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Fatiguing effects of electrical stimulation superimposed onto voluntary contraction

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FATIGUING EFFECTS OF ELECTRICAL STIMULATION SUPERIMPOSED ONTO VOLUNTARY CONTRACTION

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ABSTRACT

BACKGROUND: The current understanding of fatigue is specific to voluntary exercise (VOL) or neuromuscular electrical stimulation (NMES) separately. Currently, there is no data on the understanding of fatigue in VOL+NMES specific to motor control strategies.

PURPOSE: The main purpose of this research project was to compare the fatigability of two exercise conditions (VOL and VOL+NMES) in the elbow flexors and knee extensors.

METHODS: Thirty-six participants aged 18-35 completed this four-visit randomized, controlled study. Visit one included familiarization to procedures. Visits 2-4 included control, VOL, and VOL+NMES fatiguing exercise with the same pre- and post-measurements. Pre-measures included two isometric maximal voluntary contractions (MVC) and two trapezoids; post-measures were performed in reverse order with only one MVC. The VOL+NMES and VOL visits were identical except, NMES (50-Hertz; at maximal tolerable intensity) was superimposed onto the VOL during the VOL+NMES. The exercise consisted of five sets of 10-second-long isometric muscle contractions at 50% of MVC with two trapezoids immediately following each set. The post-measures were performed at the end of the final set. The control visit involved resting for 5-minutes between the pre- and post-measurements. A minimum of 24-hours was required between non-exercise visits and 48-hours between exercise visits. The elbow flexors (EF) were always completed first, followed by the knee extensors (KE). Several two-way repeated measures analyses of variance (ANOVA) were completed to comparing pre and post maximal voluntary force (MVF, Newtons [N]), and normalized (% pre-MVC) EMG amplitude (EMGa), and EMG median frequency (MDF) for the biceps brachii (BB), vastus lateralis (VL), and vastus medialis (VM). Several two-way repeated measures ANOVAs were completed to compare the pre and post linear slope coefficients (pulses per second [pps]/%MVC) and y-intercepts (pps) of the motor unit (MU) mean firing rate (MFR) vs. recruitment threshold (RT; %MVC) and MU RT vs. derecruitment threshold (DT; %MVC) relationships for the BB, VL, and VM. All statistical analyses were performed with an α set to 0.05.

RESULTS: A significant interaction was observed ($p < .001$) for EF MVF. The change in EF MVF was greater in VOL (-42.19 ± 53.76) and VOL+NMES (-45.81 ± 59.18) compared to the control (-3.78 ± 27.01, all $p < .001$). A significant interaction was observed ($p < .001$) for KE MVF. The change in KE MVF was greater in VOL (-80.48 ± 65.29) and VOL+NMES (-93.07 ± 78.68) compared to control (-12.52 ± 64.43, all $p < .001$). A significant interaction was observed ($p < .001$) for VM EMGa. The change in VM EMGa was greater in VOL+NMES (20.75 ± 34.66%) compared to control (-2.40 ± 25.22%, $p = .002$). A significant interaction was observed ($p < .001$) for VM EMG MDF. The change in VM EMG MDF was greater in VOL+NMES (10.62 ± 14.43%) compared to control (1.66 ± 19.14%) $p = .009$). The slope of the MFR vs. RT relationship was significantly more negative post- (-.704 ± .30), compared to pre-exercise (-.601 ± .28; *p* = .007) in the BB. The slope was significantly more negative in post- (-.777 ± .68), compared to pre-exercise (-.404 ± .26; *p* = .047) in the VM. The MU RT vs. DT, the slope was significantly more positive in post- (1.51 ± .016), compared to pre-exercise (1.35 ± .52; *p* = .044) in the BB.

CONCLUSION: This study suggests that VOL+NMES exercise appears to induce a similar level of fatigue as VOL exercise alone, in the EF and KE muscle groups. This is shown by similar changes in neuromuscular functions and MU firing properties. The MU firing property changes suggest that the addition of NMES increased recruitment of higher-threshold MUs with higher discharge rates, and caused those higher-threshold MUs to derecruit at higher force levels. This study is the first to demonstrate these findings regarding VOL+NMES fatiguing exercise and, thus, provides a foundation for future studies to continue to develop exercise paradigms to examine the fatigability of VOL+NMES.

DEDICATION

I dedicate this dissertation to my wife, Eden, and my son, Elliott Beau. I am overwhelmed with gratitude for Eden, who has been an irreplaceable and unremitting source of support for the past six years. I am beyond thankful for her. If it were not for your unwavering motivation, pep-talks, celebratory outings, countless conversations where she lent her listening ear (especially when I was on the brink), and most of all her love, I would not be here, I would not be writing this dedication page as one of the final steps toward completion of my dream. For that, I am eternally thankful for you and your kind, warm, and compassionate heart. To my son, Elliott (Elbie), you have been a bright light in these otherwise gloomy and difficult years, and I hope one day you truly know how thankful I am to be your dad. Here we go on our next adventure. I cannot wait!

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LIST OF ABBREVIATIONS AND SYMBOLS

ANOVA	Analysis of variance
CI	Confidence interval
dEMG	decomposition electromyography
EMG	Electromyography
ES	Effect size
G-G	Greenhouse-Geisser
MVC	Maximal voluntary contraction
MU	Motor unit
NMES	Neuromuscular electrical stimulation
PPS	Pulses per second
VOL+NMES	Voluntary muscle contraction with superimposed neuromuscular electrical stimulation
RMS	Root-mean-square
VOL	Voluntary muscle contraction

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER I: INTRODUCTION

Neuromuscular electrical stimulation (NMES) involves applying high frequency and intensity electrical stimuli to elicit involuntary visible muscle contractions, and focuses on enhancements in muscle size and strength and/or rehabilitation of injuries (Doucet et al., 2012; Maffiuletti et al., 2018; Valenti, 1964). Specific to the electrically evoked muscle contractions, the motor control strategies and the muscle energetics differ from that of voluntary muscle contractions (VOL) (Vanderthommen & Duchateau, 2007). For example, during VOL submaximal exercise the motor unit (MU) recruitment strategy is ordered following the Henneman size principle (Henneman et al., 1965). That is, slower twitch muscle fibers that are smaller in diameter and associated with lower-threshold MUs are recruited first; to follow, the faster twitch muscle fibers that are larger in diameter and associated with higher-threshold MUs are recruited after (Henneman et al., 1965) as contraction intensity increases, which serves a primary purpose of reducing fatigue (Calancie & Bawa, 1984; Contessa & De Luca, 2013). In contrast, NMES evokes involuntary muscle contractions by delivering predetermined sequences of electrical stimuli to single or multiple active electrodes placed on the surface of the skin. These electrodes are typically placed at or near where the intramuscular nerve motor branches enter the muscle belly (i.e., motor points) (Botter et al., 2011; Hultman et al., 1983). In turn, muscle fibers that are found directly beneath the electrodes are recruited first, and as NMES intensity increases more muscle fibers will be recruited. Like VOLs, to continue to produce more force, more muscle fibers need to be recruited during NMES, however, this is dictated by the stimulation parameters (i.e., pulse amplitude [voltage/resistance or duration) (Adams et al., 1993; Gorgey et al., 2006). In turn, during NMES, it does not matter the diameter, type of muscle fiber, nor the excitability of the MU, as muscle fibers are recruited randomly and are spatially fixed (i.e., disordered recruitment). Of note, the effects of NMES are dependent upon the muscle being stimulated (i.e., distribution of slow- and fast-twitch muscle fibers) (Adams et al., 1993). About muscle energetics, NMES has a greater metabolic demand (Vanderthommen & Duchateau, 2007) also, showing greater oxidation of carbohydrates, glucose uptake of the whole body, and energy consumption, compared to VOLs (Hamada et al., 2004). Overall, the ordered recruitment of MUs during VOL serves the purpose of reducing fatigue, however the disordered recruitment during NMES induces greater fatigue (Feiereisen et al., 1997; Gregory & Bickel, 2005; Vanderthommen et al., 2003). Therefore, the nature of the motor control strategies in fatiguing VOL and NMES exercise differ, with each inducing distinctive acute physiological effects on the neuromuscular system, however, importantly, they may also be complimentary.

In theory, if NMES were superimposed onto VOL (VOL+NMES) then the acute physiological effects on the neuromuscular system could be augmented. Koutedakis et al. (1995) supplies evidence of this. In an acute fashion, they examined individuals who were injured or overtrained and found them to have a reduced ability to activate the muscle fully voluntarily (i.e., central activation was lowered). The use of VOL+NMES enhanced muscle fiber recruitment allowing the injured/overtrained individuals to increase their force production (Koutedakis et al., 1995). On the contrary, the use of VOL+NMES is not as effective in healthy individuals (i.e., voluntary activation is sufficient) (Hortobagyi et al., 1992), meaning, if individuals who have full capability to voluntarily contract their muscle, then the addition of NMES appears to not be as beneficial. However, this still does not explain the fatigability of VOL+NMES. Following the same line of thinking, fatigue should be accumulated (i.e., higher level of fatigue), through more recruitment of muscle fibers (i.e., low- and high-threshold MUs). However, the fatiguing effects of VOL+NMES are not well known.

One method that has been used for several years to examine the fatiguing properties of different exercise conditions and muscles is automated decomposition. These techniques have continually developed over several years and provide a non-invasive picture of the MU firing behavior through breakdown of the surface electromyography (EMG) signal into its constituent MU action potential trains (De Luca et al., 2006; Nawab et al., 2010). This is carried out by linear regression analysis to examine the relationships between the MU mean firing rate and recruitment threshold during isometric voluntary contractions. This relationship, as described by De Luca et al. (1982) and later by De Luca and Erim (1994), is referenced as the “onion skin” phenomenon, which is defined as an inverse relationship between the MU mean firing rate and recruitment threshold at any force level (De Luca et al., 1982; C. J. De Luca & Erim, 1994). Hence, the firing rates of earlier recruited MUs are greater than later recruited MUs, and the firing rates of all MUs are proportional as excitation of the motoneuron pool changes. Another important piece of information the relationship provides is that it suggests how the central nervous system controls the motoneuron pool. For example, when the intensity of the contraction is increased the slope typically becomes less negative and the y-intercept typically increases, suggesting that, more high-threshold MUs are recruited and the firing rates of those recruited MUs are increased to meet the required force demand (De Luca & Hostage, 2010). Decomposition has also allowed researchers to study the relationship (which is positive in nature) between MU recruitment threshold and MU derecruitment threshold. Higher threshold

MUs are typically derecruited at higher force thresholds than when they were recruited in the beginning, and lower threshold MUs are typically derecruited at lower thresholds than when they were recruited in the beginning (De Luca & Hostage, 2010; Stock & Mota, 2017). For example, Stock et al. (2012) examined fatigue in the vastus lateralis with a fatiguing protocol of 10 maximal intermittent isometric knee extensions. They demonstrated an increase in the mean linear slope coefficients (i.e., less negative) and a decreased mean y-intercept for the MU mean firing rate versus recruitment threshold relationship (Stock et al., 2012). Based on this, the findings suggest increases in MU recruitment to adjust for the force lost due to muscle fatigue. Alternately, examining similar MU firing properties, Ye et. al. (2015) used a fatigue protocol involving six sets of 10 maximal concentric and six sets of 10 maximal eccentric isokinetic muscle contractions in separate visits in the elbow flexors. They reported a significant decrease in the mean linear slope coefficient (i.e., more negative) and significant increases in the mean y-intercepts for the MU mean firing rate versus recruitment threshold relationship. Together, the examination of these relationships using surface EMG decomposition has been shown to be a valuable tool for investigating MU control strategies during fatiguing isometric and dynamic VOL exercise. In that sense, it would also be beneficial for examining MU control strategies during fatiguing isometric VOL+NMES exercise.

Purpose

The main purpose of this research project was to examine the acute neuromuscular functions and motor control strategies, after separate bouts of fatiguing VOL and VOL+NMES exercise in the elbow flexor and knee extensor muscle groups. Although it was our intention originally, we did not implement an NMES alone condition because during piloting, participants were unable to withstand the discomfort associated with prolonged NMES at the highest tolerable intensity. In addition, we chose these two muscle groups because the motor control strategies have been examined previously (although using different fatigue protocols) and are widely used in the NMES literature.

Research Questions

1. Are the neuromuscular functions (i.e., maximal voluntary force, EMG amplitude, EMG median frequency different between VOL, VOL+NMES, and control conditions in the elbow flexors and knee extensors?
2. Are the firing patterns of recorded MUs different between VOL, VOL+NMES, and control conditions in the biceps brachii, vastus lateralis, and vastus medialis?
    a. The linear slope coefficients and y-intercepts of the MU mean firing rate vs. recruitment threshold relationship.
    b. The linear slope coefficients and y-intercepts of the MU recruitment threshold vs. derecruitment threshold relationship.

Hypotheses

1. The VOL+NMES condition would result in a significant decrease in maximal voluntary force, compared to the VOL condition, for both the elbow flexor and knee extensor muscle groups.
2. The VOL+NMES condition would result in a significant increase in EMG amplitude, compared to the VOL condition, for the biceps brachii, vastus lateralis and vastus medialis muscles.

3. The VOL+NMES condition would result in a significant decrease in EMG median frequency, compared to the VOL condition, for the biceps brachii, vastus lateralis and vastus medialis muscles.
4. The linear slope coefficients of the MU mean firing rate vs. recruitment threshold relationship would be significantly more negative in the VOL+NMES condition compared to the VOL condition, for the biceps brachii, vastus lateralis and vastus medialis muscles.
5. The y-intercepts of the MU mean firing rate vs. recruitment threshold relationship would be significantly lower in the VOL+NMES condition compared to the VOL condition, for the biceps brachii, vastus lateralis and vastus medialis muscles.
6. The linear slope coefficients of the MU recruitment threshold vs. derecruitment threshold relationship would be significantly greater in the VOL+NMES condition compared to the VOL condition, for the biceps brachii, vastus lateralis and vastus medialis muscles.
7. The y-intercepts of the MU recruitment threshold vs. derecruitment threshold relationship would be significantly more negative in the VOL+NMES condition compared to the VOL condition, for the biceps brachii, vastus lateralis and vastus medialis muscles.

Significance of the Study

Researchers have explored the combination of VOL+NMES, theorizing that it would augment force production above that of VOL. VOL+NMES has also been associated with less discomfort. If VOL+NMES "potentially" has an accumulation of effects then it may be beneficial to add VOL+NMES in training programs aiming at increasing muscle strength, power, and/or endurance. Alternately, if this were the case, then it is entirely likely that VOL+NMES would be more fatiguing because it is well known that NMES induces a prominent level of muscular fatigue. It is plausible that the fatigue accrual during VOL+NMES may be higher compared to VOL, however, this is still not known. Findings from this study would provide researchers and clinicians with a greater understanding of the fatigability of VOL+NMES (and NMES as well) and may provide information toward development of new training paradigms and/or VOL+NMES protocols.

Delimitations

1. 35 – 40 males and females were needed to complete this investigation.
2. Participants must have been between the ages of 18 – 35 years.
3. Participants must have been healthy and had no current or recent neuromuscular or musculoskeletal injury or disorder of the spine or any joint involved in the study.
4. Participants must have been physically or recreationally active (not sedentary).
5. Participants were asked to maintain their normal daily activity, sleep, and eating habits; and to refrain from strenuous or highly intense activity/exercise and alcohol a minimum of 24 hours prior to any experimental visit.
6. Participants were required to visit the laboratory on four separate occasions and to be able to perform elbow flexor and knee extensor exercise.

Limitations

1. Participants were recruited through email, spoken communication (i.e., classrooms and word of mouth), and through University announcements. Since this is a convenience sample, students were likely from the Health, Exercise Science, and Recreation

Management Department. However, it is highly likely that the distribution of students within the department is like the entire student body at the university.

2. There are inherent limitations with the technology and equipment used to assess surface electromyography and the MU firing behaviors (i.e., inaccuracy of the algorithms used in the decomposition software). Although there are limitations, as there are with all equipment, previous studies have validated the accuracy of the technology (i.e., Nawab et al. 2010; De Luca et al. 2006).

Assumptions

1. Participants answer health questionnaires honestly and accurately.
2. Participants do not exercise during the 24-hour window prior to each visit.
3. Each isometric maximal voluntary contraction is performed under specified criteria.
4. Bipolar and decomposition sensor locations accurately detect electromyographical signals and represent motor unit firing behaviors of the whole muscle.
5. Each sensor location accurately demonstrates activation of the whole muscle.

Threats to Validity

1. Each exercise visit is designed to be fatiguing, but not create task failure. This should allow the participant to complete all the necessary isometric ramping contractions effectively. The elbow flexors were always completed first to mitigate any non-local effects of fatigue if the knee extensors were to be completed first.

2. Participants will be familiarized with all the contractions being performed during the study, which may induce a learning effect. However, each visit was randomized, and explicit instruction was given for each outcome.
3. Intra-subject variability. Every measure was taken by the researcher to mitigate this variability as much as possible. Such as, marking electrode location with sharpie and adjusting equipment and recording the positions.

CHAPTER II: LITERATURE REVIEW

This review summarizes research pertinent to the topics discussed in each section, and is not entirely exhaustive, as numerous studies are not relevant to the foci. The foci of this review are 1) to provide a general understanding of the origins of electrical stimulation, 2) to describe operative definitions to ensure clarity throughout, 3) to discuss the current applications and limitations of NMES, and 4) to discuss the acute physiological characteristics of VOL, NMES and VOL+NMES on the neuromuscular system regarding fatigue.

Historical Overview of Electrical Stimulation

The history of electrical stimulation dates to the middle of the 15th century, where Gerolamo Cardano, an Italian mathematician/physician, discovered electricity. However, Cardanos' work remained undiscovered until the 18th century when many scientists began experimentation of human electrification within the medical field. The earliest work on human electrification was mostly therapeutic in nature, but the interest within the field was lost by the end of the 18th century. This was until Luigi Galvani, an Italian physicist/anatomist, began expanding upon the work of previous scientists, and discovered that the skeletal muscles of frogs' legs twitched when electrical stimulation was administered (Cambridge, 1977). The findings of Galvani are most mentioned when looking deep into the history of electrical stimulation, but one must not forget Michael Faraday, an English physicist/chemist. Faraday, was the first to demonstrate the use of electrical current to stimulate human nerves (i.e., “Faradism”) to create movement (Cambridge, 1977). Numerous scientists continued to experiment with electrical current, mostly for therapeutic purposes, but it was not until the middle of the 20th century until electrical stimulation gained popularity again. In the early 1960’s the first experiments involving electrical stimulation examined individuals with foot drop after hemiplegic stroke (Liberson et al., 1961) and finger movement (Long, 1963) and walking ability in individuals with spinal cord injury (Kantrowitz, 1960). The studies were mostly feasibility studies examining how electrical stimulation may be used as a modality for reducing patient burden (i.e., therapeutic benefits). These studies helped set the foundation for future research in examining electrical stimulation, as well as development and engineering of new electrical stimulation devices (Peckham, 2018).

Operative Definitions

Electrical stimulation has a long and rich history, with early works of (Kantrowitz, 1960; Liberson et al., 1961; Long, 1963) utilizing what is currently known as functional electrical stimulation. However, at the time, many individuals loosely used the terms functional electrical stimulation and/or electrical stimulation for all forms of electrical stimulation. As will be discussed, there are distinct differences between the three primary forms of electrical stimulation used currently: functional and transcutaneous electrical stimulation, and NMES.

Functional electrical stimulation involves delivering a moderate-intensity (e.g., 10-40-Hertz) electrical current to intact lower motoneurons (i.e., connection from anterior horn of spinal cord to the neuromuscular junction) to replace/restore lost function (Doucet et al., 2012; Maffiuletti et al., 2018; Peckham & Knutson, 2005). Functional electrical stimulation is applied in a cyclical fashion (i.e., increase current while performing a movement and decrease but not turn off when at rest) to the specified nerve to imitate a VOL, and the beneficial effects are commonly demonstrated during the bout of stimulation (Maffiuletti et al., 2018). Another form of electrical stimulation is transcutaneous electrical stimulation, consisting of a continuous application of low-intensity (e.g., 2-10-Hertz) electrical current to activate cutaneous sensory nerve fibers without achieving the depolarization threshold of motor fibers (i.e., no observable muscle contraction occurs). The primary focus of transcutaneous electrical stimulation is for treatment of acute and chronic pain with the beneficial effects occurring during and after stimulation (Doucet et al., 2012; Maffiuletti et al., 2018; Sluka & Walsh, 2003). NMES differentiates itself from functional and transcutaneous electrical stimulation because the electrical current encompasses delivering preset sequences of high frequency (e.g., 50-100-Hertz) and high intensity continuous or intermittent electrical current to superficial layers of the muscle (Maffiuletti et al., 2018). NMES evokes visible tetanic (i.e., a significant increase in action potential frequency to a point where muscle tension is maximized), often submaximal, muscle contractions. Typically, the electrical current is applied percutaneously by connecting self-adhesive electrodes to a portable current generator at the muscle motor point(s) (Maffiuletti, 2010). The motor point is the location on the skin's surface (above the muscle) where the lowest level of electrical current is required to evoke a muscle twitch (i.e., the lowest motor threshold for a specified electrical current) (Botter et al., 2011). Determination of the muscle motor point allows for reductions in the required electrical current, thereby typically leading to decreased discomfort on behalf of the participant (Maffiuletti, 2010). Establishing a framework for understanding the three main modalities of electrical stimulation is especially important. As discussed, the three distinct types of electrical stimulation each have their own specific purposes.

An understanding of the differences is imperative to ensure clarity throughout this paper, especially since the focus will be placed on NMES.

Use of Neuromuscular Electrical Stimulation

Current Applications

NMES is primarily used in rehabilitation settings for the benefit of safeguarding, restoring and/or preserving neuromuscular function changes caused by disuse (e.g., injury, disease, post-operation, and aging) (Gibson et al., 1988; Seyri & Maffiuletti, 2011; Snyder-Mackler et al., 1994). NMES is also used in strength training settings to augment muscle activation in able-bodied individuals focusing on strength and range of motion improvements, decreasing muscle atrophy, and preserving muscle mass (Maffiuletti, 2010). The beneficial effects NMES are mostly obtained after several sessions (Doucet et al., 2012; Maffiuletti et al., 2018), thus, both clinical and healthy able-bodied individuals (including athletes) may benefit from the use of NMES. NMES has been shown to be beneficial for preserving muscle mass and neuromuscular function (e.g., strength, twitch force, force development, voluntary activation, etc.) in astronauts (Maffiuletti et al., 2019); critically ill patients (Maffiuletti et al., 2013); and in individuals who have endured limb immobilization (Dirks et al., 2014). Therefore, in situations where it is contraindicated (e.g., injury, immobilization) or not plausible (e.g., microgravity) to resistance train NMES may be advantageous.

Since the 1960's, NMES has been primarily examined in clinical populations resulting in several published reviews (Alamer et al., 2020; Barss et al., 2018; Burgess et al., 2019; Enoka et al., 2020; Maffiuletti et al., 2018; Monte-Silva et al., 2019; Mooney & Rose, 2019; Paillard, 2008; Valenzuela et al., 2020; Wu et al., 2020; Zayed et al., 2020). An overarching theme of all the reviews has been to examine the effectiveness of differing NMES treatments in those with neurological disorders or diseases (Sheffler & Chae, 2007), specifically multiple sclerosis (Almuklass et al., 2018), post-stroke hemiplegia (Chae et al., 2008) and spinal cord injury (Crameri et al., 2002; Downey et al., 2015). In addition, individuals, immobilized due to illness or injury (Dirks et al., 2014); with respiratory disease (Maddocks et al., 2016); who are older adults (Mani et al., 2018); that are pre- or post-operation (e.g., knee arthroplasty) (Demircioglu et al., 2015; Vaz et al., 2013; Yoshida et al., 2017); and that are critically ill (Dirks et al., 2015; Maffiuletti et al., 2013). Also, NMES has been used to combat muscle disuse atrophy and associated weakness in space medicine (Maffiuletti et al., 2019). A few previously mentioned studies demonstrated the beneficial effects of NMES, such as enhanced walking performance in multiple sclerosis patients (Almuklass et al., 2018), improved lower limb function in spinal cord patients (Crameri et al., 2002), and attenuation of muscle loss during an acute spell of disuse (Dirks et al., 2014). Improved functional ability (i.e., gait speed, sit-to-stand quickness, and plantar flexor strength) in older adults (Mani et al., 2018) has also been shown. Additionally, patients with severe chronic obstructive pulmonary disease increased their six-minute walk time and quadriceps strength (Maddocks et al., 2016). Further benefits of NMES were also shown as reductions in knee pain and enhanced quality of life (Demircioglu et al., 2015) as well as improved knee function and health (Vaz et al., 2013) in post-knee arthroplasty patients. On the contrary, there are several instances where the effects of NMES were not beneficial. The administration of NMES to the quadriceps and gastrocnemius muscles as part of a cardiac rehabilitation program (i.e., post-cardiac valve reconstruction surgery) showed no effect on gait ability or speed, muscular strength of the quadriceps or gastrocnemius, or functional independence (Fontes Cerqueira et al., 2018). NMES added to palliative chemotherapy for patients with advanced non-small cell lung cancer did not provide any effect on quadriceps strength, lean mass of the thigh, or ability to be physically active (Maddocks et al., 2013). Moreover, quadriceps strength was not changed in women with mild-to-moderate radiographic osteoarthritis when NMES was applied (Palmieri-Smith et al., 2010). Furthermore, NMES had no effect on handgrip strength and functional independence of intensive care unit survivors (Patsaki et al., 2017), and had no effect on enhancing the ability to provoke an acceptable quadriceps muscle contraction in critically ill patients (e.g., organ transplant, surgery, respiratory failure, etc.) (Segers et al., 2014). Overall, there is ambiguity regarding the evidence of NMES effectiveness in clinical populations, however, importantly, we must consider the weight of the evidence showing the effectiveness of NMES in restoring physical function within clinical populations. Additionally, the differences in results are commonly attributed to study design (e.g., stimulation parameters, training protocol, etc.). Furthermore, the beneficial effects of NMES in clinical populations do not always crossover to healthy populations.

A primary purpose of examining NMES in healthy populations is to strengthen the activation of intact healthy muscle (Enoka et al., 2020; Gondin et al., 2011). More specifically, to determine the effectiveness of NMES regarding isometric and dynamic strength; power and explosiveness; sprint, jumping, and endurance performance; and muscle size and fatigability (Gondin et al., 2011; Veldman et al., 2016). Intuitively, this differs from NMES use in clinical populations when the traditional focus is primarily on returning or maintaining physical function when the muscle is unhealthy (e.g., injured) or not fully intact (e.g., spinal cord injury). Previous research has demonstrated increased muscle size and strength of the quadriceps after 8-weeks of NMES training at high (i.e., evoked force of $62.5 \pm 4.6\%$ of MVC) and low (i.e., evoked force

32.6 ± 2.6% MVC) intensities, with greater improvements in the high-intensity group, in young (i.e., 28 ± 1 years), healthy, untrained males (Natsume et al., 2018). The authors attributed the larger increases in size and strength to the higher stimulation intensity. In addition, improvements in MVC strength were demonstrated in the hamstrings, biceps brachii, triceps brachii, triceps surae, and most commonly the quadriceps (Gondin et al., 2011), but it is important to mention that VOL still is superior for enhancing strength in healthy populations (Maffiuletti, 2010).

Limitations

An understanding of the shortcomings related to NMES (which inevitably reduce the effectiveness) is crucial when developing experimental studies. Across the literature, four primary limitations are commonly discussed, and include: 1) a high level of discomfort associated with the electrical stimulation (Lake, 1992); 2) the recruitment of muscle fibers is spatially fixed and mostly superficial (C. S. Bickel et al., 2011); 3) high fatigability due to disordered recruitment of muscle fibers which preferentially activate fast twitch fibers (Barss et al., 2018); and 4) exceedingly variable individual responses due to a lack of consensus on appropriate stimulation parameters (Maffiuletti, 2010; Maffiuletti et al., 2018). While the stimulation parameters may play a sizable role in the effectiveness of NMES, it is believed the largest contributor is the interindividual anatomical or morphological differences in the nervous system. In other words, the way in which the axonal branches are distributed within the body (Gondin et al., 2011). With respect to limitations one, two, and three, several studies have been conducted (over a few decades) which experimentally manipulated the stimulation parameters, pulse characteristics (i.e., pulse frequency, shape, duration, and intensity) and duty cycles

(Bickel et al., 2012; Gorgey et al., 2006; Gorgey & Dudley, 2008; Gregory et al., 2007; Kesar et al., 2008; Kesar & Binder-Macleod, 2006; Lieber & Kelly, 1993; Medeiros et al., 2017; Scott et al., 2007). Moreover, experiments have also investigated how altering the stimulation electrode type (Lieber & Kelly, 1993), size (Alon et al., 1985; Lyons et al., 2004), and location would affect the perception of discomfort (Gobbo et al., 2011; Lyons et al., 2004; Vieira et al., 2016). The overarching purpose of all the studies has been to reduce discomfort, produce the greatest involuntary evoked force, and most importantly, reduce fatigability. However, as mentioned previously there is large heterogeneity between studies, making it difficult to develop an agreement on the appropriate protocols. Further, the recruitment strategies (i.e., MU recruitment, discharge frequency, discharge pattern) during NMES has been focused on in the past decade, with several reviews discussing the research on the topic (Barss et al., 2018; Bergquist, Clair, & Collins, 2011; Bergquist, Clair, Lagerquist, et al., 2011; Bickel et al., 2011; Gondin et al., 2011; Maffiuletti, 2010; Maffiuletti et al., 2018). The consensus from these studies was that MU recruitment during NMES is disordered, and this method of MU recruitment has numerous physiological implications (e.g., higher fatigability).

Acute Physiological Characteristics of Fatigue in VOL, NMES and VOL+NMES

Motor Control Strategy and Fatigability of VOL

When motoneurons are depolarized in the spinal cord by supraspinal input and sensory receptors in the periphery (e.g., muscle, joints, skin) MUs are recruited in an ordered and fixed manner, which follows the Henneman size principle (Henneman & Olson, 1965), That is, the lower-threshold fatigue resistant MUs are recruited first, followed by the more fatigable higher-threshold MUs (Calancie & Bawa, 1984; Contessa & De Luca, 2013). In combination with MU recruitment, the discharge frequency (i.e., rate coding) is dependent upon the amount of descending drive to the motoneurons, and increasing discharge frequency produces increases in the contraction amplitude of the VOLs (Bigland & Lippold, 1954; Enoka & Duchateau, 2017). Rate coding helps avoid excessive discharge rates, meaning a maximal limit for discharge is set to ensure that small or moderate muscle contractions do not have unnecessarily high discharge rates occurring (Bigland & Lippold, 1954). Additionally, once recruited, individual MUs discharge asynchronously to allow for smooth and fused muscle contractions to occur (Bellemare et al., 1983). Moreover, regarding MU discharge pattern, MUs will increase discharge rate until a steady state is achieved which is specific to the intensity of the muscle contraction. From there, the discharge pattern may follow a sharp increase to a plateau (Stock & Thompson, 2016) and then discharge in doublet (i.e., 2 times in close succession) (Binder-Macleod & Kesar, 2005) or triplet (i.e., 3 times in close succession) (Kudina & Andreeva, 2016) patterns, and MU rotation (Bawa et al., 2006) may occur to prevent fatigue. These quick succession firing events have been shown to enhance torque by playing on the catch-like property of muscle (i.e., increase tension through series elastic component of muscle and enhance calcium release) (Binder-Macleod & Kesar, 2005).

It is well known that neuromuscular fatigue during sustained VOL may occur at several points within the central (i.e., from spinal cord to brain) and peripheral (i.e., from spinal cord to muscle) nervous system (Boyas & Guével, 2011). More specifically, central fatigue refers to a decrease in the ability to voluntarily activate the muscle (i.e., reduced motor cortex output and motoneuron excitability), and includes decreases in the number of MUs recruited and their associated discharge frequencies. In contrast, peripheral fatigue refers to a decrease in muscle fiber function, which may include reductions in action potential propagation, excitation-contraction coupling, substrate depletion (e.g., glycogen, creatine phosphate), and state of intracellular environment (e.g., accumulation of inorganic phosphate, adenosine phosphate) (Allen et al., 2008; Boyas & Guével, 2011; Gandevia, 2001; Kent-Braun et al., 2012; Merton, 1954).

Motor Control Strategy and Fatigability of NMES

The methods of MU recruitment and discharge frequency and pattern for NMES are in stark contrast to the physiological recruitment of MU during VOL. The consensus in neurophysiological research is, small-diameter motor axons have greater resistance and higher depolarization thresholds, and typically innervate slower twitch muscle fibers. In contrast, large-diameter motor axons have smaller resistance and lower depolarization thresholds, and typically innervate faster twitch muscle fibers (Blair & Erlanger, 1933; Solomonow, 1984). With that said, during NMES, the MUs are recruited in a disordered fashion. This, in part, is a function of the size of the motor axon diameter and its depolarization threshold. Since NMES is applied over the skin, the diameter and distance of the axons underneath the skin will influence which motor axons will be depolarized (i.e., recruited) (Blair & Erlanger, 1933; Solomonow, 1984). Meaning, if small-diameter motor axons are close to the active stimulation electrodes they will be depolarized at lower stimulus amplitudes, as compared to the larger diameter motor axons which are further away from the electrodes. Thus, to depolarize the more distant motor axons it would require a greater stimulus amplitude (Feiereisen et al., 1997; Gregory & Bickel, 2005; Grill & Mortimer, 1995; Vanderthommen et al., 2003). Therefore, resulting in disordered (or random) MU recruitment by primarily recruiting the fatigable higher-threshold MUs, with less recruitment of the lower-threshold fatigue resistance MUs (Barss et al., 2018). The basis for MU discharge frequency for NMES is determined by the stimulation pulse duration (i.e., length of time in microseconds between the initiation and end of the electrical pulse) and frequency (i.e., rate of pulse delivery in pulses per second and/or Hertz) (C. S. Bickel et al., 2011). Additionally, the discharge pattern of MU during NMES also depends upon the stimulation frequency, assuming the NMES is administered at a constant frequency. Hence, when delivering the electrical current, the discharge frequency of MU will be fixed based on the stimulation parameters (Barss et al., 2018).

Knowing that MUs are recruited in a disordered fashion during NMES, researchers previously hypothesized that the involuntary muscle contractions induced by NMES occur because of activating peripheral pathways (i.e., motor branches underneath the applied surface electrode) (Maffiuletti, 2010). However, a recent review published by (Maffiuletti et al., 2018) discusses that NMES operates through both peripheral and central pathways. More specifically, when the volley of electrical stimuli is administered in the periphery – muscle or motor points/branches – both the cutaneous and muscle sensory fibers are activated (e.g., Ia, Ib, II) which leads to depolarization of the alpha motoneurons. In turn, the afferent volley then ascends to other spinal or supraspinal cortical regions. In fact, cortical plasticity changes have been demonstrated as augmented cortical excitability after a single bout of NMES (Chipchase et al., 2011), and activation of cortical (e.g., primary motor and somatosensory cortices) and subcortical (e.g., thalamus, putamen) structures, as determined by functional imaging (Blickenstorfer et al., 2009; Francis et al., 2009; Smith et al., 2003). Therefore, the evidence demonstrates that NMES operates through both peripheral and central (i.e., spinal, and cortical regions) mechanisms (like VOL), which has provided knowledge toward a greater understanding of how higher levels of fatigue occur during NMES.

The primary reason NMES induces a large amount of fatigue is due to the non-physiological recruitment of MU (i.e., unordered, and fixed) (Bickel et al., 2011; Jubeau et al., 2007), however, the types of fatigue are like that of VOL. More specifically, peripheral fatigue is most common with NMES due to the location of the stimulation electrodes and often has a rapid onset. The peripheral fatigue is thought to be caused by excitation-contraction coupling failure (Allen et al., 2008; Boyas & Guével, 2011; Gandevia, 2001; Kent-Braun et al., 2012; Merton, 1954) and/or compromised neuromuscular transmission (i.e., action potential propagation) across the neuromuscular junction or sarcolemma due to too much potassium in the extracellular matrix (Jones, 1996; Quinonez et al., 2010). On the contrary, central fatigue is also thought to occur during sustained NMES, which includes a decrease in motoneuron excitability.

Motor Control Strategy and Fatigability of VOL+NMES

Understanding the motor control strategies between VOL and NMES allows for speculation on the effects of combining the two, specifically, simultaneously superimposing NMES onto VOL (VOL+NMES). In theory, the acute application of VOL+NMES should augment the acute physiological effects within the neuromuscular system, by way of increased force production (i.e., increased MU recruitment) to a level above what VOL and NMES would induce separately. Moreover, since it is likely that VOL+NMES involves more muscle fibers for a given muscle contraction, it seems plausible that the combination would provide greater chronic benefits (e.g., muscular strength, power, or endurance) (Paillard, 2018). For example, comparing training programs involving VOL+NMES, and VOL and NMES separately, recent evidence suggests the possibility of improvements in motor performance (i.e., heart rate, peak oxygen consumption, strength, endurance, etc.) when using VOL+NMES (Mathes et al., 2017; Matsuse et al., 2013; Wahl et al., 2012, 2014, 2015). In clinical populations, such as post-operation rehabilitation, the chronic application of VOL+NMES achieved greater effectiveness than VOL alone, in injury recovery (Draper et al., 1991). Yet, most of the literature demonstrates that the long-term adaptations of VOL+NMES in healthy individuals are not present, and do not surpass VOL alone (Wirtz et al., 2015). Thus, the ineffectiveness of the chronic application of VOL+NMES in healthy individuals is because their ability to voluntarily activate the muscle is efficient.

Acutely, VOL+NMES appears to be beneficial for specific populations. For example, in overtrained Olympic athletes (demonstrated by an impaired central drive), the VOL+NMES combination facilitated force production, through increased MU recruitment and/or discharge rate (Koutedakis et al., 1995). The findings of both Koutedakis et al. (1995) and Draper et al. (1991) allowed researchers to determine that VOL+NMES may be useful in individuals with impaired central drive. In contrast, VOL+NMES in healthy individuals appears to not be as beneficial regarding force production when compared to VOL alone (Hortobagyi et al., 1992). Additionally, the benefits of VOL+NMES do not supersede the benefits achieved in VOL or NMES separately in healthy individuals (Paillard et al., 2004). The results of the studies do provide a greater understanding of the effects of VOL+NMES in healthy and clinical populations, with the majority showing VOL+NMES to be of more benefit in clinical individuals. The long-term beneficial effects of VOL+NMES in healthy populations, however, remain to be well established.

Regarding the examination of VOL+NMES there are two major limitations to consider. NMES is associated with an elevated level of discomfort due to the noxious effects of electrical stimulation. Thus, the fascinating approach of combining VOL+NMES can be taken, which subsequently decreases the discomfort through the gate control theory of pain (Melzack & Wall, 1965). In other words, when performing a VOL, it activates an inhibitory interneuron, subsequently blocking the nociceptive feedback (i.e., noxious effect) induced by NMES. Second, and most important, NMES alone is highly fatigable (compared to VOL) due to the disordered recruitment of MUs. The pathways of fatigue for both NMES and VOL include both peripheral and central components, with the former being of greater influence in NMES. However, what is not well known is the fatigability of VOL+NMES.

The determination of fatigue by using the VOL+NMES method was first examined in 1954 (Merton, 1954). The author was able to distinguish between peripheral and central fatigue using VOL+NMES by having participants perform exercise to exhaustion which resulted in decreased muscular force output. If the decreased post-fatigue force output was not affected by VOL+NMES, then peripheral fatigue was determined. In contrast, if the post-fatigue force output was greater in VOL+NMES compared to VOL, then central fatigue was determined. Central fatigue is exhibited as gradual decline in voluntary activation (i.e., a reduction in recruited MUs and their frequency of discharges from the onset of exercise) of the exercising muscle. This involves the primary motor cortex – extent of descending drive reaching the motoneurons – and the MU and muscle activation (Boyas & Guével, 2011; Gandevia, 2001). Peripheral fatigue may include changes in neuromuscular transmission, reductions in intrinsic contractile strength of the muscle fibers, and involves all neuromuscular locations at, or distal to, the neuromuscular junction (Boyas & Guével, 2011; Gandevia, 2001). More specifically, accumulation of multiple metabolites (e.g., adenosine diphosphate, inorganic phosphate), and reduced levels of glycogen result in impaired excitation-contraction coupling (Allen et al., 2008). The causes of fatigue during NMES and VOL separately, are similar regarding peripheral and central mechanisms. The primary difference is that fatigue occurs rapidly within the periphery (i.e., where the active electrodes are placed) in NMES, due to the high frequency and stimulus amplitude of electrical stimulation. Considering, VOL+NMES induced fatigue, impaired muscle spindle function has been previously shown; specifically, the NMES caused a decrease in discharge frequency of the Ia afferent pathway, thereby causing inhibition of the motoneuron pool (Paillard, 2005). The current understanding of fatigue is specific to VOL or NMES separately, and NMES appears to have greater fatigability. Nonetheless, there is no data regarding how the motor control strategies may be affected in VOL+NMES fatiguing exercise.

CHAPTER III: METHODS

Participants

Prior to the recruitment of the participants, an *a priori* statistical power analysis for sample size estimation using G*Power software (3.1.9.4; Heinrich Heine University, Dusseldorf, Germany) (Faul et al., 2007) was completed. The following parameters were included in the power analysis, looking at within-participants' effects for separate 3 (VOL vs. VOL+NMES vs. control) × 2 (pre vs. post) repeated measures analyses of variance (ANOVA): effect size (ES) $F = 0.25$; alpha (α) level = 0.05, power level = 0.80, and correlation among repeated measures = 0.5. The resultant recommended sample size of 36 for the within-participants' effects was used. We chose this ES because no previous research has been completed on this topic and we wanted to avoid using a calculated ES from a separate (unrelated) experimental study or meta-analysis. Recruitment was performed through email, spoken communication (i.e., classrooms and word of mouth), and through University announcements. The inclusion criteria were as follows: (a) males and females within the age range of 18- to 35-years; (b) have no current or recent neuromuscular or musculoskeletal injury or disorder of the spine or any joint involved in the study; and (c) be physically or recreationally active (not sedentary) based on the 2019 Physical Activity Guidelines Advisory Committee (Piercy et al., 2018). Habitually active individuals were chosen based on our pilot work because it became apparent that the fatiguing protocol was unable to be completed by some untrained participants and was incredibly difficult for those who were trained. Consequently, the exclusion criteria were as follows: (a) < 18- and > 35-years of age;

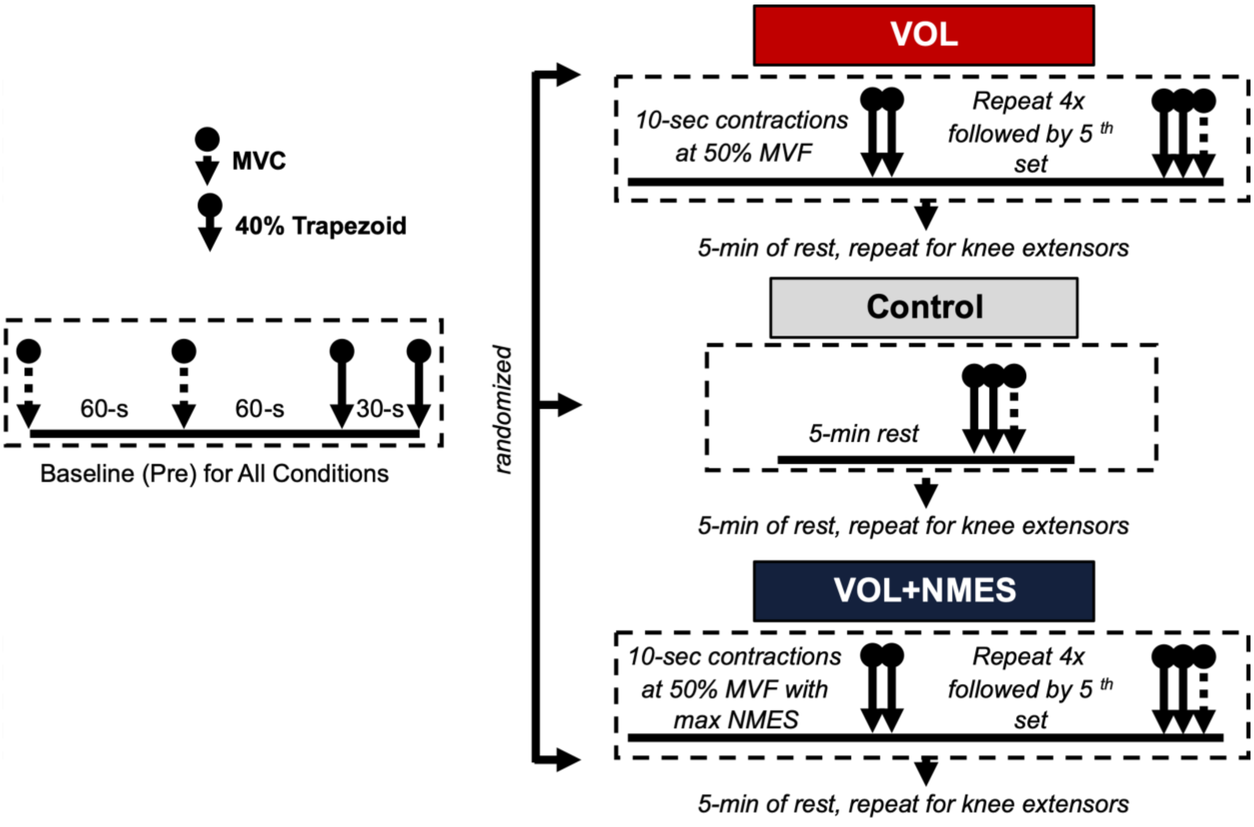
and (b) have a current or recent (≤ 6 months) neuromuscular or musculoskeletal injury or disorder of the spine or any joint involved in the study. Eligibility was determined based on the aforementioned criteria with each participant completing the following: (a) An informed consent explaining all possible risks and/or benefits of the study; (b) A pre-exercise health and exercise status questionnaire to determine if physically or recreationally active, resistance or aerobic trained, or untrained; and (c) the 2020 Physical Activity Readiness Questionnaire (Warburton et al., 2011), to determine and ensure no underlying health conditions exist. The 2019 Physical Activity Guidelines Advisory Committee (Piercy et al., 2018) was used to determine if participants are physically or recreationally active or untrained, based on the minimum recommended amount of weekly activity (i.e., ≥ 150 to ≤ 300-minutes of moderate-intensity or ≥ 75 to ≤ 150-minutes of vigorous-intensity aerobic activity weekly, and whole-body strengthening for ≥ 2-days weekly of moderate- to vigorous-intensity). Prior to any familiarization or experimental visit, all participants were asked to maintain their normal daily activity, sleep, and eating habits; and to refrain from strenuous or highly intense activity/exercise and alcohol a minimum of 24 hours prior to any experimental visit. All experimental procedures in this project were in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments or comparable ethical standards and are approved by the University's Institutional Review Board (IRB Protocol # 21-008) for the Protection of Human Participants.

Experimental Design

A graphical overview of the protocol is shown in Figure 1. This study employed a within-participant and controlled design to directly compare the neuromuscular functions (i.e., maximal voluntary force, EMG amplitude, and EMG median frequency) and MU firing properties of the lower- (i.e., vastus lateralis, vastus medialis) and upper-body (i.e., biceps brachii) muscles pre- and post-submaximal VOL+NMES and VOL exercise. All participants visited the laboratory on four separate occasions to complete the study. The first included familiarization to the equipment and procedures for the isometric maximal voluntary contraction (MVC; measures maximal voluntary force) submaximal isometric trapezoid muscle contractions (i.e., hereby referred to as trapezoids) at 40% maximal voluntary force; and NMES acclimation with determination of the maximal tolerable stimulation intensity, to be superimposed onto VOL for the VOL+NMES condition. Visits two through four were randomized, counterbalanced, and included either the VOL+NMES, VOL, or control conditions. The exercise conditions encompassed performing five sets of 10-second VOLs at 50% of maximal voluntary force, immediately followed by two trapezoids at the end of each set. At the end of the fifth and final set, two MVC measurements were performed after the final two trapezoids with no rest in between any contraction. The VOL condition included a 10-second VOL at 50% of maximal voluntary force, immediately followed by two trapezoids at 40% maximal voluntary force for set one, immediately followed by set two, and so on. After the final two trapezoids at 40% maximal voluntary force were completed, an MVC was completed. The exact same exercise was performed for the VOL+NMES, with the NMES at the maximal tolerable intensity being provided during each 10-second VOL at 50% of maximal voluntary force for each set. The control performed the same pre- and post-measurements (i.e., MVC and two trapezoids at 40% maximal voluntary force) without exercise. Lastly, the elbow flexor muscle group always finished first in each visit to prevent the potential fatiguing effects of lower body exercise on upper body exercise performance.

For all conditions and within each condition, the exact protocol was repeated. During all visits, five minutes of rest were provided between each muscle group being tested. In the exercise visits, minimal rest (5 seconds of rest were provided between each 10-second VOL at 50% of maximal voluntary force, and each trapezoid) was provided between each contraction and each set; a minimum of 24-hours of rest was required after the familiarization and control visits. The rest periods were unavoidable due to the nature of the exercise protocol setup in the computer software. A minimum of 48-hours of rest was required between each exercise visit. All visits were performed at the same time of day (± 2-hours). The dependent variables of normalized maximal voluntary force (%Pre-MVC), EMG amplitude, and EMG median frequency were collected and analyzed at the pre- and post-exercise (i.e., after the 5th set) time points for each condition. In addition, the linear slope coefficients and y-intercepts of the MU mean firing rate vs. recruitment threshold and MU recruitment vs. derecruitment relationship were collected and analyzed during the pre-and post-exercise trapezoids (specifically the 5th set trapezoid) contractions for each condition.

Figure 1. An overview of the experimental design



MVC: isometric maximal voluntary contraction; MVF: maximal voluntary force; NMES: neuromuscular electrical stimulation; VOL: voluntary contraction; VOL+NMES: voluntary contraction with superimposed NMES

Isometric MVC Testing

For the elbow flexors, participants were instructed to maintain a seated upright posture while placing the posterior aspect of their upper arm onto a square-shaped padded surface. A padded cuff was placed around the wrist and connected to one end of a tensiometer (Model SSM-AJ-500; Interface, Scottsdale, AZ, USA), with the other end of the tensiometer connected to a rigid constraint. Next, participants were instructed to obtain 90° of elbow flexion with palm facing toward them, and the opposite side of the limb against a solid surface. In this position, participants were able to passively obtain 90° of elbow flexion (Figure 2a). For the knee extensors, participants were instructed to sit on a plate-loaded knee extension machine (Steelflex PLLE 200; Steelflex Fitness, Taipei, Taiwan) which was adjusted to ensure the back of the participants remained upright; that the knee joint was in approximately 75° of flexion, and that the ankle roller pad of the tested limb was in the most comfortable position. Next, the participants' upper thighs were strapped in with a Velcro® belt to mitigate hip involvement during the trial. A load cell was connected to the lever of the ankle roller pad and connected to one end of a tensiometer (Model SSM-AJ-500; Interface, Scottsdale, AZ, USA), with the other end of the tensiometer connected to the rear plate loading bar of the machine via a steel chain (Figure 2b).

Upon setting the participant up in the station, the following parameters were used to measure maximal voluntary force for all MVC measurements for all muscles: (a) Participants were first familiarized with the MVC testing protocol, and once participants verbalized their comfortability and readiness for MVC testing, familiarization was terminated; (b) The warmup consisted of performing six to eight submaximal (i.e., 50% of perceived maximal voluntary force) isometric muscle contractions; (c) Each participant then completed only two trials of five-second MVCs with one-minute of rest in between each. Two trials have been shown to be sufficient for determining the highest reliability (Jeon et al., 2019); (d) Prior to each MVC trial, the researcher provided the same explicit instructions to either "pull" or "push as hard as you can" and, ensured each participant performed no countermovement prior to the MVC (Maffiuletti et al., 2016); (e) During each MVC trial, the researcher provided a verbal countdown of "three," "two," "one," and verbal encouragement of "pull," "push," and/or "kick," along with visual feedback administered via real-time force output displayed on a computer monitor (Dell

XPS 8900; Dell, Inc., Round Rock, TX, USA) stationed approximately 16-inches and one meter away for the elbow flexors and knee extensors, respectively. The verbal encouragement provided was at a volume slightly greater than normal conversational volume and was spoken at a high frequency for the duration of all MVCs for all muscles. If a countermovement was performed, the MVC trial was scrubbed, and another trial was completed.

Figure 2. Experimental setup for isometric MVC testing in the elbow flexors and knee extensors

Submaximal Isometric Trapezoid

Participants were instructed to complete the following: (a) Begin with a three-second rest at 0% (resting); (b) then produce force gradually, from 0% to 40% of maximal voluntary force for four seconds (i.e., an increase of 10% per second); (c) Hold at 40% of maximal voluntary force for ten seconds; and (d) gradually reduce force from 40% to 0% (resting) for four seconds, followed by a three-second rest at 0%. After performing the pre-MVCs, a one-minute rest was provided before two trapezoids were performed, and 30-seconds of rest was provided between each trapezoid. During the experimental exercise visits, two trapezoids were performed immediately at the end of each 10-second VOL at 50% of maximal voluntary force. The same equipment and setup procedures as in the MVC trials were used for the trapezoid trials. There was a monitor (Dell XPS 8900; Dell, Inc., Round Rock, TX, USA) provided showing the trapezoid target force template and the participants' real-time force.

Experimental Conditions

VOL Exercise

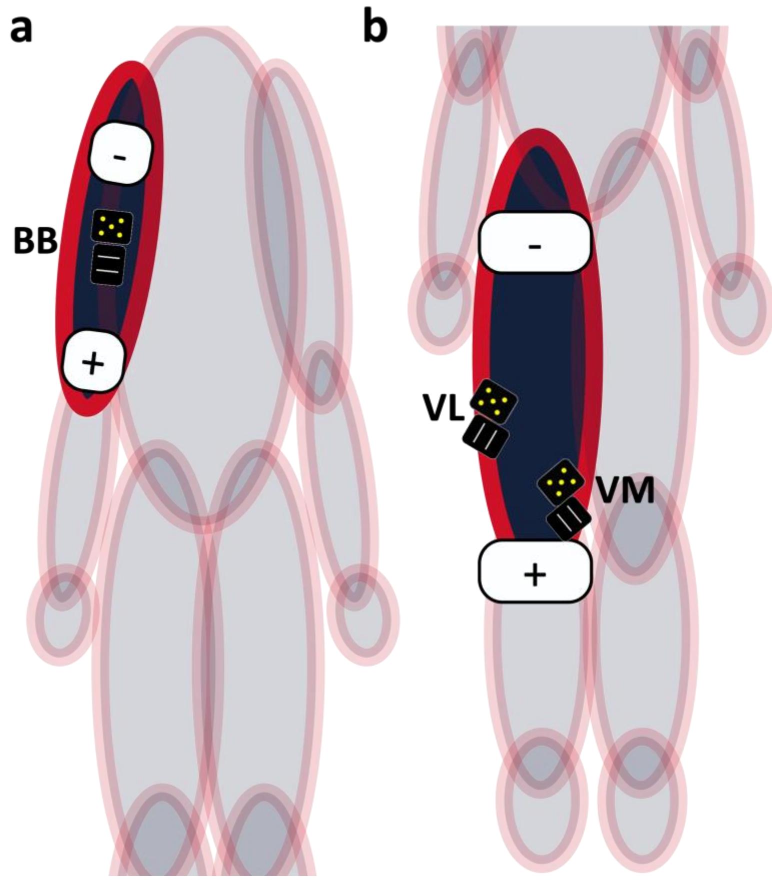
The fatigue protocol for the elbow flexors and knee extensors was identical, but the elbow flexor completed the exercise first. Specifically, the participant performed five sets of 10-second VOLs at 50% of maximal voluntary force, and at the end of each set, two trapezoids were completed back-to-back with approximately six seconds of rest in between. After the fifth and final set, the last trapezoid was followed by an MVC. Once the post measurements were completed, a five-minute rest was provided prior to testing the knee extensors.

VOL+NMES Exercise

The exact same exercise protocol as mentioned in the VOL section was performed, however, stimulation electrode pads were placed on the exercising muscle during the five sets of 10-second VOLs at 50% of maximal voluntary force. Prior to placement of the stimulation electrodes, the skin was shaved and cleansed with an isopropyl alcohol swab to remove hair and contaminants in accordance with the SENIAM guidelines (Hermens et al., 1999). The participants positioned themselves as instructed by the researcher, into the equipment for the specific muscle being tested. Two, 2" × 2" stimulation electrodes (Dermatrode HE-R, American Imex, Irvine, CA, USA) were used to stimulate the biceps brachii muscle. Two, 2" × 4" stimulation electrodes (Dermatrode HE-R, American Imex, Irvine, CA, USA) were used to stimulate the vastus lateralis and vastus medialis muscles. The electrodes were then connected to a constant current, high-voltage Digitimer DS7AH stimulator (Digitimer; Hertfordshire, UK). Centered on the anatomical landmarks for the origin (proximal) and insertion (distal) of each muscle, the cathode (-) and anode (+) stimulation electrodes were always placed at the proximal and distal regions of the muscle, respectively. The specific stimulation electrode sites for the biceps brachii encompassed placing the cathode at the most proximal portion of the biceps brachii, and the anode placed on the most distal portion, the bicipital tendon (Figure 3a). Combining the findings of motor point identification for the lower-limb muscles from (Botter et al., 2011) and (Gobbo et al., 2014), the stimulation electrode sites for the vastus lateralis and vastus medialis encompassed placing the cathode horizontally across the anterior thigh at 45% of the distance between the anterior superior iliac spine and the patella, and the anode placed horizontally across the anterior thigh at the superior portion of the patella (Figure 3b).

Based on the combined recommendations from several researchers (Doucet et al., 2012; Maffiuletti, 2010; Sheffler & Chae, 2007; Vanderthommen & Duchateau, 2007), the stimulation parameters were as follows: (a) Stimulation frequency of 50-Hz; (b) Stimulation pulse width/duration as biphasic rectangular pulses of 400-µs; (c) Duty cycle of 50%; and (d) stimulation amplitude/intensity at highest tolerated current intensity. All the parameters were identical across all muscles, except the stimulation amplitude/intensity were different between muscles based on each participant's relative maximal tolerable stimulation intensity. In addition, the stimulation amplitude/intensity was determined for all muscles during the familiarization visit and the VOL+NMES and VOL protocols for each muscle were performed with the exact same equipment and participant setup as previously mentioned in the isometric testing section.

Figure 3. Experimental setup for stimulation and EMG sensor placement



A graphical depiction of the experimental setup used in the laboratory for placement of the stimulation pads (anode [-]), cathode [+]), bipolar EMG (parallel bars) and dEMG sensors (five pins) in the (a) elbow flexors and (b) knee extensors.

Control

The control visit was identical to the VOL and VOL+NMES visits, including the same pre- and post-measurements, except no exercise was performed and participants rested for 5-minutes between the pre- and post-measurements. The purpose of this control was to limit the amount of fatigue accrued during to allow for a comparison, although complete fatigue prevention was not possible even with performing only two isometric MVCs and four trapezoids.

Surface EMG Recording

The surface EMG signals were recorded during each pre- and post-MVC and trapezoid, from the vastus lateralis, vastus medialis, and biceps brachii muscles. Before bipolar EMG and dEMG sensor and reference electrode placement, the skin was shaved and cleansed with an isopropyl alcohol swab to remove hair and contaminants in accordance with the SENIAM guidelines (Hermens et al., 1999). Bipolar EMG and dEMG placement followed modified guidelines (Hermens et al., 1999; Zaheer et al., 2012). Single bipolar EMG (DE 2.1 Single Differential Surface EMG Sensors, 10-mm interelectrode distance) and 5-pin surface array sensors (dEMG sensor; 0.5-millimeter pin diameter; 5×5-millimeter square; Delsys, Inc., Natick, MA, USA) were placed at the following specific sites: (a) Biceps brachii, oriented in the direction of the muscle fibers at 33% of the distance from the antecubital fossa and acromion process (Figure 3a); and (b) Vastus lateralis, oriented in the direction of the muscle fibers at 65% of the distance from the anterior superior iliac spine and the lateral patella, and (c) vastus medialis, oriented in the perpendicular direction to the line constituting 85% of the distance from the anterior superior iliac spine and anterior border of medial ligament (Figure 3b). The reference sensor (5.08-cm diameter; Dermatrode HE-R, American Imex, Irvine, CA, USA) was placed on the spinous process of the seventh cervical vertebrae.

Surface EMG Signal Processing and Decomposition

A 16-channel Bagnoli™ desktop EMG system (Delsys, Inc., Natick, MA, USA) sampled the force, EMG and dEMG signals. The force, EMG, and dEMG signals were subsequently handled offline using customized software (LabVIEW, National Instruments, Austin, TX). The surface EMG signals were pre-amplified (gain: 1,000), high- (20-Hz) and low-pass (450-Hz) filtered, and then smoothed with a 100-ms zero-shift moving root-mean-square (RMS). The filtered EMG signals were then digitized at a sample rate of 20 kHz with a 16-bit analog-to-digital converter (input range: 0-10-V, resolution = 0.153-mV; Model USB-6259; National Instruments, Austin, TX, USA). Briefly, the bipolar EMG sensors were needed for surface EMG amplitude (quantified as the root-mean-square [RMS]) and median frequency of the biceps brachii, vastus lateralis, and vastus medialis. The Discrete Fourier Transform algorithm was used to derive the EMG signal into a power spectrum, and the EMG median frequency of the spectrum was then calculated. The surface EMG amplitude and median frequency of the selected EMG signal were determined by selecting the highest 500-ms window of the non-smoothed EMG signal collected during the MVC. The maximal voluntary force was determined by selecting the peak one-second window within the plateau region of the five-second contraction. The EMG amplitude, median frequency and maximal voluntary force were normalized as a percentage of the baseline MVC (%Pre-MVC) value for the specific muscle during all conditions.

For the 40% trapezoid muscle contractions, the dEMG sensor (which provides four channels of surface EMG signals) was processed by the Precision Decomposition III Algorithm previously described by (De Luca et al., 2006), using the dEMG Analysis software (dEMG 1.1 Analysis, Delsys, Inc., Natick, MA, USA). The surface EMG signal was decomposed into constituent MU action potential trains with an accuracy of ≥ 90%, using the Decompose-Synthesize-Decompose-Compare process described by (Nawab et al., 2010). For each individual MU action potential waveform, the mean firing rate, recruitment threshold, and derecruitment threshold were analyzed. The MU mean firing rate was calculated by selecting the middle six seconds of the 10-second plateau region of each trapezoid. The recruitment threshold and derecruitment threshold were expressed as the first and last MU action potential firing instances, respectively, and was shown as a percentage of the baseline MVC (%Pre-MVC). To ensure the recruitment threshold and derecruitment threshold of MU action potential firing instances were correct for each MU action potential, the Decompose-Synthesize-Decompose-Compare accuracy test was used, and only the MUs with at least 90% accuracy levels were used for subsequent analyses. Then, linear regression analyses were performed to assess the relationship between MU recruitment threshold and mean firing rate, and the relationship between MU recruitment threshold and derecruitment threshold (De Luca & Hostage, 2010), yielding linear slope coefficients and y-intercepts. The trapezoid that yields a greater number of MU and a higher r^2 from the linear regression analysis was selected for statistical analysis, and those with an $r^2 < 0.60$ were excluded during data analyses.

Statistical Analysis

Normality was assessed via the Shapiro-Wilk test, determination of skewness and kurtosis values being within ± 2, and through visual inspection of Q-Q plots (for outlier identification) and histograms for all dependent variables. If outliers were present the data was analyzed with and without the outliers. Test-retest reliability for maximal voluntary force (of the elbow flexors and knee extensors), EMG amplitude and EMG median frequency (of biceps brachii, vastus lateralis, and vastus medialis) values between the three visits (VOL+NMES vs. VOL vs. Control) were assessed using the intraclass correlation coefficient (ICC) model (3,1). A two-way mixed effect model based on single measures and absolute agreement was used. Mean estimations along with 95% confidence intervals (CI) were reported for each ICC. Interpretation was as follows: <0.50, poor; between 0.50 and 0.75, fair; between 0.75 and 0.90, good; above

0.90, excellent (Koo & Li, 2016). Separate two-way (condition: VOL+NMES vs. VOL vs. Control × time: pre vs. post) repeated measures analyses of variance (ANOVAs) were completed to compare the neuromuscular functions, including the isometric maximal voluntary force of the elbow flexors and knee extensors, and the normalized EMG amplitude and EMG median frequency values for the biceps brachii, vastus lateralis, and vastus medialis during the MVC. For the MU decomposition analysis, separate two-way (condition: VOL+NMES vs. VOL vs. Control × time: pre vs. post) repeated measures ANOVAs were completed to compare the linear slope coefficients and y-intercepts of the MU mean firing rate vs. recruitment threshold, and recruitment threshold vs. derecruitment threshold relationships for the biceps brachii, vastus lateralis, and vastus medialis muscles, separately. For all repeated measures comparisons, the sphericity assumption was tested using Mauchly's test. If sphericity was violated, Greenhouse-Geisser (G-G) adjusted F and degrees of freedom were applied. When appropriate, follow-up analysis for main effects included paired-sample t-tests with Bonferroni corrections. For significant interactions follow-up analysis included simple effects ANOVAs comparing the pre-to-post change score between condition. Effect sizes (Partial eta-squared [η_p^2]) were computed to assess the condition effects, and were categorized as small (0.01), medium (0.06), and large (0.14), as suggested by (Cohen, 1973). To assess the magnitude of the condition effects on the neuromuscular functions and the slopes of the MU mean firing rate vs. recruitment threshold relationship, Cohen's d ESs were computed, and were categorized as small (0.2), medium (0.5), and large (0.8) (Cohen, 1988). All data are reported as mean ± standard deviation (SD) unless stated otherwise. All statistical tests were conducted using the Statistical Package for the Social Sciences software (IBM SPSS Statistics 28.0, IBM, Armonk, NY, USA) with an α set to 0.05.

CHAPTER IV: RESULTS

Data are presented as mean ± standard deviation (SD) in the text and tables, unless otherwise stated. Participant characteristics are presented in Table 1. The distributions (Table 2) were significantly non-normal, and skewness and/or kurtosis were not within agreeable limits for several variables (George & Mallery, 2017).

Test-retest Reliability

The ICCs for the elbow flexors and knee extensors maximal voluntary force were excellent, being .932 (.886-.962) and .925 (.874-.958), respectively. The ICCs for the biceps brachii EMG amplitude and EMG median frequency were good and fair, being .707 (.555-.825) and .559 (.372-.722), respectively. The ICCs for the vastus lateralis EMG amplitude and EMG median frequency were poor, being .277 (.072-.497) and .384 (.179-.589), respectively. The ICCs for the vastus medialis EMG amplitude and EMG median frequency were fair and poor, being .626 (.451-.771) and .162 (-.31-.388), respectively.

Neuromuscular Functions

Maximal Voluntary Force

Table 3 displays the pre-post data for the isometric maximal voluntary force of the elbow flexors for each participant. Not all subjects exhibited decreases in maximal voluntary force after the VOL and VOL+NMES exercise visits for the elbow flexors and knee extensors (e.g., Subject 2, Tables 3-4). The two-way repeated measures ANOVA comparing the average pre and post isometric maximal voluntary force of the elbow flexors showed a significant condition × time interaction $F(2, 70) = 15.347$, $p < .001$, $\eta_p^2 = .305$, along with significant main effects for condition $F(2, 70) = 6.404$, $p = .003$, $\eta_p^2 = .155$, and time $F(2, 35) = 22.084$, $p < .001$, $\eta_p^2 = .387$. The follow-up analysis comparing the pre-post change in maximal voluntary force for the elbow flexors between condition found a significant difference between the control (-3.78 ± 27.01 N) and VOL (-42.19 ± 53.76 N, $p < .001$, $d = .90$), and control and VOL+NMES (-45.81 ± 59.18 N, $p <.001$, $d = .91$). No other statistically significant differences were observed between the VOL and VOL+NMES conditions ($p = 1.00$, $d = .06$).

Table 4 displays the pre-post data for the isometric maximal voluntary force of the knee extensors for each participant. The two-way repeated measures ANOVA comparing the average pre and post isometric maximal voluntary force of the knee extensors showed a significant condition × time interaction $F(2, 70) = 21.841$, $p < .001$, $\eta_p^2 = .384$, along with significant main effects for condition $F(2, 70) = 29.867$, $p = < .001$, $\eta_p^2 = .460$, and time $F(2, 35) = 49.368$, $p < .001$, $\eta_p^2 = .585$. The follow-up analysis comparing the pre-post change in maximal voluntary force for the knee extensors between condition found a significant difference between the control (-12.52 ± 64.43 N) and VOL (-80.48 ± 65.29 N, $p < .001$ $d = 1.04$), and control and VOL+NMES (-93.07 ± 78.68 N, $p <.001$, $d = 1.12$). No other statistically significant differences were observed between the VOL and VOL+NMES conditions ($p = 1.00$, $d = .17$).

Electromyography Amplitude

Table 5 displays the average data for the post-exercise normalized EMG amplitude and EMG median frequency for the biceps brachii, vastus lateralis, and vastus medialis across all conditions. The two-way repeated measures ANOVA comparing the biceps brachii normalized EMG amplitude during the MVC showed no significant condition × time interaction $F(2, 70) = .011$, $p = .989$, $\eta_p^2 = .000$ or main effects for condition $F(2, 70) = .011$, $p = .989$, $\eta_p^2 = .000$ or time $F(1, 35) = .075$, $p = .786$, $\eta_p^2 = .002$. The two-way repeated measures ANOVA comparing the vastus lateralis normalized EMG amplitude during the MVC showed no significant condition × time interaction $F(2, 70) = .197$, $p = .821$, $\eta_p^2 = .006$ or main effect for condition $F(2, 70) = .197$, $p = .821$, $\eta_p^2 = .006$, but a main effect for time was observed $F(1, 35) = 6.064$, $p = .019$, $\eta_p^2 = .148$. Bonferroni-corrected pairwise comparisons revealed vastus lateralis normalized EMG amplitude to be significantly higher at the post-time point (109.7 ± 3.1%, $p = .019$, $d = .44$; collapsed across condition). The two-way repeated measures ANOVA comparing the vastus medialis normalized EMG amplitude during the MVC was completed with 35 subjects due to one subject having poor EMG vastus medialis amplitude data. The results showed a significant condition × time interaction $F\ (2, 68) = 6.061$, $p = .004$, $\eta_p^2 = .151$, along with significant main effects for condition $F(2, 68) = 6.061$, $p = .004$, $\eta_p^2 = .151$, and time $F(1, 34) = 9.687$, $p = .004$, $\eta_p^2 = .222$. The follow-up analysis comparing the pre-post change in EMG amplitude for the vastus medialis between conditions found a significant difference between the control (-2.40 ± 25.22%) and VOL+NMES (20.75 ± 34.66%, $p = .002$, $d = .61$). No other statistically significant differences were observed between the control and VOL conditions (13.47 ± 32.75%, $p = .054$, $d = .38$) and the VOL and VOL+NMES conditions ($p = .751$, $d = .22$).

Electromyography Median Frequency

Table 5 displays the data for the average post-exercise normalized EMG median frequency for the biceps brachii, vastus lateralis, and vastus medialis across all conditions. The two-way repeated measures ANOVA comparing the biceps brachii normalized EMG median frequency during the MVC showed no significant condition × time interaction $F(2, 70) = .864$, $p = .426$, $\eta_p^2 = .024$ or a main effect for condition $F(2, 70) = .864$, $p = .426$, $\eta_p^2 = .024$, but a main effect for time was observed $F(1, 35) = 7.217$, $p = .011$, $\eta_p^2 = .171$. Bonferroni-corrected pairwise comparisons revealed post-exercise biceps brachii normalized EMG median frequency to be significantly lower at the post-time point (95.17 ± 17.10%, $p = .011$, $d = .40$; collapsed across condition). The two-way repeated measures ANOVA comparing the post-exercise vastus lateralis normalized EMG median frequency during the MVC showed no significant condition × time interaction $F(2, 70) = .764$, $p = .470$, $\eta_p^2 = .021$ or main effects for condition $F(2, 70) = .764$, $p = .470$, $\eta_p^2 = .021$ or time $F(1, 35) = 3.082$, $p = .088$, $\eta_p^2 = .081$. The two-way repeated measures ANOVA comparing the post-exercise vastus medialis normalized EMG median frequency during the MVC showed a significant condition × time interaction $F(2, 70) = 6.858$, $p = .002$, $\eta_p^2 = .164$, and main effects for condition $F(2, 70) = 6.858$, $p = .002$, $\eta_p^2 = .164$, and time $F(1, 35) = 4.524$, $p = .041$, $\eta_p^2 = .114$. The follow-up analysis comparing the pre-post change in EMG median frequency for the vastus medialis between conditions found a significant difference between the control (1.66 ± 19.14%) and VOL+NMES (10.62 ± 14.43%, $p = .009$, $d = .53$). No other statistically significant differences were observed between the control and VOL conditions (-3.95 ± 16.28%, $p = .270$, $d = .31$) and the VOL and VOL+NMES conditions ($p = .073$, $d = .95$).

Motor Unit Firing Properties

Motor Unit Mean Firing Rate vs. Recruitment Threshold Relationship

Table 6 shows the overall mean linear slope coefficients and y-intercepts of the MU mean firing rate versus recruitment threshold relationship for the biceps brachii, vastus lateralis, and vastus medialis for each condition. All data analyses were performed with 18 samples, due to poor data quality. The mean ± SD number of MUs for the biceps brachii prior to each condition were 16 ± 6, 18 ± 5, and 17 ± 6 per contraction for the control, VOL, and VOL+NMES conditions, respectively. After each condition, the number of MUs remained similar 17 ± 5, 20 ± 6, and 20 ± 6 per contraction for the control, VOL, and VOL+NMES conditions, respectively (Appendix Tables 8-10). After the VOL exercise, 9 participants had decreased linear slopes with increased y-intercepts; three participants had increased linear slopes with increased y-intercepts; three participants had decreased linear slopes with decreased y-intercepts; and three had increased linear slopes with decreased y-intercepts (Appendix Table 9). After the VOL+NMES exercise, 12 participants had decreased linear slopes with increased y-intercepts; three participants had decreased linear slopes with decreased y-intercepts; and three had increased linear slopes with decreased y-intercepts (Appendix Table 10). After combining the individual participant data, the slope coefficients showed no significant condition × time interaction $F(2, 34) = 1.022$, $p = .371$, $\eta_p^2 = .057$ or main effect for condition, $F(2, 34) = 1.019$, $p = .372$, $\eta_p^2 = .057$. Alternately, a significant main effect for time was observed $F(1, 17) = 9.469$, $p = .007$, $\eta_p^2 = .358$. Bonferroni-corrected pairwise comparisons revealed the slope coefficients were significantly more negative in the post- (-.704 ± .30) compared to the pre-exercise (-.601 ± .28, $p = .007$, $d = .35$, collapsed across condition, Table 5). For the y-intercepts, the results showed no significant condition × time interaction $F(2, 34) = .717$, $p = .496$, $\eta_p^2 = .047$ or main effects for condition $F(2, 34) = .840$, $p = .441$, $\eta_p^2 = .047$ or time $F(1, 17) = 2.910$, $p = .106$, $\eta_p^2 = .147$.

Appendix tables 11-13 show the overall mean linear slope coefficients and y-intercepts of the MU mean firing rate versus recruitment threshold relationship for the vastus lateralis for each condition. The two-way repeated measures ANOVAs comparing the linear slope coefficients and y-intercepts of the vastus lateralis were performed with four samples, due to poor data quality. For the slope coefficients, the results showed no significant condition × time interaction $F(2, 6) = 3.108$, $p = .118$, $\eta_p^2 = .509$ or main effects for condition $F(2, 6) = .322$, $p = .736$, $\eta_p^2 = .097$ or time $F(1, 3) = 4.246$, $p = .131$, $\eta_p^2 = .586$. For the y-intercepts, the results showed no significant condition × time interaction $F(2, 6) = 2.122$, $p = .201$, $\eta_p^2 = .414$ or main effects for condition $F(2, 6) = .164$, $p = .852$, $\eta_p^2 = .052$ or time $F(1, 3) = 6.555$, $p = .083$, $\eta_p^2 = .686$.

All data analyses for the vastus medialis were performed with seven samples, due to poor data quality. The mean ± SD number of MUs for the vastus medialis prior to each condition were 18 ± 5, 15 ± 2, and 13 ± 4 per contraction for the control, VOL, and VOL+NMES conditions, respectively. After each condition, the number of MUs remained similar 13 ± 4, 16 ± 5, and 15 ± 7 per contraction for the control, VOL, and VOL+NMES conditions, respectively (Appendix Tables 14-16). After the VOL exercise, five participants had decreased linear slopes with increased y-intercepts and two participants had decreased linear slopes with decreased y-intercepts (Appendix Table 15). After the VOL+NMES exercise, five participants had decreased linear slopes with increased y-intercepts and two participants had increased linear slopes with increased y-intercepts (Appendix Table 16). After combining the individual participant data, the slope coefficients showed no significant condition × time interaction $F(2, 12) = .115$, $p = .893$, $\eta_p^2 = .019$ or main effect for condition $F(2, 12) = .690$, $p = .521$, $\eta_p^2 = .103$. Alternately, a significant main effect for time was shown $F(1, 6) = 6.225$, G-G $p = .047$, $\eta_p^2 = .509$. Bonferroni-corrected pairwise comparisons revealed the slope coefficients were significantly more negative in the post- (-.777 ± .68) compared to the pre-exercise (-.404 ± .26), $p = .047$, $d = .73$, collapsed across condition, Table 5). For the y-intercepts, the results showed no significant condition × time interaction $F(2, 12) = 1.143$, $p = .351$, $\eta_p^2 = .160$ or main effect for condition $F(2, 12) = 1.673$, $p = .229$, $\eta_p^2 = .218$ or time $F(1, 6) = 3.559$, $p = .108$, $\eta_p^2 = .372$.

Motor Unit Recruitment Threshold vs. Derecruitment Threshold Relationship

Table 7 shows the overall mean linear slope coefficients and y-intercepts of the MU recruitment versus derecruitment threshold relationship for the biceps brachii, vastus lateralis, and vastus medialis for each condition. The mean ± SD number of MUs for the biceps brachii prior to, and after each condition were identical to the MU mean firing rate vs. recruitment threshold relationship section (Appendix Tables 17-19). After each condition, the number of MUs remained similar 17 ± 5, 20 ± 6, and 20 ± 6 per contraction for the control, VOL, and VOL+NMES conditions, respectively. After the VOL exercise, seven participants had increased linear slopes with decreased y-intercepts; six had decreased linear slopes with increased y-intercepts; three had increased linear slopes and increased y-intercepts; one had decreased linear slopes and decreased y-intercepts; and one had no change in slope and an increased y-intercept (Appendix Table 18). After the VOL+NMES exercise, eight participants had increased linear slopes with decreased y-intercepts; six had decreased linear slopes with increased y-intercepts; and four had increased linear slopes with increased y-intercepts (Appendix Table 19). For the slope coefficients, the results showed no significant condition × time interaction $F(2, 34) = .962$, $p = .392$, $\eta_p^2 = .054$ or main effect for condition $F(2, 34) = 2.608$, $p = .088$, $\eta_p^2 = .133$.

Alternately, a significant main effect for time was shown $F(1, 17) = 4.740$, $p = .044$, $\eta_p^2 = .218$. Bonferroni-corrected pairwise comparisons for time revealed the slope coefficients were significantly more positive in the post- (1.51 ± .50) compared to pre-exercise (1.35 ± .52, $p = .044$, $d = .31$, collapsed across condition). For the y-intercepts, the results showed no significant condition × time interaction $F(2, 34) = .416$, $p = .663$, $\eta_p^2 = .024$ or main effects for condition $F(2, 34) = .332$, $p = .720$, $\eta_p^2 = .019$ or time $F(1, 17) = 1.377$, $p = .257$, $\eta_p^2 = .075$.

Appendix tables 20-22 show the overall mean linear slope coefficients and y-intercepts of the MU recruitment versus derecruitment threshold relationship for the for the vastus lateralis for each condition. The two-way repeated measures ANOVAs comparing the linear slope coefficients and y-intercepts of the vastus lateralis were performed with four samples, due to poor data quality. For the slope coefficients, the results showed no significant condition × time interaction $F(2, 6) = 2.155$, $p = .197$, $\eta_p^2 = .418$ or main effects for condition $F(2, 6) = 1.820$, $p = .241$, $\eta_p^2 = .378$ or time $F(1, 3) = .579$, $p = .502$, $\eta_p^2 = .162$. For the y-intercepts, the results showed no significant condition × time interaction $F(2, 6) = 1.524$, $p = .292$, $\eta_p^2 = .337$ or main effects for condition $F(2, 6) = 1.519$, $p = .293$, $\eta_p^2 = .336$ or time $F(1, 3) = .554$, $p = .511$, $\eta_p^2 = .156$.

Appendix tables 23-25 show the overall mean linear slope coefficients and y-intercepts of the MU recruitment versus derecruitment threshold relationship for the for the vastus medialis for each condition. The two-way repeated measures ANOVAs comparing the linear slope coefficients and y-intercepts of the vastus medialis were performed with seven samples, due to poor data quality. For the slope coefficients, the results showed no significant condition × time interaction $F(2, 12) = .622$, $p = .553$, $\eta_p^2 = .094$ or main effects for condition $F(2, 12) = .011$, $p = .990$, $\eta_p^2 = .002$ or time $F(1, 6) = 1.514$, $p = .265$, $\eta_p^2 = .202$. For the y-intercepts, the results showed no significant condition × time interaction $F(2, 12) = .849$, $p = .452$, $\eta_p^2 = .124$ or main effects for condition $F(2, 12) = .027$, $p = .973$, $\eta_p^2 = .005$ or time $F(1, 6) = 1.293$, $p = .299$, $\eta_p^2 = .177$.

Table 1. Participant Characteristics

	Age (yr)			Mass (kg)			Height (cm)			Stimulation Intensity (mA)					
										Elbow Flexor			Knee Extensor		
	Min	*Max*	*Mean (SD)*	*Min*	*Max*	*Mean (SD)*	*Min*	*Max*	*Mean (SD)*	*Min*	*Max*	*Mean (SD)*	*Min*	*Max*	*Mean (SD)*
Male	18	33	25(5)	66.00	101.50	83.43(10.53)	161.00	192.60	178.56(8.39)	19	99	45(25)	31	137	72(35)
Female	18	28	21(3)	48.40	80.10	62.83(8.38)	158.20	176.70	166.89(5.65)	15	45	25(8)	20	52	34(10)
Total	18	33	24(5)	48.40	101.50	71.98(13.91)	158.20	192.60	172.07(9.06)	15	99	34(20)	20	137	51(31)

Note. mA = milliamp; N = newton; SD = standard deviation

Table 2. Normality, skewness, and kurtosis

	Shapiro-Wilk [*W(p)*]			Skewness			Kurtosis		
	Control	VOL	VOL+NMES	Control	VOL	VOL+NMES	Control	VOL	VOL+NMES
MVF									
EF	.916(.10)*	.897(.003)*	.925(.017)*	.361	.441	.414	-1.256	-1.247	-1.078
KE	.929(.024)*	.918(.011)*	.922(.014)*	.607	.609	.888	-.689	-.803	.140
EMGa									
BB	.952(.118)	.851(<.001)*	.910(.007)*	.858	1.438	1.148	.680	1.823	1.207
VL	.944(.070)*	.469(<.001)*	.917(.010)*	.825	4.798$^{\$}$	.964	.467	25.987$^{\$}$	.450
VM	.950(.101)	.928(.021)	.926(.019)*	.688	.893	1.082	-.099	.778	1.225
EMG MDF									
BB	.860(<.001)*	.849(<.001)*	.938(.044)*	1.248	1.228	.904	.870	.624	.516
VL	.936(.038)*	.910(.006)*	.949(.094)	.904	1.058	.821	.743	1.747	.905
VM	.593(<.001)*	.965(.308)	.942(.060)	4.093$^{\$}$	.271	.737	20.879$^{\$}$	-.275	.104

Note. BB = biceps brachii; EF = elbow flexors; EMG = electromyography; EMG = EMG amplitude; EMG MDF = EMG median frequency; VL = vastus lateralis; VM = vastus medialis; VOL = voluntary exercise; VOL+ NMES = voluntary exercise with neuromuscular electrical stimulation

*Significant non-normal distribution $p < 0.05$; $^{\$}$Skewness and/or Kurtosis were outside agreeable limits of ± 2

Table 3. Individual subject data for the isometric strength values pre- and immediately post-exercise conditions for the elbow flexors

	Control			VOL			VOL+NMES			Control vs. VOL	Control vs. VOL+NMES	VOL vs. VOL+NMES
Subject	Pre-MVF (N)	Post-MVF (N)	Difference	Pre-MVF (N)	Post-MVF (N)	Difference	Pre-MVF (N)	Post-MVF (N)	Difference	Difference	Difference	Difference
1	181.82	181.11	0.71	192.60	166.28	26.32	169.76	171.00	-1.24	-25.61	1.95	27.56
2	258.74	231.52	27.22	228.18	254.17	-25.99	264.40	317.04	-52.64	53.21	79.86	26.65
3	172.82	160.31	12.51	127.57	141.87	-14.30	136.47	133.82	2.65	26.81	9.86	-16.95
4	140.01	205.34	-65.33	195.24	212.69	-17.45	194.13	192.86	1.27	-47.88	-66.6	-18.72
5	193.31	161.98	31.33	191.56	170.25	21.31	222.06	126.01	96.05	10.02	-64.72	-74.74
6	133.39	142.98	-9.59	211.40	93.47	117.93	214.89	221.39	-6.50	-127.52	-3.09	124.43
7	117.24	158.49	-41.25	163.15	217.59	-54.44	155.52	150.53	4.99	13.19	-46.24	-59.43
8	201.11	195.38	5.73	210.37	188.72	21.65	207.37	178.20	29.17	-15.92	-23.44	-7.52
9	220.24	199.59	20.65	200.14	186.03	14.11	176.82	168.31	8.51	6.54	12.14	5.6
10	197.73	221.66	-23.93	221.39	220.49	0.90	217.43	226.28	-8.85	-24.83	-15.08	9.75
11	426.29	434.08	-7.79	366.31	333.72	32.59	338.80	311.91	26.89	-40.38	-34.68	5.7
12	127.99	152.62	-24.63	114.07	108.82	5.25	115.97	132.60	-16.63	-29.88	-8	21.88
13	196.57	212.88	-16.31	189.79	196.89	-7.10	192.12	194.82	-2.70	-9.21	-13.61	-4.4
14	216.11	205.41	10.70	222.25	199.95	22.30	234.36	200.38	33.98	-11.6	-23.28	-11.68
15	346.22	378.84	-32.62	347.65	352.20	-4.55	319.21	368.50	-49.29	-28.07	16.67	44.74
16	307.41	259.85	47.56	202.82	129.42	73.40	309.35	213.33	96.02	-25.84	-48.46	-22.62
17	394.20	360.99	33.21	412.36	358.72	53.64	433.91	312.70	121.21	-20.43	-88	-67.57
18	223.15	229.63	-6.48	220.03	197.10	22.93	210.28	217.08	-6.80	-29.41	0.32	29.73
19	480.60	459.60	21.00	471.46	345.37	126.09	516.36	315.57	200.79	-105.09	-179.79	-74.7
20	201.28	215.63	-14.35	138.21	93.20	45.01	210.28	158.12	52.16	-59.36	-66.51	-7.15
21	267.74	290.51	-22.77	224.00	170.62	53.38	304.86	227.71	77.15	-76.15	-99.92	-23.77
22	288.45	326.84	-38.39	339.71	263.37	76.34	354.06	299.00	55.06	-114.73	-93.45	21.28
23	344.37	320.80	23.57	412.25	247.78	164.47	407.26	343.94	63.32	-140.9	-39.75	101.15
24	474.90	486.16	-11.26	466.00	411.67	54.33	387.63	375.03	12.60	-65.59	-23.86	41.73
25	386.90	380.69	6.21	349.29	360.32	-11.03	420.30	371.74	48.56	17.24	-42.35	-59.59
26	415.96	425.12	-9.16	470.29	344.42	125.87	364.28	231.57	132.71	-135.03	-141.87	-6.84
27	308.67	293.98	14.69	286.70	271.82	14.88	264.24	222.50	41.74	-0.19	-27.05	-26.86
28	435.89	374.41	61.48	424.81	299.30	125.51	381.06	218.84	162.22	-64.03	-100.74	-36.71
29	216.59	211.40	5.19	263.40	184.92	78.48	202.24	225.19	-22.95	-73.29	28.14	101.43
30	240.96	233.90	7.06	236.29	188.04	48.25	210.39	136.99	73.40	-41.19	-66.34	-25.15
31	471.90	422.10	49.80	482.90	318.52	164.38	433.60	350.03	83.57	-114.58	-33.77	80.81
32	185.77	169.34	16.43	172.37	154.63	17.74	202.80	162.94	39.86	-1.31	-23.43	-22.12
33	432.92	428.09	4.83	440.48	428.09	12.39	452.08	381.49	70.59	-7.56	-65.76	-58.2
34	219.12	195.51	23.61	208.38	210.17	-1.79	201.39	169.56	31.83	25.4	-8.22	-33.62
35	455.68	432.32	23.36	395.10	351.11	43.99	408.55	268.58	139.97	-20.63	-116.61	-95.98
36	389.11	376.14	12.97	402.20	310.16	92.04	437.75	327.32	110.43	-79.07	-97.46	-18.39
Mean	**285.31**	**281.53**	**3.78**	**283.35**	**241.16**	**42.19**	**285.33**	**239.52**	**45.81**	**-38.41**	**-42.03**	**-3.62**
SD	**113.91**	**105.52**	**27.01**	**113.50**	**90.89**	**53.76**	**107.29**	**79.93**	**79.93**	**49.05**	**51.19**	**51.09**
CI			**-8.70, 16.26**			**17.35, 67.03**			**18.47, 73.15**	**-61.07, -15.75**	**-65.68, -18.38**	**-27.22, 19.98**

Note. MVF = maximal voluntary force; N = Newton; VOL+ NMES = voluntary exercise with neuromuscular electrical stimulation; VOL = voluntary exercise
SD = standard deviation; CI = Confidence interval

Table 4. Individual subject data for the isometric strength values pre- and immediately post-exercise conditions for the knee extensors

Subject	Control			VOL			VOL+NMES			Control vs. VOL	Control vs. VOL+NMES	VOL vs. VOL+NMES
	Pre-MVF (N)	Post-MVF (N)	Difference	Pre-MVF (N)	Post-MVF (N)	Difference	Pre-MVF (N)	Post-MVF (N)	Difference	Difference	Difference	Difference
1	290.30	342.43	-52.13	351.20	315.66	35.54	287.18	255.98	31.20	-38.36	-34.02	4.34
2	419.93	426.55	-6.62	391.23	343.20	48.03	398.01	259.11	138.90	-0.69	-91.56	-90.87
3	339.02	281.09	57.93	206.15	161.51	44.64	213.04	176.61	36.43	17.79	26.00	8.21
4	424.70	397.69	27.01	370.69	368.25	2.44	355.86	370.84	-14.98	-42.58	-25.16	17.42
5	320.75	289.40	31.35	324.06	274.00	50.06	259.48	186.93	72.55	13.01	-9.48	-22.49
6	317.73	344.37	-26.64	362.64	343.63	19.01	393.30	324.35	68.95	43.37	-6.57	-49.94
7	311.22	308.15	3.07	251.11	281.93	-30.82	243.91	204.25	39.66	-166.10	-236.58	-70.48
8	339.87	353.26	-13.39	317.36	227.28	90.08	308.30	193.71	114.59	-77.64	-102.15	-24.51
9	264.51	237.72	26.79	219.55	182.59	36.96	244.18	155.11	89.07	212.62	160.51	-52.11
10	285.06	271.82	13.24	273.09	242.43	30.66	237.13	224.53	12.60	27.38	45.44	18.06
11	388.48	391.30	-2.82	321.75	255.03	66.72	339.64	282.14	57.50	-74.56	-65.34	9.22
12	277.64	203.24	74.40	178.25	141.34	36.91	230.09	168.45	61.64	-18.43	-43.16	-24.73
13	328.48	329.80	-1.32	277.64	237.19	40.45	298.93	239.73	59.20	-4.00	-22.75	-18.75
14	316.19	306.40	9.79	334.46	135.04	199.42	322.13	249.42	72.71	-173.68	-46.97	126.71
15	661.14	613.80	47.34	655.53	560.63	94.90	624.76	476.01	148.75	-143.04	-196.89	-53.85
16	455.73	393.30	62.43	446.36	366.71	79.65	415.27	295.57	119.70	-17.76	-57.81	-40.05
17	623.39	663.53	-40.14	677.88	561.69	116.19	825.09	472.99	352.10	-168.32	-404.23	-235.91
18	298.56	296.18	2.38	323.40	267.79	55.61	355.91	274.78	81.13	-62.23	-87.75	-25.52
19	687.46	624.39	63.07	655.69	458.96	196.73	589.44	412.63	176.81	-138.80	-118.88	19.92
20	348.57	380.23	-31.66	274.04	214.47	59.57	320.64	269.93	50.71	-32.56	-23.70	8.86
21	485.81	423.43	62.38	344.21	209.70	134.51	496.48	316.09	180.39	-103.16	-149.04	-45.88
22	396.47	593.39	-196.92	409.24	287.02	122.22	378.84	274.73	104.11	-148.86	-130.75	18.11
23	459.65	447.21	12.44	500.95	314.82	186.13	484.20	339.92	144.28	-183.06	-141.21	41.85
24	643.24	580.10	63.24	607.45	393.67	213.78	538.77	360.99	177.78	-227.18	-191.18	36.00
25	444.35	386.31	58.04	445.43	362.58	82.85	434.72	363.71	71.01	-56.05	-44.21	11.84
26	586.32	594.16	-7.84	688.85	527.33	161.52	731.10	508.63	222.47	-148.28	-209.23	-60.95
27	447.44	411.88	35.56	417.13	377.62	39.51	405.26	397.16	8.10	34.89	66.30	31.41
28	494.55	476.07	18.48	588.05	391.01	197.04	438.89	424.88	14.01	-198.36	-15.33	183.03
29	202.55	221.30	-18.75	259.65	187.78	71.87	204.41	185.93	18.48	-62.07	-8.68	53.39
30	331.40	371.00	-39.60	350.95	352.82	-1.87	306.19	257.41	48.78	4.25	-46.40	-50.65
31	564.13	527.68	36.45	565.70	439.63	126.07	611.31	396.96	214.35	-157.73	-246.01	-88.28
32	246.45	297.87	-51.42	249.16	247.16	2.00	254.59	265.01	-10.42	33.56	45.98	12.42
33	695.50	669.76	25.74	695.50	589.02	106.48	710.66	540.99	169.67	-125.23	-188.42	-63.19
34	260.12	251.29	8.83	272.57	225.68	46.89	218.23	202.18	16.05	-86.50	-55.66	30.84
35	474.79	522.93	-48.14	454.41	459.60	-5.19	505.15	468.33	36.82	-46.22	-88.23	-42.01
36	572.75	510.85	61.90	558.73	418.03	140.70	553.96	388.53	165.43	-131.87	-156.60	-24.73
Mean	**416.78**	**404.26**	**12.52**	**406.11**	**325.63**	**80.48**	**403.75**	**310.68**	**93.07**	**-67.96**	**-80.55**	**-12.59**
SD	**137.45**	**128.87**	**64.43**	**152.34**	**121.16**	**65.29**	**160.58**	**105.20**	**78.68**	**90.16**	**105.61**	**67.07**
CI			**-17.24, 42.29**			**50.32, 110.64**			**56.72, 129.42**	**-109.61, -26.30**	**-129.33, -31.76**	**-43.58, 18.39**

Note. MVF = maximal voluntary force; N = Newton; VOL+ NMES = voluntary exercise with neuromuscular electrical stimulation; VOL = voluntary exercise
SD = standard deviation; CI = Confidence interval

Table 5. Individual subject data for the post exercise normalized electromyography amplitude and median frequency for each muscle (%)

	Control		VOL		VOL+NMES	
	Mean(SD)	% Change	Mean(SD)	% Change	Mean(SD)	% Change
EMGa						
BB	99.37(23.39)	-.63%	98.26(46.01)	-1.74%	99.34(38.98)	-0.66%
VL	107.98(19.70)	7.98%	111.66(36.75)	11.66%	109.37(34.53)	9.37%
VM	100.39(19.15)	.39%	113.47(32.75)	13.47%	120.75(34.66)$	20.75%
EMG MDF						
BB	97.02(19.31)	-2.98%	96.20(16.60)	-3.80%	92.29(15.21)	-7.71%
VL	99.59(14.22)	-.41%	95.78(14.83)	-4.22%	95.84(18.07)	-4.16%
VM	101.66(19.14)	1.66%	96.05(16.28)	-3.95%	89.38(14.43)$	-10.62%

Note. BB = biceps brachii; EF = elbow flexors; EMG = electromyography; EMG = EMG amplitude; EMG MDF = EMG median frequency; VL = vastus lateralis; VM = vastus medialis; VOL = voluntary exercise; VOL+ NMES = voluntary exercise with neuromuscular electrical stimulation

% = All data are normalized and presented as a percentage of the pre-exercise isometric maximal voluntary contraction force, meaning the pre-value was always set to 100%.

$ = Denotes significant difference compared to the control condition

Table 6. Mean slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the biceps brachii (BB), vastus lateralis (VL), and vastus medialis (VM) pre- and post-exercise conditions

	Control				VOL				VOL+NMES			
	Pre		Post		Pre		Post		Pre		Post	
	Slope coefficient	y-intercept	Slope coefficient	y-intercept	Slope coefficient	y-intercept	Slope coefficient	y-intercept	Slope coefficient	y-intercept	Slope coefficient	y-intercept
BB	-.602	30.09	-.621	29.91	-.594	30.50	-.707	33.37	-.607	30.40	-.783	34.14
	(.274)	(8.27)	(.329)	(11.32)	(.280)	(10.63)	(.302)	(8.82)	(.290)	(8.54)	(.275)	(9.11)
VL	-.358	23.20	-.327	22.20	-.356	19.39	-.460	23.59	-.278	20.23	-.554	25.75
	(.116)	(2.85)	(.506)	(2.21)	(.237)	(4.55)	(.198)	(2.46)	(.190)	(4.43)	(.172)	(6.88)
VM	-.434	20.72	-.740	23.49	-.496	23.01	-.936	32.01	-.283	19.19	-.654	26.67
	(.260)	(4.42)	(.736)	(5.50)	(.304)	(5.93)	(.534)	(12.63)	(.172)	(3.37)	(.809)	(15.13)

Note. pps = pulses per second; MVC = maximal voluntary contraction; VOL = voluntary exercise visit; VOL+ NMES = voluntary exercise visit with neuromuscular electrical stimulation; Data are mean ± standard deviation (SD)

Table 7. Mean slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the biceps brachii (BB), vastus lateralis (VL), and vastus medialis (VM) pre- and post-exercise conditions

	Control				VOL				VOL+NMES			
	Pre		Post		Pre		Post		Pre		Post	
	Slope coefficient	y-intercept	Slope coefficient	y-intercept	Slope coefficient	y-intercept	Slope coefficient	y-intercept	Slope coefficient	y-intercept	Slope coefficient	y-intercept
BB	1.27	-14.04	1.30	-11.80	1.50	-18.35	1.61	-13.02	1.27	-14.71	1.61	-15.44
	(.538)	(12.60)	(.416)	(12.20)	(.471)	(16.74)	(.378)	(11.45)	(.556)	(17.07)	(.634)	(21.28)
VL	.943	4.72	.803	6.43	.911	7.14	1.19	-.709	.977	3.16	1.37	-1.73
	(.239)	(3.95)	(.226)	(6.17)	(.486)	(3.18)	(.372)	(8.35)	(.436)	(4.79)	(.479)	(13.14)
VM	1.25	3.98	1.40	.421	1.01	8.97	1.69	-6.10	1.13	5.82	1.62	-.310
	(.355)	(4.18)	(.693)	(10.44)	(.561)	(7.85)	(1.04)	(28.10)	(.433)	(7.59)	(1.59)	(28.72)

Note. BB = biceps brachii; VL = vastus lateralis; VM = vastus medialis; VOL+ NMES = voluntary exercise visit with neuromuscular electrical stimulation; VOL = voluntary exercise visit; pps = pulses per second; MVC = maximal voluntary contraction; Data are mean ± standard deviation (SD)

CHAPTER V: DISCUSSION

The aim of this study was to compare the neuromuscular functions and the MU firing properties in the elbow flexors and knee extensors after performing a novel fatigue protocol with (VOL+NMES) and without (VOL) neuromuscular electrical stimulation. The key findings from this study were: 1) the maximal voluntary force was impaired to a similar extent in both the elbow flexors and knee extensors after VOL and VOL+NMES exercise (see tables 3-4); 2) vastus lateralis normalized EMG amplitude was significantly higher post-exercise (collapsed across condition), vastus medialis normalized EMG amplitude was significantly higher post VOL+NMES and VOL exercise within each condition, and compared to the control; 3) biceps brachii normalized EMG median frequency was significantly lower post-exercise (collapsed across condition), vastus medialis normalized EMG median frequency was significantly lower post-VOL+NMES exercise within condition, and compared to the control; 4) the slope coefficients of the MU mean firing rate vs. recruitment threshold relationship were more negative post-exercise (collapsed across conditions) in the biceps brachii and vastus medialis; and 5) the slope coefficients of the MU recruitment threshold vs. derecruitment threshold relationship were more positive post-exercise (collapsed across conditions) in the biceps brachii.

Maximal Voluntary Force

We provide evidence that the decrease in maximal voluntary force immediately post-exercise was similar between the VOL and VOL+NMES conditions for both the elbow flexors and knee extensors (Tables 3-4). Two things are important to mention as they are likely the most influential factors involved in the changes in maximal voluntary force, 1) NMES alone has been shown to be more metabolically demanding compared to VOL alone (Hamada et al., 2004; Vanderthommen et al., 2003), and 2) the MU recruitment order in NMES is spatially fixed and disordered (Barss et al., 2018; Bickel et al., 2011). Importantly, as mentioned previously, a primary focus of our study was to examine the effects of adding neuromuscular electrical stimulation onto VOL exercise because previous research has yet to examine the combined effect on maximal voluntary force (and MU firing properties as well), but only the metabolic demand during cycling exercise.

For example, Hamada et al. (2004) compared low-intensity VOL cycling (i.e., 20-minutes supine at 50 rpms) to NMES (i.e., 20-Hertz, milliamp intensity not reported) at equivalent exercise intensities (based on oxygen consumption), and found NMES increased the oxidation of carbohydrates, uptake of glucose in the whole body, and energy consumption more than VOL cycling. More recently, Wahl et al. (2012) found VOL+NMES (i.e., 30-Hertz, maximal tolerable intensity of NMES) cycling (i.e., stepwise cycling protocol starting at 100 Watts and increasing 40 Watts every 5 minutes) to produce greater metabolic changes (e.g., higher lactate and respiratory exchange ratio) when compared to VOL cycling (Wahl et al., 2012). Based on these findings it is likely that our VOL and VOL+NMES fatiguing protocols were both metabolically demanding (i.e., the force decreased significantly compared to the control condition for both conditions), yet this is only speculatory as our design was not structured to measure such outcomes. Additionally, there was no difference in force decrease between the VOL and VOL+NMES conditions for either muscle even though NMES was superimposed at the maximal tolerable intensity. This is a difficult finding to explain but it may be a result of the maximal tolerable stimulation level not being high enough. Typically, when providing maximal NMES the goal would be to evoke near or full tetanic contractions. Although not specifically measured in our study, it was very unlikely that any participants reached stimulation levels high enough to evoke such a response due to the occurrence of elevated levels of discomfort. These results are partially supported by the size of the effect. For example, in the elbow flexors, large ESs were observed regarding the change in maximal voluntary force between the VOL+NMES and control (d = .91) and VOL and control (d = .90) conditions, and a trivial ES was observed between the VOL+NMES and VOL condition (d = .02). Similarly, in the knee extensors, large ESs were observed regarding the change in maximal voluntary force between the VOL+NMES and control (d = 1.12) and VOL and control (d = 1.04) conditions, and a small ES was observed between the VOL+NMES and VOL condition (d = .17). Thus, the VOL+NMES and VOL exercise conditions imposed a greater effect in the knee extensors than in the elbow flexors. It is also plausible that the intensity level of the VOL exercise was high enough, causing a reduction in the effectiveness of the superimposed NMES. This is supported by the findings of Watanabe et al. (2021) who had participants perform cycling exercise at randomized intensities (i.e., 3-minutes at each intensity and 60-rpm) set as a percentage of the participant's known ventilatory threshold (i.e., 50%, 75%, 100%, and 175%) with and without NMES. It was reported that oxygen consumption, lactate, and the respiratory exchange ratio were all significantly greater in the VOL+NMES group, compared to VOL group (Watanabe et al., 2021). The authors reported that, as exercise intensity increased above the ventilatory threshold, the magnitude of the difference in oxygen consumption decreased, and suggested this to be a result of MU recruitment overlap between the two conditions (Watanabe et al., 2021). This means, if maximal VOL efforts are suggested to recruit all muscle fibers and their MUs, then the superimposition of NMES could not recruit any more muscle fibers or MUs (Hortobagyi et al., 1992; Koutedakis et al., 1995). Thus, our isometric fatiguing protocol of 50% of maximal voluntary force used in our study may have created a situation where the addition of NMES did not augment the recruitment of more muscle fibers/MUs because no statistically significant differences were seen between the two exercise conditions. Caution should be used when extrapolating however, especially since these studies used cycling as a fatiguing protocol, an entirely different motor movement than isometric fatiguing exercise.

Electromyography Amplitude and Median Frequency

The maximal voluntary force results are partially corroborated by the similar responses in EMG amplitude between the VOL and VOL+NMES conditions for the vastus lateralis and vastus medialis muscles, as no statistically significant finding was observed in the biceps brachii. The vastus medialis muscle demonstrated significantly higher post-exercise normalized EMG amplitude in the VOL+NMES and VOL, compared to the control conditions. Previous studies have shown increased normalized EMG amplitude during the MVC through a variety of differing fatiguing protocols and muscles. For example, Clark et al. (2005) demonstrated increased EMG amplitude in both the vastus lateralis and vastus medialis after performing a sustained submaximal isometric contraction at 25% of MVC to task failure (Clark et al., 2005) and suggested this to be a result of changes in central activation (although this was speculatory because it was not directly measured). Carr & Ye (2020) showed a decrease in EMG amplitude in both the biceps brachii and vastus lateralis after performing maximal isometric fatiguing exercise (i.e., 6 repetitions, 30-seconds each, 30-seconds rest). Physiologically, several factors may be playing a role. First, increases in EMG amplitude are thought to be attributed to increases in MU recruitment and/or discharge rate of the recruited MUs (De Luca, 1984). In addition, during sustained fatiguing exercise (maximal or submaximal) the neural drive to the muscle must increase to overcome any fatigue-related loss in force, and thus, may be presented as an increase in normalized EMG amplitude (measured during the MVC). Second, sustained submaximal contractions are known to have greater plasticity, meaning, the central nervous system can continually recruit higher-threshold MUs as neural drive increases to overcome any force loss in the active muscle fibers. These factors are based on changes that occur during VOL exercise and not VOL+NMES. As previously mentioned, if NMES causes preferential recruitment of higher-threshold MUs then it would seem possible to see an even greater increase in EMG amplitude (compared to VOL). But again, this could be a result of the stimulation level being too low (i.e., did not penetrate deeper into the muscle volume, recruiting more muscle fibers), therefore, the VOL contraction aspect of the VOL+NMES condition may have been able to 'override' the stimulation.

Changes in the frequency spectrum of the EMG signal (i.e., compression) are thought to be explained by alterations in the muscle fiber conduction velocity (Lindstrom et al., 1970) and changes in the shape of the MU action potential (De Luca, 1997) and the EMG median frequency is particularly sensitive to changes in the intramuscular metabolic environment (e.g., increased [H^+, P_i, K^+]) (Merletti et al., 1984). EMG median frequency decreased in the VOL+NMES condition compared to the control condition in the vastus medialis only and an overall decrease (collapsed across condition) in EMG median frequency in the biceps brachii was observed. Mechanistically, a decrease in EMG median frequency suggests that the muscle fiber action potential shapes have widened (i.e., longer time to complete). This would reduce the muscle fiber conduction velocity and would be due to peripheral accumulation of metabolites in the exercising muscle. Since NMES is known to recruit more fatigable higher-threshold (i.e., larger Type-II MUs) and cause non-physiologically high discharge rates of MUs it seems possible that the nature of VOL+NMES caused more peripheral fatigue in the vastus medialis only. Yet, table 5 shows that normalized EMG median frequency did decrease across all muscles in the VOL+NMES and VOL conditions. It is difficult to determine why there were no differences between the VOL+NMES and VOL conditions, which goes back to a previous point. The VOL exercise was intense enough (overall) that the addition of NMES did not increase the intensity any further.

A final piece that may have impacted the neuromuscular function findings is specific to our fatiguing protocol. We had participants perform a novel fatiguing protocol of five sets of 10-second long submaximal (i.e., 50% MVC) isometric contractions with two trapezoids performed between each set that was not to task failure. As minimal rest as possible was provided before, between, and after each trapezoid, equating to 12-seconds of total rest for each pair of trapezoids. The rest was unavoidable due to the nature of the software used to perform the exercise protocol (Delsys, Inc., Natick, MA, USA). We did not want task failure to occur because the participants would not have been able to fully complete the trapezoid contractions, which were used for analysis of the MU firing properties.

Motor Unit Mean Firing Rate vs. Recruitment Threshold Relationship

Our study aimed to examine any changes in the MU mean firing rate vs. recruitment threshold relationship after performing VOL and VOL+NMES exercise. This approach is novel as no study has examined the motor control strategy after fatiguing isometric exercise combined with electrical stimulation. Previous research performed by De Luca and Hostage (2010) had participants perform a ramp MVC protocol (i.e., MVCs at 20, 50, 80, and 100%) in the tibialis anterior, first dorsal interosseous, and vastus lateralis to examine changes in the relationship of the MU mean firing rate vs. recruitment threshold. In general, they determined that the motor control strategy was similar across muscles (i.e., the slope of the linear regression line to be less negative [more flat] and an increased y-intercept, and proposed the changes to be a result of recruiting newer higher threshold MUs to maintain the increase in required force (De Luca & Hostage, 2010). To examine changes in this relationship in the vastus lateralis and vastus medialis during fatiguing exercise, Stock et al. (2012) employed a fatiguing protocol involving 10 maximal isometric knee extension contractions (10 seconds on/off). They found a significant increase in the mean linear slope coefficients (i.e., less negative slope) and a decrease in the y-intercepts for the MU mean firing rate vs. recruitment threshold relationship for the vastus lateralis only. The authors suggested that an increase in drive to the motoneuron pool – meaning more recruitment of higher-threshold MUs – occurred, to counteract any fatigue-related loss in force (Stock et al., 2012). In our study, the typical changes in the relationship between the MU mean firing rate and recruitment threshold (i.e., the mean linear slope coefficient became more negative, and the y-intercept increased) were not observed in the biceps brachii in most subjects in the VOL+NMES and VOL conditions (Tables 6, 8-10), which is inconsistent with the findings of previous studies (De Luca et al., 1982b; De Luca & Erim, 1994). For the biceps brachii and vastus medialis, there were no observed differences between the VOL and VOL+NMES conditions, but there was a significant time effect demonstrating a more negative mean linear slope coefficient (steeper regression line) with no significant change in the mean y-intercepts for both muscles. We also observed non-significant decreases in the mean linear slope coefficients and increases in the mean y-intercepts for both VOL and VOL+NMES conditions (Table 5 and

Appendix Tables 10-13). In the biceps brachii, there was a small-medium effect for VOL exercise (*d* = .39) and a medium-large effect for VOL+NMES exercise (*d* = .62). Further, there was a small effect comparing control to VOL (*d* = .27) and a medium effect comparing control to VOL+NMES (*d* = .53). Together, this suggests that the significant time effect may be driven by the changes in the linear slope coefficients and mean y-intercepts in the VOL+NMES condition. Regarding the vastus medialis, caution needs to be taken when extrapolating the results as there were only seven viable subjects for analysis out of 36, due to data loss. Nonetheless, there was a large effect for VOL exercise (*d* = 1.01) and a medium-large effect for VOL+NMES exercise (*d* = .64). Further, there was a small effect comparing control to VOL (*d* = .31) and the control to VOL+NMES (*d* = .11). Based on this alone, this suggests that the time effect may have been driven by the VOL condition in the vastus medialis, which is opposite of the biceps brachii. However, this is not the case because the linear slope coefficients and y-intercept changes were like that of the biceps in our study and in contrast to those found after fatigue in Stock et al. (2012). There are a few plausible explanations for these effects. When the conventional method of NMES is applied (i.e., an anode and cathode placed on the belly of the muscle, which was used in our study), involuntary muscle contractions occur because of depolarization of motoneurons, and the MU recruitment is time-fixed (i.e., synchronized to the stimulation pulse parameters and has a constant discharge rate) (Bergquist, Clair, & Collins, 2011). On the contrary, the normal recruitment pattern occurring during VOLs, is asynchronous in nature. This means, if you were to "simulate" a VOL (i.e., create tetatanic contractions) using NMES, the intensity would need to be increased, causing the discharge rate of MUs to be non-physiological in nature. The non-physiologically high discharge rates create a greater metabolic demand on the muscle (Vanderthommen et al., 2003; Vanderthommen & Duchateau, 2007), the excitability of motoneurons decreases, and the motoneuron becomes less capable of achieving the threshold for depolarization (i.e., MU "drop out") (Luu et al., 2021). Additionally, during lower intensity (i.e., amplitude) NMES, higher-threshold MU – comprised of larger Type-II muscle fibers, commonly located in more superficial regions of the muscle volume – are initially recruited (Bickel et al., 2011). Also, deeper muscle fibers are recruited – consisting of a mixture of lower- and higher-threshold MUs – as the NMES intensity increases (Maffiuletti, 2010). Thus, the superimposition of NMES creates a chaotic environment within the neuromuscular system, causing selective recruitment of higher-threshold MUs, in turn fatiguing these recruited MUs more quickly. These high-threshold MUs then become less excitable because they cannot handle the continued external electrical stimulus and, therefore, the central nervous system becomes more reliant on recruitment of lower-threshold MUs and/or increasing the firing rates of the already recruited MUs.

Motor Unit Recruitment Threshold vs. Derecruitment Threshold Relationship

An additional novel approach to our study was to examine the MU recruitment threshold vs. derecruitment threshold relationships after fatiguing VOL and VOL+NMES exercise. Previous research has shown that the MU recruitment threshold vs. derecruitment threshold relationship is linear, typically positive in nature, and is different among different muscles (De Luca et al., 1982a; De Luca & Hostage, 2010; Farina et al., 2009). The results of this study demonstrated that biceps brachii fatigue resulted in shifts in the MU recruitment vs. derecruitment threshold relationship, with significantly higher slopes (i.e., more positive) and no significant change in the y-intercepts at the end of the fatiguing protocol (collapsed across time). As mentioned previously, De Luca and Hostage (2010) examined the MU mean firing rate vs.

recruitment threshold relationship, but also examined the recruitment vs. derecruitment threshold relationship. In the vastus lateralis, they observed slopes above one and negative y-intercepts, suggesting low-threshold MUs were derecruiting at lower force levels than when recruited, and theorized the opposite to be true for high-threshold MUs (i.e., derecruit at higher force levels than when recruited) (De Luca & Hostage, 2010). Previous research examining the same relationship in the vastus lateralis after performing repeated 50% isometric MVCs until exhaustion, found a shift in the MU recruitment vs. derecruitment relationship showing a decrease in the slope and an increase in the y-intercept (Stock & Mota, 2017). The authors postulated that it is plausible that the recruitment thresholds could be decreasing and/or the derecruitment thresholds could be increasing (Adam & De Luca, 2003; Christova & Kossev, 2001; Contessa et al., 2016; Farina et al., 2009).

As completed previously, it is interesting to determine the magnitude of the effect to potentially see if there is a specific condition that may be driving the finding. Specific to the change in the slope only (since that is where the significant finding occurred), there was a small effect for the VOL condition (d = .26) and a medium effect for the VOL+NMES condition (d = .58). In comparison to the control, there were large (d = .76) and medium effects (d = .58) for the VOL and VOL+NMES conditions, respectively. This data does support the previously mentioned notion (i.e., VOL+NMES is the main driver for the MU mean firing rate vs. recruitment threshold slope change) that the VOL+NMES may be a driver in the significant slope change, although it is difficult to discern based on this alone. Together, we suggest that much of the recruited MU would be derecruiting at higher force levels than when recruited and the lower-threshold MU would continue to be derecruited at even lower force levels.

Conclusions

The aim of this investigation was to examine the changes in maximal voluntary force and surface EMG parameters and the relationship between the mean firing rate and recruitment threshold and recruitment and derecruitment threshold after VOL and VOL+NMES fatiguing exercise. Our findings provide evidence that our fatiguing protocol did induce some level of fatigue and did affect the neuromuscular functions and motor unit firing properties. The change in the slopes of the MU mean firing rate and recruitment threshold relationship may be a result of a greater reliance on lower-threshold MUs as high-threshold MUs fatigue due to the superimposition of NMES. In addition, changes in the slopes of the MU recruitment threshold and derecruitment threshold relationship is possibly due to the derecruitment of higher-threshold MUs at even higher force levels, causing the lower-threshold MUs to increase firing rates and derecruit at much lower forces than recruitment.

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APPENDIX

Table 8. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the biceps brachii pre- and post- control condition

	Control					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	6	-0.234	17.94	10	-0.767	33.18
2	19	-0.492	27.59	24	-0.413	24.90
3	19	-0.191	19.79	17	-0.458	25.53
4	10	-0.353	23.34	13	-0.210	21.06
5	17	-0.247	21.52	17	-0.373	21.07
6	22	-0.549	28.39	22	-0.549	28.39
7	12	-0.926	39.20	15	-0.475	27.64
8	25	-0.706	32.76	11	-0.433	26.55
9	13	-0.956	42.28	23	-1.159	44.52
10	21	-0.733	36.88	20	-1.038	51.45
11	11	-0.392	23.59	12	-0.521	25.22
12	17	-0.279	18.97	17	-0.426	21.80
13	13	-0.881	33.34	14	-0.386	17.87
14	26	-0.857	32.95	15	-1.005	34.94
15	11	-0.642	32.63	14	-0.652	32.21
16	20	-0.555	26.61	24	-0.382	20.05
17	12	-0.982	44.41	22	-0.495	22.74
18	18	-0.864	39.41	16	-1.440	59.22
Mean	**16**	**-0.602**	**30.09**	**17**	**-0.621**	**29.91**
SD	**6**	**0.274**	**8.27**	**5**	**0.329**	**11.31**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 9. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the biceps brachii pre- and post- voluntary (VOL) exercise condition

	VOL					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	20	-0.462	24.74	26	-0.669	29.18
2	31	-0.528	25.60	10	-1.260	48.36
3	17	-0.203	17.35	20	-0.300	21.70
4	18	-0.422	27.81	17	-1.068	35.65
5	19	-0.244	19.93	25	-0.467	21.87
6	15	-0.625	33.06	14	-0.058	47.25
7	13	-0.636	30.66	18	-0.568	30.91
8	21	-0.696	31.00	17	-0.603	32.04
9	25	-0.748	35.53	19	-0.674	32.40
10	15	-0.623	40.45	24	-0.994	37.47
11	18	-0.476	23.48	20	-0.646	27.56
12	15	-0.557	27.29	25	-0.752	34.44
13	21	-1.078	45.99	29	-0.901	40.66
14	13	-0.487	23.50	17	-0.893	36.77
15	16	-1.014	50.43	13	-1.121	48.92
16	22	-0.151	15.70	31	-0.406	20.66
17	10	-0.578	24.92	8	-0.594	24.63
18	18	-1.171	51.63	18	-0.749	30.17
Mean	**18**	**-0.594**	**30.50**	**20**	**-0.707**	**33.37**
SD	**5**	**0.280**	**10.63**	**6**	**0.302**	**8.82**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 10. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the biceps brachii pre- and post- voluntary exercise with superimposed electrical stimulation (VOL+NMES) condition

	VOL+NMES					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	7	-0.605	27.20	22	-0.696	36.32
2	24	-0.373	22.36	31	-0.422	21.33
3	18	-0.593	30.84	17	-0.335	21.82
4	10	-0.555	32.42	15	-0.804	35.32
5	20	-0.311	24.27	15	-0.540	24.35
6	19	-0.397	25.68	14	-0.773	35.67
7	24	-0.263	19.09	15	-0.505	20.45
8	7	-0.679	32.54	16	-1.131	46.72
9	11	-0.939	38.20	24	-1.081	40.77
10	22	-0.998	43.57	28	-1.005	43.69
11	10	-1.199	33.16	24	-0.884	30.05
12	15	-0.300	18.20	20	-0.996	41.33
13	19	-0.536	29.27	32	-1.078	42.49
14	25	-0.473	25.42	20	-0.842	44.53
15	19	-0.675	38.22	20	-0.564	26.48
16	17	-0.301	23.83	23	-0.341	23.05
17	14	-0.586	31.54	16	-0.946	42.59
18	29	-1.143	51.48	14	-1.148	37.53
Mean	**17**	**-0.607**	**30.40**	**20**	**-0.783**	**34.14**
SD	**6**	**0.290**	**8.54**	**6**	**0.275**	**9.11**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 11. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the vastus lateralis pre- and post- control condition

	Control					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	11	-0.513	27.05	8	-0.375	24.29
2	19	-0.234	20.32	18	-0.361	23.10
3	17	-0.347	23.36	15	-0.309	22.27
4	23	-0.339	22.06	15	-0.265	19.12
Mean	**18**	**-0.358**	**23.20**	**14**	**-0.327**	**22.20**
SD	**5**	**0.116**	**2.86**	**4**	**0.051**	**2.21**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 12. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the vastus lateralis pre- and post- voluntary (VOL) exercise condition

	VOL					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	26	-0.461	24.20	22	-0.357	24.51
2	7	-0.150	15.38	24	-0.302	21.01
3	19	-0.642	22.34	17	-0.746	26.57
4	17	-0.174	15.63	10	-0.437	22.27
Mean	**17**	**-0.357**	**19.39**	**8**	**-0.460**	**23.59**
SD	**8**	**0.237**	**4.55**	**6**	**0.198**	**2.46**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 13. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the vastus lateralis pre- and post- voluntary exercise with superimposed electrical stimulation (VOL+NMES) condition

	VOL+NMES					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	3	-0.076	14.19	19	-0.450	20.22
2	23	-0.216	21.51	23	-0.493	21.23
3	20	-0.531	24.77	9	-0.464	26.26
4	23	-0.288	20.47	20	-0.810	35.27
Mean	**17**	**-0.278**	**20.23**	**18**	**-0.554**	**25.75**
SD	**10**	**0.190**	**4.43**	**6**	**0.172**	**6.88**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 14. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the vastus medialis pre- and post- control condition

	Control					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	21	-0.214	15.26	15	-0.238	17.42
2	12	-0.778	28.64	6	-2.208	28.35
3	11	-0.829	22.33	16	-1.218	29.49
4	22	-0.307	20.16	10	-0.494	26.63
5	16	-0.405	20.42	12	-0.550	25.36
6	24	-0.247	16.24	18	-0.188	15.16
7	19	-0.258	21.20	15	-0.283	22.04
Mean	**18**	**-0.434**	**20.72**	**13**	**-0.740**	**23.49**
SD	**5**	**0.260**	**4.420**	**4**	**0.736**	**5.50**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 15. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the vastus medialis pre- and post- voluntary (VOL) exercise condition

	VOL					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	15	-0.191	15.32	10	-1.225	34.15
2	10	-1.091	34.57	9	-1.359	32.93
3	15	-0.611	24.07	21	-0.629	22.90
4	15	-0.342	22.98	17	-0.465	25.63
5	18	-0.515	23.63	16	-1.825	58.83
6	14	-0.489	21.13	17	-0.490	23.11
7	15	-0.233	19.37	22	-0.557	26.52
Mean	**15**	**-0.496**	**23.01**	**16**	**-0.936**	**32.01**
SD	**2**	**0.304**	**5.93**	**5**	**0.534**	**12.63**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 16. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between average firing rate and recruitment threshold in the vastus medialis pre- and post- voluntary exercise with superimposed electrical stimulation (VOL+NMES) condition

	VOL+NMES					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	13	-0.315	19.78	11	-0.523	22.91
2	9	-0.082	15.00	17	-0.241	15.75
3	8	-0.104	16.34	9	-0.275	19.06
4	12	-0.262	19.34	22	-0.260	21.13
5	16	-0.552	22.39	3	-2.473	60.06
6	16	-0.450	24.43	21	-0.428	27.04
7	17	-0.217	17.08	21	-0.379	20.72
Mean	**13**	**-0.283**	**19.19**	**15**	**-0.654**	**26.67**
SD	**4**	**0.172**	**3.37**	**7**	**0.809**	**15.13**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 17. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the biceps brachii pre- and post- control condition

	Control					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	6	0.658	2.60	10	1.322	-20.96
2	19	1.362	-13.87	24	1.465	-18.92
3	19	0.748	-7.55	17	1.231	-12.01
4	10	1.324	-14.59	13	0.494	4.33
5	17	1.018	-6.08	17	1.296	-1.45
6	22	1.280	-8.35	22	1.280	-8.35
7	12	0.594	4.71	15	0.751	1.09
8	25	1.723	-25.00	11	1.070	-5.61
9	13	1.858	-28.18	23	2.313	-24.13
10	21	1.676	-22.95	20	1.771	-37.43
11	11	0.674	0.161	12	0.909	-3.17
12	17	0.910	-4.54	17	0.970	-6.62
13	13	2.049	-22.71	14	1.456	-2.31
14	26	0.966	-3.81	15	1.573	-11.34
15	11	0.860	-12.46	14	1.073	-14.40
16	20	2.506	-36.80	24	1.428	-10.06
17	12	1.074	-18.44	22	1.265	-2.42
18	18	1.597	-34.90	16	1.779	-38.56
Mean	**16**	**1.271**	**-14.04**	**17**	**1.303**	**-11.80**
SD	**6**	**0.538**	**12.40**	**5**	**0.416**	**12.21**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 18. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the biceps brachii pre- and post- voluntary (VOL) exercise condition

	VOL					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	20	1.165	-7.53	26	1.890	-14.42
2	31	1.955	-21.50	10	1.927	-33.49
3	17	1.320	-12.92	20	1.660	-25.23
4	18	1.150	-16.59	17	2.249	-18.29
5	19	1.482	4.97	25	2.294	-7.02
6	15	1.320	-16.36	14	1.280	-5.81
7	13	1.857	-22.40	18	0.966	-1.53
8	21	1.973	-29.01	17	1.460	-19.47
9	25	1.847	-31.38	19	1.516	-14.03
10	15	0.781	-3.80	24	1.452	-1.22
11	18	1.220	-5.90	20	1.734	-13.57
12	15	2.472	-46.97	25	0.944	2.09
13	21	1.835	-37.70	29	1.832	-27.20
14	13	0.912	-1.92	17	1.233	6.35
15	16	1.628	-35.37	13	1.785	-32.18
16	22	0.906	9.45	31	1.820	-9.65
17	10	1.104	-9.20	8	1.500	-13.59
18	18	2.023	-46.27	18	1.367	-6.19
Mean	**18**	**1.497**	**-18.36**	**20**	**1.606**	**-13.03**
SD	**5**	**0.471**	**16.74**	**6**	**0.378**	**11.45**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 19. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the biceps brachii pre- and post- voluntary exercise with superimposed electrical stimulation (VOL+NMES) condition

	VOL+NMES					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	7	1.247	-14.76	22	1.192	-12.02
2	24	0.905	-2.55	31	1.293	-0.62
3	18	2.451	-48.95	17	0.917	-1.08
4	10	1.366	-23.66	15	2.315	-40.89
5	20	0.826	5.98	15	1.101	4.97
6	19	1.206	-7.98	14	1.142	-2.92
7	24	1.123	5.59	15	0.994	6.41
8	7	1.141	-17.05	16	2.109	-38.93
9	11	2.828	-52.32	24	2.445	-35.67
10	22	1.214	-16.97	28	0.615	19.13
11	10	1.398	-5.00	24	1.965	-8.77
12	15	1.126	-1.33	20	1.579	-14.83
13	19	1.353	-33.09	32	2.961	-56.66
14	25	1.150	-4.52	20	2.119	-40.06
15	19	0.870	-8.27	20	1.635	-7.54
16	17	0.746	-4.79	23	0.953	3.850
17	14	0.541	-3.91	16	1.933	-40.12
18	29	1.394	-31.22	14	1.800	-12.24
Mean	**17**	**1.271**	**-14.71**	**20**	**1.615**	**-15.44**
SD	**6**	**0.556**	**17.07**	**6**	**0.634**	**21.28**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 20. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the vastus lateralis pre- and post- control condition

	Control					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	11	1.239	1.62	8	0.494	14.85
2	19	0.696	9.96	18	0.924	3.73
3	17	0.815	1.71	15	0.784	0.42
4	23	1.022	5.57	15	1.011	6.72
Mean	**18**	**0.943**	**4.72**	**14**	**0.803**	**6.43**
SD	**5**	**0.239**	**3.95**	**4**	**0.226**	**6.17**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 21. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the vastus lateralis pre- and post- voluntary (VOL) exercise condition

	VOL					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	26	1.510	4.35	22	0.682	5.94
2	7	0.321	5.51	24	1.152	1.98
3	19	0.926	11.60	17	1.454	2.17
4	17	0.887	7.09	10	1.483	-12.93
Mean	**17**	**0.911**	**7.14**	**18**	**1.193**	**-0.71**
SD	**8**	**0.486**	**3.18**	**6**	**0.372**	**8.35**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 22. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the vastus lateralis pre- and post- voluntary exercise with superimposed electrical stimulation (VOL+NMES) condition

	VOL+NMES					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	3	1.583	-3.90	19	0.682	5.94
2	23	0.547	6.32	23	1.152	1.98
3	20	0.929	4.25	9	1.454	2.17
4	23	0.849	5.97	20	1.483	-12.93
Mean	**17**	**0.977**	**3.16**	**18**	**1.193**	**-0.71**
SD	**10**	**0.436**	**4.79**	**6**	**0.372**	**8.35**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 23. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the vastus medialis pre- and post- control condition

	Control					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	21	1.293	4.10	15	0.591	10.23
2	12	1.318	4.29	6	2.096	2.17
3	11	1.896	-0.97	16	2.495	-10.04
4	22	1.222	1.22	10	1.621	-15.83
5	16	0.853	7.86	12	1.150	-2.88
6	24	1.314	0.59	18	0.935	9.16
7	19	0.836	10.77	15	0.930	10.13
Mean	**18**	**1.247**	**3.98**	**13**	**1.403**	**0.42**
SD	**5**	**0.355**	**4.18**	**4**	**0.693**	**10.44**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 24. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the vastus medialis pre- and post- voluntary (VOL) exercise condition

	VOL					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	15	1.044	11.05	10	2.321	-13.84
2	10	0.411	21.64	9	1.032	7.90
3	15	1.032	6.79	21	1.024	23.53
4	15	0.734	10.65	17	0.980	1.42
5	18	0.941	3.06	16	3.806	-64.66
6	14	2.180	-3.19	17	1.394	-0.09
7	15	0.735	12.83	22	1.274	3.03
Mean	**15**	**1.011**	**8.97**	**16**	**1.690**	**-6.10**
SD	**2**	**0.561**	**7.85**	**5**	**1.042**	**28.10**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

Table 25. Individual data for the linear slope coefficients (pps/%MVC) and y-intercepts (pps) for the relationship between recruitment threshold and derecruitment threshold in the vastus medialis pre- and post- voluntary exercise with superimposed electrical stimulation (VOL+NMES) condition

	VOL+NMES					
	Pre			Post		
Subject	No. of MUs	Slope coefficient	Y-intercept	No. of MUs	Slope coefficient	Y-intercept
1	13	0.985	0.45	11	1.120	10.84
2	9	1.907	-6.75	17	2.354	6.13
3	8	0.667	13.23	9	0.910	10.73
4	12	0.758	14.25	22	0.609	12.66
5	16	0.910	8.37	3	4.961	-64.98
6	16	1.376	1.97	21	0.630	6.57
7	17	1.326	9.20	21	0.747	15.88
Mean	**13**	**1.133**	**5.82**	**15**	**1.619**	**-0.31**
SD	**4**	**0.433**	**7.59**	**7**	**1.593**	**28.72**

Note. pps = pulses per second; MVC = maximal voluntary contraction; MU = motor unit

VITA

William M. Miller MS, Ph.D.(c)

University of Evansville, Evansville IN, 47714 wm114@evansville.edu

PROFESSIONAL EXPERIENCE

University of Evansville, Evansville, IN August 2022
Assistant Professor Exercise Science, School of Health Sciences

University of Mississippi 2017-Present
Graduate Assistant, Health, Exercise Science, and Recreation Management

Logan University 2018
Adjunct Graduate Instructor, Sports Rehabilitation

University of Central Missouri 2015-17
Instructor, Nutrition, Kinesiology, and Psychological Science

Southeast Missouri State University 2013-15
Graduate Assistant, Health, Human Performance and Recreation

EDUCATION

University of Mississippi, University, MS August 2022
Doctor of Philosophy in Health and Kinesiology

Southeast Missouri State University, Cape Girardeau, MO 2015
Master of Science in Nutrition and Exercise Science

University of Central Missouri, Warrensburg, MO 2013
Bachelor of Science in Physical Education: Emphasis in Exercise Science

THESIS AND DISSERTATION

Dissertation : Fatiguing effects of electrical stimulation superimposed onto voluntary contraction 2022
Committee: Drs. Matthew Jessee (Chair), Xin Ye, Mark Loftin, Stephanie Miller

Thesis: Assessment of electromyographic activity during a TRX and traditional split-squat 2015
Committee: Drs. Jason Wagganer (Chair), Jeremy Barnes, Seidu Sofo

RESEARCH EXPERTISE

My research interest is in neuromuscular physiology, including the neural control of movement and its plasticity (i.e., fatigue, adaptations to training, and muscle damage). The primary focus is to examine the acute neuromuscular responses (motor control strategies) in healthy and clinical populations, using voluntary exercise as an intervention. This is accomplished by using non-invasive techniques, such as surface electromyography and neuromuscular electrical stimulation.

PEER-REVIEWED JOURNAL PUBLICATIONS

1. Chatlaong, M.A, Stanford, D.M., Miller, W.M., & Jessee, M.B. (2022). Whole body vibration and blood flow restriction for muscle recovery following exercise-induced muscle damage. Submitted to the *Physiology International - Under Review.*

2. Olivia K. Anderson, Caleb C. Voskuil, M. Travis Byrd, Matthew J. Garver, Alex J. Rickard, **William M. Miller**, Steve Burns, Haley C. Bergstrom, Taylor K. Dinyer McNeely. (2022). Affective and perceptual responses during an 8-week resistance training to failure intervention at low vs. high loads in untrained women. *Journal of Strength and Conditioning Research.* Epub ahead of print.

3. Stanford, D.M., Chatlaong, M.A., **Miller, W.M**., Mouser, J.G., Dankel, S.J., & Jessee, M.B. (2022). A comparison of variability between absolute and relative blood flow restriction pressures**.** *Clinical Physiology Functional Imaging*. *42*(4), 278-285.

4. Jeon, S., **Miller, W.M.**, Song, J.S., & Ye, X. (2021). Effect of repeated eccentric exercise on muscle damage markers and motor unit control strategies in arm and hand muscle. *Journal of Sports Medicine and Health Science. 4*(1), 44-53.

5. Ye, X., **Miller, W.M.**, Jeon, S., Song, J.S., & West, T.J. (2021). Effect of arm eccentric exercise on muscle damage of the knee flexors after high-intensity eccentric exercise. *Frontiers in Physiology 12*(464).

6. **Miller, W.M.**, Jeon, S., Kang, M., Seob Song, J., & Ye, X. (2021). Does performance-related information augment the maximal isometric force in the elbow flexors? *Journal of Applied Psychophysiology and Biofeedback 46*, 91-101.

7. Ye, X., Benton, R.J., **Miller, W.M.**, Jeon, S., & Song, J.S. (2020). Downhill running impairs peripheral but not central neuromuscular indices in upper limb elbow flexor muscles. *Journal of Sports Medicine and Health Science 3*(2), 101-109.

8. **Miller, W.M.**, Jeon, S., & Ye, X. (2020). An examination of acute cross-over effects following unilateral low-intensity concentric and eccentric exercise. *Journal of Sports Medicine and Health Science 2*(3), 141-152.

9. **Miller, W.M.**, Ye, X., & Jeon, S. (2020). Effects of maximal vs. submaximal isometric fatiguing exercise on subsequent submaximal exercise performance*. Journal of Strength and Conditioning 34*(7), 1875-1883.

10. Jeon, S., **Miller, W.M.**, & Ye, X. (2020). A comparison of motor unit control strategies between two different isometric tasks. *International Journal of Environmental Research and Public Health 17*(8):2799.

11. West, J.T., **Miller, W.M.**, Jeon, S., & Ye, X. (2020). The effects of a preconditioning foam rolling session on subsequent eccentric exercise-induced muscle damage. *Journal of Strength and Conditioning Research 34(*8):2112-2119.

12. Jeon S., **Miller, W.M.**, Kang, M., & Ye, X. (2019). The minimum number of attempts for a reliable isometric strength test score. *Journal of Science in Sports and Exercise 2*(1):89-92.

13. **Miller, W.M.**, Kang, M., Jeon, S., & Ye, X. (2019). A meta-analysis of non-local heterologous muscle fatigue. *Journal of Trainology 8*(1):9-18.

14. **Miller, W.M.**, Barnes, J.T., Sofu, S.S., & Wagganer, J.D. (2019). Comparison of myoelectric activity during a suspension-based and traditional split squat. *Journal of Strength and Conditioning Research 33*(12):3236-3241.

15. Dinyer, T.K., Byrd, M.T., Garver, M.J., Rickard, A.J., **Miller, W.M.**, Burns, S., & Bergstrom, H.C. (2019). Low intensity versus high intensity resistance training to failure on one-repetition maximum strength and body composition in untrained females. *Journal of Strength and Conditioning Research 33*(7):1737-1744.

16. Jeon, S., **Miller, W.M.**, & Ye, X. (2019) Sex comparisons of agonist and antagonist muscle electromyographic parameters during two different submaximal isometric fatiguing tasks. *Physiological Reports 7*(5):1-10.e14022.

17. Ye, X., **Miller, W.M.**, Jeon, S., & Carr, J.C. (2019). Sex comparisons of the bilateral deficit in proximal and distal upper body limb muscles. *Human Movement Science 64*(10):329-337. doi: 10.1016/j.humov.2019.02.017.

18. Ye, X., Killen, B.S., Zelizney, K.L., **Miller, W.M.**, & Jeon, S. (2019). Unilateral hamstring foam rolling does not impair strength but the rate of force development of the contralateral muscle. *Peer-Reviewed Journal 29*(7):e7028.

19. Syed-Abdul, M.M., Soni, D.S., **Miller, W.M.**, Johnson, R.J., Barnes, J.T., Pujol, T.J., & Wagganer, J.D. (2018). Traditional vs. suspended pushup muscle activation in athletes and sedentary females. *Journal of Strength and Conditioning Research Strength 32*(7):1816-1820.

TEACHING EXPERIENCE

*Instructor of Record: Created course syllabus, independently developed and taught activities/labs/lectures; developed, administered, and graded midterm and final exams

Assistant Professor, University of Evansville — 2022-Present
School of Health Sciences

- *Course: EXSS 244 Practicum

Semester/Year Taught: Fall 2022

- *Course: EXSS 388 Exercise Prescription
  Semester/Year Taught: Fall 2022

- *Course: EXSS 417 Advanced Exercise Science
  Semester/Year Taught: Fall 2022

- *Course: EXSS 427 Exercise Testing and Leadership
  Semester/Year Taught: Fall 2022

Doctoral Graduate Student, The University of Mississippi 2017-2022
Department of Health, Exercise Science, and Recreation Management

<u>Undergraduate Courses</u> (Overall Evaluation Score: 4.5/5)

- *Course: ES 350 Research Methods
  Semester/Year Taught: Fall 2021; Spring 2022
  Class Size: 60-75

- *Course: ES 338 Motor Learning and Control
  Semester/Year Taught: Summer 2019; 2020 (WEB); Spring 2021 (WEB); Fall 2021 (WEB); Spring 2022; Summer 2022 (WEB)
  Class Size: 12-95

- *Course: ES 402 Exercise Leadership
  Semester/Year Taught: Spring/Fall 2018; Spring/Fall 2019; Spring 2020
  Class Size: 25-62

- *Course: HP 191 Personal & Community Health
  Semester/Year Taught: Fall 2018; Spring 2019; Spring 2020 (WEB); Spring 2021 (WEB)
  Class Size: 50-65

- *Course: HP 203 First Aid and CPR
  Semester/Year Taught: Summer 2020 (WEB)
  Class Size 20-25

- *Course: ES 347 Kinesiology Laboratory
  Semester/Year Taught: Fall 2019
  Class Size: 16

- *Course: ES 348 Physiology of Exercise
  Semester/Year Taught: Summer 2018
  Class Size: 25-35

- *Course: ES 349 Physiology of Exercise Laboratory
  Semester/Year Taught: Fall 2017; 2019
  Class Size: 20-25

- *Course: ES 457 Exercise Testing and Prescription Laboratory
  Semester/Year Taught: Fall 2019
  Class Size: 16

- *Course: EL 151 Weightlifting
  Semester/Year Taught: Fall 2017; Spring 2018
  Class Size: 20-25

- *Course: ES 100 Introduction to Exercise Science
  Semester/Year Taught: Summer 2018; 2019
  Class Size: 25-30

Adjunct Graduate Instructor, Logan University 2018
Department of Master's-Sports Rehabilitation

<u>Graduate Courses</u> (Overall Evaluation Score: N/A)

- *Course: ANAT 06201 Anatomy of Human Motion
  Semester/Year Taught: Summer 2018
  Class Size: 29

- *Course: ANAT 062L1 Anatomy of Human Motion Lab – Prosection
  Semester/Year Taught: Summer 2018
  Class Size: 31

Instructor, The University of Central Missouri 2015-17
School of Nutrition, Kinesiology, and Psychological Science

<u>Graduate Courses</u> (Overall Evaluation Score: N/A)

- Course: PE 6980 Independent Study (Graduate 3 cr. internship)
  Semester/Year Taught: Spring 2017
  Class Size: 3

<u>Undergraduate Courses</u> (Overall Evaluation Score: 4.8/5)

- *Course: PE 1101 Introduction to Exercise Science
  Semester/Year Taught: Fall 2015
  Class Size: 39

- *Course: PE 1800 Functional Anatomy (1-2 sections each semester)
  Semester/Year Taught: Fall/Spring 2015-2017
  Class Size: 10-40

- *Course: PE 2472 Communicating Ideas on Sport
  Semester/Year Taught: Fall 2016
  Class Size: 16

- *Course: PE 2850 Foundations of Exercise Physiology
  Semester/Year Taught: Summer 2016 (hybrid course), Spring 2016; 2017
  Class Size: 32-34

- *Course: PE 2900 Essentials of Personal Training
  Semester/Year Taught: Fall 2016
  Class Size: 30

- Course: PE 4000 Independent Study (Undergraduate 2-6 cr. /hr. internship)
  Semester/Year Taught: Spring 2016; 2017
  Class Size: 15-30

- Course: PE 4341 Physical Activity for Special Populations
  Semester/Year Taught: Fall 2015, Spring 2016
  Class Size: 20-30

- Course: PE 4860 Fitness Programming & Implementation
  Semester/Year Taught: Fall/Spring 2015-2017
  Class Size: 15-25

Graduate Student, Southeast Missouri State University 2013-15
Department of Health, Human Performance and Recreation

Undergraduate Courses (Overall Evaluation Score: 4.5/5)

- *Course: HL 031 Exercise Physiology Laboratory
  Semester/Year Taught: Fall/Spring 2013-2015
  Class Size 10-23

- *Course: HL 120 Health Perspectives
  Semester/Year Taught: Fall/Spring 2013-2015
  Class Size: 20-40

Guest Lecturer, The University of Mississippi 2019
Department of Biomedical Engineering

- Course: General Human Physiology – Urinary System Fundamentals

GRANTS

1. **American College of Sports Medicine Doctoral Student Research Grant** 2022
   M.B. Jessee, Stanford, D.M., Chatlaong, M.A., & **Miller, W.M.**
   Project Title: The acute hemodynamic response to occlusive or partial blood flow restriction
   Role: Co-investigator
   Funding: $3649; Status: Under Review

2. **Mississippi Center for Clinical and Translational Research – Pilot Projects Program** 2022
   M.B. Jessee, Bentley, J., Chatlaong, M.A., Stanford, D.M., & **Miller, W.M.**
   Project Title: Vascular adaptations to single-sprint training
   Role: Co-investigator
   Funding: $39,513; Status: Under Review

3. **University of Mississippi Critical Thinking Redesign Grant** 2021
Miller, W.M.
Project Title: An evidence-based approach to designing a resistance
training program
Role: Principal Investigator
Funding: $1000; Status: Funded

4. **Mississippi Space Grant Consortium Student Grant for NASA-Related Research** 2020
Miller, W.M., Ye, X.
Project Title: Effects of combining neuromuscular electrical stimulation and
voluntary isometric training on neuromuscular functions
Role: Principal Investigator
Funding: $6000; Status: Funded

5. **National Strength and Conditioning Association Graduate Student Research Grant** 2020
Miller, W.M., Jeon, S., Song, J.S., and Ye, X.
Project Title: Effects of transcutaneous neuromuscular electrical stimulation
combined with submaximal voluntary isometric exercise on the neuromuscular
function of the knee extensors after a one-week immobilization period
Role: Principal Investigator
Funding Requested: $10,640; Status: Not Funded

6. **National Strength and Conditioning Association Graduate Student Research Grant** 2020
Song, J.S., Jeon, S., **Miller, W.M.**, and Ye, X.
Project Title: Acute effects of combining neuromuscular electrical stimulation
and voluntary isometric exercise on neuromuscular functions
Role: Co-investigator
Funding Requested: $8,740; Status: Not Funded

7. **National Strength and Conditioning Association Young Investigator Research Grant** 2020
Research Grant
Ye, X., **Miller, W.M.**, Jeon, S., and Song, J.S.
Project Title: Effects of a novel resistance training program on human neuromuscular
adaptations
Role: Co-investigator
Funding Requested: 23,639; Status: Not Funded

8. **National Strength and Conditioning Association Young Investigator Research Grant** 2020
Ye, X., **Miller, W.M.**, and Jeon, S.
Project Title: The examination of global effects of high-intensity upper/lower-
body resistance exercise
Role: Co-investigator
Funding Requested: $20,363; Status: Not Funded

9. **National Strength and Conditioning Association Graduate Student Research Grant** 2018
Miller, W.M., Ye, X., and Jeon, S.
Project Title: Comparison of contralateral elbow flexor rate of force development after
concentric and eccentric exercise to failure
Role: Principal Investigator
Funding Requested: $7,573; Status: Not Funded

FELLOWSHIPS

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1. **The University of Mississippi Dissertation Fellowship** 2020
A semester long fellowship which relinquishes instructor of record duties for doctoral students thereby increasing time commitment toward dissertation completion
Funding: $6400; Status: Funded

2. **Mississippi Space Grant Consortium Graduate Fellowship for NASA-Related Research** 2020
Project Title: A Direct Comparison of Motor Unit Control Strategies After a Fatiguing Bout of Electrically Evoked and Voluntary Muscle Actions
Role: Principal Investigator
Funding Requested: $22,000; Status: Not Funded

3. **The Southeast Missouri State University Summer Research Fellowship** 2014
Wagganer, J.D., **Miller, W.M.**, and Syed-Abdul, M.M.
Project Title: High-intensity interval training on cardiac rehabilitation patients
Role: Co-investigator
Funding Requested: $5,000; Status: Funded

AWARDS

1. **American Kinesiology Association Doctoral Scholar Award Recipient** 2022
Recognized as a doctoral scholar committed to promoting and enhancing kinesiology as a unified field of study and to advancing its many applications

2. **The UM J. Robert Blackburn Graduate Award in Exercise Science** 2020
Ranked 1st in research, teaching, and service out of all graduate students in the Department of Health, Exercise Science, and Recreation Management

3. **The UM Summer Graduate Research Assistantship Award** 2018-19
Competitive graduate student award for students who seek to perform research outside of the academic calendar year

4. **The UM Travel Award** 2018-19
Competitive grant for graduate students seeking to present and travel to regional and national conferences

CONFERENCE PROCEEDINGS

1. **Miller, W.M.**, Chatlaong, M.A., Stanford, D.M., Davidson, C.J. & Jessee, M.B. Effects of caffeine abstinence on the acute response to low-load blood flow restriction exercise. Abstract submitted for presentation at the 2022 National ACSM Conference, San Diego, CA. May 31-June 4, 2022.

2. Davidson, C.J., Chatlaong, M.A., Stanford, D.M., **Miller, W.M.**, & Jessee, M.B. Caffeine abstinence in habituated users: Cardiovascular and perceptual responses to exercise with blood flow restriction. Abstract submitted for presentation at the 2022 National ACSM Conference, San Diego, CA. May 31-June 4, 2022.

3. Stanford, D.M., Chatlaong, M.A., **Miller, W.M.**, & Jessee, M.B. Comparing the exercise response and immediate recovery between two different blood flow restriction devices. Abstract submitted for presentation at the 2022 National ACSM Conference, San Diego, CA. May 31-June 4, 2022.

4. Chatlaong, M.A., Stanford, D.M., **Miller, W.M.**, & Jessee, M.B. Whole body vibration and blood flow restriction for muscle recovery following exercise-induced muscle damage. Abstract submitted for presentation at the 2022 National ACSM Conference, San Diego, CA. May 31-June 4, 2022.

5. Jessee, M.B., Stanford, D.M., Chatlaong, M.A., & **Miller, W.M.** Comparing the resting cardiovascular response to commonly used blood flow restriction devices. Abstract submitted for presentation at the 2022 National ACSM Conference, San Diego, CA. May 31-June 4, 2022.

6. **Miller, W.M.**, Chatlaong, M.A., Stanford, D.M., & Jessee, M.B. Effects of caffeine abstinence on the acute neuromuscular response to low-load blood flow restriction exercise. Abstract submitted for presentation at the 2022 University of Mississippi Graduate Research Symposium, Oxford, MS. March 10, 2022.

7. Stanford, D.M., Chatlaong, M.A., **Miller, W.M.**, & Jessee, M.B. Comparing the exercise response and immediate recovery between two different blood flow restriction devices. Abstract submitted for presentation at the 2022 University of Mississippi Graduate Research Symposium, Oxford, MS. March 10, 2022.

8. Benton, B., Stanford, D.M., Chatlaong, M.A., **Miller, W.M.**, & Jessee, M.B. Comparing the resting cardiovascular response to commonly used blood flow restriction devices. Abstract submitted for presentation at the 2022 Southeast ACSM Conference, Greenville, SC. February 17-19, 2022.

9. Davidson, C.J., Chatlaong, M.A., Stanford, D.M., **Miller, W.M.**, & Jessee, M.B. Caffeine abstinence in habituated users: Cardiovascular and perceptual responses to exercise with blood flow restriction. Abstract submitted for presentation at the 2022 Southeast ACSM Conference, Greenville, SC. February 17-19, 2022.

10. Chatlaong, M.A., Stanford, D.M., **Miller, W.M.**, & Jessee, M.B. Whole body vibration and blood flow restriction for muscle recovery following exercise-induced muscle damage. Abstract submitted for presentation at the 2022 Southeast ACSM Conference, Greenville, SC. February 17-19, 2022.

11. Stanford, D.M., Chatlaong, M.A., **Miller, W.M.**, & Jessee, M.B. Comparing the exercise response and immediate recovery between two different blood flow restriction devices. Abstract submitted for presentation at the 2022 Southeast ACSM Conference, Greenville, SC. February 17-19, 2022.

12. **Miller, W.M.**, Chatlaong, M.A., Stanford, D.M., & Jessee, M.B. Effects of caffeine abstinence on the acute response to low-load blood flow restriction exercise. Abstract submitted for presentation at the 2022 Southeast ACSM Conference, Greenville, SC. February 17-19, 2022.

13. Stanford, D.M., Chatlaong, M.A., **Miller, W.M**., & Jessee, M.B. Applying relative and absolute blood flow restriction alters blood flow velocity but not blood profiles. Abstract submitted for presentation at the Virtual 2021 National ACSM Conference, June 1-5, 2021.

14. Jessee, M.B., Stanford, D.M., Chatlaong, M.A., **Miller, W.M**., Dankel, S.J., & Mouser, J.G. Blood flow restriction stimulus differs between absolute and relative pressure. Abstract submitted for presentation at the Virtual 2021 National ACSM Conference, June 1-5, 2021.

15. Jeon, S., **Miller, W.M.**, Song, J.S., & Ye, X. Motor unit control strategies following contralateral repeated bouts on arm and hand muscles. Abstract submitted for presentation at the Virtual 2021 National ACSM Conference, June 1-5, 2021.

16. Jeon, S., **Miller, W.M.**, Song, J.S., & Ye, X. Motor unit control strategies following contralateral repeated bouts on arm and hand muscles. Abstract submitted for presentation at the Virtual CSACSM Regional Conference, March 3-4, 2021.

17. Ye, X., Benton, R., **Miller, W.M.**, Jeon, S., & Song, J.S. Correlations between thigh muscle soreness and arm muscle neuromuscular indices after prolonged downhill running exercises. Abstract submitted for presentation at the Virtual 2021 National ACSM Conference, June 1-5, 2021.

18. **Miller, W.M.**, Ye, X., Jeon, S., West, T.J., & Benton, R. A preliminary report of the nonlocal repeated bout effect of the elbow flexor muscles. Abstract submitted for presentation at the Virtual 2021 SEACSM Regional Conference, February 18-19, 2021.

19. Jessee, M., Stanford, D., Chatlaong, M., & **Miller, W.M.**, Blood flow restriction stimulus differs between absolute and relative pressure. Abstract submitted for presentation at the Virtual 2021 SEACSM Regional Conference, February 18-19, 2021.

20. Voskuil, C.C., Dinyer, T.K., Succi, P.J., Byrd, M.T., Garver, M.J., Rickard, A.J., **Miller, W.M.,** Burns, S., & Bergstrom, H.C. Affective and perceptual responses during a 4-week low- vs. high-load resistance training intervention. Abstract submitted for presentation at the Virtual 2021 National ACSM Conference, February 18-19, 2021

21. Voskuil, C.C., Dinyer, T.K., Succi, P.J., Byrd, M.T., Garver, M.J., Rickard, A.J., **Miller, W.M.,** Burns, S., & Bergstrom, H.C. Affective and perceptual responses during a 4-week low- vs. high-load resistance training intervention. Abstract submitted for presentation at the Virtual 2021 SEACSM Regional Conference, February 18-19, 2021.

22. Song, J.S., Jeon, S., **Miller, W.M.**, Kang, M., & Ye, X. An examination of the nonlocal repeated bout effect of the elbow flexor muscles. Medicine & Science in Sports & Exercise. 52(Suppl.):5. Abstract submitted for presentation at the 2020 ACSM National Conference, San Francisco, CA. May 26-30, 2020.

23. Jeon, S., **Miller, W.M.,** Song, J.S., & Ye, X. The comparison of contralateral repeated bout effects on arm muscle and hand muscle. Medicine & Science in Sports & Exercise. 52(Suppl.):5. Abstract submitted for presentation at the 2020 ACSM National Conference, San Francisco, CA. May 26-30, 2020.

24. Voskuil, C.C., Dinyer, T.K., Succi, P.J., Byrd, M.T., Garver, M.J., Rickard, A.J., **Miller, W.M.,** Burns, S., Souci, E.P., & Bergstrom, H.C. Acute and early-phase perceptual responses to 30% 1RM training to failure in untrained women. Abstract submitted for presentation at the 2020 NSCA National Conference, Las Vegas, NV. July 8-11, 2020.

25. Ye, X., Benton, R.J., **Miller, W.M.,** Jeon, S., Song, J.S. Prolonged effects of a one-hour downhill running exercise on upper limb muscle neuromuscular functions. Abstract submitted for presentation at the 2020 NSCA National Conference, Las Vegas, NV. July 8-11, 2020.

26. **Miller, W.M.,** Jeon, S., Song, J., Kang., M., & Ye, X. How do different forms of feedback effect maximal voluntary force in the forearm flexors? Medicine & Science in Sports & Exercise. 52(Suppl.):5. Abstract submitted for presentation at the 2020 ACSM National Conference, San Francisco, CA. May 26-30, 2020.

27. **Miller, W.M.**, Ye, X., & Jeon, S. Comparison of contralateral rate of force development after separate concentric and eccentric exercise to failure in the elbow flexors. Abstract submitted for presentation at the 2019 NSCA National Conference, Washington, DC. July 13-16, 2019.

28. Jeon, S. Ye, X. & **Miller, W.M.** A comparison of motor unit control strategies between two different isometric muscle actions. Medicine & Science in Sports & Exercise. 51(Suppl.):341. Abstract submitted for presentation at the 2019 ACSM National Conference, Orlando, FL. May 26-30, 2019.

29. **Miller, W.M.** & Ye, X. Comparisons of time to failure in different isometric fatiguing muscle actions. Abstract submitted for presentation at the 2018 NSCA National Conference, Indianapolis, IN. July 11-14, 2018.

30. Dinyer, T., Byrd, M., Garver, M., Rickard, A., **Miller, W.M**., Burns, S., & Bergstrom, H. Low-intensity versus high-intensity resistance training to failure on one-repetition maximum strength in untrained females. Abstract submitted for presentation at the 2018 NSCA National Conference, Indianapolis, IN. July 11-14, 2018.

31. Barnes, J.T., Wagganer, J.D., Loenneke, J.P., & **Miller, W.M**. Validity of ultrasound and skinfolds for the measurement of body composition in collegiate basketball players. Medicine & Science in Sports & Exercise**.** 50(Suppl. 5):166. Abstract submitted for presentation at the 2018 ACSM National Conference Minneapolis, MN. May 29-June 2, 2018.

32. Shrum, L.K., Wagganer, J.D., **Miller, W.M**., Syed-Abdul, M.M., Soni, D.S., Hoover, B.J., McCrate, M., Kester, B., Nguyen, D.T., & Pujol, T.J. Comparison of six-minute walk test vo2peak prediction equations in cardiac rehabilitation patients. Medicine & Science in Sports & Exercise**.** 50(Suppl. 5):359. Abstract submitted for presentation at the 2018 ACSM National Conference Minneapolis, MN. May 29-June 2, 2018.

33. Dinyer, T.K., Garver, M.J., Rickard, A.J., **Miller, W**., Burns, S., & Bergstrom, H.C. Low intensity resistance training to failure on 1RM strength in untrained females. Abstract submitted for presentation at the 2018 Southeast ACSM Regional Conference Chattanooga, TN. Feb 15-17, 2018.

34. Garver, M.J., Burns, S., Hughes, B.J., Glover, D., Dinyer, T.K., Rickard, A., Jennings, M.A., Wilson, L.A., Lewis, T. **Miller, W**., Brown, R.K., Burnett, D.M., & Godard, M.P. Asthma, undiagnosed asthma, and exercise-induced bronchoconstriction in collegiate men's basketball. Medicine and Science in Sports and Exercise, 49(Suppl. 5):1045. Abstract submitted for presentation at the 2017 ACSM National Conference Denver, CO. May 29-June 3, 2017.

35. Barnes, J.T., Wagganer, J.D., Loenneke, J.P., **Miller, W.M.,** Gegg, C.R., McDowell, K.W., Shrum, L.K., & Barns, K.D. A comparison of DXA and a joint diameter-based system for the measurement of body composition. Medicine and Science in Sports and Exercise, 49(Suppl. 5):259-260. Abstract submitted for presentation at the 2017 ACSM National Conference Denver, CO. May 29-June 3, 2017.

36. Williamson, K.A., **Miller, W.M.,** Syed Abdul, M.M., McDowell, K.W., Gegg, C.R., Wagganer, J.D., & Barnes, J.T. A comparison of total bone mineral density between college baseball players and recreationally active students. Medicine and Science in Sports and Exercise, 48(Suppl. 5):1009. Abstract submitted for presentation at the 2016 ACSM National Conference Boston, MA. May 31-June 4, 2016.

37. **Miller, W.M**., Wagganer, J.D., Barnes, J.T., Sofo, S.S., & Godard, M.P. Assessment of electromyographic activity during a TRX and traditional split squat. Medicine and Science in Sports and Exercise, 48(Suppl. 5):733. Abstract submitted for presentation at the 2016 ACSM National Conference Boston, MA. May 31-June 4, 2016.

38. Barnes, J.T., Wagganer, J.D., Loenneke, J.P., **Miller, W.M**., Gegg, C.R., Williamson, K.A., McDowell, K.W., & Guy, J.D. Validity of ultrasound and skinfolds for the measurement of body composition in collegiate baseball players. Medicine and Science in Sports and Exercise, 48(Suppl. 5):994. Abstract submitted for presentation at the 2016 ACSM National Conference Boston, MA. May 31-June 4, 2016.

39. Wagganer, J.D., **Miller, W.M.,** Syed Abdul, M.M., Soni, D.S., Hoover, B.J., McCrate, M.K., Kester, B.A., Nguyen, D.T., & Pujol, T.J. Effects of high-intensity interval training vs. moderate intensity continuous exercise in cardiac rehabilitation patients. Medicine and Science in Sports and Exercise, 48(Suppl. 5):659. Abstract submitted for presentation at the 2016 ACSM National Conference Boston, MA. May 31-June 4, 2016.

40. Gegg C.R., Barnes, J.T., Wagganer, J.D., Loenneke J.P., **Miller, W.M.**, Soni D.S., & Johnson R.J. A comparison of skinfolds to dual energy x-ray absorptiometry for body composition analysis in division I collegiate basketball players. International Journal of Exercise Science, 11(3): Article 43. Abstract submitted for presentation at the 2015 Central States ACSM Regional Conference Warrensburg, MO. Oct 25-27, 2015.

41. **Miller, W.M**., Wagganer, J.D., Barnes, J.T., & Sofo S. Assessment of electromyographic activity during a TRX and traditional split squat. International Journal of Exercise Science, 11(3): Article 74. Abstract submitted for presentation at the 2015 Central States ACSM Regional Conference Warrensburg, MO. Oct 25-27, 2015.

42. Abdul, M.M., Soni, D.S., **Miller, W.M**., Passini, B.A., Patel, P.A., Koeller, R.G., Baker, D.M., Miller, D.T., Pujol, T.J., FACSM, Barnes, J.T., Johnson, R.J. & Wagganer, J.D. Traditional vs. suspended push-up muscle activation in collegiate female soccer players and gymnasts. Medicine & Science in Sports & Exercise, 47(Suppl. 5):472. Abstract submitted for presentation at the 2015 ACSM National Conference San Diego, CA. May 31-June 4, 2015.

43. Barnes, J.T., Wagganer, J.D., Loenneke, J.P., **Miller, W.M.,** Abdul, M.M., & Soni, D.S. Validity of a Joint Diameter-based System for the Measurement of Body Composition. Medicine & Science in Sports & Exercise, 47(Suppl. 5):41. Abstract submitted for presentation at the 2015 ACSM National Conference San Diego, CA. May 26-30, 2015.

44. **Miller, W.M**., Abdul, M.M., Soni, D.S., Wagganer, J.D., Hoover, B.J., & Nguyen, D.T. Effects of High-Intensity Interval Training (HIT) on Maximal Oxygen Consumption in Cardiac Rehabilitation Patients. Medicine & Science in Sports & Exercise, 47(Suppl. 5):789. Abstract submitted for presentation at the 2015 ACSM National Conference San Diego, CA. May 26-30, 2015.

45. Williamson, K.A., **Miller, W.M.,** Abdul, M.M., Johnson, R.J., Wagganer, J.D. & Barnes, JT. Laboratory Height and Weight Measurements in Collegiate American Football Players Compared to Athletic Program Measurements. Medicine & Science in Sports & Exercise, 47(Suppl. 5):43. Abstract submitted for presentation at the 2015 ACSM National Conference San Diego, CA. May 26-30, 2015.

46. Abdul, M.M., Soni, D.S., **Miller, W.M.,** Passini, B.A., Patel, P.A., Koeller, R.G., Baker, D.M., Miller, D.T., Pujol, T.J., Barnes, J.T., Johnson, R.J., & Wagganer, J.D. Traditional vs. suspended push-up muscle activation in sedentary and collegiate female soccer players. Medicine & Science in Sports & Exercise, 46(Suppl. 5):190. Abstract submitted for presentation at the 2014 ACSM National Conference Orlando, FL. May 31-June 4, 2014.

47. **Miller, W.M.**, Abdul, M.M., Wagganer, J.D., Pujol, T.J., Langenfeld, M.E., Barnes, J.T., Loenneke, J.P., & Logan, W.V. Predicting maximal oxygen consumption in normal weight cyclists using lean leg mass. Medicine & Science in Sports & Exercise, 46(Suppl. 5):935-936. Abstract submitted for presentation at the 2014 ACSM National Conference Orlando, FL. May 31-June 4, 2014.

48. Soni, D.S., Abdul, M.M., **Miller, W.M.**, Wagganer, J.D., Pujol, T.J., Langenfeld, M.E., Barnes, J.T., Loenneke, J.P., & Logan, W.V. Predicting maximal oxygen consumption in normal weight cyclists using lean arm mass. Medicine & Science in Sports & Exercise, 46(Suppl. 5):937. Abstract submitted for presentation at the 2014 ACSM National Conference Orlando, FL. May 31-June 4, 2014.

49. **Miller, W.M.,** Abdul, M.M., Wagganer, J.D., Pujol, T.J., Langenfeld, M.E., Barnes, J.T., Loenneke, J.P., & Logan, W.V. Predicting maximal oxygen consumption in normal weight cyclists using lean leg mass. International Journal of Exercise Science, 11(1), Article 32. Abstract submitted for presentation at the 2014 Central States ACSM Regional Conference Overland Park, KS. Oct 25-27, 2015.

50. Syed, M.A., Soni, D.S., Passini, B.A., Patel, P.A., Koeller, R.G., Baker, D.M., Miller, D.T., Pujol, T.J., Barnes, J.T., Johnson, R.J., **Miller, W.M.,** & Wagganer, J.D. Muscle activation during pushups performed in a stable and unstable environment in female collegiate soccer players. International Journal of Exercise Science, 11(1): Article 40. Abstract submitted for presentation at the 2014 Central States ACSM Regional Conference Overland Park, KS. Oct 25-27, 2015.

PODIUM PRESENTATIONS

1. **Miller, W.M.,** (2022). Effects of caffeine abstinence on the acute neuromuscular response to low-load blood flow restriction exercise. Abstract submitted for presentation at the Damien Moore Memorial Lecture, Oxford, MS. April 28, 2022.

2. **Miller, W.M.**, Chatlaong, M., Stanford, D., & Jessee, M.B. (2021). Whole body vibration and blood flow restriction for recovery of muscle function following exercise-induced muscle damage. Abstract submitted for presentation at the Trainology Conference, Oxford, M.S. July 19, 2021.

3. **Miller, W.M.** (2019). NASA's mission to Mars: Combating muscle atrophy with neuromuscular electrical stimulation. University of Mississippi 3-Minute Thesis Competition, Oxford, M.S. October 22, 2019.

4. **Miller, W. M.**, Jeon, S., & Ye, Xin. (2019). Contralateral rate of force development in the forearm flexors. Abstract submitted for presentation at the NSCA National Conference, Washington, DC. July 13-16, 2019.

ACADEMIC/PROFESSIONAL SERVICE

Invited Reviewer for Peer-Reviewed Journals

International Journal of Environmental Research and Public Health	2021-Present
Journal of Strength and Conditioning Research	2019-Present
Journal of Trainology	2020-Present
Journal of Sports Medicine	2020-Present
Journal of Sports Biomechanics	2020-Present
Journal of Physical Activity & Health	2019-Present
International Journal of Therapy and Rehabilitation	2019-Present
Journal of Human Bodywork and Movement Therapies	2019-Present

Journal of Human Kinetics	2018-Present
International Journal of Exercise Science	2012-13

Professional Committees

Graduate Professional Development, University of Mississippi	2021
Faculty Website Task Force, University of Central Missouri	2016-17
Faculty Search Committee, University of Central Missouri	2016
General Education Awards Committee Member, University of Central Missouri	2016

Professional Development

Workshop on Resilient Pedagogy for Graduate Students	2020
How to Write a Diversity Statement	2020
Pursuing Academic Jobs – Applying for Academic Jobs	2019
Navigating Imposter Syndrome – A Seminar Series	2019
Graduate Writing Center Workshop – Writing Professional Documents	2018
Getting Your Research Funded	2018

Service/Outreach

Allies Training for the LGBTQIA+ Community, University of Mississippi	2020
Stronger Together Series for Diversity and Community Engagement, University of Mississippi	2020
Mississippi Region VII Science Fair Judge	2020
Exercise Science Admitted Student Day, University of Mississippi	2020
Ole Miss Junior Preview Day, University of Mississippi	2019
Academic Advisor, University of Mississippi	2018-19
Conference Abstract Reviewer Committee, Central States ACSM	2016-17
Educator "Being a Responsible and Active Learner," Warrensburg, MO	2016
Faculty Mentor ACSM Quiz Bowl Team, Warrensburg, MO	2015-16

PROFESSIONAL AFFILIATIONS/MEMBERSHIPS

International Society for Electromyography and Kinesiology	2020-Present
Southeast States American College of Sports Medicine Regional Member	2020-Present
National Center for Faculty Development and Diversity Member	2018-Present
National Strength and Conditioning Association Member	2018-Present
National American College of Sports Medicine Member	2014-Present
Central States American College of Sports Medicine Regional Member	2012-17

CERTIFICATIONS

eLearning Training Course Certification	2019-Present
American Red Cross, First Aid/CPR/AED Instructor	2018-Present
American Red Cross, First Aid/CPR/AED	2018-Present
X-Ray Safety Certified	2014-15