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SEX DIFFERENCES IN MUSCLE FORCE SIGNAL COMPLEXITY AND VARIABILIY DURING MAXIMAL AND SUBMAXIMAL EXERCISE

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ABSTRACT

Sex differences have been a topic of interest in exercise physiology as of late, especially the possibility of a sex-dependent fatigue mechanism. Signal complexity has the potential to provide a better picture of fatigue by examining the behavior of a signal produced throughout a fatiguing task. Complexity measures the self-similarity and regularity of a signal and is associated with a system's ability to respond to a change in condition. **PURPOSE:** To determine if there are sex differences in variability and complexity of a force signal before and/or after maximal and or/submaximal exercise. **METHODS:** 16 healthy untrained individuals (9 females, 7 males) completed a maximal and submaximal isometric resistance exercise test using a handmade dynamometer. The maximal exercise test consisted of a 5-minute all-out test with 30 maximal effort isometric knee extensions at a 60% duty cycle (6s contraction, 4s rest). The submaximal exercise consisted of a submaximal test performed at 50% of their maximal voluntary contraction until task failure at a 60% duty cycle. Complexity and variability measures were calculated from the first and last three contractions. Performance measures included pre and post MVC, blood lactate, rating of perceived exertion (RPE), Time-to-Exhaustion (TTE), and force decrement. **RESULTS:** There were significant sex differences found in complexity and performance measures. Males had greater fatigue and levels of complexity. **CONCLUSION:** Further research is needed to determine the significance and applicability of complexity measures in exercise physiology. However, it appears low complexity in females is associated with fatigue resistance in a healthy untrained population.

CHAPTER I: INTRODUCTION

Muscle fatigue, defined by Bigland-Ritchie et al, is the decrease in maximum force-generating capacity of the muscle. Muscle fatigue during exercise has been attributed to both central and peripheral factors (Zając et al., 2015). Central factors of fatigue are associated with interruptions between central command and the alpha motor neuron including malfunction of neurons, inhibition of motor cortex, and psychological factors (Gandevia, 2001). Peripheral factors associated with muscle fatigue include complications at the neuromuscular junction, t-tubules, and sarcoplasmic reticulum, depletion of muscle metabolite stores, and accumulation of metabolic byproducts (Gandevia, 2001).

The identification of muscle fatigue includes direct and indirect assessments of force production (Vøllestad, 1997). Direct assessment involves measuring the decline of maximal force and power output over time using equipment capable of quantifying force production. Indirect assessments observe the physiological responses involved in fatigue and the decline in muscle activation. These methods serve as a foundation for the observation of muscle fatigue and have played a significant role in the current understanding of the mechanisms that influence muscle force production.

The topic of surrounding fatigue is sex-dependent fatiguability, or how an individual's biological sex influences the ability to maintain force production during exercise is of growing interest. Current literature consistently supports the idea that females are more fatigue resistant than males (Critchfield & Kravitz, 2008, Hicks et al., 2001, Sheel, 2016). This is often attributed to reduced muscle mass, which limits blood flow restriction and the removal metabolic byproduct. (Critchfield & Kravitz, 2008). However, there is little research to

support that this is a sex-dependent limiting factor after the identification of sex differences during similar levels of blood flow occlusion and intramuscular pressure (Wüst et al., 2008). They attributed sex differences to changes in muscle activation achieved changes in firing rates and motor recruitment. This directs the observation of sex differences elsewhere. There is research that attributes the sex differences in fatigue to muscle fiber type, and energy utilization (Critchfield & Kravitz, & 2008 (Hicks et al., 2001), but these are often invasive assessments that directly measure peripheral fatigue and do not include central fatigue interaction. If we are to determine if fatigue resistance is truly influenced by biological sex, we need to assess the neuromuscular system. This can be accomplished through the assessment of force signal variation and structure during exercise. Variability has been found to differentiate between males and females due to reduced motor control during fatigue (Svendsen & Madeleine, 2010). Although this does help identify a sex difference through magnitude and amount of variability in force signals, it does not paint the full picture of how force signals can describe fatigue.

Recently, the concept of signal complexity, or signal structure, has been introduced into the field of exercise physiology and is thought to reflect a system's ability to adapt during dynamic and steady-state conditions by measuring the irregularity or unpredictability of a dynamic system described by signal self-similarity and regularity (Peng et al., 2009). The loss of complexity hypothesis states that when a system loses complexity (less variable and more regular) there is a corresponding loss in function (Lipsitz & Goldberger, 1992). This has been observed in several physiological systems including heart rate dynamics, respiratory frequency, stride timing, and recently muscle force output (Lipsitz, 2002). Although this is a novel method of describing muscle fatigue, the findings by Pethick and colleagues suggest

complexity is a capable method of measuring the ability of the neuromuscular system to adapt during the onset of fatigue and describe motor output behavior (Pethick et al., 2016).

The ability to successfully assess the ability of the neuromuscular system to adapt using signal complexity opens the door for several research possibilities to help better understand the interaction between physiological systems. A beneficial next step would be to examine sex differences in force complexity for males and females. This study will help build on the novelty of assessing muscle force complexity and provide potentially new information regarding gender differences in fatigue.

Purpose

The purpose of this study is to determine sex differences in the complexity and variability of force signals produced before and after maximal and submaximal isometric resistance exercise.

Research Question

1. Are there sex differences in knee extensor force signal variability before and/or after a maximal and/or submaximal isometric resistance exercise test?
2. Are there sex differences in knee extensor force signal complexity before and/or after a maximal and/or submaximal isometric resistance exercise test?

Research Hypotheses

1.

H0). There will be no sex differences in knee extensor force signal variability at the beginning and/or end of maximal and/or submaximal isometric resistance exercise.

i. Standard Deviation
ii. Coefficient of Variation

H1). Males will have a change knee extensor force signal variability compared to females at the end of maximal and submaximal isometric resistance.

i. Standard Deviation- Increase
ii. Coefficient of Variation- Increase

2.

H0). There will be no sex differences in knee extensor force signal complexity at the beginning and/or end of maximal and/or submaximal isometric resistance exercise.

i. Detrended Fluctuation Analysis
ii. Approximate Entropy

H1). Males will have a change knee extensor force signal complexity compared to females at end of maximal and submaximal isometric resistance.

i. Detrended Fluctuation Analysis- Decrease or Increase
ii. Approximate Entropy- Decrease or Increase

Significance of the Study

The concept of complexity theory in the field of exercise physiology is novel and has potential for new research. This study aims to build on the foundation of force signal complexity and variability through the identification of sex differences in performance influenced by maximal and submaximal exercise. The ability to measure and understand force signal complexity, and its behavior during exercise has the potential to be a method capable of describing the neuromuscular system's ability to adapt during high demands. The demand placed on the body to produce and sustain force during exercise requires effective adaptative responses from the neuromuscular system. The onset of fatigue prevents the body's ability to maintain performance, forcing the body to make adaptations necessary to maintain desired force. If we can successfully identify the point where these adaptations occur and determine if this is a sex-dependent factor this could open the door for opportunities to identify deficiencies of the neuromuscular system responsible for reduced performance. The use of complexity measures will not be able to define or explain the mechanisms of fatigue, but it has the potential to identify when fatigue occurs. This will allow for future research to use complexity measures to detect the onset of fatigue and use other methods to focus on the specific mechanisms of fatigue. From there, testing protocols and exercise prescriptions could be designed to help different populations detect and reach an ideal state of muscle force complexity. This could be beneficial in helping athletes identify weaknesses and improve performance. It also has the potential to identify the onset or severity of diseases that limit the neuromuscular system ability to supply resources during daily activities. Clinical exercise prescriptions could then be designed to improve daily living and quality of life. The benefit of muscle force complexity measures to simplify the identification of fatigue opens the door for

future research opportunities. However, the foundation of complexity measures in exercise physiology needs to be built upon. There are simple questions that need to be explored. One of these being the identification of complexity differences between males and females. This study hopes to supply basic research that force signal complexity is a valid and reliable method of detecting fatigue, and if complexity differences exist between males and females.

Delimitations

1. Healthy males and females, ages 18-35 from Norman and surrounding areas
2. No prior major injury or surgery to the dominant leg and hip within the past year.
3. No neuromuscular or neurological diseases/disorders that limit muscle function
4. Sleep, caffeine, training status, and hydration status will be controlled
5. Inclusion of males and females who qualify as "not trained" individuals:
    a. Aerobic trained: Train less than 4 hours per week with less than 1.5 hours of resistance training.
    b. Resistance trained: Train less than 3 days per week for at least 4 hours with less than 1.5 hours of aerobic training.
6. Fatigue will be determined through decline in maximal voluntary contraction

Limitations

1. There is no random assignment of groups.
2. There is no control group.
3. Participants will be recruited from the Norman and Oklahoma City Area

Assumptions

1. Participants have not participated in vigorous activity 12 hours prior to the test.
2. Participants will perform at maximal effort during the maximal and submaximal exercise tests.
3. Individuals will provide accurate medical information and health history

Operational Definitions

1. Muscle Fatigue-is the decrease in maximum force-generating capacity of the muscle (Bigland-Ritchie 1984)
2. Peripheral Fatigue- A reduction in the force generating capacity of the skeletal muscle that may occur within muscle, or at the neuromuscular junction. (Sadri et al., 2014)
3. Central Fatigue- A progressive loss of voluntary activation or reduced nervous excitation into muscle and thus decreased maximal force production during exercise (Sadri et al., 2014)
4. Complexity- irregularity or unpredictability of a dynamic system (Lipsitz and Goldberger, 1992).
5. Entropy (ApEn)- average amount of information conveyed by an event or the inherent uncertainty of a string of data (Richman & Moorman, 2000).
6. Detrended fluctuation analysis (DFA)- The self-similarity of a signal produced by system over a time series (Pethick et al. 2015).
7. Variability- Standard deviation and Coefficient of Variation of a signal (Pethick et al. 2015)
8. Coefficient of Variation- the amount of variation in a signal (Pethick et al. 2015)
9. Standard Deviation- the magnitude of the variation in a signal (Pethick et al. 2015)

CHAPTER II: LITERATURE REVIEW

Introduction

This review of literature will present the current understanding of muscle fatigue, complexity, and sex differences during resistance exercise. The search process included literature found using google scholar, MEDLINE(EBSCO) and SportsDiscuss with full text. The search criteria used a combination of keywords such as: complexity, isometric exercise, force production, muscle fatigue, sex differences, central fatigue, peripheral fatigue, and critical torque, found in the text, abstract and title.

Muscle Fatigue: Peripheral and Central Mechanisms

A general definition of muscle fatigue as described by Bigland-Ritchie et al is a reduction in the maximal capacity of a muscle to generate a force (Bigland-Ritchie et al 1984). The cause of this reduction in muscle force production can be attributed to central and peripheral factors. Additionally, fatigue can be influenced by the type of exercise and for this project we will be talking about resistance exercise more specifically. Peripheral fatigue is the reduction of force generating capacity due to factors within the muscle or at the neuromuscular junction (Sadri et al., 2014). It can be difficult to distinguish the differences between peripheral and central fatigue due to the interacting components of the peripheral and central nervous systems. There are numerous studies that identify the factors of peripheral fatigue as a decrease in energy storage and increase in metabolic byproducts. (Joan Dawson et al. 1978, Hirvonen et al. 1987, Green 1997, Takada et al, 2012). This can occur when sustained or intermittent contractions are performed for prolonged periods of time during submaximal and maximal resistance exercise intensities (Babault et al., 2006, and St Clair Gibson et al., 2001).

The ability to produce and sustain a force is dependent on the muscle's capability to receive a signal, participate in excitation-contraction coupling, and form cross-bridges. These actions require the breakdown of carbohydrate stores for the utilization of ATP, resulting in metabolic byproducts that disrupt force production. These byproducts include the accumulation of H+ ions and inorganic phosphate.

The increase in H+ ion concentration is attributed to the breakdown of lactate during a state of anaerobic metabolism. An increase in H+ ions decrease blood and intracellular pH, which can reduce enzyme and protein function (Wilson 1988). In the muscle, increased H+ ions interfere with actin-myosin cross bridges, and myosin ATPase (Metzger 1990 and Fitts 2008). The increase in inorganic phosphate concentration from creatine phosphate breakdown has an additive effect with the accumulation of H+ ions on the availability of calcium (Ca2+) during muscle contractions (Potmac 1995). Sarcoplasmic reticulum calcium is necessary for excitation contraction coupling and cross bridge formation. H+ and inorganic phosphate interfere with the enzymes that are responsible for the reuptake of cellular calcium thus reducing calcium availability for muscle force production (Westerblad 2000).

During a muscle contraction, the pressure created during contractions can result in the occlusion of muscle blood flow. This prevents muscle recovery through reduced removal of metabolic byproducts. Therefore, the body must efficiently remove these byproducts to sustain force. However, intramuscular pressure reduces blood flow and removal of interfering metabolites resulting in reduced force due to the inability to activate excitation contraction coupling and cross-bridge formation. The increase in intramuscular pressure and metabolites also activates the mechanosensitive myelinated type III afferents and the metabosensitive unmyelinated type IV afferents. The activation of these afferents sends feedback to the central

nervous system that a disruption in neuromuscular homeostasis has occurred. Interestingly, the activation of these afferent groups is capable of attributing to central fatigue through an interference of central motor drive (Gandevia, 2001)

Central fatigue is a cumulative reduction in voluntary activation of muscle during exercise (Gandevia, 2001). Voluntary activation is managed by high-level neural regulation centers responsible for the activation of efferent neurons. These high-level functional components make up the integration center of the neuromuscular system and include the prefrontal cortex, motor cortex, basal ganglia, and cerebellum. They play a role in the basic rhythmic patterns produced by the spinal cord locomotor system that help regulate motor drive (Guertin 2012). When the brain receives a signal via afferent neurons this indicates a change in stimulus or disruption in homeostasis at the muscle. During periods of stress such as exercise, the integration center is believed to signal increased motor unit firing rates to maintain force production. However, when fatigue occurs, muscle activation is inhibited through reduced signal transmission to the motor units (Zając et al., 2015). Muscle activation can be inhibited through a decrease in motor unit activation and neurotransmitters initiated by stimulation of type III/IV afferents (Sadri et al., 2014). There have been several proposed mechanisms that influence the reduction in neural excitation and signal transmission of these brain regions to perform their role during exercise. These mechanisms include changes in neurotransmitter activity, increased temperature, and perceived exertion to reduce voluntary muscle activation. This inhibition on central drive aims to prevent energy depletion, muscle damage, injury, pain, and return the body to a state of homeostasis (Sadri et al., 2014).

The level and origin of fatigue can be attributed to the type of activity, depending on the amount of force produced and the speed of the movement (Sadri et al., 2014). For example,

isometric resistance exercise has been used in numerous studies to observe the development of central fatigue (Babault et al., 2006, Berchicci et al., 2013, Zając et al., 2015). During this type of exercise, whether the contractions are sustained or intermittent, the activation of large muscle groups requires consistent coordination between the peripheral and central nervous systems to maintain force production (Sadri et al., 2014). This strain of the motor output on the motor control regions of the brain affects the physiological and perceptual components. As fatigue is introduced, the accumulation of metabolic byproducts and change in neurotransmitter activity can lead to adaptations in motor activation to limit the perceived exertion and sustain force production (Berchicci et al., 2013). However, there is a limit to how far these adaptations can go and decline in performance eventually occurs.

A major factor that can contribute to fatigue during isometric resistance exercise is the ischemic conditions large muscle groups can experience due to the contraction of the muscle group (Sjogaard et al., 1988). The contraction of large muscles can cause reductions in blood flow of the muscle which leads to accumulation of metabolic byproducts and the activation of pain afferents (Zając et al., 2015). This results in a response from the autonomic nervous system to maintain blood flow through vasodilation and reduction of the force of the contractions (Rossman et al., 2012). Despite this response, voluntary activation can continue to sustain contraction through the recruitment of different motor units and alternating firing rates (Sadri et al., 2014). However, as the duration of the activity is prolonged the accumulation of the byproducts and perception of effort increases. As a result, the ability of the nervous system to adapt becomes reduced and eventually fatigue becomes so severe the body is incapable of sustaining the desired force.

Sex Differences in Force Production and Fatigability

A popular topic in the field of exercise physiology is the possibility of sex-dependent factors that affect performance during exercise. It is widely accepted that males typically have higher force production and increased fatigability compared to reduced force production and increased fatigue in females during low-moderate exercise with sustained and intermittent contractions (Critchfield & Kravitz, 2008). A variety of factors are attributed to these findings such as differences in muscle mass, energy utilization, and muscle activation.

Males typically have increased muscle mass compared to females. Whether this increased muscle mass is due to a larger body size or increased type-II muscle fiber percentage there is still increased force production compared to females. Both factors influence energy utilization during exercise. The larger body size requires more force to perform a task and therefore more energy to maintain the desired force. Although the increased percentage of type-II muscle fibers can maintain force, type-I fibers are more fatigue resistant due to increased oxidative phosphorylation capacity (Hicks et al. 2001). This is one reason females are believed to be more fatigue resistant than males because of their increased percentage of type-I muscle fibers (Hicks et al. 2001). However, another factor related to muscle mass and fatigue is that increased muscle mass results in increased intramuscular pressure and blood flow occlusion. This reduces blood flow to the muscle and the removal of metabolic byproducts during exercise thus reducing the ability to sustain performance (Hicks et al. 2001). However, findings by Wust et al. (2008) and Hunter et al. (2004) show sex differences in performance despite equal occlusion of blood flow and strength matching. This indicates that females are still capable of increased fatigue resistance despite the influence of increased muscle mass. Their findings point to muscle activation, and energy utilization.

Muscle activation has been explored using electromyography (EMG) to explain sex differences. However, these findings are conflicting and cannot fully describe the ability of the neuromuscular system to maintain performance through changes in motor recruitment and firing rates. These measures can describe how much they change but don't fully describe the behavior of how they change. If we look at how much and the way the behavior of a signal changes this can help us better understand how the neuromuscular system adjust muscle activation. This can be accomplished through the observation of force signal complexity, a measure that will help determine if a sex-dependent of fatigue truly exists.

Complexity

The concept of complexity in exercise physiology has recently become an intriguing topic when investigating muscle fatigue. The neuromuscular system is an interconnected network composed of motor cortical neurons, spinal motor neurons, muscle fibers, and muscle afferents that interact to produce complex patterns of force production (Pethick et al., 2015). This complex system allows for sustained force production during times of fatigue through changes in motor control mechanisms over time. The changes or adaptations of the neuromuscular system during fatigue can be observed through force signal time series complexity (Pethick et al., 2016). The loss of complexity in a torque time series during fatigue is associated with a loss of motor control (Pethick et al., 2020). It has also been determined complexity is reduced when exercise intensity is performed above critical torque (Pethick et al., 2016). Therefore, a relationship between complexity and fatigue exists which can signify the failure of the neuromuscular system to adapt due to the loss of motor control during muscle fatigue. This relationship needs to be examined further to determine if torque complexity can

potentially be an important component in explaining the interaction between central and peripheral fatigue.

The behavior of force signals has typically been examined by the standard deviation (SD) and coefficient of variation (CV) which measures the magnitude and amount of variation in a signal. Although these measures have been capable of identifying the loss of motor control through changes in muscle activation, they do completely describe a force signal. However, there are properties of a complex signal such as temporal irregularity, and long-range fractal correlations that cannot be observed using these typical methods (Pethick et al., 2016). Temporal regularity is the regularity or predictability of a signal in time series data. This is quantified through ApEn or approximate entropy, which is the likelihood that a series of data points are within a certain distance of each other in consecutive readings (Lipsitz, 2002). When ApEn is decreased there is a corresponding reduction in torque complexity (Lipsitz & Goldberger, 1992). Long-range correlations reflect signal self-similarity throughout multiple time scales. Detrended fluctuation analysis (DFA) scaling exponent is used to describe the shift in the signal patterns generated during torque production. When DFA detects an increase in self-similarity there is reduced complexity (Lipsitz & Goldberger, 1992). This can be detected in the estimation of noise color and temporal fractal scaling. When the fractal scaling component value, $\boldsymbol{\alpha}$, is >0.5(white noise) but <1.5 (brownian noise) this indicates healthy physiological system outputs. Any shift in the fractal structure resulting in a change towards white or brownian noise that detects a complexity change that indicates system dysfunction [$\boldsymbol{\alpha}$~1.0] (Goldberger et al., 2002). These properties can essentially be described as signal complexity or signal structure, which can describe the pattern of a signal.

Complexity indicates healthy and adaptive physiological systems (Peng, et al., 2009). The physiological significance of signal complexity has been observed in many processes such as in heart rate dynamics, respiratory frequency, and stride timing (Lipsitz 2002). Researchers have found increased signal complexity in cardiopulmonary measures and gait mechanics in healthy populations compared to diseased populations (Goldberger et al., 2002). In addition, research has been done on the neuromuscular system more specifically, force signal complexity which is thought to reflect the ability of the neuromuscular system to adapt and respond to changes in intensity (Pethick et al., 2015, Pethick et al., 2016, Pethick et al., 2019). This is significant because the neuromuscular system must find a way to sustain force production during high intensity or prolonged exercise to sustain performance. When force signal complexity decreases, the ability to sustain the exercise has been shown to be correlated to task failure, fatigue, and overall decline in force (Pethick et al., 2015).

The loss in force signal complexity has been shown to occur during maximal and submaximal exercise, sustained and intermittent exercise and exercise that occurs above critical torque (Pethick et al., 2015, Pethick et al., 2016, Pethick et al., 2019). These are modes of exercise correlated with high levels of central and peripheral fatigue due to the demand placed on the neuromuscular components associated with force production and sustainability (St Clair Gibson et al., 2001). The first published study to observe torque complexity had participants (10 Males, 1 Female) perform a maximal test of 5 minutes of intermittent isometric knee extensor maximal voluntary contractions, and a submaximal test at 40% of MVC performed until task failure, both at a 60% duty factor (6 second contraction, 4 second rest). The researchers found that fatigue significantly reduced signal complexity of both maximal (ApEn to 0.10 ± 0.02; DFA α to 1.63 ± 0.02; all $P < 0.01$) and submaximal

contractions (ApEn to 0.24 ± 0.05; SampEn to 0.22 ± 0.04; DFA α to 1.55 ± 0.03; all $P < 0.005$) (Pethick et al., 2015). Another study found that signal complexity was lost exclusively above critical torque (Pethick et al, 2016). In the study, healthy participants (5 males, 4 females) performed isometric knee extension exercises for 30 minutes or until task failure on 6 occasions. The first 4 visits were used to establish critical torque and the last 2 visits were performed at 50% and 90% of the established critical torque. They found that the fatigue-induced loss of complexity occurred in the contractions performed above CT (ApEn for S1: from 0.67 ± 0.06 to 0.14 ± 0.01,, 0.33; DFA- from 1.38 ± 0.03 to 1.58 ± 0.01, 95% CI 0.12, 0.29) but it did not decrease in the trials performed below critical torque despite a reduced MVC (ApEn for 90%CT: from 0.82 ±0.03 to 0.75 ±0.06,, DFA- from 1.36 ± 0.01 to 1.32 ± 0.03). Finally, it has been found that fatigue reduces the signal complexity of the knee extensors during sustained isometric contractions. In the study, healthy participants (7 male, 2 female) performed sustained isometric knee extensor exercise at 20% MVC until task failure and 100% of MVC for 60 seconds. They found that fatigue reduced the complexity in both the sustained submaximal (ApEn from 1.02 ± 0.06 to 0.41 ± 0.04, $P < 0.05$) and maximal voluntary contractions (ApEn from 0.34 ± 0.05 to 0.26 ± 0.04, $P < 0.05$; DFA α from 1.41 ± 0.04 to 1.52 ± 0.03, $P < 0.05$) (Pethick et al., 2019). In these studies, the loss in complexity was accompanied by and attributed to the central, and peripheral fatigue detected by voluntary activation via twitch interpolation technique and fall in potentiated doublet torque, respectively (Pethick et al., 2019). The relevancy of complexity measurements for motor output behaviors across a wide range of exercise modalities and intensities indicate that torque complexity is potentially a viable method for detecting fatigue and describing the neuromuscular system's ability to adapt during physiological stress such as exercise.

Sex Differences in Force Signal Complexity

Force signal complexity is such a novel method of describing muscle fatigue that there are only a handful of studies that examine it (Pethick et al., 2015, Pethick et al., 2016, Pethick et al., 2019). One major research area that needs to be explored is possible sex differences in force complexity. Biological sex has been shown to influence muscle fatigue due to consistent findings in sex difference performance measures (Hicks et al., 2001). Therefore, it would be interesting to determine if sex has a role in the complexity of force signals. This would be significant as differences in complexity would indicate that sex is a factor in the body's ability to make adaptions to sustain exercise in response to fatigue. The current literature involving force complexity does not distinguish changes between males and females outside of Svendsen and Madeline (2010), which found that temporal regularity measurements were higher in males than females indicating reduced complexity changes in males post exercise (Svendsen & Madeleine, 2010). This indicates that there could be sex-dependent force control mechanisms that influence signal variability outside of the strictly peripheral components. However, this leaves an apparent gap in force complexity research. There is already a lack of research in the field of exercise physiology for females compared to males therefore it is crucial that the early forced complexity research includes females to prevent a possible distance in available literature between the sexes.

Although the research examining sex differences in torque complexity is minimal, there is research regarding sex differences in terms of muscle force production, muscle endurance and muscle fatigue (Hicks et al., 2001). A well accepted finding is that the average female is more fatigue resistant compared to the average male (Hakkinen 2003). This can be attributed to a couple of factors. One factor includes the increased concentration of type I

muscle fibers in females compared to males (Hicks et al, 2001). Because males have a higher concentration of type II fibers, they are more likely to produce more force, but their force production decreases faster due to the reduced oxidative metabolic capability of type II fibers compared to type I (Hicks et al., 2001). Another factor is the increased muscle mass found in males compared to the average female (Wüst et al., 2008). Increased muscle mass is correlated with increased energy use by the muscle fibers and increased muscle fiber area; therefore, it is possible that the increased fatigue seen in males is due to the increased energy required to contract the increased muscle mass (Wüst et al., 2008). There is an argument that the increased muscle mass causes ischemia-like conditions due the intramuscular pressure caused by the muscle on the blood flow, however Wust et al. (2008) determined that this is not a sex dependent factor but rather a coincidental finding after testing fatigability with blood flow occlusion. This raises the question on whether the fluctuations in torque complexity are different between the sexes. If females are typically more fatigue resistant than males, will torque complexity be influenced in a similar manner? In the one study by Svendsen & Madeleine regarding sex differences observed that males had increased complexity or signal variability during an endurance test while males had decreased endurance duration. However, the endurance test consisted of a protocol that fatigued the elbow flexors. Although this muscle group can generate force, it would be beneficial to take this further and observe complexity during a protocol that fatigues a larger muscle group capable of producing greater levels of force such as the knee extensors during a maximal intermittent voluntary contraction test. This could be significant in a way that further questions the mechanisms that play into central and peripheral fatigue. Whether or not there is a sex difference in force signal complexity, further

exploration of signal variation and structure can help determine if these measures are useful in identifying and describing muscle fatigue.

Summary

There has been extensive research regarding fatigue. Fatigue influences the muscle's force generation capacity through central and peripheral factors. When fatigue becomes so severe that performance can no longer be sustained, the body must make adaptations to adjust for the physiological changes that occur. When observing torque output across a time series there are fluctuations in torque production that relate to motor control. The regularity and self-similarity of torque signals can be described as signal complexity. A decline in torque complexity occurs during fatiguing tasks and is associated with the neuromuscular system's ability to adapt during increased demand. Essentially, it is possible to detect the capability of the neuromuscular system to adapt during exercise through measures such as ApEn and DFA. Since this is such a novel area of research there is an abundance of research possibilities that need to be explored. One includes sex differences in torque complexity. There is already evidence that females have an increased ability to resist muscular fatigue, which is why it would be important to explore if there are similar differences pertaining to torque complexity. This would not only further solidify the known mechanisms of fatigue but open new doors to other potential mechanisms that explain muscle fatigue.

CHAPTER III: METHODOLOGY

This chapter describes the methodology used in this study to examine potential sex differences in force signal complexity produced by maximal and submaximal isometric resistance exercise.

Study Sample

The participants consisted of low-to-moderately active healthy males and females from the local community between the ages 18-35. A power analysis using G*power (version 3.1.9.7), 2 by 2 by 2 repeated measures ANOVA within-between group was used to determine the sample size with an alpha level of 0.05, statistical power of 0.80, and effect size of 0.27 (Black, 2017). This equated to a sample size of 18 participants (9 female, 9 male),

Research Design

This study was a cross-sectional, repeated measures, quasi-experimental design that examined sex differences in force signal complexity and variability before and after a maximal and submaximal fatiguing exercise task. Participants were asked to visit the University of Oklahoma Human Performance and Body Composition lab on 3 occasions.

Visit #1. The first visit consisted of the completion of study documents and procedure familiarization. They were provided an informed consent document describing the procedures, risks, compensation, and confidentiality of the study. They completed a physical activity readiness (PAR-Q) questionnaire that assured their ability to perform maximal and submaximal fatigue protocols. They completed an Internal Physical Activity Questionnaire (IPAQ) to assure that they were not sedentary according to ACSM. A training diary was used

to determine training status, and to assure that they were not aerobically (Train less than 4 hours per week with less than 1.5 hours of resistance training), or resistance (Train less than 3 days per week for at least 4 hours with less than 1.5 hours of aerobic training) trained. Females completed a menstrual history questionnaire to ensure that testing does not occur during menses. A Profile of Mood States (POMS) was used to assure that they were mentally and emotionally capable of performing exercise and as a control variable between test visits. Height (cm) and weight (kg) were measured and rounded to the tenth decimal place. Followed by a submaximal familiarization procedure of the Burnley (2009) fatigue protocol. The participants were familiarized with the timing of the 60% duty cycle (6 second contraction, 4 second rest) stop-go PowerPoint, and equipment as they performed a lesser version of the maximal exercise test. The familiarization was performed at an intensity left to the discretion of the participant for 2 minutes on a custom-made dynamometer. The participants were asked to refrain from caffeine, alcohol, nicotine, and exercise 12 hours prior to visits 2 and 3. Visit 2 was scheduled at least 24 hours after visit 1. Visit 3 was scheduled at least 48 hours after visit 2.

Visit #2 (Maximal Exercise Test): Upon arrival, participants were asked if they had refrained from caffeine, alcohol, nicotine, and exercise 12 hours prior to the visit, and completed a POMS to assess mood disturbance. The individuals' shins were then strapped into a custom-made dynamometer. A seatbelt and side handles were used to secure the participants' position in the chair. The hip angle was set at 90-degree flexion and their knee fixed at an angle of 70 degrees below the horizontal. The participants were asked to perform 3 maximal voluntary contractions (MVC) for 6 seconds with 1-minute rest periods in between MVCs. The highest of the 3 MVCs was used to determine the maximum force. Prior to the maximal

test, the participant was given a 10-minute rest period. At 5 minutes, resting Rate of Perceived Exertion on scale of 6-20 (Borg, 1982) and lactate measures were recorded before the protocol. The maximal exercise test consisted of a series of intermittent dominant knee extensor maximal contractions performed at 60% duty cycle (6 seconds on, 4 seconds off) for 5 minutes for a total of 30 contractions. There was a timed PowerPoint display using green and red signaling to indicate when to contract and when to rest. The participant was instructed to sit up straight and look at the PowerPoint throughout the entire protocol. After the protocol was completed RPE and blood lactate (immediate and 1-minute post) were recorded. The first and last three contractions of the protocol were used to assess fatigue and calculate torque complexity via approximate entropy (ApEn), and detrended fluctuation analysis (DFA).

Visit #3 (Submaximal Exercise Test): The procedure of the submaximal exercise test was like the maximal test in visit 1. However, after the initial three MVCs and resting RPE were recorded, the participants highest force value was used to establish 50% of their maximal force production. This value was set on a computer monitor as the midpoint represented by a red line on grid created in Biopac. After the MVCs, the participants were given a 10-minute rest period. At the 5-minute mark baseline RPE was measured. The participants were instructed to contract until the force signal reached this midpoint and to hold at that value for 6 seconds followed by 4 seconds of rest. This protocol was performed until task failure, determined by the participant's verbal request to end the protocol, or the failure to maintain 50% of their MVC for two consecutive contractions. Immediately after task failure RPE was recorded followed by 3 MVCs with 1 minute rest periods in between contractions.

Control Variables: Participants were asked to abstain from alcohol, caffeine, exercise, and nicotine for 12 hours prior to each visit. In addition, the participants were encouraged to

consume a light meal 2-3 hours before testing and to be hydrated. Females were not tested during the follicular phase the menstrual cycle, this phase is associated with reduced RPE and arterial resistance during resistance exercise (Augustine et al., 2018 & Hooper et al., 2011, Delp 2019). This will be assessed using a menstrual cycle questionnaire. POMS was used to assure that they were mentally and emotionally capable of performing exercise and as a control variable between test visits

Instrumentation: Basic anthropometric data such as height and weight were recorded using a Physician's Scale [Detecto USA, Webb City, MO] to the nearest .5 cm and .1 kg. Force signals were measured using a custom-made dynamometer connected to a force transducer [model SB-500; Transducer Techniques, Temecula, CA] sampled at 2000 Hz a Biopac MP150 for the maximal and submaximal exercise tests. Lactate was measured using a Lactate plus analyzer [Nova Biomedical Corporation Waltham, MA 02454, U.S.A]

Complexity and Variability Measurements: The complexity and variability measurements were calculated using the average of the first three (Fresh) and last three (End Task) contractions. These measurements were found to be reliable methods for calculating variability and complexity measurements during a fatigue test using intermittent maximal voluntary contractions (Pethick et al., 2015). The most stable 5 seconds (10,000 samples) determined by smallest SD was used for data analysis. The variability measurements include SD and CV. SD is the absolute variability in a time series. CV is the amount of variability in a time series normalized to the mean of the time series. The temporal complexity measurement includes ApEn, while the temporal fractal scaling and noise color estimation was calculated using DFA.

ApEn, approximate entropy, uses the negative logarithm of the conditional probability to determine the complexity of torque output signals (Pincus 1992). This is represented by the probability that a template length m (set at 2) is repeated during a time series. If the data set conditional probability is close to 1 the negative log and ApEn will be close to 0 signifying low complexity and high predictability.

$$ApEn(m, r, N) = \frac{1}{N-m}\sum_{i=1}^{N-m} \quad log\frac{A}{B}$$

The variables of ApEn calculation include *m*=embedding dimension (2), *r*=within tolerance unit(0.1SD), *N*= number of data points in time series, *A*= number of matches of the ith template of length m+1 data points, *B*= the number of matches of the ith template of length *m* data points. Values closest to 2 are more irregular or unpredictable while values closer to 0 are more regular or predictable (Lipsitz & Goldberger, 1992).

DFA, detrended fluctuation analysis, assesses the fractal scaling of the force time series (Peng et al. 1994). An integrated time series is divided into boxes of length n, and a least squares line is fitted, indicating the trend in each box. The relationship between box size and f(n) is determined, and the slope of the log-log plot of n and F(n) determines **α**, the scaling parameter to determine self-similarity. The characteristics size of fluctuation for the time series is given by:

$$F(n) = \sqrt{\frac{1}{N}\sum_{k=1}^{N} \quad [y(k0 - y_n(k)]^2}$$

The variables of DFA calculation includes *N*= number of data points in a time series, *n*= length of box, $y_n(k)$ = y coordinate of the straight-line segment of length *n* in the *k*th box. The values of 0.5, 1.0, and 1.5 all represent a white, pink, and red noise respectively. Lower

values are considered to have reduced self-similarity while values closer to two are repeating patterns (Goldberger et al., 2002).

Force (N) will be converted to torque (Nm) using the force produced multiplied by the length moment arm (m) using the equation:

Torque= F x L

Data Management: Participants had an individual data collection folder containing study documents and data collection sheets kept under lock and key in the Human Performance and Body Composition lab at the University of Oklahoma. A designated flash drive was used to store and save collected data recorded by the instruments used in the study. Standardized data collection sheets were used to collect pre and post MVCs.

Statistical Analysis: Force complexity and variability data recorded from the Biopac will be analyzed using a MATLAB code R2018b. After SD, CV, DFA, AE, and SE have been calculated from the first three and last three contractions, a 2 group (Males v. Females) by 2 conditions (Maximal v. Submaximal) by 2 time point (Fresh v. End Task) repeated measures ANOVA was performed to determine if there are significant sex differences in force signal complexity and variability between males and females during maximal and submaximal exercise with Bonferroni corrections. A 2 condition (Maximal vs Submaximal) by 2 time point (Fresh v. End Task) repeated measures ANOVA was performed to determine within-group effects on complexity and variability measures with Bonferroni corrections. Effect sizes were determined using partial eta squared (ηp^2, small=0.01, moderate=0.06, large=0.14). Independent sample t-tests were used to determine if there are sex or time differences in

performance measures. Effect sizes were determined using Hedges G for unequal sampling (g, small=0.2, medium=0.5, large=0.8). The analyses were performed using SPSS software v. 28.0 (SPSS, Inc., Chicago, IL). Data will be presented as Means (SD) and $p<0.05$.

CHAPTER IV: RESULTS

Subject Characteristics: A total of 18 untrained subjects (10 females and 8 males) agreed to participation in the study following informed consent, and 16 of these subjects (9 females and 7 males) finished the study's protocols and procedures. One participant dropped out due to a sudden injury outside of the study, and one was removed due to a health condition that could've limited exercise. They consisted of males and females recruited primarily from the University of Oklahoma and surrounding areas. All subjects met the minimum ACSM guidelines to be considered non-sedentary and did not meet the requirements to be considered aerobically or resistance trained. The subject characteristics data can be found in Table 1. There was a significant sex difference in height ($t=5.1$, $p<0.001$, $g=2.4$) and weight ($t=2.3$,$p=0.037$,$g=1.1$), indicating the males were significantly taller and heavier than females.

Table 1: Subject Characteristics

	Male (n=7)	**Female (n=9)**	**Total (n=16)**
Age (years)	25.1(5.3)	21.0(3.2)	22.8(4.60)
Height (cm)	179.4(7.7)	163.5(4.7) *	170.4(10.1)
Weight (kg)	81.4(4.9)	65.3(4.8) *	72.4(15.7)
TMD	2.0(4.4)	1.0(14.8)	1.4(13.1)
Physical Activity (MET.min)	4475.7(3146.3)	6026.7(4375.2)	5348.2(3847.1)

*Values are expressed as mean (SD) between untrained males and females for age(years), height(cm), weight(kg), TMD (total mood disturbance), *Significantly different from males.*

Maximal Exercise Test: The performance measures collected during the maximal exercise test from can be found in Table 2. The MVC recorded prior to the test was significantly higher in males compared to females (t=3.3, p=.0.005, g=1.6), indicating a sex difference in quadricep force production. There was a significant increase in blood lactate levels (t=9.3, p<0.001, g=2.2), and RPE (t=16.2, p<0.001, g=3.8) from rest to immediate post exercise for both males and females indicating a time effect on carbohydrate metabolism. Males increased in blood lactate (t=5.7, p=0.001, g=1.86) and RPE (t=11.4, p<0.001, g=3.8) from beginning to end of the protocol. Females increased in blood lactate (t=7.1, p<0.001, g=2.1) and RPE (t=11.1, p<0.001, g=3.3) as well as from beginning to end of the maximal test.

Table 2: Performances Measures during Maximal Exercise Test

	Male (n=7)	**Female (n=9)**	**Total (n=16)**
TMD	-0.4(9.8)	0.6(18.0)	0.13(14.6)
Pre-MVC (N)	492.6(98.2)	346.4(78.1) *	410.3(112.9)
Last Contraction (N)	210.5(77.7) #	188.6(47.9) #	198.2(61.4)
Force % Difference	-54.01(13.1)	-45.4(9.0)	-49.14(11.5)
Torque (Nm)	321.6(24.2)	226.2(51.0) *	267.9(73.6)
Pre-RPE	7.7(2.0)	7.2(1.8)	7.44(1.8)
IP RPE	17.3(1.4) #	17.0(1.5) #	17.12(1.4) #
Pre-Lactate (mmol/dL)	1.6(0.5)	1.3(0.3)	1.4(0.5)
IP Lactate (mmol/dL)	6.3(2.6) #	5.5(2.0) #	5.8(2.2) #

*Values are expressed as mean (SD) for TMD (total mood disturbance), MVC (Maximal Voluntary Contraction, Torque (Nm), RPE (Rate of Perceived Exertion), IP(Immediate Post). *Significantly different from males. #Significantly different from Pre.*

Submaximal Exercise Test: The performance measures collected during the submaximal exercise test can be found in Table 3. There was a significant sex difference in force production at Pre (t=3.4, p=.0.004, g=1.6) and Post (t=3.04, p=0.009, g=1.5) with

increased force production in males. Force production decreased (t=10.2, p<0.001, g=2.4) and RPE (t=13.0, p<0.001, g=3.1) increased significantly at the end of exercise. Males had a significant decrease in force production (t=9.3, p<0.001, g=3.04) and increased RPE (t-7.9, p<0.001, g=2.6) at the end of exercise. Females had a significant drop in force production (t=7.2, p<0.001, g=2.2) and increased RPE (t=9.9, p<0.001, g=3.0) at the end of exercise.

Table 3: Performance Measures during Submaximal Exercise Test

	Male (n=7)	**Female (n=9)**	**Total (n=16)**
TMD	-1.0(3.5)	-2.9(11.0)	-2.1(10.2)
Pre-MVC (N)	504.8(90.2)	354.01(85.5) *	420.0(114.6)
Post-MVC (N)	321.8(63.7) #	229.7(57.2) *#	270.0(74.8) #
Pre-Torque (Nm)	329.6(58.9)	231.2(55.8) *	274.2(74.8)
Post-Torque (Nm)	210.2(41.6) #	150.0(37.4) *#	176.3(48.9) #
Pre-RPE	7.0(1.8)	7.0(1.2)	7.4(1.8)
Post-RPE	16.3(2.4) #	16.6(2.6) #	16.4(2.4) #
Force % Difference	-36.0(7.3)	-35.0(9.1)	-35.2(8.1)
TTF (s)	319.0(99.0)	438.0(221.0)	385.7(184.0)

*Values are expressed as mean (SD) between untrained males and females for TMD(total mood disturbance), MVC RPE(Rate of Perceived Exertion), percent change(%), MVC, and TTF(Time-to-Task Failure). *Significantly different from males. # Significant different from Pre.*

Force Signal Variability and Complexity Measures

The measurements used to determine force signal complexity include SD, CV, DFA, and AE can be found in table 4. The average of each measure from the first and last three contractions were compared to determine if there were significant condition, time, and sex interactions.

Table 4: Complexity and Variability Measures in Males and Females, before and after Maximal and Submaximal Exercise

	Maximal		***Submaximal***	
	Start	*End*	*Start*	*End*
Variability				
SD(N)				
Group	18.4(7.4)	20.5(10.5)	7.63(2.9) $	24.6(13.7) #
Male	21.9(9.9)	22.1(14.7)	9.08(2.4) $	29.2(14.5) #, ג
Female	15.7(4.1)	19.4(6.4)	6.51(2.8) $	21.1(12.7) #
CV (%)				
Group	5.23(1.3)	17.3(13.7) #	3.77(0.9)	13.9(6.3) #
Male	5.02(1.7)	14.0(3.6) #	3.80(0.8)	13.6(5.8) #
Female	5.40(0.9)	19.4(6.4) #	3.74(1.0)	14.2(7.0) #
Complexity				
DFA				
Group	1.72(0.1)	1.77(0.2)	1.64(0.1)	1.73(0.1) #
Male	1.75(0.1)	1.67(0.2)	1.59(0.1) $	1.74(0.1) ג, #
Female	1.71(0.1)	1.85(0.1) *, #	1.67(0.1) *	1.73(0.2) ג, #
AE				
Group	0.22(0.1)	0.16(0.1)	0.36(0.1) $	0.17(0.1) #
Male	0.25(0.1)	0.21(0.1)	0.36(0.1) $	0.16(0.1) #
Female	0.18(0.1) *	0.11(0.1) *, #	0.35(0.1) $	0.17(0.1) #

*Values are expressed as mean (SD) between untrained males and females for standard deviation (SD), Coefficient of Variation (CV), Detrended Fluctuation Analysis (DFA), and Approximate Entropy (AE) of the first and last three contractions during maximal and submaximal exercise.*Significantly different from males. #Significantly different from Start. $ Significantly different from start of Maximal exercise. ג Significantly different from end of maximal exercise.*

Standard Deviation (SD): The SD measures for the first and last three contractions during maximal and submaximal exercise can be found in Table 4 and Figure 1. There was a significant condition by time interaction ($F_{1,14}=24.002$, $p<0.001$, $\eta p^2 =0.632$). Males and females SD increased significantly ($p<0.001$) at the end of submaximal exercise (Figure 1).

There was a condition by time interaction for males ($F_{1,6}=20.973$, $p=0.004$, $\eta p^2=0.78$). Standard deviation was higher at the beginning of exercise in the maximal test compared to the submaximal test for males ($p=0.012$, $\eta p^2=0.68$) (Figure 1). SD was higher at end task in the submaximal test than the maximal test for males ($p=0.017$, $\eta p^2=0.64$) (Figure 1). There was a condition by time interaction for females ($F_{1,8}=6.23$, $p<0.037$, $\eta p^2=0.44$). Standard deviation was higher at beginning of exercise for the maximal exercise test compared to submaximal test for females ($p<0.001$, $\eta p^2=0.815$) (Figure 1).

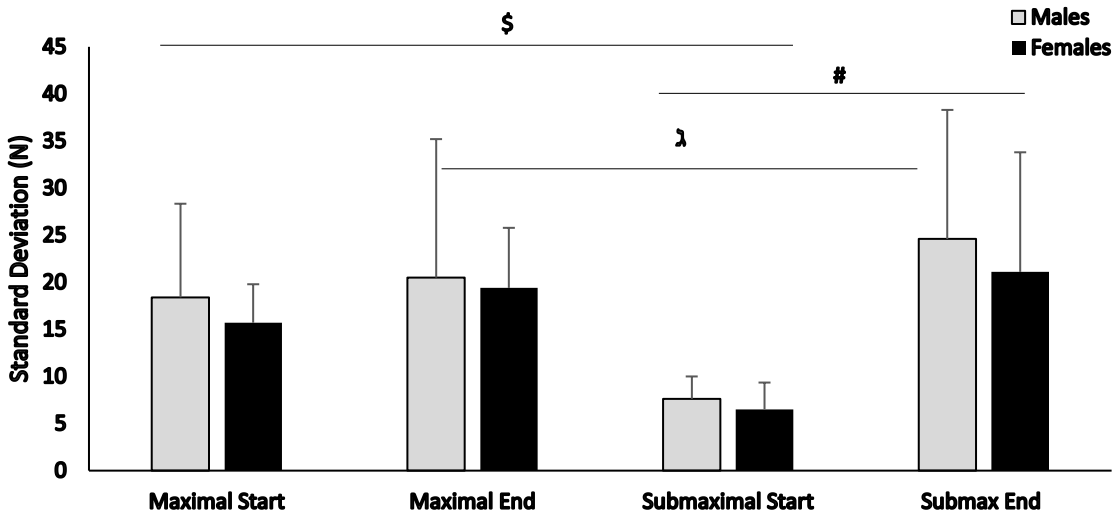

Figure 1: *Standard Deviation. – Grey Bars: Males, Black bars: Females, [#]Significantly different from start. [$] Significantly different from start of maximal. [ג] Significantly different from end of maximal. All values are Mean (SD).*

Coefficient of Variation (CV): The CV measures for the first and last three contractions during maximal and submaximal exercise can be found in table 4 and Figure 2. There was a significant main effect of time ($F_{1,14}=33.883$, $p<0.001$, $\eta p^2=0.708$) as CV increased from beginning to end during maximal and submaximal exercise (Figure 2). CV in males increased

for both conditions from beginning to end (F1,6=28.45, p=0.002, ηp^2=0.826) (figure 2). CV in females increased for both conditions from beginning to end (F1,8=17.31, p=0.003, ηp^2=0.684) (Figure 2).

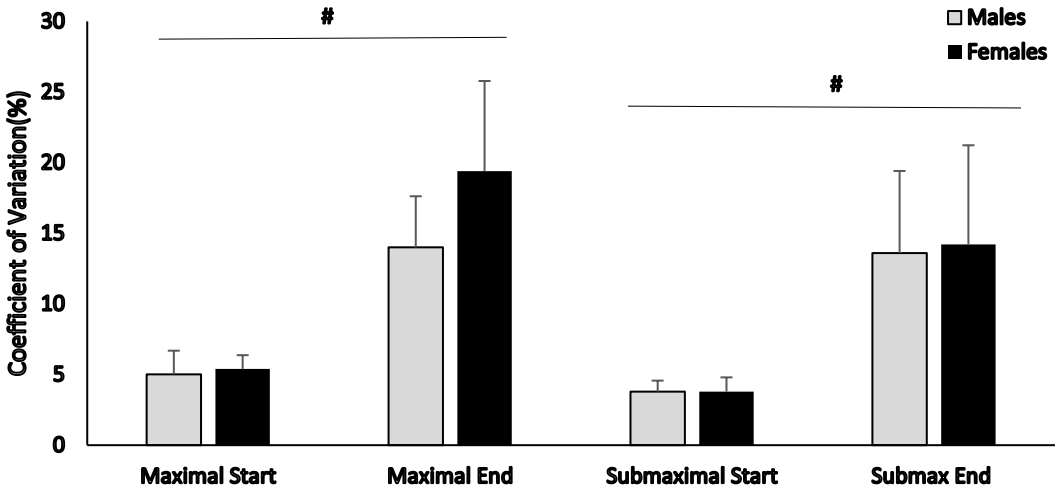

Figure 2: *Coefficient of Variation. – Grey Bars: Males, Black bars: Females. #Signifcantly different from start. All values are Mean (SD).*

Detrended Fluctuation Analysis (DFA): The DFA measures for the average of the first and last three contractions during maximal and submaximal exercise can be found in Table 4 and Figure 3. There was a significant condition by time by sex interaction (F1,14=14.983, p=0.002, ηp^2=0.517) with DFA was significantly higher in females compared to males at the end of maximal exercise and the beginning of submaximal exercise (p=0.002, ηp^2=0.517) (Figure 3). Males had significant within-group condition by time interactions (F1,6=10.9, p=0.016, ηp^2=0.646) (Figure 3). There was an increase in DFA at the end of submaximal exercise (p<0.001, ηp^2=0.889) and a higher DFA at the beginning of maximal exercise

compared to submaximal ($p<0.001$, $\eta p^2=0.893$) (Figure 3). Females had significant time effect ($F1,8=7.95, p=0.022$, $\eta p^2=0.499$) (Figure 3). DFA increased significantly at the end of maximal and submaximal exercise in females ($p=0.022$, $\eta p^2=0.499$) (Figure 3).

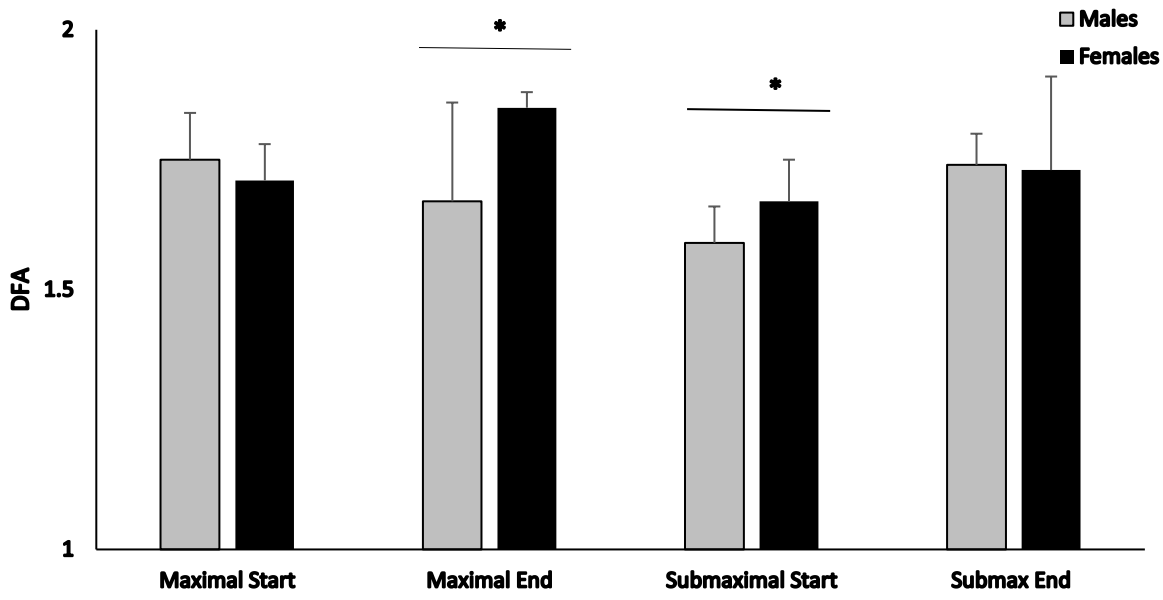

Figure 3: *Detrended Fluctuation Analysis. – Grey Bars: Males, Black bars: * Significant sex difference. All values are Mean (SD).*

Approximate Entropy (AE): The AE measures for the first and last three contractions during maximal and submaximal exercise can be found in Table 4 and Figure 4. There was a significant condition by time interaction ($F1,14=19.802$, $p<0.001$, $\eta p^2 =0.586$) (Figure 4). Males and females had an increased AE at the start of submaximal exercise compared to the start of maximal exercise (Figure 4). There was a condition by time interaction for males ($F1,6=12.2$, $p=0.013$, $\eta p^2=0.85$) (Figure 4). AE decreased significantly after submaximal exercise for males ($p=0.001$, $\eta p^2=0.001$) (Figure 4). AE was significantly higher at the beginning of maximal exercise compared to submaximal exercise in males ($p=0.013$,

ηp^2=0.67) (Figure 4). There was a significant condition by time interaction for females (F1,8=7.4, p=0.026, ηp^2=0.481) (Figure 4). AE decreased significantly after maximal (p=0.002, ηp^2=0.73) and submaximal exercise for females (p<0.001, ηp^2=0.78) (Figure 4). There was a condition by sex interaction (F1,14=14.973, p=0.002, ηp^2=0.517), where males had a higher AE than females at the beginning and end of maximal exercise (Figure 4).

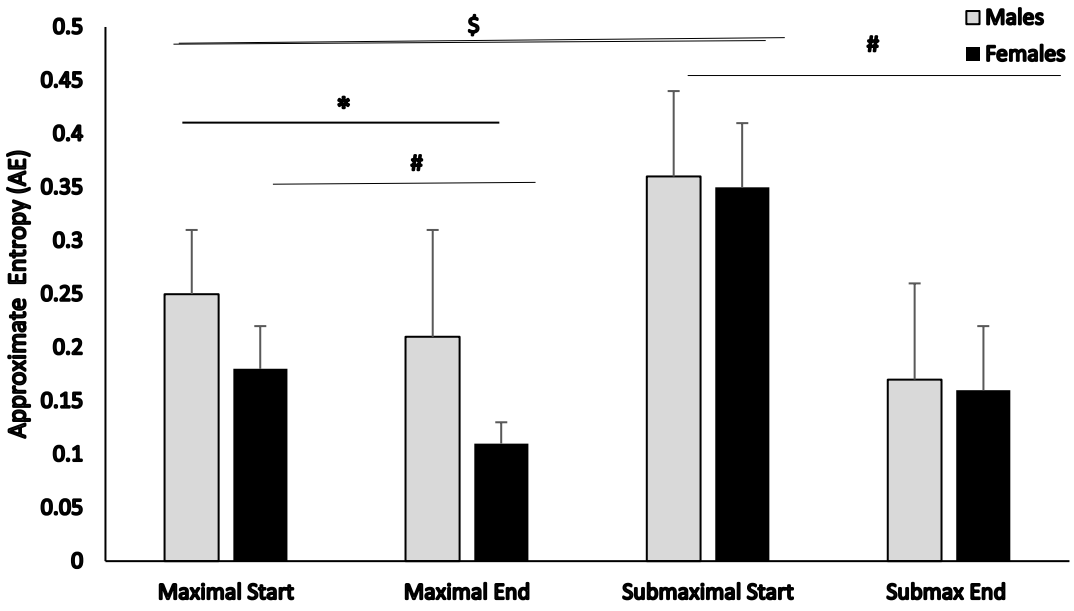

Figure 4: *Approximate Entropy. – Grey Bars: Males, Black bars.* ******* *Significantly different sex difference.* [#]*Signifcantly different at the end of exercise.* [$]*Significantly different from the start of maximal exercise. All values are Mean (SD).*

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CHAPTER V: DISCUSSION AND LIMITATIONS

The primary findings from this study were determined using the performance, variability, and complexity measurements collected during maximal and submaximal exercise. The maximal and submaximal exercise tests were successful in inducing fatigue (Bigland-Ritchie et al., 1986) in the quadricep muscles for males and females, indicated by a decline in force production and supported by increased pre/post RPE and lactate measures (Table 2 & 3).

Maximal force production was similar at the beginning and end of the maximal and submaximal exercise tests. Males produced greater force than females at the start of both intensities and end of submaximal exercise, but there was no significant sex difference in force at the end of maximal exercise (Table 2 & 3). Increased force production in males is a characteristic often seen during resistance exercise (Critchfield & Kravitz, 2008 & Hicks et al., 2001). This is attributed to increased muscle mass and type II fiber concentration capable of generating more force (Hicks et al., 2001). Although muscle mass and fiber percentage were not directly measured, the sex difference in body size (Table 1) found in the sample can be attributed to the difference in force production. Increased body size is often related to increased muscle mass and force production (Sjogaard et al., 1988).

The sex difference in body size and force production observed in this study are like other studies that observe muscle fatigue, as males tend to be larger than females with reduced fatigue resistance (Critchfield & Kravitz, 2008, Hicks et al., 2001, & Pincivero et al., n.d.). Females are typically more fatigue resistant compared to males due to increased type-I muscle fiber concentration and reduced muscle mass, this often leads to reduced force decrement and

increased time-to-task failure during resistance exercise (Pincivero et al. 2000, & Yoon et al., 2007). However, these studies report significant sex differences in fatigue resistance identified by increased time to exhaustion during isometric resistance exercise that were not observed in this study. Although females in this study had increased time to exhaustion with a moderate effect size during submaximal exercise this was not considered statistically significant ($p=.211$, $g=0.64$). ($n=16$). Force decrement behaved similarly, as there was no significant sex difference, but males did decrease at a higher percentage compared to females with a moderate-large effect size ($p=0.14$, $g=0.75$). This could be attributed to the study being underpowered because of the small sample size. Despite the lack of significance, female time to exhaustion during submaximal exercise behaved like females in other studies characterized by increased endurance and lower force production (Yoon et al., 2007).

Force signal variability behaved similarly for males and females before and after the onset of fatigue (Table 4). Force variability, described by the magnitude (SD) and amount (CV) of variability, is affected by maximal exercise as CV was found to increase significantly from the start to the end of exercise (Table 4). Variability in submaximal exercise behaved like maximal exercise with the addition of significant increase in SD from start to end. The difference in force variability between submaximal and maximal exercise can be identified by a larger SD at the beginning of maximal exercise (Figure 1). These findings were like force variability measures observed in a study by Pethick et al. (2015), where force variability increased significantly at the end of exercise. However, one difference between these two studies is the significant increase in SD after submaximal exercise compared to the end of maximal exercise males found in this study. In the study by Pethick et al. (2015), the participants performed at 40% of their MVC compared to 50% of their MVC in the current

study. The increase in intensity in this study is a potential factor for the difference in male force signal SD behavior at the end of submaximal exercise compared to maximal exercise. Despite this difference, the increase in variability with the onset of fatigue can be attributed to the adjustment in motor unit recruitment and firing rates after the onset of fatigue observed consistently in other studies (Contessa et al., 2009, Hunter & Enoka, 2003).

Despite the lack of statistically significant sex differences in time-to-exhaustion, force decrement, and force signal variability, the evidence shown by Wust et al. (2008) points that there is a sex-dependent factor that influences force production with the onset of fatigue. In their study they provided evidence that there is a sex-dependent mechanism during maximal exercise that is independent from blood flow occlusion and voluntary activation with the use of electrical stimulation. Therefore, they determined the sex difference occurs at a peripheral origin related to energy utilization and contractile speed. Since the current study did not directly measure energy utilization, contractile speed can be observed by changes in motor recruitment and firing rates indicated by force signal variability. However, because there was no significant sex difference in variability related to the influence of fatigue on muscle activation, and central fatigue was not removed from the current study this leaves us wondering if there is truly a sex-dependent fatigue component when central and peripheral fatigue are present during exercise. Variability is how much a signal changes, and for males and females the variability is expected to increase as intensity changes (Davids et al., 2003). How variability changes within a signal can identify patterns and predictability that equate to adaptations (Davids et al., 2003). This is where the observation of the neuromuscular system as whole becomes essential and where force signal complexity measures play a role.

Signal complexity described by the systems regularity (AE) and self-similarity (DFA), can describe the system's ability to adapt to dynamic change (Lipsitz & Goldberger, 1992). There is evidence to support that systems with high complexity (high AE and low DFA) are highly adaptive and better equipped to adjust to changes in their environment (Lipsitz & Goldberger, 1992). This presents the idea that healthier and more adaptive systems produce more complex signals in a time series capable of performing a task (Lipsitz, 2002). Therefore, complexity measures have the potential to assess the ability of the neuromuscular system to adapt with the onset of fatigue.

In this study, signal complexity decreased at the end of maximal and submaximal exercise. Males and females behaved similar in submaximal exercise as complexity signals decreased significantly during submaximal exercise (Table 4). Complexity was higher at the start of submaximal exercise compared to maximal exercise. These findings were like those found in the studies by Pethick and colleagues that examine the effect of fatigue on the ability of the neuromuscular systems ability to adapt during exercise (Pethick et al. 2015, 2016, 2019, & 2020). They attributed the change in signal complexity to the adaptations made by the neuromuscular system through motor control adjustments. However, this study was able to identify sex differences in force signal complexity during maximal and submaximal exercise (Table 4). Males had higher AE measures at the beginning and end of maximal exercise. Males had reduced DFA at the end of maximal and start of submaximal exercise. This indicates that untrained female's force signals are less complex than males at the beginning and end of maximal exercise and the start of submaximal exercise. These findings point to the possibility of a motor control sex-dependent factor that influence the neuromuscular system's ability to adapt during isometric resistance exercise.

Although the complexity measures of females were lower than that of males, we cannot assume that females are less capable of neuromuscular adaptation or performance during exercise. Again, despite the lack of significance, the effect size of the increased TTE and reduced force decrement indicate that females are more fatigue resistant than males. Therefore, we must look at the performance, variability, and complexity measures to describe how these measures interact with each other during fatigue to influence force production. We know that the males produced significantly more force at the beginning of maximal and submaximal exercise, and the end of submaximal exercise (Table 2 & 3). This can be attributed to the larger size of the males and increased muscle mass because of increased percentage of type II (Hicks et al. 2001). However, since the end-task maximal exercise force production was similar between males and female, potential explanations need to be explored. The identification of energy utilization and contractile speed as potential sex-dependent factors during blood occlusion in the study by Wust et al. (2008) suggest that that there is another factor at play in how males and females adapt to fatigue. Although the magnitude of variability did not change during maximal exercise the amount of variability did for both males and females. This indicates that contractile speed was influenced by motor recruitment and firing rates (St Clair Gibson et al., 2001). However, the lack of sex differences in the variability measures points at the signal complexity to describe the effect of fatigue on exercise. The force signals produced by females had similar structure and were more regular at the end of maximal exercise. Since there was a moderate-large effect size of reduced force decrement at the end of maximal exercise, and variability and overall force production in females were like males. The difference in the structure of the signal between males and females suggests that the force signals produced by female's neuromuscular system are not as complex at the beginning and

end of maximal exercise. However, we cannot confidently state that females have reduced ability to adapt to exercise but rather males produce more complex signals to maintain maximal exercise performance. The ability to maintain force production requires the neuromuscular system to provide all adaptations necessary to perform (St Clair Gibson et al., 2001). Because males are more likely to have increased muscle mass and type II muscle fiber percentage that contribute increased force production (Critchfield & Kravitz, 2008). These components are more likely to contribute to fatigue due to the occlusion of blood flow that limit metabolic byproduct removal and reduced oxidative capacity to replenish energy stores (Wüst et al., 2008). Therefore, it is possible that males require different patterns of muscle activation to maintain performance during fatigue through various combinations of motor recruitment and firing rates which could explain the sex differences observed in force signal complexity.

Limitations: The findings in these studies were primarily limited by an underpowered sample size. Because of the small sample significant sex differences in TTE, force decrement, and variability were not present despite moderate-large effect sizes. However, despite this limitation, there were still significant sex differences in complexity and performance measures, and significant within group condition by time interactions for performance, variability, and complexity measures. The explanations for the findings are also limited due to the lack of direct central and peripheral fatigue measurement. Central fatigue could be assessed using voluntary activation or EEG, while peripheral fatigue could be assessed using electrical stimulation or EMG. The use of a lactate curve or metabolic cart could be used to identify if the differences found were due to substrate utilization. The use of any of these measures

combined with complexity measures would be beneficial in determining if there is a limiting factor between males and females during fatigue.

CHAPTER VI: CONCLUSION

In conclusion, the research hypothesis pertaining to complexity was accepted, and the null hypotheses for variability was accepted. This states that there was a significant sex different in complexity but not variability. The major novel finding of this study includes reduced force signal complexity in females at the beginning and end of maximal exercise and the start of submaximal exercise. Other findings support the loss of complexity fatigue, increased variability with fatigue, increased force production in males, and reduced fatiguability in females.

Females are generally considered more fatigue resistant than males. This is attributed to multiple factors but agreement on whether this is a sex-dependent mechanism is still being explored. The recent use of signal complexity measures through signal regularity and self-similarity to describe a system's ability to adapt has shown potential to be a measure that can effectively describe the neuromuscular system's ability to respond to fatigue during exercise. This study found that males produce force signals that are more complex than females at the beginning and end of maximal exercise, and the beginning of submaximal exercise. Although it is not certain, the current and previous studies findings suggest that males produce more complex force signals indicating a greater range of muscle activation patterns through a combination of motor recruitment and firing rates to maintain performance during fatigue. Despite these interesting findings, further research is needed to build on the foundation of sex

differences in fatigue and complexity measures before a sex-dependent limiting factor can be determined.

References

Augustine, J. A., Nunemacher, K. N., & Heffernan, K. S. (2018). Menstrual phase and the vascular response to acute resistance exercise. European Journal of Applied Physiology, 118(5), 937–946. https://doi.org/10.1007/s00421-018-3815-1

Babault, N., Desbrosses, K., Fabre, M.-S., Michaut, A., & Pousson, M. (2006). Neuromuscular fatigue development during maximal concentric and isometric knee extensions. Journal of Applied Physiology, 100(3), 780–785. https://doi.org/10.1152/japplphysiol.00737.2005

Berchicci, M., Menotti, F., Macaluso, A., & Di Russo, F. (2013). The neurophysiology of central and peripheral fatigue during submaximal lower limb isometric contractions. Frontiers in Human Neuroscience, 7, 135. https://doi.org/10.3389/fnhum.2013.00135

Bigland-Ritchie B. (1984). Muscle fatigue and the influence of changing neural drive. Clinics in chest medicine, 5(1), 21–34.

Bigland-Ritchie, B., Furbush, F., & Woods, J. J. (1986). Fatigue of intermittent submaximal voluntary contractions: Central and peripheral factors. Journal of Applied Physiology (Bethesda, Md.: 1985), 61(2), 421–429. https://doi.org/10.1152/jappl.1986.61.2.421

Burnley, M., Vanhatalo, A., & Jones, A. M. (2012). Distinct profiles of neuromuscular fatigue during muscle contractions below and above the critical torque in humans. Journal of Applied

Physiology (Bethesda, Md.: 1985), 113(2), 215–223. https://doi.org/10.1152/japplphysiol.00022.2012

Contessa, P., Adam, A., & De Luca, C. J. (2009). Motor unit control and force fluctuation during fatigue. Journal of Applied Physiology, 107(1), 235–243. https://doi.org/10.1152/japplphysiol.00035.2009

Critchfield, B., & Kravitz, L. (2008). Fatigue Resistance: An Intriguing Difference in Gender.DEA Fitness Journal, 5(6), 19–21.

Davids, K., Glazier, P., Araújo, D., & Bartlett, R. (2003). Movement systems as dynamical systems: The functional role of variability and its implications for sports medicine. *Sports Medicine (Auckland, N.Z.)*, *33*(4), 245–260. https://doi.org/10.2165/00007256-200333040-00001

Gandevia S. C. (2001). Spinal and supraspinal factors in human muscle fatigue. Physiological reviews, 81(4), 1725–1789. https://doi.org/10.1152/physrev.2001.81.4.1725

Goldberger, A. L., Peng, C.-K., & Lipsitz, L. A. (2002). What is physiologic complexity and how does it change with aging and disease? *Neurobiology of Aging*, *23*(1), 23–26. https://doi.org/10.1016/s0197-4580(01)00266-4

Green, H. J. (1997). Mechanisms of muscle fatigue in intense exercise. Journal of Sports Sciences, 15(3), 247–256. https://doi.org/10.1080/026404197367254

Guertin, P. A. (2013). Central Pattern Generator for Locomotion: Anatomical, Physiological, and Pathophysiological Considerations. Frontiers in Neurology, 3, 183. https://doi.org/10.3389/fneur.2012.00183

Hirvonen, J., Rehunen, S., Rusko, H., & Härkönen, M. (1987). Breakdown of high-energy phosphate compounds and lactate accumulation during short supramaximal exercise. European Journal of Applied Physiology and Occupational Physiology, 56(3), 253–259. https://doi.org/10.1007/BF00690889

Hicks, A. L., Kent-Braun, J., & Ditor, D. S. (2001). Sex Differences in Human Skeletal Muscle Fatigue. Exercise and Sport Sciences Reviews, 29(3), 109–112.

Hooper, A. E. C., Bryan, A. D., & Eaton, M. (2011). Menstrual Cycle Effects on Perceived Exertion and Pain During Exercise Among Sedentary Women. *Journal of Women's Health*, *20*(3), 439–446. https://doi.org/10.1089/jwh.2010.2042

Hunter, S. K., & Enoka, R. M. (2003). Changes in muscle activation can prolong the endurance time of a submaximal isometric contraction in humans. Journal of Applied Physiology, 94(1), 108–118. https://doi.org/10.1152/japplphysiol.00635.2002

Joan Dawson, M., Gadian, D. G., & Wilkie, D. R. (1978). Muscular fatigue investigated by phosphorus nuclear magnetic resonance. Nature, 274(5674), 861–866. https://doi.org/10.1038/274861a0

Lipsitz, L. A., & Goldberger, A. L. (1992). Loss of 'complexity' and aging. Potential applications of fractals and chaos theory to senescence. *JAMA, 267*(13), 1806–1809.

Lipsitz, L. A. (2002). Dynamics of Stability: The Physiologic Basis of Functional Health and Frailty. *The Journals of Gerontology: Series A, 57*(3), B115–B125. https://doi.org/10.1093/gerona/57.3.B115

Mills, K. R. (2005). The basics of electromyography. Journal of Neurology, Neurosurgery & Psychiatry, 76(suppl 2), ii32–ii35. https://doi.org/10.1136/jnnp.2005.069211

Monod H, Scherrer J. The work capacity of a synergic muscle group. Ergonomics. 1965;8(3):329–38.

Pethick, J., Winter, S. L., & Burnley, M. (2015). Fatigue reduces the complexity of knee extensor torque fluctuations during maximal and submaximal intermittent isometric contractions in man. *The Journal of Physiology, 593*(8), 2085–2096. https://doi.org/10.1113/jphysiol.2015.284380

Pethick, J., Winter, S. L., & Burnley, M. (2016). Loss of knee extensor torque complexity during fatiguing isometric muscle contractions occurs exclusively above the critical torque. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 310(11), R1144–R1153. https://doi.org/10.1152/ajpregu.00019.2016

Pethick, J., Winter, S. L., & Burnley, M. (2019). Fatigue reduces the complexity of knee extensor torque during fatiguing sustained isometric contractions. European Journal of Sport Science, 19(10), 1349–1358. https://doi.org/10.1080/17461391.2019.1599450

Pethick, J., Winter, S. L., & Burnley M. (2020). Physiological Evidence That the Critical Torque Is a Phase Transition, Not a Threshold. Medicine and Science in Sports and Exercise, 52(11), 2390–2401. https://doi.org/10.1249/MSS.0000000000002389

Peng, C.-K., Costa, M., & Goldberger, A. L. (2009). Adaptive Data Analysis of complex Fluctuations in physiologic time series. Advances in Adaptive Data Analysis, 1(1), 61–70. https://doi.org/10.1142/S1793536909000035

Poole, D. C., Burnley, M., Vanhatalo, A., Rossiter, H. B., & Jones, A. M. (2016). Critical Power: An Important Fatigue Threshold in Exercise Physiology. Medicine and Science in Sports and Exercise, 48(11), 2320–2334. https://doi.org/10.1249/MSS.0000000000000939

Sadri, K., Khani, M., & Sadri, I. (2014). Role of Central Fatigue in Resistance and Endurance Exercises: An Emphasis on Mechanisms and Potential Sites. SportLogia, 10(2), 65–80.

Sojgaard, G., Savard, G., & Juel, C. (1988). Muscle blood flow during isometric activity and its relation to muscle fatigue. *European Journal of Applied Physiology and Occupational Physiology*, *57*(3), 327–335. https://doi.org/10.1007/BF00635992

St Clair Gibson, A., Lambert, M. I., & Noakes, T. D. (2001). Neural Control of Force Output During Maximal and Submaximal Exercise: Sports Medicine, 31(9), 637–650. https://doi.org/10.2165/00007256-200131090-00001

Wang, L., & Buchanan, T. S. (2002). Prediction of joint moments using a neural network model of muscle activations from EMG signals. IEEE Transactions on Neural Systems and Rehabilitation Engineering, 10(1), 30–37. https://doi.org/10.1109/TNSRE.2002.1021584

Wüst, R. C. I., Morse, C. I., De Haan, A., Jones, D. A., & Degens, H. (2008). Sex differences in contractile properties and fatigue resistance of human skeletal muscle. Experimental Physiology, 93(7), 843–850. https://doi.org/10.1113/expphysiol.2007.041764

Zając, A., Chalimoniuk, M., Maszczyk, A., Gołaś, A., & Lngfort, J. (2015). Central and Peripheral Fatigue During Resistance Exercise – A Critical Review. Journal of Human Kinetics, 49, 159–169. https://doi.org/10.1515/hukin-2015-0118

Vøllestad, N. K. (1997). Measurement of human muscle fatigue. Journal of Neuroscience Methods, 74(2), 219–227. https://doi.org/10.1016/S0165-0270(97)02251-6

Signed Consent to Participate in Research

Would you like to be involved in research at the University of Oklahoma?

I am (BLANK) from the Department of Health and Exercise Science and I invite you to participate in my research project entitled “Examining the effects of fatigue on the complexity of force production during a maximal and submaximal test.” This research is being conducted at the Human Performance and Body Composition Laboratory in the Sarkeys Fitness Center on the Norman Campus of the University of Oklahoma. You were selected as a possible participant because you are a man or a woman between the ages of 18-35 years old and are deemed at a low risk of cardiac arrest during exercise based upon your responses to the PAQ-Q questionnaire, the Health Screening Questionnaire, and your physician (if necessary). You must be at least 18 years of age to participate in this study.

Please read this document and contact me to ask any questions that you may have BEFORE agreeing to take part in my research.

What is the purpose of this research? 1) To examine the effect of training status on muscle torque and muscle electrical activity (EMG) signal complexity during a fatiguing exercise test. 2) examine sex differences in muscle torque signal complexity during a fatiguing exercise test.

How many participants will be in this research? Up to 60 people will take part in this research

What will I be asked to do? If you agree to be in this research, you will be asked to complete 3 visits to the Human Performance and Body Composition Lab.

The first visit will include the completion of medical history, exercise screening, and physical activity questionnaires, and height and weight measurement. These will be used to ensure that you can complete a fatiguing exercise task. A submaximal familiarization procedure will be conducted using a special piece of equipment called Kin-Com Isokinetic Dynamometer. This piece of equipment will measure how strong your leg muscles are. You will also be given a sleep diary to ensure you are getting a proper night's sleep prior to the following visits. For female participants, a menstrual cycle questionnaire will be asked to be completed on the first visit. The following visits will be corresponded with the information provided in the questionnaire.

The second and third visits will consist of a fatiguing exercise task. Force and muscle activity will be measured using approved and official testing procedures. At the beginning of both tests, 3 maximal voluntary contractions will be performed, followed by 10 minutes of rest. The test on the second visit includes an all-out maximal test consisting of 30 leg extensions for 5 minutes. The test on the third visit includes a submaximal test performed until failure.

How long will this take? Your participation will include 3 visits with approximately 30-60 minutes per day for completion.

What are the risks and/or benefits if I participate? There are no intended direct benefits from participation. The risks include those associated with typical exercise such as muscle soreness, dizziness, nausea, fatigue, and sudden cardiac arrest.

Risks related to COVID-19: The research protocol includes precautions that help prevent the transmission of the COVID-19 virus. Individuals who are considered high risk for COVID-19 complications such as older adults and those with health complications are excluded from the study.

What do I do if I am injured? Any injury during participation needs to be reported to the active researcher immediately. Care will be provided to the researcher's knowledge of care along with access to emergency medical services. However, any medical cost will not be covered for treatment as the University of Oklahoma Norman Campus has not set aside funds for compensation in the event of an injury.

Will I be compensated for participating? Participants will receive a $15 gift card at the end of the study.

Who will see my information? All research reports will have de-identified data that make it impossible to identify you. The research records will only be accessible to approved researchers and the OU institutional Review Board, and will be stored in a secure location.

You reserve the right to access any of your collected research data at the end of the entire research and consensus to this temporary restriction.

Do I have to participate? There is no penalty or loss in benefits if you do not participate. You reserve the right to not answer any question and can stop participation at any time.

What will happen to my data in the future? After your data is de-identified, your data may be shared with other researchers or used in other research without obtaining additional consent from you.

Will I be contacted again? The researcher may contact you for other research possibilities or collect additional data.

I give my permission for the researcher to contact me in the future. ____ Yes ____ No

Who do I contact with questions,concerns, or complaints? If you have questions, concerns or complaints about the research or have experienced a research-related injury, contact me at rdlarson@ou.edu or at 353-359-8432.

You can also contact the University of Oklahoma – Norman Campus Institutional Review Board (OU-NC IRB) at 405-325-8110 or irb@ou.edu if you have questions about your rights as
a research participant, concerns, or complaints about the research and wish to talk to someone other than the researcher(s) or if you cannot reach the researcher(s).

You will be given a copy of this document for your records. By providing information to the researcher(s), I am agreeing to participate in this research.

Participant Signature	**Print Name**	**Date**
Signature of Researcher Obtaining Consent	**Print Name**	**Date**
SIgnature of Witness (if applicable)	**Print Name**	**Date**

AUTHORIZATION TO USE or SHARE

HEALTH INFORMATION THAT IDENTIFIES YOU FOR RESEARCH

An Informed Consent Document for Research Participation may also be required.

Title of Research Project**: Examining the Effects of Fatigue on the Complexity of Force Production, Brain Activity, and Muscle Activity during a Maximal and Submaximal Exercise Test**

IRB Number:
Leader of Research Team: **Rebecca Larson**

Address: **Department of Health and Exercise Science, 1401 Asp Avenue SJSC 117, Norman, OK, 73019**
Phone Number: **405-325-6325**

If you decide to sign this document, University of Oklahoma (OU) researchers may use or share information that identifies you (protected health information) for their research. Protected health information will be called PHI in this document.

PHI To Be Used or Shared. Federal law requires that researchers get your permission (authorization) to use or share your PHI. If you give permission, the researchers may use or share with the people identified in this Authorization any PHI related to this research from your medical records and from any test results. Information used or shared may include all information relating to any tests, procedures, surveys, or interviews as outlined in the consent form; medical records and charts; name, address, telephone number, date of birth, race, government-issued identification numbers, and can include physical findings from questionnaires, basal body temperature readings,anthropometric measures, and graded-exercise tests.

Purposes for Using or Sharing PHI. If you give permission, the researchers may use your PHI to examine how signal complexity in EEG, EMG, and Force production changes overtime during fatigue.

Other Use and Sharing of PHI. If you give permission, the researchers may also use your PHI to develop new procedures or commercial products. They may share your PHI with other researchers, the research sponsor and its agents, the OU Institutional Review Board, auditors and inspectors who check the research, and government agencies such as the Department of Health and Human Services Health whether past, present or future, created or maintained by a Covered

Entity.(HHS), and when required by law. The researchers may also share your PHI with no one outside of the main research team.

Confidentiality. Although the researchers may report their findings in scientific journals or meetings,they will not identify you in their reports. The researchers will try to keep your information confidential, but confidentiality is not guaranteed. The law does not require everyone receiving the information covered by this document to keep it confidential, so they could release it to others, and federal law may no longer protect it.

YOU UNDERSTAND THAT YOUR PROTECTED HEALTH INFORMATION MAY INCLUDE INFORMATION REGARDING A COMMUNICABLE OR NONCOMMUNICABLE DISEASE.

Voluntary Choice. The choice to give OU researchers permission to use or share your PHI for their research is voluntary. It is completely up to you. No one can force you to give permission. However, you must give permission for OU researchers to use or share your PHI if you want to participate in the research and, if you cancel your authorization, you can no longer participate in this study.

Refusing to give permission will not affect your ability to get routine treatment or health care unrelated to this study from OU.

Canceling Permission. If you give the OU researchers permission to use or share your PHI, you have a right to cancel your permission whenever you want. However, canceling your permission will not apply to information that the researchers have already used, relied on, or shared or to information necessary to maintain the reliability or integrity of this research.

End of Permission. Unless you cancel it, permission for OU researchers to use or share your PHI for their research will never end.

Contacting OU: You may find out if your PHI has been shared, get a copy of your PHI, or cancel your permission at any time by writing to:
Privacy Official or Privacy Board
University of Oklahoma, PO Box 26901 201 Oklahoma City, OK 73190
Stephenson Pkwy, Suite 4300A Norman, OK 73019
If you have questions, call: (405) 271-2511 or (405) 325-8110

Access to Information. You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this

medical information until the entire research study is completely finished. You consent to this temporary restriction.

Giving Permission. By signing this form, you give OU and OU researchers, led by the ResearchTeam Leader permission to share your PHI for the research project listed at the top of this form.

Participant Name (Print): _____

_____ _____
Signature of Participant Date
or Parent if Participant is a minor

Or

_____ _____
Signature of Legal Representative** Date

**If signed by a Legal Representative of the Participant, provide a description of the relationship to the Participant and the authority to act as Legal Representative:

_____
OU may ask you to produce evidence of your relationship.

A signed copy of this form must be given to the Participant or the Legal Representative at thetime this signed form is provided to the researcher or his representative.

Research Participants Needed

Are you interested in contributing to the understanding of the neuromuscular system and shortening the research gap between males and females?

The Body composition and Human Performance lab is conducting a study titled: "Examining the Effects of Fatigue on the Complexity of Force Production, Brain Activity, and Muscle Activity During a Maximal and Submaximal Exercise Test".

To participate

- Healthy male and female participants with no cardiovascular or neurological/neuromuscular disorders and are free from any major dominant leg injuries/surgeries within the past year.

- Individuals who meet the ACSM activity recommendations of **at least**: -150 mins of moderate-intensity activity or 75 minutes of vigorous-intensity activity/week **AND** 2 or more days of resistance training activity/week, **but** are not considered elite/national level athletes.

- Females: You cannot be pregnant.

3 visits required (~ 1 hour per visit)

- Total time commitment is approximately 3 hours.
- Testing will take place in the Human Body Composition Lab at the University of Oklahoma Norman Campus
- Participants will be compensated with a $15 Amazon gift card for their time.

If you are eligible and interested, please contact: Brady Rule (brady.d.rule-1@ou.edu), Grant Chesbro (gchesbro@ou.edu) or Dr. Rebecca Larson (Primary Investigator, rdlarson@ou.edu) The University of Oklahoma is an equal opportunity institution.

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Training Diary

1. In the last week, how many days did you train?

2. How many days per week did you participate in resistance training?

3. For how long each day did you resistance train?

4. How many days did you participant in aerobic training?

5. What type of aerobic training did you participate in (e.g., running, cycling, swimming, etc.)?

6. How long each day did you participate in aerobic training?

7. How long have you engaged in this routine?

To: Whom it may concern,

Healthy participants needed to further the understanding of the neuromuscular system, and to shorten the research gap between males and females. Participants will receive a $15 dollar Amazon gift card for their time commitment.

Principle Investigator: Rebecca D Larson, PhD

Study Title: "Examining the Effects of Fatigue on the Complexity of Force Production, Brain Activity, and Muscle Activity During a Maximal and Submaximal Exercise Test"

To Participate: Healthy Males and Females, ages 18-35, without neuromuscular disease/disorders, or major injuries to their dominant leg in the past year. Females that are not pregnant. Individuals who meet the ACSM activity recommendations of at least: -150 mins of moderate-intensity activity or 75 minutes of vigorous-intensity activity/week

AND

-2 or more days of resistance training activity/week

Required Time Commitment: 3 visits

Visit 1: Paperwork, and protocol familiarization (~ 1 hour)

Visit 2: Brief questionnaire and maximal effort fatigue test, (~ 1 hour)

Visit 3: Brief questionnaire and submaximal effort fatigue test, (~ 1 hour)

If you are interested in participating in this study please contact: Brady Rule or Grant Chesbro.

Brady.D.Rule-1@ou.edu or 918-720-3112

Gchesbro@ou.edu or 913-594-1119

Department of Health and Exercise Science

Body Composition & Human Performance Laboratory

Participants cleared for the study will be asked to report to the Human Performance & Body Composition Lab in the Department of Health & Exercise Science for experimental testing. All participants will be asked to refrain from any strenuous activity, alcohol, caffeine, non-steroidal anti-inflammatory drugs , and smoking for 12 hours prior to each visit. Additionally, participants will be asked to come to the lab in a hydrated state and having eaten at least 3 hours prior to each visit. All individuals will provide verbal and written informed consent of the procedures and protocols associated with the study design.

Visit 1 – Familiarization (~60 Minutes)

Participants will read the consent form and be briefed on the purpose and procedures of the study. After reading the consent form, participants will confirm their understanding that they may withdraw their consent at any point and for any reason without penalty. If they wish to participate, they will sign the informed consent form, a Health Insurance Portability and Accountability Act (HIPPA) form, and fill out the following questionnaires; Physical Activity Readiness Questionnaire (PAR-Q), International Physical Activity Questionnaire (IPAQ), self-reported training status,and finally the Profile of Mood States. Additionally, female participants will be asked to complete a Menstrual History Questionnaire to ensure they are not performing the task during menses. The participants will be provided sufficient time to review the documents, ask questions, and consult their primary physician, family members, etc.

Once the paperwork is completed, the participants height and weight will be recorded. Standing height will be measured to the nearest 0.5 cm using a calibrated stadiometer. Body weight will be measured to the nearest 0.01 kg using a clinical scale which has been calibrated. During the body weight measurements, the participants will be asked to wear minimal clothing such as a t-shirt and shorts. Body weight will be measured at each visit.

Participants will then be familiarized with the maximal voluntary contraction (MVC) protocol. These contractions will be performed using a special piece of equipment that measures force production called a KinCom isokinetic dynamometer. The participants will be seated upright in the dynamometer with the hips at a 90-degree angle and the knee extended out to an angle of 110 degrees. The participants will be strapped into the dynamometer using straps positioned to go across the waist and chest and at the ankle to prevent extra movement that could arise from the MVC. The participants will be asked to complete 3 maximal contractions using their thigh muscles. The contractions will last for 6 seconds with 60 seconds of rest between the contractions. The participants will be instructed to contract and relax by the investigator.

Finally the participants will be familiarized with the fatiguing protocol. The participants will remain seated and secured to the dynamometer. For the testing day protocols, a 6-second contraction followed by a 4-second rest duty cycle will be used. A Stop-Go PowerPoint will be shown to the participant and the participants will perform 2-minutes of practice contractions for familiarization.

Visit 2 – Maximal Testing (60 Minutes)

There will be a minimum of 24 hours between visits 1 and 2. First, the participants will fill out the Profile of Mood States. If participants do not get at least 5 hours of sleep the night before the visit, the visit will be rescheduled. The participants will be fitted with EMG before the protocol begins. Then the participants will complete 3 MVCs with the same protocol as in Visit 1. Following the MVC protocol, the participants will have a 10-minute rest period.

Before the maximal protocol, blood lactate and rating of perceived exertion (RPE) will be measured. For blood lactate measurement, the participants will be seated and using a small finger stick on their left hand, a blood sample will be obtained on an analysis strip. The strip will be inserted into a calibrated blood lactate analyzer. RPE is measured on a scale of 6-20 with 6 being low exertion and 20 being maximal exertion. A scale will be presented to the participants with verbal anchors. The participant will be asked to rate their current perceived exertion.

After the 10-minute rest period, the participants will be asked to perform a maximal protocol that they were familiarized with during Visit 1. This protocol will consist of 30 contractions over 5 minutes with a 6 second contraction followed by a 4 second rest. A stop-go PowerPoint will be provided visually for the participants to follow. The participants will be instructed to give a maximal effort on each of the 30 contractions. Their maximal force production from the MVC protocol will be provided visually and the participants will be asked to match this force output for at least the first 3 contractions during the maximal protocol. The participants will be informed that their force production may decrease during the protocol, but to continue to provide maximal effort. At 30-second intervals during a rest interval, the participants will be asked a yes-no question on whether or not they feel fatigued. Immediately following the 5-minute protocol, blood lactate and RPE will be assessed for the participants. Blood lactate will also be assessed 1-minute post exercise[LDJ7] .Participants will not be given verbal encouragement due to possible influence of the EEG.

Following the maximal protocol, the participants will be given a 20-minute rest period. Following the rest period, the participants will be instructed to hold a 6-second contraction at various percentages of their MVC (20, 40, 60, & 80%), determined from the protocol at the start of the visit. Sixty (60) seconds of rest will be provided between contractions.

Visit 3 – Submaximal Testing (60 Minutes)

First, participants will need to wait at least a minimum of 48 hours between visits 2 and 3. The participants will fill out the Profile of Mood States. Similar to visit 2 if the participants do not get at least 5 hours of sleep the night before the visit, the visit will be rescheduled. The participants will be fitted with EMG. Before the submaximal protocol, RPE will be assessed. Then the participants will complete 3 MVCs with the same protocol as in Visit 1. Following the MVC protocol, the participants will have a 10-minute rest period.

The submaximal test will be performed at 50% of their maximal voluntary contraction, which will be determined from the data from the maximal test in Visit 2. The target force will be provided to the participants through visual feedback. The participants will be asked to perform intermittent contractions until task failure. The participants will be asked to match force production to the line

on the screen for 6 seconds followed by a 4 second rest. The test will end at voluntary termination or if the participants cannot reach the target force on two consecutive contractions. At the end of the test, RPE will be assessed. Time to task failure will be recorded. Immediately following the test, the participant will perform 3 MVCs with 1 minute rest in between each contraction.

(October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000).

Assessment of Physical Activity: An International Perspective. Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

Yes ☐

☐ No → Skip to PART 2: TRANSPORTATION

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

   _____ **days per week**

   ☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

   _____ **days per week**

   ☐ No job-related walking → Skip to PART 2: TRANSPORTATION

7. How much time did you usually spend on one of those days **walking** as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

   _____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

   _____ **hours per day**
   _____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

    _____ **days per week**

    ☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

    _____ **hours per day**
    _____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

    _____ **days per week**

    ☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK,*** HOUSE MAINTENANCE, AND CARING FOR FAMILY

13. How much time did you usually spend on one of those days **walking** from place to place?

    _____ **hours per day**
    _____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

    _____ **days per week**

    ☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

    _____ **hours per day**
    _____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

    _____ **days per week**

    ☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

    _____ **hours per day**
    _____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

    _____ **days per week**

    ☐ No moderate activity inside home → ***Skip to PART 4: RECREATION,***

SPORT AND LEISURE-TIME PHYSICAL ACTIVITY

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise, or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities

like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
    _____ **hours per day**
    _____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

    _____ **hours per day**
    _____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

    _____ **hours per day**
    _____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

I.D. Number: _____ Session Number: _____ Date:

_____

POMS-B QUESTIONNAIRE

INSTRUCTIONS: Below is a list of words that describe feelings that people have. Please read each word carefully. Then circle the number that best describes:

☐ How you have been feeling during the PAST WEEK, INCLUDING TODAY.

☐ How you feel RIGHT NOW.

	Not At All	A Little	Moderately	Quite a Bit	Extremely
1. Tense	0	1	2	3	4
2. Angry	0	1	2	3	4
3. Worn out	0	1	2	3	4
4. Lively	0	1	2	3	4
5. Confused	0	1	2	3	4
6. Shaky	0	1	2	3	4
7. Sad	0	1	2	3	4
8. Active	0	1	2	3	4
9. Grouchy	0	1	2	3	4
10. Energetic	0	1	2	3	4
11. Unworthy	0	1	2	3	4
12. Uneasy	0	1	2	3	4
13. Fatigued	0	1	2	3	4
14. Annoyed	0	1	2	3	4
15. Discouraged	0	1	2	3	4

PLEASE ANSWER QUESTIONS ON OTHER SIDE

I.D. Number: _____ Session Number: _____ Date: _____

POMS-B QUESTIONNAIRE

INSTRUCTIONS: Below is a list of words that describe feelings that people have. Please read each word carefully. Then circle the number that best describes:

☐ How you have been feeling during the PAST WEEK, INCLUDING TODAY.

☐ How you have been feeling during the PAST 24 HOURS.

	Not At All	A Little	Moderately	Quite a Bit	Extremely
16. Nervous	0	1	2	3	4
17. Lonely	0	1	2	3	4
18. Muddled	0	1	2	3	4
19. Exhausted	0	1	2	3	4
20. Anxious	0	1	2	3	4
21. Gloomy	0	1	2	3	4
22. Sluggish	0	1	2	3	4
23. Weary	0	1	2	3	4
24. Bewildered	0	1	2	3	4
25. Furious	0	1	2	3	4
26. Efficient	0	1	2	3	4
27. Full of Pep	0	1	2	3	4

28. Bad-tempered	0	1	2	3	4
29. Forgetful	0	1	2	3	4
30. Vigorous	0	1	2	3	4

Approval of Study Modification – Expedited Review – AP0

Date: April 27, 2023 **IRB#:** 15502

Principal Investigator: Rebecca Larson, PhD **Reference No: 747453**

Study Title: Examining the Effects of Fatigue on the Complexity of Force Production and Muscle Activity during a Maximal and Submaximal Exercise Test

Approval Date: 04/27/2023

Modification Description: Brady is being removed as per graduate school requirement as Brady is graduating this spring

The review and approval of this submission is based on the determination that the study, as amended, will continue to be conducted in a manner consistent with the requirements of 45 CFR 46.

To view the approved documents for this submission, open this study from the My Studies option, go to Submission History, go to Completed Submissions tab and then click the Details icon.

If the consent form(s) were revised as a part of this modification, discontinue use of all previous versions of the consent form.

If you have questions about this notification or using iRIS, contact the HRPP office at (405) 325-8110 or irb@ou.edu. The HRPP Administrator assigned for this submission: Kat L Braswell.

Cordially,

Kendra Williams-Diehm, Ph.D.
Vice Chair, Institutional Review Board

Approval of Study Modification – Expedited Review – AP0

Date: February 08, 2023 **IRB#:** 15502

Principal Investigator: Rebecca Larson, PhD **Reference No: 744929**

Study Title: Examining the Effects of Fatigue on the Complexity of Force Production, Brain Activity, and Muscle Activity during a Maximal and Submaximal Exercise Test

Approval Date: 02/08/2023

Modification Description:
Remove EEG. Add MVCs to Visit 3.

The review and approval of this submission is based on the determination that the study, as amended, will continue to be conducted in a manner consistent with the requirements of 45 CFR 46.

To view the approved documents for this submission, open this study from the My Studies option, go to Submission History, go to Completed Submissions tab and then click the Details icon.

If the consent form(s) were revised as a part of this modification, discontinue use of all previous versions of the consent form.

If you have questions about this notification or using iRIS, contact the HRPP office at (405) 325-8110 or irb@ou.edu. The HRPP Administrator assigned for this submission: Nicole A Cunningham.

Cordially,

Kendra Williams-Diehm, Ph.D.
Vice Chair, Institutional Review Board
Approval of Initial Submission – Exempt from IRB Review – AP01

Date: January 31, 2023 **IRB#:** 15502

Principal Investigator: Rebecca Larson, PhD

Approval Date: 01/30/2023

Exempt Category: 2

Study Title: Examining the Effects of Fatigue on the Complexity of Force Production, Brain Activity, and Muscle Activity during a Maximal and Submaximal Exercise Test

On behalf of the Institutional Review Board (IRB), I have reviewed the above-referenced research study and determined that it meets the criteria for exemption from IRB review. To view the documents approved
for this submission, open this study from the *My Studies* option, go to *Submission History*, go to *Completed Submissions* tab and then click the *Details* icon.

As principal investigator of this research study, you are responsible to:

- Conduct the research study in a manner consistent with the requirements of the IRB and federal regulations 45 CFR 46.
- Request approval from the IRB prior to implementing any/all modifications as changes could affect the exempt status determination.
- Maintain accurate and complete study records for evaluation by the HRPP Quality Improvement Program and, if applicable, inspection by regulatory agencies and/or the study sponsor. Notify the IRB at the completion of the project.

If you have questions about this notification or using iRIS, contact the IRB @ 405-325-8110 or irb@ou.edu.

Cordially,

Kendra Williams-Diehm, Ph.D.
Vice Chair, Institutional Review Board