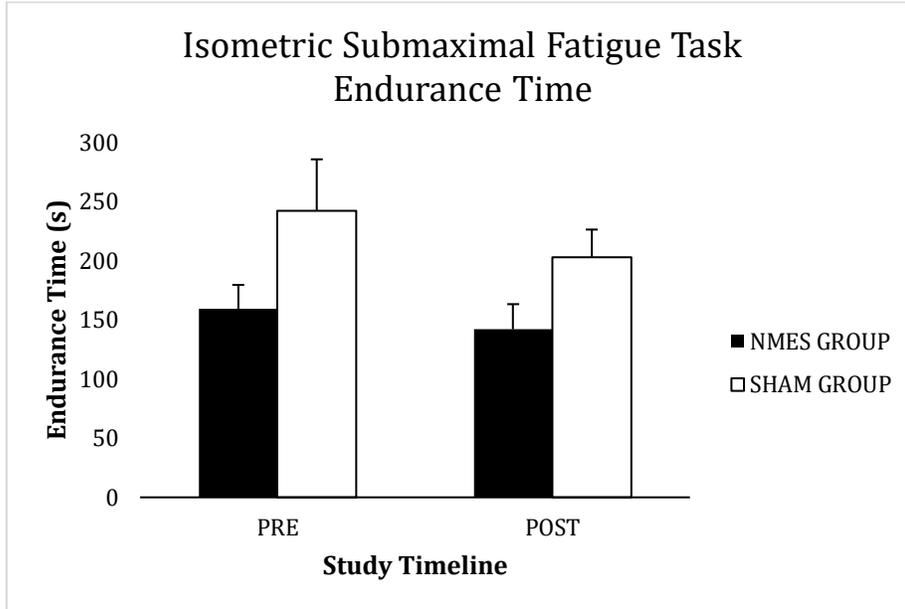


Figure 11. Isometric submaximal fatigue task endurance time in seconds. No significant changes pre- to post-training and no difference between groups ($p > 0.05$). Data are presented as mean \pm SE.

Figure 12

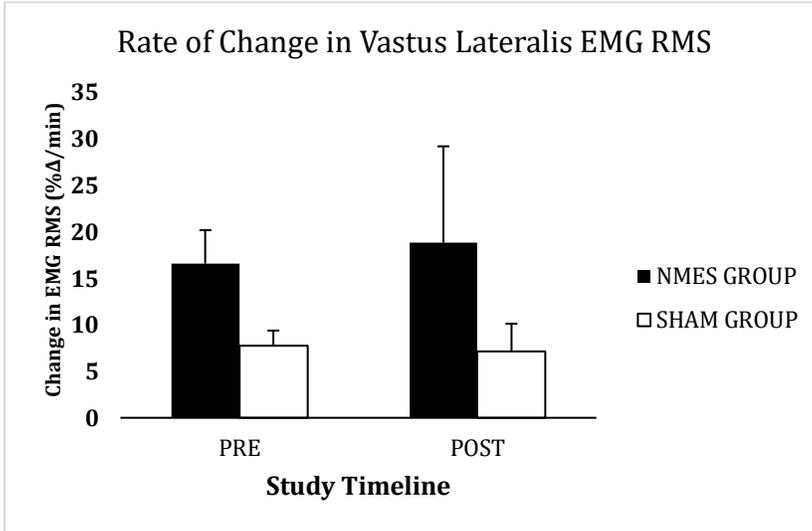


Figure 12a. Changes in electromyography (EMG) root mean square (RMS) for the vastus lateralis muscle pre-training and post-training. No significant changes for training or between groups ($p > 0.05$). Data are analyzed and displayed as an average of right and left legs. Data are normalized to pre-training maximal voluntary contraction (MVC) EMG RMS. Data are presented as mean \pm SE.

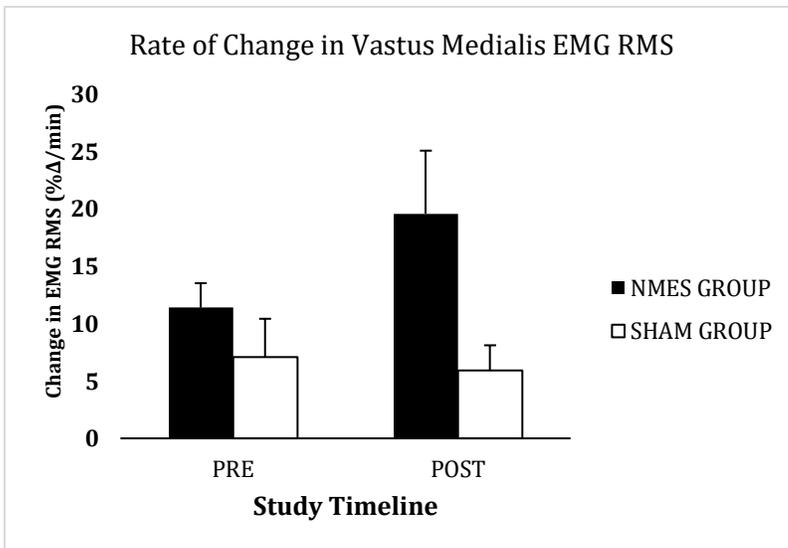


Figure 12b. Changes in electromyography (EMG) root mean square (RMS) for the vastus medialis muscle pre-training and post-training. No significant changes for training or between groups ($p > 0.05$). Data are analyzed and displayed as an average of right and left legs. Data are normalized to pre-training maximal voluntary contraction (MVC) EMG RMS and are presented as mean percent change of initial contraction value per minute \pm SE.

Figure 13

Figure 13a.

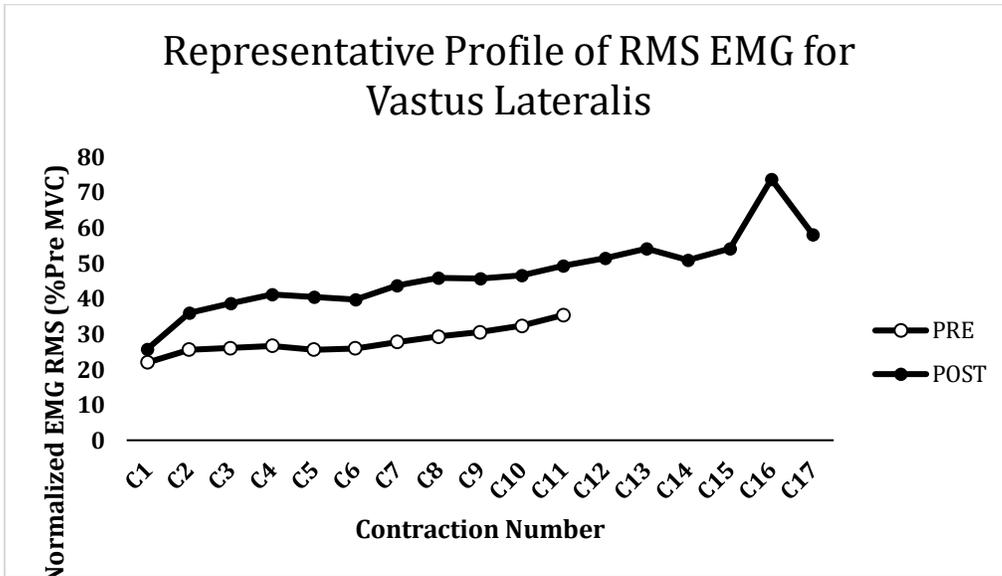


Figure 13b.

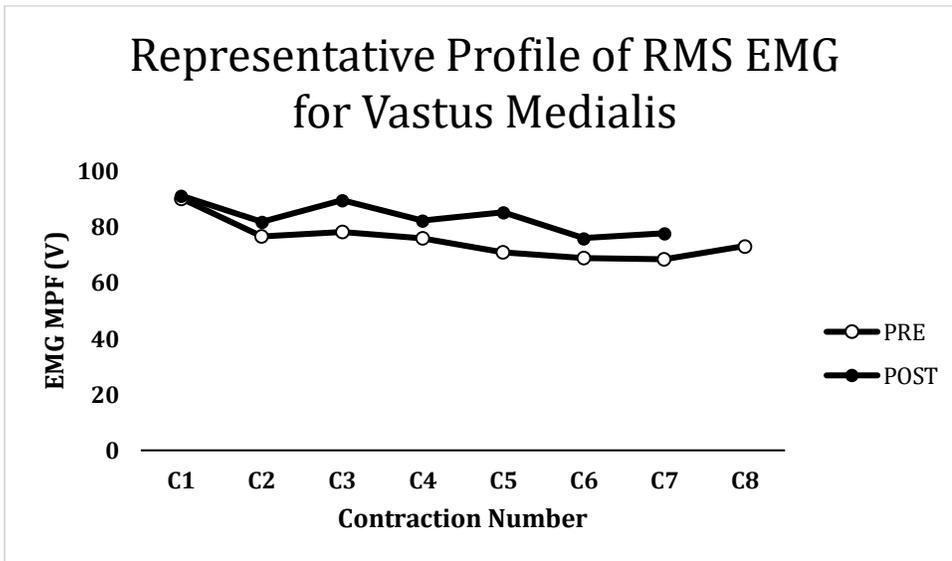


Figure 13. Representative vastus lateralis electromyography (EMG) root mean square (RMS) profile (a) and median power frequency (b) for one subject during the fatigue task. Data are presented as means during each submaximal isometric contraction throughout the submaximal isometric fatigue task.

Figure 14

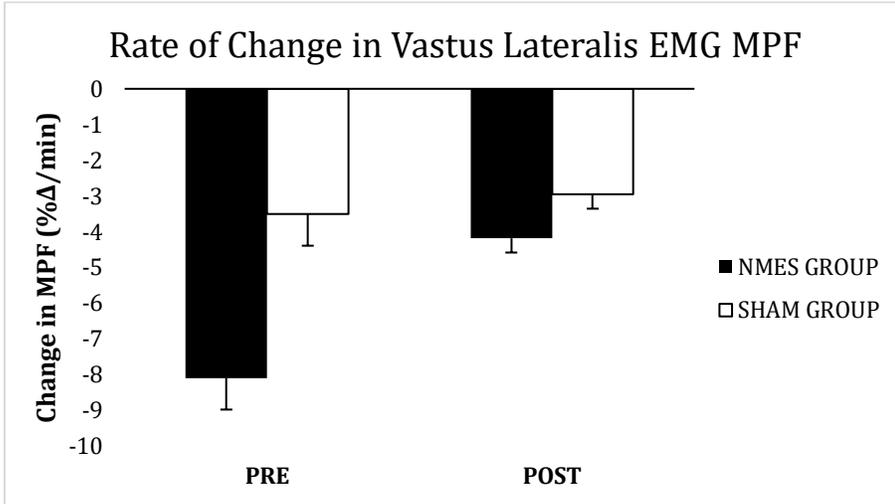


Figure 14a. Changes in electromyography (EMG) median power frequency (MPF) for the vastus lateralis muscle pre-training and post-training. No significant changes for training or between groups ($p > 0.05$). There was a medium effect size for the rate of change in vastus lateralis MPF EMG pre-post NMES training for the NMES group with lower rate of change post-training (Cohen's $d = 0.53$). Data are analyzed and displayed as an average of right and left legs. Data are presented as mean percent change of initial contraction value per minute \pm SE.

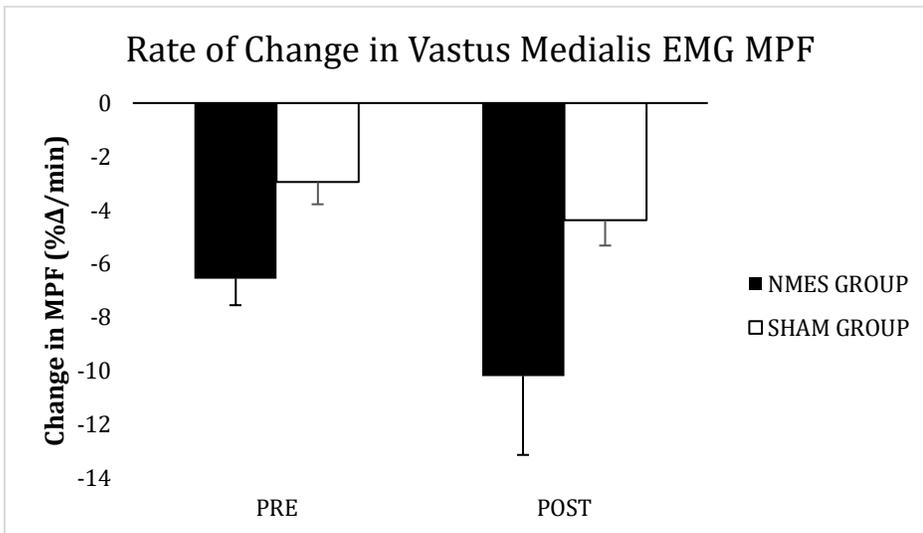


Figure 14b. Changes in electromyography (EMG) median power frequency (MPF) for the vastus medialis muscle pre-training and post-training. No significant changes for training or between groups ($p > 0.05$). However, there was a medium effect size for pre-post change in the NMES group (Cohen's $d = 0.53$). Data are analyzed and displayed as an average of right and left legs. Data are presented as mean percent change of initial contraction value per minute \pm SE.

Figure 15

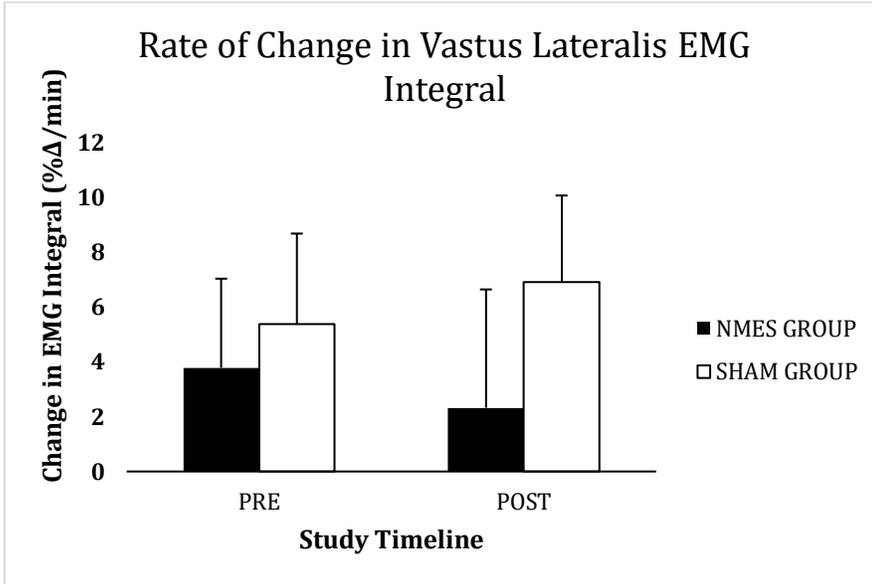


Figure 15a. Changes in electromyography (EMG) integral for the vastus lateralis muscle pre-training and post-training. No significant changes for training or between groups ($p > 0.05$). Data are analyzed and displayed as an average of right and left legs. Data are normalized to pre-training maximal voluntary contraction (MVC) EMG integral and are presented as mean percent change of initial contraction value per minute \pm SE.

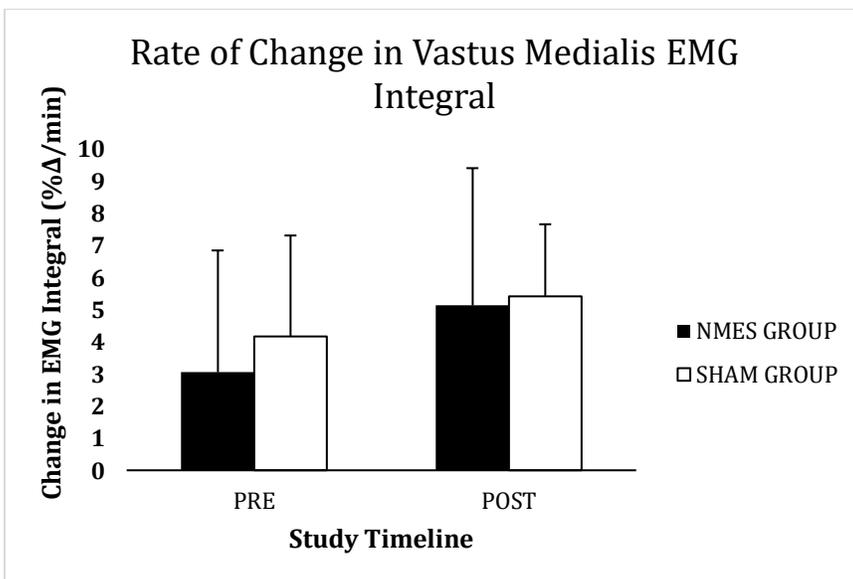


Figure 15b. Changes in electromyography (EMG) integral for the vastus medialis muscle pre-training and post-training. No significant changes for training or between groups ($p > 0.05$). Data are analyzed and displayed as an average of right and left legs. Data are normalized to pre-training maximal voluntary contraction (MVC) EMG integral and are presented as mean percent change of initial contraction value per minute \pm SE.

Table 1. Subject characteristics for NMES and SHAM group presented as a mean \pm SE.

Characteristic	NMES group	SHAM group	OVERALL
Height (in)	65.24 \pm 0.59	64.69 \pm 0.97	65.08 \pm 0.49
Weight (lbs)	158.62 \pm 7.87	167.04 \pm 17.64	161.09 \pm 7.34
BMI (kg/m ²)	26.06 \pm 1.08	28.06 \pm 2.88	26.65 \pm 1.11
% Body Fat	34.71 \pm 1.55	41.26 \pm 2.25	36.64 \pm 1.45

Table 2. Cohen’s *d* effect size for each outcome measure for respective functional assessments. Direction of change is presented and change in means pre-post NMES intervention are presented as a mean \pm SD.

Variable	Pre- and Post-Test Scores	Cohen’s <i>d</i>	Direction of Change
MVC			
Peak Torque	Pre: 117.09 \pm 29.97; Post: 127.55 \pm 38.30	Small effect, 0.31	Increase
RMS EMG			
VL	Pre: 100 \pm 0.00 Post: 186.83 \pm 208.31	Large effect, 0.83	Increase
VM	Pre: 100 \pm 0.00 Post: 106.36 \pm 43.59	Small effect, 0.29	Increase
MPF EMG			
VL	Pre: 82.14 \pm 21.56 Post: 89.07 \pm 39.65	Small effect, 0.23	Increase
VM	Pre: 5.77 \pm 18.69 Post: 85.65 \pm 16.98	Medium effect, 0.55	Increase
EMG Peak			
VL	Pre: 100 \pm 0.00 Post: 193.93 \pm 213.79	Large effect, 0.88	Increase
VM	Pre: 100 \pm 0.00 Post: 107.18 \pm 42.41	Small effect, 0.34	Increase
Non-Fatiguing Isometric Submaximal Contractions			
RMS EMG			
VL			
20%	Pre: 22.13 \pm 6.31 Post: 36.23 \pm 44.15	Medium effect, 0.56	Increase
30%	Pre: 29.55 \pm 8.99 Post: 44.72 \pm 52.93	Small effect, 0.49	Increase
40%	Pre: 37.49 \pm 10.36 Post: 57.16 \pm 65.89	Medium effect, 0.52	Increase
60%	Pre: 54.47 \pm 9.91 Post: 79.98 \pm 97.45	Small effect, 0.48	Increase
80%	Pre: 78.29 \pm 30.57 Post: 114.96 \pm 148.19	Small effect, 0.41	Increase
VM			
20%	Pre: 18.33 \pm 8.17 Post: 21.45 \pm 10.31	Small effect, 0.34	Increase
30%	Pre: 25.87 \pm 9.28 Post: 26.46 \pm 9.96	No effect, 0.06	No change

Table 2. Continued

40%	Pre: 35.15 ± 13.27 Post: 35.08 ± 13.61	No effect, -0.01	No change
60%	Pre: 50.89 ± 12.39 Post: 52.84 ± 20.56	No effect, 0.12	No change
80%	Pre: 67.22 ± 15.53 Post: 77.59 ± 29.77	Small effect, 0.46	Increase
MPF EMG			
VL			
20%	Pre: 82.93 ± 21.24 Post: 72.23 ± 19.29	Medium effect, -0.53	Decrease
30%	Pre: 79.74 ± 16.72 Post: 74.95 ± 19.68	Small effect, -0.26	Decrease
40%	Pre: 83.03 ± 17.33 Post: 77.71 ± 18.75	Small effect, -0.29	Decrease
60%	Pre: 81.64 ± 15.02 Post: 84.94 ± 19.37	No effect, 0.19	No change
80%	Pre: 84.82 ± 19.10 Post: 88.51 ± 14.37	Small effect, 0.22	Increase
VM			
20%	Pre: 75.83 ± 17.89 Post: 73.89 ± 12.03	No effect, -0.13	Decrease
30%	Pre: 73.95 ± 13.56 Post: 73.32 ± 9.89	No effect, -0.05	No change
40%	Pre: 75.28 ± 10.69 Post: 78.09 ± 8.12	Small effect, 0.29	Increase
60%	Pre: 76.32 ± 11.19 Post: 81.09 ± 10.61	Small effect, 0.44	Increase
80%	Pre: 83.58 ± 9.71 Post: 82.88 ± 10.79	No effect, -0.07	No change
Isometric Submaximal Fatigue Task			
RMS EMG Rate of Change			
VL	Pre: 16.58 ± 12.47 Post: 18.84 ± 35.90	No effect, 0.09	No change
VM	Pre: 11.39 ± 7.37 Post: 19.57 ± 19.03	Medium effect, 0.62	Increase
MPF EMG Rate of Change			
VL	Pre: -9.57 ± 7.83 Post: 17.08 ± 93.27	Medium effect, 0.53	Increase
VM	Pre: -6.57 ± 3.46 Post: -10.21 ± 10.24	Medium effect, -0.53	Decrease

Table 2. Continued

EMG Integral Rate of Change			
VL	Pre: 3.78 ± 11.25 Post: 2.32 ± 14.94	No effect, -0.11	No change
VM	Pre: 3.05 ± 13.13 Post: 5.13 ± 14.80	No effect, 0.15	No change
Endurance Time	Pre: 159.31 ± 69.75 Post: 141.95 ± 73.49	Small effect, -0.24	Decrease
6MWT Distance	Pre: 610.25 ± 78.69 Post: 624.51 ± 51.94	Small effect, 0.22	Increase

Table 3. Number of participants in the NMES group that improved after 4 weeks of NMES. Data presented as mean percent improvement \pm SE.

Variable	Number of Improved Participants	Percent Improvement
MVC	9	14.4 increase
MVC (Met MCID of 4%) ¹⁰⁵	8	16.4 increase
Endurance Time	4	24.4 increase
6MWT Distance	8	7.8 increase
6MWT (Met MCID of 20m) ¹²¹	4	15.4% increase

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