11-8-2023 11:30 AM

Force Variability and Neural Control Differences in an Upper and Lower Limb Muscle

Kherto Ahmed, *Western University*

Supervisor: Christie, Anita D., *The University of Western Ontario*
A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Kinesiology

Recommended Citation

Ahmed, Kherto, "Force Variability and Neural Control Differences in an Upper and Lower Limb Muscle" (2023). *Electronic Thesis and Dissertation Repository*. 9761.
https://ir.lib.uwo.ca/etd/9761

Abstract

This study examined force and motor unit firing rate variability in the first dorsal interosseous (FDI) and the tibialis anterior (TA), focusing on sex-related differences and physical activity. Isometric contractions in the FDI and TA muscles in 12 males and 12 females were examined using electromyography and custom-built dynamometers. Physical activity was monitored using tri-axial accelerometers over seven days. Findings revealed that females exhibited higher CV (coefficient of variation) of force in the TA than FDI, while males displayed higher force variability in the FDI than the TA. Across all contraction intensities, the FDI showed higher firing rate variability than the TA, with no significant difference of muscle in CV of force. Moderate to strong relationships between activity levels and force variability in both FDI and TA at 10, 20 and 50% maximal voluntary contractions were observed. This study prompts further investigation into the neuromuscular control of force in upper and lower limbs, as well as interactions with sex and physical activity.

Keywords

motor unit, electromyography, force steadiness, force variability, motor unit firing rate variability, coefficient of variation, first dorsal interosseous, tibialis anterior

Summary for Lay Audience

Whether engaging in daily tasks or robust exercises, the nervous system and muscles work simultaneously to coordinate movements. The center of this process consists of motor units, where upon receiving a signal, the motor neuron sends electrical signals to the muscle fibers it controls, resulting in muscle contraction. We tend to perceive upper and lower limb muscles as more different than alike. This can be attributed to their differences in anatomical and physiological characteristics that allow them to execute a range of functions in the body. However, research remains inconclusive regarding whether significant differences exist in the fundamental processes through which upper and lower limb muscles perform their functions. The first dorsal interosseous (FDI) and tibialis anterior (TA) muscles have each been widely examined, but there has been limited research into the differences between them, especially regarding the neural control of force production. Enhancing our understanding of neuromuscular control entails exploring key factors like force and how muscle fibers are activated. As such, this research aims to investigate the differences in force variability and neural control between the FDI and TA. In accounting for potential influences of sex and physical activity levels on motor output variability in these muscle groups, we found that both males and females demonstrated higher motor unit firing rate variability in the FDI than TA. We also found that females had higher variability of force in the TA than in the FDI and females had a higher variability of force in the FDI than the TA. Additionally, across certain contraction intensities, levels of light, moderate, and vigorous physical activity were associated with force variability in the FDI and the TA. This study provides a comprehensive analysis of the control of force and motor unit firing rates in both the FDI and the TA, as well as their interactions with sex and physical activity.

Co-Authorship Statement

Anita D. Christie has been actively involved in the development of this study while providing feedback and guidance throughout this study and manuscript. Data was analyzed and interpreted by Kherto Ahmed.

Acknowledgments

Alhamdulillah (All praise is due to God) for allowing me to reach this point in my life gracefully and in good health.

To my supervisor Anita, thank you for this incredible journey. I am extremely grateful for your unwavering support and dedication since you first welcomed me into your lab. Your mentorship and guidance have not only expanded my knowledge but also played a significant role in shaping my confidence. I will forever cherish the lessons learned, the challenges overcome, and the insights I have gained from our time working together.

To my parents, friends, and family, your support has been my anchor throughout the last two years. I have never doubted the strength of your support, but words cannot describe my gratitude for everything you all have done for me. Although this process has been tough, your belief in me has been my driving force to overcome all of life's challenges. And a special thanks to my sister, Rachel; your presence and inquisitive nature have boosted my confidence immeasurably! Thank you for being there for me through the highs and lows and for being my reason to take breaks and take care. I cannot wait to see all the big things you do in life, and I can’t wait to support you through them.

To my lab mates Michael, Ali, Taia, KJ, Jonah, Alicia & Bernadette, it was a great pleasure to learn from you all. I am confident that each of you will achieve great things in the future, and I will eagerly watch your successes unfold! A huge thanks to Michael for the constant support and for being such an integral part of our lab. Your willingness to share your knowledge, especially in navigating the complexities of MATLAB has been a game-changer for me. I might be a MATLAB connoisseur after everything you have taught me!

Thank you to every single one of you who has been a part of this journey. Your support, mentorship, and friendship have enhanced my research project and transformed me as an individual. I am grateful for all the lessons, memories and experiences that will stay with me forever.

To Abdulaziz Dubet, thank you for reminding me to smile.

Table of Contents

List of Tables

List of Figures

List of Appendices

List of Abbreviations

ACh – acetylcholine

ANOVA – analysis of variance

ATP – adenine triphosphate

CV – coefficient of variation

CVISI- coefficient of variation of interspike interval

EMG – electromyography

FDI – first dorsal interosseous

FR – firing rate

ISI – interspike interval

MU – motor unit

MUFR – motor unit firing rate

MVC – maximal voluntary contraction

PA – physical activity

SD – standard deviation

sEMG – surface electromyography

TA – tibialis anterior

Chapter 1

1 Literature Review

1.1 Overview

The force produced by a muscle during a voluntary contraction depends on the number of active motor units (MU) and the rate at which those units discharge action potentials (Adrian & Bronk, 1929; Enoka & Duchateau, 2017; Macefield et al., 1996; Seyffarth, 1940). Current literature on the relative contribution of these two mechanisms indicates a comprehensive understanding that force varies across the capacity of the muscle (Enoka & Duchateau, 2017; Turchick, 2015). However, this fluctuation in the control of force and MU firing behaviour is often analysed within architecturally similar muscles (Ross et al., 1999; Hu et al., 2014). A direct comparison of both force control and MU firing behaviour measured from different muscles in the same individual has yet to be assessed. As such, the neuromuscular mechanisms contributing to maintaining force during sustained and force-varying contractions require further investigation.

1.2 Neuromuscular Control

Motor neurons are nerve cells responsible for carrying motor information from the central nervous system toward muscles to generate movement. These nerve cells control the contraction of skeletal muscles and are the final pathway responsible for motor behaviour. The upper and lower motor neurons interact, forming a two-neuron circuit to generate movement and responses (Zayia & Tadi, 2021). Upper motor neurons originate in the cerebral cortex and proceed to the brainstem or spinal cord (Zayia & Tadi, 2021). In contrast, lower motor neurons originate in the spinal cord and innervate muscles and glands. Lower motor neurons transmit the signal from upper motor neurons to effector muscles to execute a movement. Somatic motor neurons extend to skeletal muscles to regulate movement and muscle tone and are classified into alpha, beta, and gamma motor neurons. Alpha motor neurons innervate the extrafusal fibers that generate muscular contractions (Webb, 2017).

When a muscle is required to contract, the summation of afferent signals, primarily from the upper motor neurons during a voluntary contraction, increases the lower motor neuron's resting membrane potential, causing it to depolarize at the axon hillock. Action potentials are then generated and propagate along the length of the axon towards the neuromuscular junction a synaptic connection between the muscle fiber and motor neuron, leading to the activation of skeletal muscle fibers. When the action potential reaches the axon terminal, the neurotransmitter acetylcholine (ACh) is released from vesicles into the synaptic cleft and interacts with nicotinic ACh receptors on the motor endplate of the muscle fibers (Omar et al., 2017; Witzemann, 2006). Binding of ACh causes sodium to flow into the myocyte, resulting in an end plate potential. This depolarization leads to the opening of voltage-gated sodium channels, which causes more sodium to enter the cell, making the cell more positive, reaching its membrane threshold, and causing an action potential (Omar et al., 2017; Witzemann, 2006). The opening of voltage-gated sodium channels activates voltage-gated calcium channels lining the transverse tubules and calcium is released from the sarcoplasmic reticulum into the cytosol of the muscle cell. (Kuo & Ehrlich, 2015). Once inside the cell, calcium binds to troponin, which induces a conformational change in the troponin complex and exposes the active sites of actin. The myosin heads temporarily bind to actin forming a cross-bridge (Krans, 2010). Through the breakdown of ATP, myosin heads are able to pull the actin filaments toward the centre of the sarcomere, shortening the muscle fiber and producing a muscle contraction (Krans, 2010).

A motor unit (MU) is a functional unit of a muscle that consists of a lower motor neuron and innervated muscle fibers (Heckman and Enoka 2012; Reinking et al. 1975; Willingham et al. 2020). The relative size (number of muscle fibers) of a motor unit is partly influenced by the size of the muscle (DeLuca and Hostage, 2010), with larger muscles tending to have greater innervation ratios than comparatively smaller muscles (Doherty et al., 1995). This variation in the number of muscle fibers innervated per motor unit may be explained by the need for fine and gross motor control (Doherty et al., 1995).Regardless of the muscle, however, the force produced during a contraction is dependent on motor unit recruitment and rate coding, which are the number of motor units activated and the rate at which these units generate action potentials, respectively

(Enoka and Duchateau, 2017). During an isometric contraction, as the force generated by a muscle undergoes a gradual increase, it requires an increase in both the recruitment of additional motor units, as well as the firing rate (Enoka and Duchateau, 2017). It has been suggested that the role of motor unit recruitment in enhancing muscle force is more pronounced during the early stages of muscle contraction (Milner-Brown et al., 1973). The motor units activated earlier reach a peak value that remains relatively constant, even as the muscle force continues to increase progressively (Milner-Brown et al., 1973).

Muscle fibers are often classified according to their metabolic strategy and contraction pace, with different types better suited for specific activities (Potvin and Fuglevand, 2017). Type I, or slow twitch, muscle fibers can sustain low levels of force for long periods of time, making them useful for tasks such as maintaining posture and engaging in endurance-related movements (Sica and McComas, 1971; Bellemare et al., 1983). Type II fibers, also known as fast twitch fibers, can generate swift, explosive force, which are activated in high force, and quick movements such as running or jumping (Sica and McComas, 1971; Bellemare et al., 1983). Type II fibers can be classified into two groups, Type IIA and Type IIB fibers. Type IIA muscle fibers contain high oxidative and glycolytic capacity and are relatively resistant to fatigue (Herbison et al., 1982). Type IIB muscle fibers, on the other hand, have low oxidative and high glycolytic capacity and are subject to greater fatigue (Herbison et al., 1982). Although muscles are composed of multiple fiber types, individual motor neurons only connect with one type of muscle fiber, meaning all muscle fibers are of the same type for a given motor unit (Burke, 1999). Slow and fast twitch muscle fibers do not exist in isolated clusters within a muscle (Enoka and Fuglevand, 2001; Sica and McComas, 1971), rather, the muscle fibers connected to a single motor neuron are distributed throughout the muscle, allowing for the production of force across a large region (Enoka and Fuglevand, 2001; Sica and McComas, 1971). Recruiting Type I muscle fibers is sufficient for producing low force output; and additional recruitment of Type II muscle fibers is necessary for generating high force output (Enoka and Fuglevand, 2001; Potvin and Fuglevand, 2017).

Early research by Adrian, Bronk (1929) and Seyffarth (1940) demonstrated that as the level of muscle contraction increased, more motor units were activated, and their firing rates increased. Henneman expanded on these observations, establishing the "size principle," whereby the activation of more motor neurons as contractile intensity increases is determined by the size of their somatic and dendritic components (Henneman, 1957 Henneman et al., 1974). Motor units are activated using rate coding, in which increasing the impulse frequency translates to increased force contribution. Over most of the operating range of a muscle, the nervous system regulates muscle force by adjusting both motor unit recruitment and rate coding (Doherty, Chan, and Brown, 2002). During slow ramp contractions, motor unit firing rates (MUFR) increase gradually, while fast contractions entail high instantaneous discharge rates that subsequently decrease (Duchateau & Baudry, 2014). The maximal discharge rate achieved during slow isometric ramp contractions typically ranges from 20 to 50 Hz (Duchateau & Baudry, 2014). In contrast, fast contractions can reach higher values (>100 Hz) only briefly (Duchateau & Baudry, 2014).

In 1994, De Luca and Erim found an inverse relationship between the recruitment threshold and the firing rate of motor units at a given force level. This suggests that motor units recruited earlier have higher firing rates than motor units recruited later and that all motor units respond proportionally to changes in input to the motoneuron pool. This observation has been previously documented by researchers such as Seyffarth (1940), Person and Kudina (1972), and Tanji and Kato (1973).

1.3 Control of Force

Functional motor output refers to the capacity to effectively produce and control force in response to the demands of a given task (Davis et al., 2020). An isometric contraction occurs when the muscle length remains constant as tension is produced (Reed & Bowen, 2008). During these types of contractions, the force that fluctuates around a mean value and the standard deviation, or coefficient of variation, of these fluctuations provides an indication of force steadiness (Oomen & van Dieen, 2017; Enoka and Farina, 2021). Force steadiness is a quantitative measure used to understand the control of force while an individual strives to maintain a constant force during a brief submaximal contraction (Enoka and Farina, 2021; Castronovo et al., 2018).

While some studies have shown a connection between force steadiness and variability in the discharge rates of individual motor units (Enoka et al., 2003), other research indicates inconclusive results (Duchateau et al., 2006; Dideriksen et al. 2012). Some researchers suggest that motor unit recruitment patterns influence the variability of force output. For instance, it has been suggested by Duchateau et al. (2006) and Dideriksen et al. (2012) that variations in force result from the activation of newly recruited motor units. Furthermore, studies reveal that several internal factors affect force steadiness in individuals with a healthy neuromuscular system, and it is worth noting that no single factor is solely responsible for influencing force steadiness (Missenard et al., 2009). Instead, it is a combination of several factors that determine one's ability to maintain optimal force levels. For instance, research suggests that force steadiness varies with age and sex, and generally, older individuals are less steady than their younger counterparts and females, compared with males, exhibit lower force steadiness (Jakobi et al., 2018; Oomen and Van Dieen, 2017; Brown et al., 2010; Inglis and Gabriel, 2021).

Moreover, the coefficient of variation of force during steady isometric contractions is affected by factors such as the number of motor units, the motor unit recruitment threshold, and the contractile properties of the muscle fiber (Jesunathadas et al., 2012). For instance, muscles with a smaller number of motor units typically have a lower maximal recruitment threshold resulting in reduced force fluctuations at lower forces outputs (Enoka and Duchateau, 2012; Jesunathadas et al., 2012). In contrast, muscles with a smaller number of motor units but a higher maximal recruitment threshold experience greater force fluctuations at the same relative target force (Enoka and Duchateau, 2012; Jesunathadas et al., 2012). As a result, it has been asserted that force steadiness is impacted by the properties of its motor unit population (Enoka and Duchateau, 2012; Jesunathadas et al., 2012).

In addition to recruitment, studies suggest that force variability is inversely related to the maximal voluntary contraction (MVC) and the number of motor units the muscle contains (Hamilton et al. 2004). Muscles with greater numbers of MUs exhibit low force variability, whereas muscles with fewer motor units display higher force variability (Hamilton et al., 2004; Monster, 1979). In a study that compared the first dorsal interosseus (FDI) to larger muscles such as knee extensors and elbow flexors, force variability was greatest for the FDI (Tracy et al., 2007). Furthermore, force variability is noted to be influenced by the motor unit firing rate, where smaller muscles that exhibit higher force variability also have a wider firing rate range (Contessa et al., 2011; Moritz et al., 2005). The firing rates achieved at maximum force in the FDI are consistently reported as greater than larger muscles, including the tibialis anterior (TA) (DeLuca and Hostage, 2010; Hamilton et al., 2004).

Recent studies suggest that there is a link between the number of active motor units and force variability within a single muscle, where increased levels of active motor units decrease force variability (Hamilton et al. 2004). However, the exact nature of this link at the single muscle level remains to be tested in detail. Research on the distribution of other factors that can also influence muscle force, specifically firing rate variability, has yet to be thoroughly analysed (Moritz et al. 2005). This gap has led to an interest in comparing muscle groups that differ vastly in mechanical properties. Despite the increasing amount of research on force variability and submaximal isometric contractions, studies suggest that the magnitude of the relationship to contraction intensity should be considered "moderate" (Davis et al., 2020). Researchers assert that in order to establish a thorough understanding of these relationships, a number of significant conceptual gaps must be addressed in a more comprehensive manner, including comparisons across muscles.

1.4 First Dorsal Interosseous and Tibialis Anterior

The first dorsal interosseous (FDI) is the largest and strongest of the dorsal interossei muscles located on the dorsal aspect of the hand, and it is the only muscle responsible for the abduction and flexion of the index finger at the metacarpophalangeal joint (Infantolino and Challis, 2010). As it inserts into the base of the proximal phalanx of the thumb, the FDI arises from the metacarpal bone of the index finger and is one of the four intrinsic muscles of the hand. The FDI is highly involved in fine motor control and is innervated by the deep branch of the ulnar nerve (Valenzuela and Bordoni, 2020). Due to its unique characteristic of being the only muscle responsible for a particular joint movement, many studies have explored the FDI based on MU recruitment (Milner-Brown et al.1973; Kornatz et al. 2005), strength training (Davies et al. 1985) and tendon stiffness (Cook & McDonagh, 1996, Infantolino & Challis, 2010). The FDI assists in a wide range of hand functions, including everyday activities such as writing, grasping and manipulating objects.

The tibialis anterior (TA) is the largest of the four muscles in the anterior compartment of the lower leg. It arises from the lateral tibia and the tibialis anterior tendon inserts on the medial border of the foot. It is primarily responsible for foot inversion and is the strongest dorsiflexor of the foot at the ankle joint (Juneja and Hubbard, 2018). Due to its insertion on the medial border of the foot, the tibialis anterior also supports the medial longitudinal arch of the foot (Juneja and Hubbard, 2018). The TA is highly involved in gross motor control, such as gait, running, and maintaining balance and is innervated by the deep peroneal nerve, also known as the deep fibular nerve. Many studies have focused on the TA as it plays such an important role in gait, specifically in the swing phase (Juneja and Hubbard, 2018; Usherwood et al., 2012), provides a deeper understanding of the MU firing and recruitment threshold relationship (De Luca and Hostage, 2010), and has clinical significance (Kakouris et al., 2021; Mattock et al., 2021; Hatz et al., 2019).

The FDI contains approximately 40,500 muscle fibers, and an estimated ~119 motor units with an average of ~340 number of fibers per motor unit (Feinstein et al., 1954; MacIntosh et al., 2006, Feinstein et al., 1954). The FDI muscle is composed of approximately 57% slow-twitch (type I) fibers and 42% fast-twitch (type II) fibers (Johnson et al., 1973). Additionally, research by Thomas et al. (1986), Kamen et al. (1995), and De Luca and Hostage (2010) have shown that most MUs in the FDI are recruited by 50% MVC, with few recruited up to 70% MVC with a firing rate range of 47-92 pulses per second (pps) (Duchateau and Hainaut., 1990; Kamen et al., 1995). In contrast, the total number of muscle fibers in the TA is approximately 271,350, with an estimated ~445 motor units and a mean of ~562 fibers per MU (MacIntosh et al., 2006, Feinstein et al., 1954, Feinstein et al., 1954). Johnson et al. (1973), have demonstrated that the TA muscle contains approximately 73% slow-twitch (type I) fibers and 26% fast-twitch (type II) fibers. In a study conducted by De Luca and Kline (2011), it was reported that most MUs within the TA are recruited by 70-80% MVC with a maximum recruitment threshold of 90% MVC with a firing rate range of 40-58 pps (Connelly et al., 1999; Rubinstein and Kamen., 2005). Despite our understanding of the architectural and functional differences between the FDI and TA muscles, our current knowledge of potential differences between these muscles in the neural control of force is limited.

1.5 Sex-related Differences

Past research indicates a compelling understanding of the behaviour of motor units, as well as the capacity of the muscle to generate force in affecting variability and steadiness (Yao et al., 2000; Christou et al., 2002; Enoka et al., 2003). The number of MUs recruited, the order of recruitment, and the variability in the MUFR, for instance, have been reported as clear contributing factors in explaining MU firing patterns. However, current research has yet to reach conclusive findings regarding the sex differences that may arise when analyzing motor unit behaviour, especially in the TA and FDI.

In a comprehensive review conducted by Jakobi et al. (2018), it was noted that females often display more force variability in upper and lower limbs than males. For example, in a recent study investigating MU firing rate variability and force steadiness of the TA, Inglis and Gabriel (2021) reported that females, compared with males, exhibited greater variance in MUFR and lower force steadiness. Furthermore, females showed a greater fluctuation in force steadiness throughout the range of contraction intensities from 20 to 100% MVC (Inglis and Gabriel, 2021). This resulted in females, compared with males, having less force steadiness at both low and high force outputs. These findings are consistent with previous research conducted on the biceps across various force levels. Brown et al. (2010) examined force steadiness in three positions of the forearm in males and females across various force levels. They concluded that females exhibit less force steadiness than males in neutral, supinated, and pronated forearm positions. However, sex-related differences in force steadiness may not be ubiquitous, as there are reports of no differences between males and females (Christie & Kowalski, 2020; Yoon et al. 2014). Where sex-related differences are observed, Jakobi et al. (2018) conclude that it is not likely that differences in muscle fiber type, contractile properties, or the total number of motor units (MUs) significantly contribute to the differences in force variability. Most experimental studies indicate a weak relationship between whole-muscle contractile properties and force steadiness for short-duration contractions (Jakobi et al., 2018).

Although females and males differ in muscle contractile properties, if these factors highly contribute to force steadiness, a significant difference in CV of force would be expected. However, since the relationship between these properties and force steadiness is minimal, the differences in muscle fiber type composition do not adequately explain the sex-related differences in the CV of force. Rather, Jakobi et al (2018) assert that the observed sex-based differences in force variability is more likely caused by variables including maximal strength, agonist-antagonist muscle activity, and tendon mechanics.

Inglis and Gabriel (2020) also explored sex-related differences in MUFR at both maximal and submaximal levels of force output in the tibialis anterior reporting that MUFRs and the variability of MUFR in females were greater than males across all submaximal force levels. A similar finding of greater MUFRs in females than males at submaximal contraction intensities was also previously reported in the vastus medialis and vastus medialis oblique (Peng et al., 2018). However, comparisons of potential sex-related differences across different muscles in the same individuals are limited.

1.6 Impact of Physical Activity on Neuromuscular Function

The capacity and function of the neuromuscular system are impacted by physical activity through a complex interplay of physiological changes. As an individual engages in physical exercise, the nervous system activates the required muscles, and the body undergoes a number of physiologic changes that support and aid in facilitating the activity (Duchateau and Enoka, 2002). When the exercise is repeated, the continued exposure to the elevated demands provides a stimulus that prompts neural adaptations to increase the capacities of the affected muscles (Duchateau and Enoka, 2002). When the degree of physical activity decreases, such as immobilisation, the lowered physiologic demand generates adaptations that reduce the capability of the muscle (Duchateau and Enoka, 2002).

Studies reveal that physical activity has a direct impact on muscle fibers that lead to changes in contractile properties (Plotkin et al., 2021; Hughes et al., 2018). It has been observed that endurance training, for example, can increase the quantity and size of type I fibers, enhancing oxidative capacity and endurance performance (Huges et al., 2018;

Hendricke et al., 2021). Resistance training, on the other hand, can cause an increase in the size and number of type II fibers, leading to improved force production and power output (Grgic and Schoenfeld, 2018; Plotkin et al., 2021; Huges et al., 2018). These modifications in muscle fibers result from several cellular and molecular adaptations in response to moderate to vigorous exercise (Brandy et al., 1990; Grgic and Schoenfeld, 2018).

When partaking in vigorous physical activity, numerous muscular and neurophysiological responses can be seen in the target muscles, such as an increase in muscle mass and neural adaptations (Elgueta-Cancino et al., 2022; Gabriel et al., 2001; Aagaard et al., 2020; Pearcey et al., 2021). The neural adaptations include significant increases in motor unit firing rate and a significant decrease in recruitment threshold (Del Vecchio et al. 2019). In a study conducted by Vila Cha and Falla (2016), it was also found that strength training reduces motor unit firing rate variability and increases force steadiness in lower limbs. However, others have shown only early increases in motor unit discharge rates with no changes after weeks of vigorous training (Patten et al. 2001). This was similarly found in a study conducted by Pucci et al. (2006), who reported no significant change in motor unit discharge rate after three weeks of isometric resistance training.

Research also suggests that a lack of physical activity, including prolonged sedentary behaviour, is linked to reduced muscle strength, force control, and neuromuscular function (Engberg et al., 2017; Mear et al., 2022). Sedentary behaviour has been noted to impact neuromuscular physiology and, subsequently, function significantly. One study found that experimentally-induced durations of muscle inactivity have been shown to reduce muscle cross-sectional area, decrease the ability to activate motor units voluntarily and have an overall reduction in motor unit firing rates (Mear et al., 2022). Additionally, studies have demonstrated that an increase in sedentary behaviour is negatively associated with neuromuscular function and strength and leads to a reduction in isometric force control (Clark et al., 2007).

These diverse findings indicate a gap in understanding the effect of physical activity on neuromuscular control. Some studies conclude that physical activity may modify motor unit properties and function; however, the effects on the variability of motor performance remain largely unknown (Hunter et al., 2016; Westerberg et al., 2018). Further work is therefore necessary to understand the relationship between physical activity and neuromuscular control of force.

1.7 Study Objectives

The first primary aim of this study was to examine force variability and neural control differences, in the same individual, between an upper and lower limb muscle, specifically the FDI and the TA. While many studies compare muscles with similar muscle fiber compositions, this study aims to contribute to the limited literature that compares these variables within muscles that are different in mechanical properties and function, providing a more complete picture of differences in neuromuscular control across muscles. The second primary aim was to determine sex-related differences in force variability and neural control across these two muscles. A secondary aim was to examine potential relationships between physical activity levels and neuromuscular function outcomes of variability in force and motor unit firing rate. It was hypothesized that force variability would be lower in the TA than in the FDI, that force variability would be lower at high-intensity contractions within each muscle, and that the firing rate variability would be lower in the TA than in the FDI. It was also hypothesized that females would exhibit greater variability in force and MUFR across all contraction intensities in both muscles. Finally, it was hypothesized that individuals engaging in moderate-vigorous physical activity would exhibit lower force variability compared to individuals who engage in light physical activity.

Chapter 2

2 Force variability and neural control differences in upper and lower limb muscles

2.1 Introduction

The execution of daily activities requires coordinated muscle control, which involves various components of the central and peripheral nervous system, with the final point of this process being the motor unit (MU) (Enoka and Duchateau, 2017). All voluntary and reflex muscle contractions involve activation of motor units, which consist of a motor neuron and varying numbers of innervated muscle fibers (Enoka and Duchateau, 2017). Muscles are composed of different motor unit pools that share the same neuromuscular mechanisms governing motor unit recruitment and firing rate (Enoka and Duchateau, 2017). Motor unit activation is regulated through two main mechanisms: the selective recruitment of motor units based on their size (Henneman, 1957) and the adjustment of motor unit discharge rate (Person and Kudina, 1972; Milner-Brown et al., 1973).

During voluntary contractions, motor neurons are generally recruited from the smallest to the largest, resulting in the recruitment of smaller and low-force-producing muscle fibers first, followed by the recruitment of larger and high-force-producing fibers (Henneman and Olson, 1965). Furthermore, the frequency with which a motor neuron generates action potentials reflects its firing rate. The rate at which motor units fire plays a critical role in controlling both the magnitude and speed of muscle contractions, and it is influenced by a variety of factors, such as the particular demands of the task at hand (Doherty, Chan, and Brown, 2002; Davis et al., 2020). The ability to control one's force output is referred to as forced steadiness, which demonstrates the capacity to maintain an isometric contraction around a certain force level (Davis et al., 2020). Even during "constant force" contractions, however, inherent fluctuations in the force around the target value are evident. As a result, it has been asserted that force steadiness is impacted by the properties of its motor unit population (Jesunathadas et al., 2012).

Despite a comprehensive understanding of muscular function, motor unit behaviour and force variability remain complex and multi-dimensional aspects of neuromuscular physiology. Recent research suggests an influence of biological sex and physical activity on neuromuscular function. For instance, Inglis and Gabriel (2020) and Peng et al. (2018) found that motor unit firing rates (MUFRs) in females were greater than in males across multiple submaximal force levels. Further, a recent review conducted by Jakobi and colleagues (2018) demonstrated that in comparison to males, females tend to display a higher level of variation in force in both their upper and lower limbs. Studies also suggest that one's physical activity can lead to increased or decreased muscle strength and force control, impacting neurophysiological responses and force production (Duchateau and Enoka, 2002; Elgueta-Cancino et al., 2022; Gabriel et al., 2001). Engaging in intense physical activity leads to several observable neuromuscular adaptations including increased motor unit firing rate and decreased variability in motor unit firing rate (Del Vecchio et al. 2019; Vila Cha and Falla, 2016). Furthermore, muscle inactivity can result in diminished voluntary activation of motor units and an overall reduction in motor unit firing rates (Mear et al., 2022). As such, additional studies into the roles of external variables are essential to gain an in-depth understanding of their contributions and implications to neuromuscular function.

Differences in the neural control of force may also exist between muscles. For example, looking across studies of force steadiness and motor unit firing behaviour, it appears that the control of force may be different in the tibialis anterior (TA), a muscle in the leg, and the first dorsal interosseous (FDI), a muscle in the hand (Fling et al., 2009; Heckman and Enoka, 2004).

The tibialis anterior, involved in gross motor control, is the largest muscle in the lower leg's anterior compartment, containing approximately 271,350 muscle fibers, with a mean of 562 muscle fibers per MU (MacIntosh et al., 2006, Feinstein et al., 1954). Most MUs in the TA are recruited by 70-80% MVC (Luca and Kline, 2011). In contrast, the FDI, used for fine-motor control in the hand, contains approximately 40,500 muscle fibers, with an average of 340 fibers per motor unit, mostly recruited by 50% MVC (Feinstein et al., 1954; MacIntosh et al., 2006; De Luca and Hostage, 2010). It has been suggested that smaller muscles, like the FDI, will exhibit responses such as higher force variability and a wider firing rate range compared to large muscles, such as the TA (Contessa et al., 2011; Moritz et al., 2005). However, direct comparisons of these outcomes between the two muscles within the same individuals are limited.

Therefore, the purpose of this study was to compare force variability and motor unit firing behaviour between the FDI and the TA, and between sexes. A secondary aim was to examine the relationship between force and motor unit outcomes and physical activity levels. We hypothesized that force and MUFR variability will be higher in the FDI than in the TA, and that females will exhibit greater variability in force and MUFR across all contraction intensities, regardless of muscle. We also hypothesized that there would be an inverse relationship between physical activity and force variability, such that individuals engaging in moderate-vigorous physical activity would exhibit lower force variability than those who engage in light physical activity. The findings of this study will advance our understanding of muscle- and sex-specific differences in neuromuscular control.

2.2 Methods

2.2.1 Participants

Twenty-four young, healthy individuals (12 females, 12 males (22.04 ± 2.40 years)) were recruited for this study. Participants had normal or corrected to normal vision and no history of any neuromuscular, neurological, musculoskeletal or cardiovascular impairments that would impact the ability to complete the tasks of the study. All participants refrained from exercise, alcohol and central nervous system stimulant and depressant pharmacological agents within 12 hours of participating in this study. It was critical to ensure that participants avoided these factors as they can induce temporary changes in muscle performance, motor unit recruitment, and neural conductivity, which may confound the results of EMG data (Pesta et al., 2013). All participants provided informed consent, and the study was approved by The University of Western Ontario Health Sciences Research Ethics Board.

2.2.2 Experimental Protocol

Testing included two visits to the Neurophysiology Lab at the University of Western Ontario. During the initial laboratory visit, eligible participants were introduced to the apparatus and underwent a practice session involving the force-tracing task that would be utilized during their second visit. During this session, participants performed three trials of their MVC for both the FDI and TA muscles. If we did not obtain MVC forces within 10% of each other, a fourth trial was performed (Haynes et al., 2022). Additionally, they practiced tracing force templates. Specifically, they completed two practice trials of each of three trapezoidal force traces, plateauing at 10%, 20%, and 50% of their MVC. They also performed 10 practice trials of a sinusoidal curve, averaging around 20% MVC. Practice trial was conducted to ensure participants' ability to complete the task and familiarize them with the protocol.

Prior to leaving the lab, participants were provided with a physical activity (PA) monitor and associated instructions. Participants were asked to wear the PA monitor for seven days, including a weekend. Upon completion of the seven-day PA monitoring period, participants were scheduled for their second visit to the laboratory.

During the second visit, participants underwent the testing phase, where force output and motor unit firing characteristics were acquired in the FDI and the TA. For each muscle, participants traced six trapezoidal curves, two trials at each of three different contraction intensities: 10%, 20%, and 50% MVC. These specific intensities were selected due to observations of higher force variability at lower contraction levels (Jakobi et al., 2018) and to avoid exceeding the maximal recruitment thresholds of either muscle (Luca and Kline., 2011; De Luca and Hostage., 2010). Each tracing lasted 30-40 seconds, with 1-2 minutes of rest between tracings. Participants also performed two trials of tracing a sinusoidal wave, with the intensity varying between 15-25% MVC for 30 seconds at a rate of 0.15 Hz. The sinusoidal force tracing task was used in this study to investigate the dynamic patterns of force and motor unit firing behaviour observed in everyday human movement. Research indicates that static and variable force outputs are essential to understanding neuromuscular control (Knight and Kamen., 2007). The order of the force tracing conditions was randomized. Baseline measures of maximal voluntary contraction were obtained before initiating the force tracing protocol. Following the completion of the testing phase, participants performed an additional MVC to determine if muscle fatigue had occurred. Once the procedure for one muscle was completed, it was repeated for the subsequent muscle (Figure 2.1).

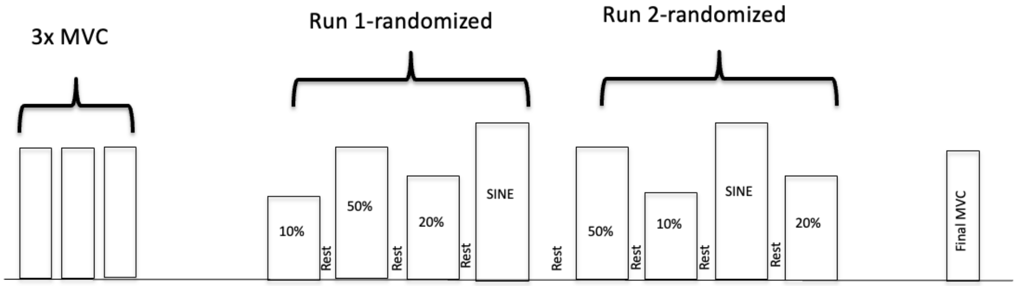


Figure 2.1. Outline of experimental protocol

Physical Activity

Physical activity (PA) levels were recorded using a wrist-worn tri-axial accelerometer (Actigraph CentrePoint Insight Watch, Pensacola, FL) over seven days, including a weekend. Participants wore the watch on their dominant hand during all waking hours except during activities that could damage the device or affect its functioning, such as showering, swimming etc. Participants also completed an activity log for the corresponding activity days to verify the accelerometer data. A custom-written MATLAB program was used to analyze a 60-sec epoch and activity counts were expressed as the average counts per minute (Freedson et al.,1998). The PA counts were light (800-1951 counts), moderate (1952-5724 counts) and vigorous (>5725 counts) PA per day and data was expressed in the number of minutes spent in each PA category (Freedson et al.,1998).

Force

Force was measured using custom-built dynamometers designed for measuring index finger abduction and ankle dorsiflexion force. Participants were seated, with their elbows resting comfortably on the armrests of a chair. Their dominant hand or foot was placed within a custom-built dynamometer.

For ankle dorsiflexion measures, participants were seated with the knee slightly bent and the ankle at 20° plantar flexion. An inflexible strap was placed across the dorsum of the foot to ensure contractions were isometric. The custom-built dynamometer was equipped with a load cell (FR5-300-B000; Tovey Engineering Inc., Phoenix, AZ, USA) from which the force signal was amplified (CP122 A.C./D.C.Strain Gage Amplifier; GRASS Instrument Co., W.Warwick, RI, USA) and sampled at 2224 Hz using a 16-bit A/D converter (NI USB-6343; National Instruments, Austin, TX, USA). To measure finger abduction, participants positioned their dominant hand on the apparatus, resisting the thumb with a special component that would allow the index finger and thumb to form a 90º angle during the isometric contractions. The custom-built dynamometer was equipped with a load cell (MBP-5; Interface, Scottsdale, AZ, USA) from which the force signal was amplified (CWE Inc; PM-1000; DataQ Instruments, Akron, OH, USA) and sampled at 2224 Hz using a 16-bit A/D converter (NI USB-6343; National Instruments, Austin, TX, USA).

To establish the maximal voluntary contraction, participants performed three maximal effort contractions, each lasting between 4 to 5 seconds. After each contraction, a rest period of 2 minutes was allocated before initiating the subsequent MVC attempt. If the peak force exhibited a variation exceeding 10%, additional trials were conducted to ensure consistency in maximal force output (Haynes et al., 2022). The trial resulting in the highest peak force measurement was selected and designated as the MVC.

Real-time feedback on force production was displayed to participants using DasyLab software (Data Acquisition System Laboratory, DasyTec, USA, Inc., Amherst, NH, USA) as they traced trapezoid figures, with target lines indicating 10%, 20%, and 50% of their MVC. Contraction duration was determined through pilot testing, to minimize the influence of muscular fatigue on neuromuscular outcomes. The 50% MVC contraction was reduced from a 30-second plateau period to 20 seconds. This was done to prevent the impact of fatigue during high-intensity contractions. Trapezoidal curves consisted of a ramp-up and ramp-down at a rate of 10% MVC/second with a 20-30 second plateau period in-between. The tracings lasted for 30 to 40 seconds. Participants also traced a sinusoidal curve at a frequency of 0.15Hz, with an amplitude that varied by ±5% around 20% of their MVC. Each sinusoidal curve tracing lasted for 30 seconds (Figure 2.2). The force was sampled at 2224 Hz with a 16-bit analog-to-digital board (NI USB-6343; National Instruments, Austin, TX, USA) and DasyLab software. Using a custom-written MatLab program (Mathworks Inc., Natick, MA, USA), the force signal was low-pass filtered at 10 Hz and sampled at 2224 Hz to match the sampling rate of motor unit recordings (see below). Measures of mean force and force variability were calculated over the middle 5-second window of the plateau region, avoiding the ramp-up and ramp-down portions of the contraction and the middle period (~6.6 seconds) of the sinusoidal condition. During each tracing, force fluctuations of the index finger abduction and foot dorsiflexion tracings were calculated by the coefficient of variation (CV) [CV of force; CV = SD of force/mean force) · 100]. The two trials at each contraction intensity (10, 20, 50% and Sine wave) were then averaged for each dependent variable.

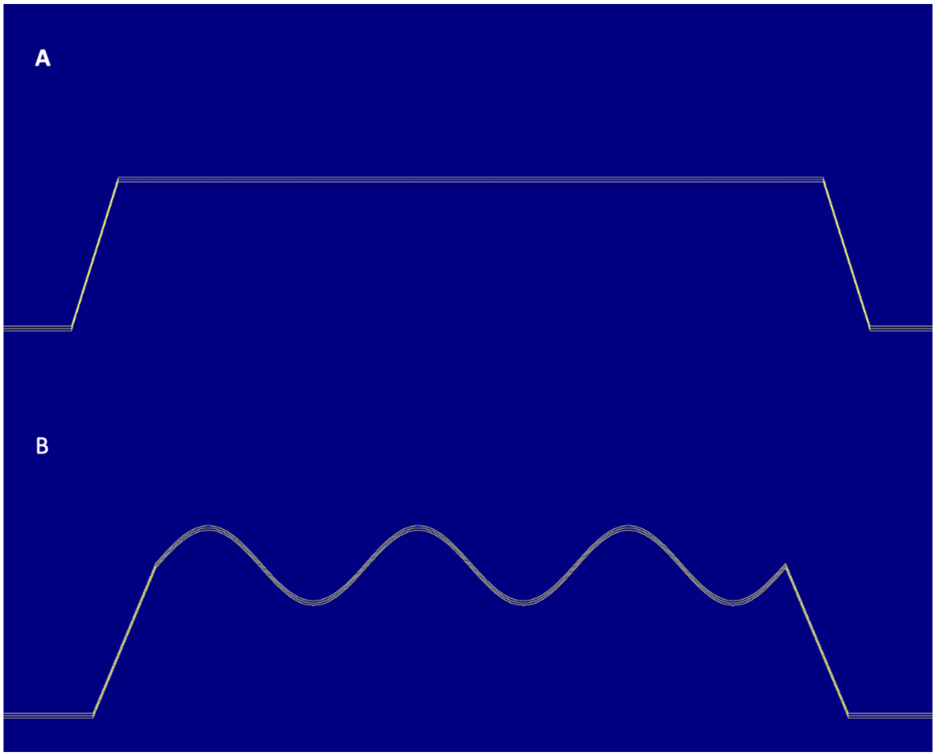


Figure 2.2. Trapezoid curve (A) and sine wave (B) templates for force tracing

Surface Electromyography

Wireless, 4-pin surface electromyography (EMG) electrodes (Galileo Wireless EMG; Delsys Inc., Natick, MA, USA) were attached to the posterior aspect of the hand, over the First Dorsal Interosseous (FDI) muscle, and on the anterior aspect of the shin, over the Tibialis Anterior (TA) muscle. Participants were asked to perform slight abduction of the finger and dorsiflexion of foot to palpate the muscles and ensure correct placement of the electrodes. A ground electrode was affixed to the distal end of the ulna, near the wrist, and the proximal end of the tibia, close to the knee. Prior to electrode placement, the skin was prepped with Nuprep (Skin Prep Gel) and alcohol prep pads to remove excess dirt from the surface of the skin. To align motor unit data with the force signal, the EMG signal was also sampled using a 16-bit A/D converter (NI USB-6343; National Instruments, Austin, TX, USA) and DasyLab software (Data Acquisition System Laboratory, DasyTec, USA, Inc., Amherst, NH, USA). Upon the completion of data collection, the EMG recordings were decomposed into constituent motor unit trains using NeuroMap software (Delsys Inc., Natick, MA, USA). A custom-written MatLab program was employed to calculate the mean motor unit firing rate (FR) and motor unit inter-spike interval (CVISI) over the same 5-second, middle plateau region, avoiding the ramp up and ramp-down portions of the contraction. Doublet (< 10ms) and long ISIs (>200ms) firings were excluded from the motor unit firing rate and CVISI calculations. Motor units below 80% accuracy were excluded from the analysis. The two trials at each contraction intensity (10, 20, 50% and Sine wave) were then averaged for each dependent variable.

2.2.3 Statistical analyses

A three-way (sex, muscle and contraction intensity) repeated measures ANOVAs were used to compare to each outcome variable (CV of force, CV of motor unit firing rate). Regression analysis was conducted to determine the relationship between levels of physical activity and the CV of force and interspike interval (ISI). All statistical analyses were performed using SPSS (IBM Corp. Released 2023. IBM SPSS Statistics for

Macintosh. Version 29.0. Armonk, NY: IBM Corp). Effect sizes were calculated for all main effects and interactions with independent factors. Significance will be set at $p \leq 0.05$.

2.3 Results

Participant Characteristics

Participant characteristics are presented in Table 1. There were no group differences in age, body mass, BMI, or physical activity levels ($p \geq 0.105$). Males and females differed in height ($p < 0.01$), FDI MVC ($p < 0.001$) and TA MVC ($p < 0.001$), with males being taller and exerting greater force in both muscle groups.

Table 2.1 Participant characteristics

	Females	Males
Age (years)	21.4 ± 1.9	22.7 ± 2.7
Height* (m)	1.6 ± 0.04	1.8 ± 0.1
Mass (kg)	64.6 ± 10.6	70.5 ± 18.5
MVC FDI* (N)	22.0 ± 4.4	29.9 ± 5.5
MVC TA* (N)	81.2 ± 29.1	160.5 ± 68.6
BMI (kg/m^2)	24.6 ± 4.0	22.1 ± 6.3
Light PA (min/day)	168.2 ± 50.0	164.6 ± 39.7
Moderate PA (min/day)	60.1 ± 27.3	55.5 ± 32.3
Vigorous PA (min/day)	0.65 ± 1.1	0.57 ± 0.89

*Indicates significant difference between sexes ($p < 0.001$). Data are presented as mean ± SD. MVC, Maximum voluntary contraction, PA, physical activity.

Force

Mean force across contraction intensities is displayed in Figure 2.2. There was no significant main effect of muscle ($p = 0.37$; $\eta^2 = 0.04$) or sex ($p = 0.43$; $\eta^2 = 0.03$) on mean force. There was a main effect of contraction intensity on mean force ($p < 0.001$, $\eta^2 = 1.0$). Post-hoc analysis showed that there was a significant difference in mean force across all contraction intensities ($p < 0.001$)), however, the difference in mean force at 20% MVC and SINE contraction was not significant ($p = 0.09$). There was no significant interaction between sex and muscle ($p = 0.66$; $\eta^2 = 0.01$), sex and contraction intensity ($p = 0.65$; $\eta^2 = 0.02$), or sex, muscle and contraction intensity ($p = 0.64$; $\eta^2 = 0.02$) on mean force. There was a significant interaction between muscle and contraction intensity on mean force ($p = 0.02$, $\eta^2 = 0.17$). Post-hoc analysis showed that in the 50% MVC contraction, the FDI had a higher mean force than the TA ($p = 0.05$). There were no other differences between muscles in the 10, 20% MVC or SINE contractions ($p \geq 0.27$).

The CV of force across contraction intensities is shown in Figure 2.2. There was no significant main effect of muscle ($p = 0.98$; $\eta^2 < 0.001$) or sex ($p = 0.66$; $\eta^2 = 0.01$) on CV of force. There was a main effect of contraction intensity on CV of force ($p < 0.001$, $\eta^2 = 0.98$). Post-hoc analysis showed that in the 10% MVC contraction, the CV of force was significantly higher than 20% MVC ($p = 0.005$) and lower than SINE contraction ($p < 0.001$). CV of force during the 20% MVC contraction was significantly lower than 50% MVC ($p = 0.003$) and SINE ($p < 0.001$). Finally, CV of force during the 50% MVC contraction was significantly lower than the SINE contraction ($p < 0.001$).

There was a significant interaction between sex and muscle on CV of force ($p = 0.008$, $\eta^2 = 0.281$), as CV of force was higher in the FDI compared to TA, but this difference was only found in males ($p = 0.05$). Females demonstrated a higher CV of force in the TA than in FDI ($p = 0.05$). There were no significant interactions of contraction intensity and sex ($p = 0.96$, $\eta^2 = 0.002$), muscle and contraction intensity ($p = 0.556$, $\eta^2 = 0.03$) or sex, muscle and contraction intensity on CV of force ($p = 0.56$, $\eta^2 = 0.03$).

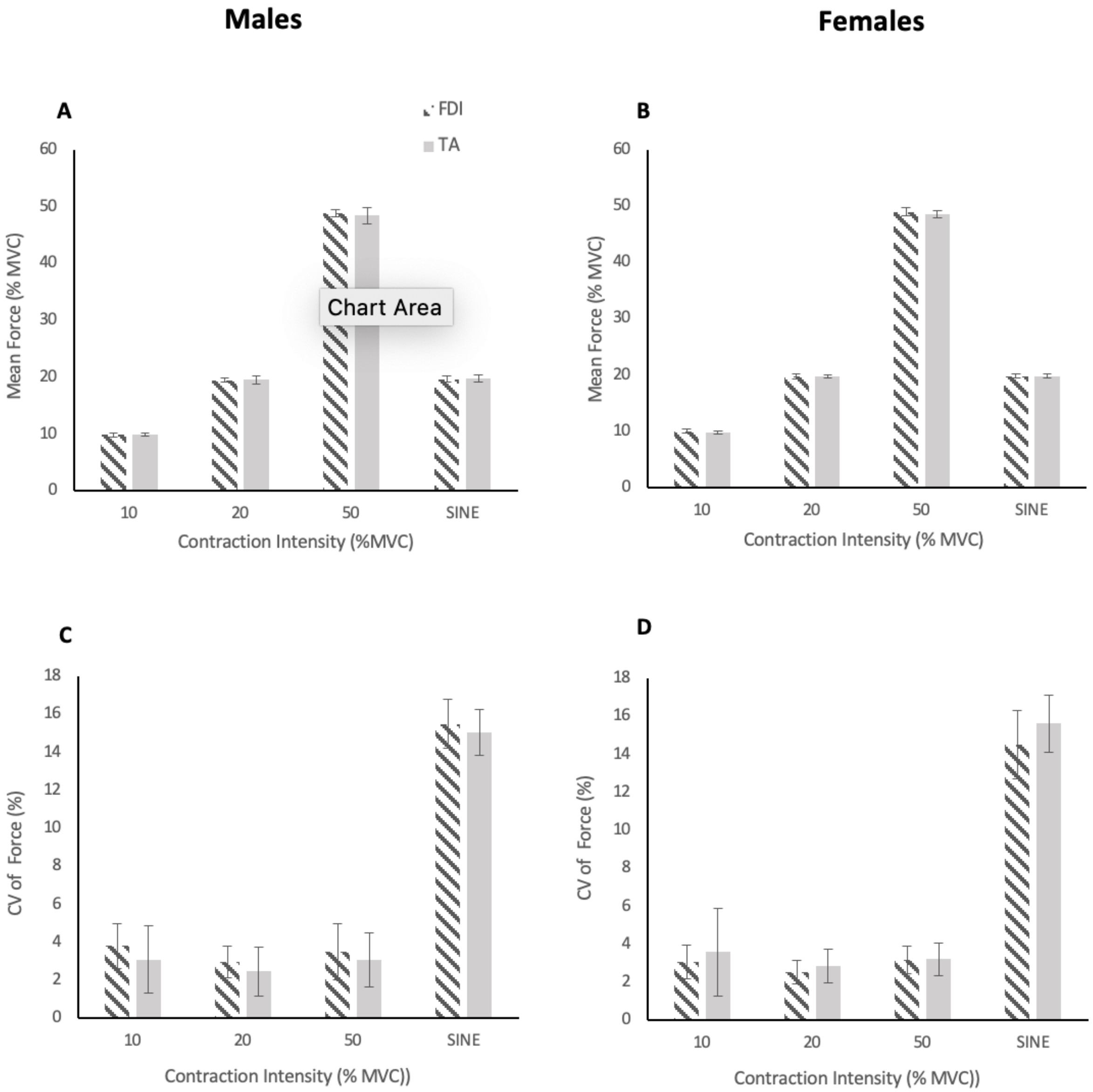


Figure 2.3. Mean and CV of force across contraction intensities.

There were no significant differences in mean force between males (A) and females (B) and no differences between muscles. Force was different across all contraction intensities except for 20% MVC and SINE. There was a significant interaction between muscle and contraction intensity where mean force was higher in the FDI than the TA at 50% MVC. Overall, there were no significant differences in CV of force between males (C) and females (D) however, there was a significant interaction between sex and muscle where males demonstrated higher CV of force in the FDI than the TA and females demonstrated higher CV of force in the TA than the FDI.

Motor Unit Firing Behaviour

Mean firing rate across contraction intensities is displayed in Figure 2.3. There was no main effect of sex ($p = 0.19$; $\eta^2 = 0.08$) on mean firing rate. However, there was a main effect of muscle ($p < 0.001$; $\eta^2 = 0.94$), as the FDI had higher mean firing rates than the TA ($p < 0.001$). Additionally, there was a main effect of contraction intensity ($p < 0.001$; $\eta^2 = 0.94$). Post-hoc analysis showed that there was a significant difference in mean firing rates across all contraction intensities ($p < 0.001$), however, the difference in mean firing rates at 20% MVC and SINE contraction was not significant ($p = 0.19$).

There were no significant interactions between sex and contraction intensity ($p = 0.20$; $\eta^2 = 0.07$), or sex, muscle and contraction intensity ($p = 0.43$; $\eta^2 = 0.04$) on mean firing rate. There was a significant interaction between muscle and contraction intensity on mean firing rate ($p < 0.001$, $\eta^2 = 0.28$). There was a significant interaction between muscle and sex on mean firing rate ($p = 0.003$, $\eta^2 = 0.34$). Post-hoc analysis showed that males had a higher mean firing rate than females in the TA ($p < 0.001$) and no significant difference between sex was seen in the FDI ($p = 0.39$).

The CVISI across contraction intensities is shown in Figure 2.3. There was a main effect of sex ($p = 0.04$; $\eta^2 = 0.19$), as males demonstrated higher CVISI than females. There was a main effect of muscle on CVISI ($p < 0.001$; $\eta^2 = 0.90$), with higher CVISI in the FDI than the TA. There was also a main effect of contraction intensity on CVISI ($p < 0.001$, $\eta^2 = 0.78$), as CVISI at 50% MVC was higher than 10 and 20% MVC ($p < 0.001$) and CVISI at 20% MVC was higher than 10% MVC ($p < 0.001$). CVISI at SINE was higher than 10 and 20% MVC ($p < 0.001$). There was no significant difference in CVISI between 50% MVC and SINE contractions ($p = 0.54$).

There was a significant interaction between sex and muscle on CVISI ($p < 0.001$, $\eta^2 = 0.42$). Males had significantly higher CVISI than females in the TA ($p < 0.001$). There was no statistically significant difference between sexes in the FDI ($p = 0.48$). There was also a significant interaction between sex and contraction intensity on CVISI ($p = 0.04$, $\eta^2 = 0.14$). Post-hoc analysis demonstrated that males had a significant difference between all contraction intensities ($p \leq 0.03$). Females also demonstrated significant differences for all pairwise comparisons ($p < 0.001$) except for 50% MVC and SINE ($p = 0.18$). Males also had a higher CVISI compared to females across all contraction intensities, however, the difference was only statistically significant at 10% MVC ($p = 0.009$) and SINE ($p = 0.02$). There was also a significant interaction between muscle and contraction intensity on CVISI ($p = 0.008$, $\eta^2 = 0.17$). Post-hoc analysis demonstrated a significant difference across all contraction intensities in the FDI ($p \leq 0.03$). Similarly, the TA showed statistically significant differences across all contraction intensities expect differences between 50% MVC and SINE ($p = 0.17$). When comparing FDI to the TA at each contraction intensity, the FDI demonstrated higher CVISI compared to TA at all levels of contraction intensities ($p < 0.001$). There was no significant interactions of sex, muscle and contraction intensity on CVISI ($p = 0.22$, $\eta^2 = 0.06$).

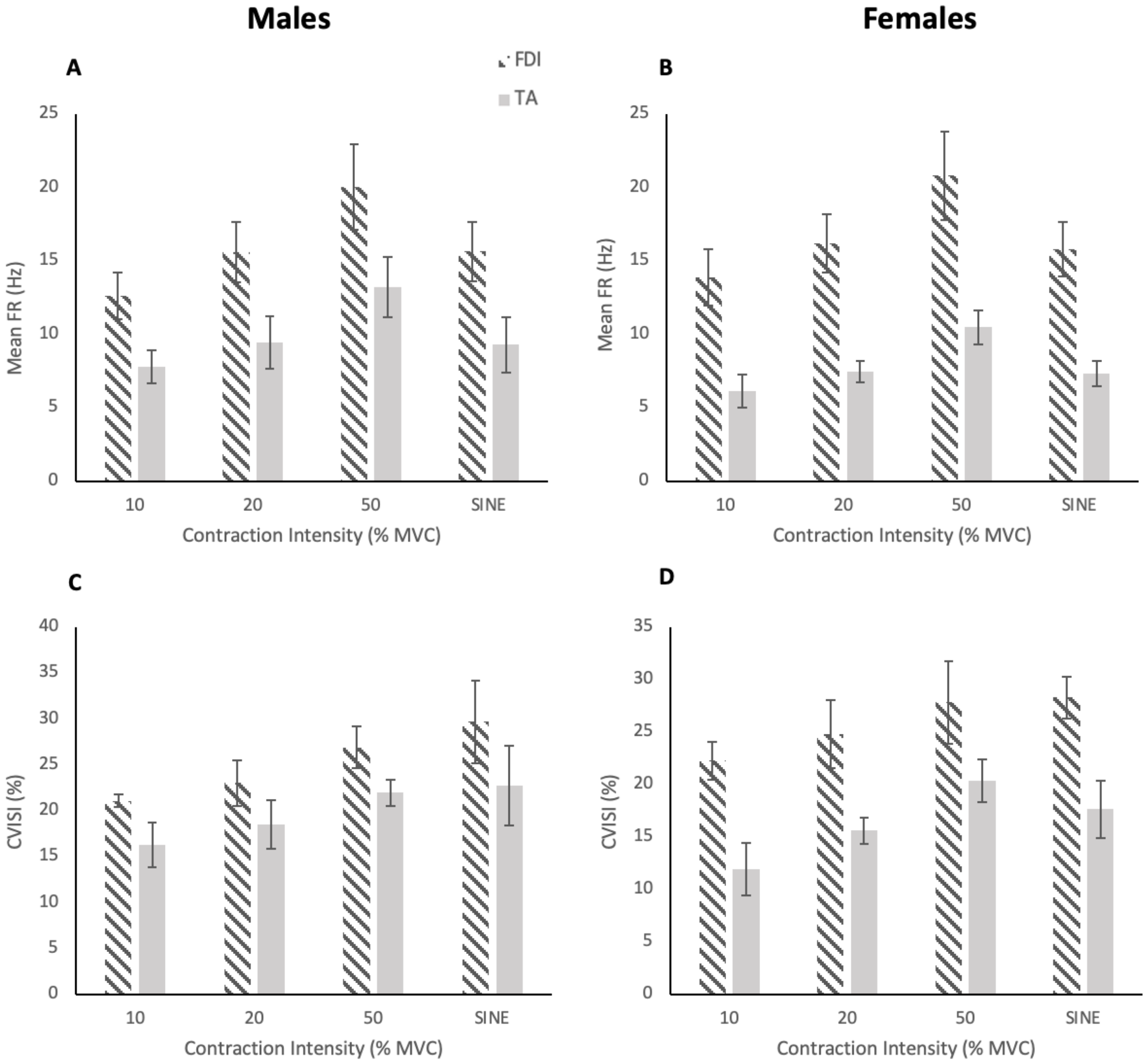


Figure 2.4. Mean firing rate and CV of interspike interval across contraction intensities.

There were no significant differences in mean firing rates between males (A) and females (B). The FDI had higher mean firing rates than the TA, and across contraction intensities, except for 20% and SINE contraction. There was a significant interaction between muscle and sex where males had a higher mean firing rate than females in the TA. There was a main effect of sex where males (C) demonstrated higher CVISI than females (D). There was a main effect of muscle where the FDI demonstrated higher CVISI values than the TA. Additionally, there was a significant interaction between sex and contraction intensity where males had a significant difference between all contraction intensity comparisons.

Physical Activity

Physical activity counts are shown in Table 2.2 for males and females. There were no significant differences between males and females at any physical activity level ($p \geq 0.71$). Results from regression analyses are presented in Table 2.3. In the FDI, CV of force at 50% MVC was positively and significantly related to light PA ($r = 0.497$; $p = 0.01$) and moderate PA ($r = 0.61$; $p = 0.001$). CV of force at 10% MVC was positively and significantly related to moderate PA ($r = 0.43$; $p = 0.04$). Additionally, CVISI at SINE contraction was positively and significantly related to vigorous PA ($r = 0.40$; $p = 0.05$). There were no other significant relationships between light, moderate or vigorous PA and CV of force, or CVISI at any contraction intensity ($r \leq 0.37$; $p \geq 0.07$). In the TA, CV of force at 10% MVC was positively and significantly related to light PA ($r = 0.58$; $p = 0.03$). Moderate PA was positively and significantly related to CV of force at 10% ($r = 0.45$; $p = 0.03$), 20% ($r = 0.44$; $p = 0.03$) and 50% MVC ($r = 0.40$; $p = 0.05$). No other significant relationships between PA and properties of the TA were observed ($r \leq 0.39$; $p \geq 0.08$).

Table 2.2 Physical Activity

Sex	**Light PA (min/day)**	**Moderate PA (min/day)**	**Vigorous PA (min/day)**
Female	168.18 ± 50.02	60.08 ± 27.32	0.65 ± 1.14
Male	164.61 ± 39.70	55.53 ± 32.30	0.57 ± 0.89

Data are presented as mean ± SD.

Table 2.3 Associations Between Neuromuscular Outcomes and Physical Activity Levels

Muscle	Neuromuscular Outcomes	Contraction Intensity (%MVC)	Light PA (r ; p)	Moderate PA (r ; p)	Vigorous PA (r ; p)
FDI	CV Force	10*	0.39; 0.08	0.43; 0.04	0.23; 0.28
		20	0.16; 0.45	0.37; 0.08	0.19; 0.36
		50*	0.49; 0.01	0.61; 0.001	0.05; 0.83
		SINE	0.06; 0.79	0.20; 0.34	0.03; 0.89
	CVISI	10	0.16; 0.46	0.01; 0.61	0.17; 0.44
		20	0.13; 0.54	0.01; 0.96	0.02; 0.95
		50	0.08; 0.69	0.07; 0.75	0.12; 0.59
		SINE*	0.05; 0.80	0.01; 0.96	0.40; 0.05
TA					
	CV Force	10*	0.58; 0.003	0.45; 0.03	0.29; 0.16
		20*	0.36; 0.08	0.44; 0.03	0.32; 0.13
		50	0.27; 0.20	0.40; 0.05	0.39; 0.06

		SINE	0.13; 0.55	0.08; 0.69	0.21; 0.34
	CVISI	10	0.12; 0.57	0.03; 0.89	0.10; 0.63
		20	0.21; 0.32	0.23; 0.29	0.09; 0.68
		50	0.03; 0.91	0.21; 0.34	0.09; 0.69
		SINE	0.06; 0.77	0.12; 0.57	0.25; 0.24

* Indicates significant relationship between variables ($p \leq 0.05$).

Chapter 3

3 Discussion

This study aimed to investigate force and motor unit firing rate variability differences between upper (FDI) and lower limb (TA) muscles. The study also sought to understand potential variations in neuromuscular control arising from sex-related differences and physical activity. We hypothesized that the FDI would have higher coefficient of variation of the interspike interval (CVISI) and coefficient of variation (CV) of force than the TA, females would demonstrate higher CVISI and CV of force than males, and moderate-vigorous physical activity would be related to lower CV of force and CVISI. We observed that CVISI was higher in the FDI than the TA, and males had a higher CVISI than females. No muscle or sex-related differences was seen in the CV of force however, we did observe that CV of force was greater in females than males in the TA, and higher in males than females in the FDI. We also observed that individuals who had increased minutes spent in moderate physical activity demonstrated greater force variability in their TA muscle.

3.1 Muscle-based differences

When comparing the FDI to larger muscles, due to characteristics such as muscle function, size and motor unit recruitment, force variability is often observed as being higher in the FDI (Tracy at al. 2007). This finding also aligns with previous studies that report that muscles that muscles that have higher numbers of MU and increased strength abilities, demonstrate lower force variability (Hamilton et al. 2004). In the current study, however, higher CV of force in the FDI compared with the TA was only observed for males. We did not observe similar findings for females, as they had a higher CV of force in the TA than the FDI. There was a greater sex-related difference in MVC force in the TA (~49%) than the FDI (~26%), which may partially explain these findings. However, the larger CV of force in the TA than the FDI in females requires further study, as this finding is in contrast to previous work (Enoka and Duchateau, 2012; Jesunathadas et al., 2012). Our observations may be explained by Dideriksen et al. (2012) who suggest that although the FDI has fewer motor units and is more susceptible to higher levels of variability, its narrow range of recruitment compensates by stabilizing force variability.

The FDI exhibited higher CVISI across all contraction intensities compared to the TA muscle, consistent with prior studies (De Luca and Hostage, 2010). We found that both males and females had a higher CVISI in the FDI than the TA, potentially suggesting that the observed differences between muscles occur irrespective of sex. It has been suggested that smaller muscles, like the FDI, will exhibit responses such as higher MUFR variability, compared to larger muscles, such as the TA, due to a wider firing rate range (Enoka and Duchateau, 2012; Jesunathadas et al., 2012). Contessa et al. (2018) notes that in the FDI, responses to fatigue include a variety of adaptations such as motor unit firing rate increases, decreases in recruitment thresholds, and new motor units being recruited. It has been noted that these adaptations are in response to the FDI attempting to sustain target force output. However, it has also been observed that the change in behaviour of motor units in the FDI during a sustained contraction causes variability in discharge rates to increase (Pascoe et al., 2014).

3.2 Sex-based differences

In the FDI muscle, males exhibited a higher CV of force than females. This result is notably inconsistent with prior research on sex-related differences in force steadiness, such as the work of Inglis and Gabriel (2021). They found that females generally show greater fluctuations in force steadiness, with an average 27.3% greater CV of force compared to males. However, Inglis and Gabriel (2021) solely examined the TA in which the size, function, and motor unit properties potentially contributed to force variability. Jakobi et al. (2018) also observed that females often display more force variability in upper and lower limbs than men do. However, Jakobi et al. (2018) also assert that differences in force variability between sexes are likely attributed to factors such as maximal strength, where males typically exert greater force and often display lower force variability. (Kowalski & Christie, 2020)Our study showed a significant sex-related difference in MVC, where males exerted greater force than females in both the FDI and TA. However, similar to a previous study (Kowalski & Christie, 2020), we did not find a significant difference in the CV of force across sexes. This lack of difference between sexes may suggest that neuromuscular control strategies and the mechanical properties of muscles and tendons are similarly efficient in both sexes (Jakobi et al., 2018). In the TA, our data revealed that females exhibited a higher CV of force than males, consistent with previous research (Inglis and Gabriel, 2021). However, the lack of statistical significance means we cannot confidently conclude that the difference in the CV of force was sex-related but could be due to chance. To gain a deeper understanding of these observations, it is essential to evaluate additional factors, including hormonal markers, strength, motor unit characteristics, and differences in muscle fiber types that may play a role in sex-related differences. The difference in findings across studies and between muscles suggests that further exploration is needed to understand sex-related differences in force variability.

Males had higher CVISI values than females in the TA and they exhibited higher CVISI values than females at both 10% contraction and during SINE contractions, with no significant sex-related difference in the FDI. These results are not consistent with previous findings in MUFR variability, as observed in the TA (Inglis and Gabriel 2021), vastus lateralis, vastus medialis, and oblique muscles (Peng et al., 2018) and the FDI (Parra et al., 2020). These previous reports demonstrated that females had an overall greater level of variability in motor unit firing rate. Our observations may be a result of the anatomical differences that exist within muscles between males and females. Males tend to possess larger muscle cross-sectional areas, along with a higher proportion of type II muscle fiber areas (Staron et al., 2000), which has been previously noted to potentially create an increase in CVISI (Parra et al., 2020, Peng et al., 2018).

3.3 Contraction intensity-related differences

As contraction levels increased— from 10% to 20% to 50% —the CVISI showed a significant corresponding increase. This finding was consistent for both sexes, indicating that higher force contractions were associated with greater motor unit firing rate variability. This observation was not part of our initial hypothesis and does not align with existing literature on the subject. Previous research, such as studies by Moritz et al. (2005) and Tanji and Kato (1973), has generally found that CVISI decreases as force levels increase. However, it should be noted that in the study by Moritz et al. (2005), there were more male subjects than females and Tanji and Kato's (1973) study included only male participants. This inconsistency across studies suggests further investigation into firing rate variability across contraction intensities is necessary, especially when considering female participants.

At all contraction levels—10% to 20% to 50% to SINE—the FDI had a higher CVISI than the TA, consistent with our study's hypothesis. We also observed that the FDI had higher mean firing rates than the TA across all contraction intensities. In a comparison between the FDI and the TA, factors like muscle function, size, and recruitment often result in higher force and motor unit firing rate variability in the FDI (Tracy et al. (2007). Due to the FDI having a smaller motor unit pool size compared to TA, this could lead to increased firing rate variability as recruitment increases. Indeed, in the FDI it has been noted that greater CVISI is associated with greater force variability (Inglis and Gabriel, 2021).

When comparing force variability between contraction intensities, we observed a significantly lower CV of force at 20% MVC, compared with 10% MVC. This is in line with previous studies, suggesting an increase in force output leads to increased force steadiness (Kunugi et al., 2021, Moritz et al., 2005). We also observed that amongst all contraction intensities (10%, 20%, 50%, SINE), SINE contractions exhibited the highest CV of force. SINE wave contractions may be more likely to exhibit higher variability compared to a constant contraction due to fluctuations in recruitment and firing rate. As the force increases and decreases with the SINE wave, motor units are recruited and de-recruited cyclically, leading to higher variability in force production compared to a static force contraction (Knight and Kamen 2007; Park et al., 2016).

3.4 Physical activity relationships

In the TA, we did not observe any significant relationships between physical activity and CVISI. However, in the TA, CV of force at 10% MVC was positively and significantly related to light PA. Moderate PA was positively and significantly related to CV of force at 10, 20, and 50% MVC. In the FDI, CV of force at 10% MVC was positively and significantly related to moderate physical activity and CVISI at SINE contraction was positively and significantly related to vigorous physical activity. More specifically, this relationship suggests that individuals engaging in greater amounts of moderate-vigorous PA exhibit increased force variability. This finding is inconsistent with the literature, where previous studies demonstrated a lower force variability and CVISI with increased strength training (Vila Cha and Falla, 2016). This could be explained by the methodological differences between studies, where other studies focused on a specific strength training intervention, with measurements taken from the specifically trained muscles of the participants, while we examined general habitual physical activity.

Prior studies have demonstrated that vigorous strength training reduces motor unit firing rate variability (Vila Cha and Falla, 2016), contrary to the lack of significant relationships between physical activity and CVISI observed in the present study. In contrast to our monitoring of habitual physical activity, the work by Vila Cha and Falla (2016) involved a short-term high intensity training intervention. It is therefore possible that the relationship between physical activity and motor unit firing behaviour following short-term training is different than the relationship to longer-term habitual physical activity levels.

3.5 Limitations and Future Directions

While our study was able to address a number of significant conceptual gaps, the exploration of these variables were collected to help us assess for sex-related differences in more detail. Limited hormonal or physiological markers were examined to potentially explain observed discrepancies. Additionally, while our participants were required to track their physical activity; the length of the protocol or muscle-specific physical activity collection may not have been enough to observe a significant relationship among variables. Finally, when compared to the FDI, the TA had a lower number of MU identified, which could have impacted the neuromuscular outcomes. Although this study adds valuable data to the existing body of literature, these limitations should be considered when interpreting the findings.

Conclusions

This study provides a unique, comprehensive analysis of the control of force and motor unit firing rates in both the FDI and the TA, as well as their interactions with sex and physical activity. Our findings contribute to the existing body of literature by demonstrating that differences in neural control were evident between muscles and sexes; however, these differences were not observed in force control. We found that the FDI, showed higher CVISI than the TA. Contrary to the common findings that females exhibit higher motor unit firing rate variability than males, our data showed that males had higher variability. This contrast in findings emphasizes the need to investigate factors such as physical training, hormonal factors and strength that may impact sex-related neuromuscular control. Using objective measures of physical activity, this work also adds to literature by assessing the relationships of habitual physical activity to neuromuscular outcomes. We found that increased levels of moderate-vigorous physical activity were related to higher force and motor unit firing rate variability, emphasizing the need for more research into these variables.

Future studies should further explore additional variables that may influence differences in motor unit firing and force variability across muscles. This work provides an in-depth overview of neuromuscular control by focusing on force and motor unit firing rate variability and how it differs between muscles. Contrary to prior findings, the study reveals differences inconsistent with the literature, suggesting the need for further investigations into other potential variables that influence neuromuscular behaviour.

References

Aagaard, P., Bojsen-Moller, J., & Lundbye-Jensen, J. (2020). Assessment of neuroplasticity with strength training. *Exercise and Sport Sciences Reviews*, *48*(4), 151-162.

Bandy, W. D., Lovelace-Chandler, V., & McKitrick-Bandy, B. (1990). Adaptation of skeletal muscle to resistance training. *Journal of Orthopaedic & Sports Physical Therapy*, *12*(6), 248-255.

Bellemare, F., Woods, J. J., Johansson, R., & Bigland-Ritchie, B. (1983). Motor-unit discharge rates in maximal voluntary contractions of three human muscles. *Journal of neurophysiology*, *50*(6), 1380-1392.

Brown, R. E., Edwards, D. L., & Jakobi, J. M. (2010). Sex differences in force steadiness in three positions of the forearm. *European journal of applied physiology*, *110*(6), 1251-1257.

Burke, R. E. (1999). Revisiting the notion of 'motor unit types'. *Progress in brain research*, *123*, 167-175.

Castronovo, A. M., Mrachacz-Kersting, N., Stevenson, A. J. T., Holobar, A., Enoka, R. M., & Farina, D. (2018). Decrease in force steadiness with aging is associated with increased power of the common but not independent input to motor neurons. *Journal of neurophysiology*, *120*(4), 1616-1624.

Cioni, R., Giannini, F., Paradiso, C., Battistini, N., Navona, C., & Starita, A. (1994). Sex differences in surface EMG interference pattern power spectrum. *Journal of Applied Physiology*, *77*(5), 2163-2168.

Clamann, H. P. (1993). Motor unit recruitment and the gradation of muscle force. *Physical therapy*, *73*(12), 830-843.

Clark, B. C., Pierce, J. R., Manini, T. M., & Ploutz-Snyder, L. L. (2007). Effect of prolonged unweighting of human skeletal muscle on neuromotor force control. *European journal of applied physiology*, *100*(1), 53–62. https://doi.org/10.1007/s00421-007-0399-6

Connelly, D. M., Rice, C. L., Roos, M. R., & Vandervoort, A. A. (1999). Motor unit firing rates and contractile properties in tibialis anterior of young and old men. *Journal of applied Physiology*, *87*(2), 843-852.

Contessa, P., Letizi, J., De Luca, G., & Kline, J. C. (2018). Contribution from motor unit firing adaptations and muscle coactivation during fatigue. *Journal of neurophysiology*, *119*(6), 2186–2193. https://doi.org/10.1152/jn.00766.2017

Contessa, P., Nawab, S. H., & De Luca, C. J. (2011, August). A model of motoneuron behavior and muscle-force generation for sustained isometric contractions. In *2011 Annual International Conference of the IEEE Engineering in Medicine and Biology Society* (pp. 4072-4075).

Davis, L. A., Alenazy, M. S., Almuklass, A. M., Feeney, D. F., Vieira, T., Botter, A., & Enoka, R. M. (2020). Force control during submaximal isometric contractions is associated with walking performance in persons with multiple sclerosis. *Journal of Neurophysiology*, *123*(6), 2191-2200.

De Luca, C. J., & Erim, Z. (1994). Common drive of motor units in regulation of muscle force. *Trends in neurosciences*, *17*(7), 299-305.

De Luca, C. J., & Hostage, E. C. (2010). Relationship between firing rate and recruitment threshold of motoneurons in voluntary isometric contractions. *Journal of neurophysiology*, *104*(2), 1034-1046.

De Luca, C. J., & Kline, J. C. (2011). Influence of proprioceptive feedback on the firing rate and recruitment of motoneurons. *Journal of Neural Engineering*, *9*(1), 016007.

Del Vecchio, A., Casolo, A., Negro, F., Scorcelletti, M., Bazzucchi, I., Enoka, R., ... & Farina, D. (2019). The increase in muscle force after 4 weeks of strength training is mediated by adaptations in motor unit recruitment and rate coding. *The Journal of physiology*, *597*(7), 1873-1887.

Dideriksen, J. L., Negro, F., Enoka, R. M., & Farina, D. (2012). Motor unit recruitment strategies and muscle properties determine the influence of synaptic noise on force steadiness. *Journal of neurophysiology*, *107*(12), 3357-3369. https://doi.org/10.1152/jn.00938.2011

Doherty, T. J., Chan, K. M., & Brown, W. F. (2002). Motor neurons, motor units, and motor unit recruitment. *Neuromuscular function and disease*, *1*, 247-273.

Doherty, T., Simmons, Z., O'Connell, B., Felice, K. J., Conwit, R., Chan, K. M., Komori, T., Brown, T., Stashuk, D. W., & Brown, W. F. (1995). Methods for estimating the numbers of motor units in human muscles. *Journal of clinical neurophysiology : official publication of the American Electroencephalographic Society*, *12*(6), 565–584. https://doi.org/10.1097/00004691-199511000-00004

Duchateau, J., & Baudry, S. (2014). Maximal discharge rate of motor units determines the maximal rate of force development during ballistic contractions in human. *Frontiers in human neuroscience*, *8*, 234.

Duchateau, J., & Enoka, R. M. (2002). Neural adaptations with chronic activity patterns in able-bodied humans. *American journal of physical medicine & rehabilitation*, *81*(11), S17-S27.

Duchateau, J., & Hainaut, K. (1990). Effects of immobilization on contractile properties, recruitment and firing rates of human motor units. *The Journal of physiology*, *422*(1), 55-65.

Duchateau, J., Semmler, J. G., & Enoka, R. M. (2006). Training adaptations in the behavior of human motor units. *Journal of applied physiology*, *101*(6), 1766-1775.

Elgueta-Cancino, E., Evans, E., Martinez-Valdes, E., & Falla, D. (2022). The Effect of Resistance Training on Motor Unit Firing Properties: A Systematic Review and Meta-Analysis. *Frontiers in physiology*, *13*, 817631. https://doi.org/10.3389/fphys.2022.817631

Enoka, R. M., & Duchateau, J. (2017). Rate Coding and the Control of Muscle Force. *Cold Spring Harbor perspectives in medicine*, *7*(10), a029702. https://doi.org/10.1101/cshperspect.a029702

Engberg, I., Segerstedt, J., Waller, G., Wennberg, P., & Eliasson, M. (2017). Fatigue in the general population- associations to age, sex, socioeconomic status, physical activity, sitting time and self-rated health: the northern Sweden MONICA study 2014. *BMC public health*, *17*(1), 654. https://doi.org/10.1186/s12889-017-4623-y

Enoka, R. M., Christou, E. A., Hunter, S. K., Kornatz, K. W., Semmler, J. G., Taylor, A. M., & Tracy, B. L. (2003). Mechanisms that contribute to differences in motor performance between young and old adults. *Journal of Electromyography and Kinesiology*, *13*(1), 1-12.

Enoka, R. M., & Duchateau, J. (2017). Rate Coding and the Control of Muscle Force. *Cold Spring Harbor perspectives in medicine*, *7*(10), a029702. https://doi.org/10.1101/cshperspect.a029702

Enoka, R. M., & Farina, D. (2021). Force steadiness: from motor units to voluntary actions. *Physiology*, *36*(2), 114-130.

Enoka, R. M., & Fuglevand, A. J. (2001). Motor unit physiology: some unresolved issues. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *24*(1), 4-17.

Freedson PS, Melanson E, Scrard J. Calibration of the Computer Science and Applications, lnc. accelerometer, http://www.wwilkins.com/

Freund, H. J. (1983). Motor unit and muscle activity in voluntary motor control. *Physiological reviews*, *63*(2), 387-436.

Feinstein, B., Lindegdrd, B., Nyman, E. and Wohlfart, G. (1954) : Morphologic studies of motor units in normal human muscles. Acta Anatomica (In preparation).

Feinstein, B., Lindegarrd, B., Nyman, E., & Wohlfart, G. (1954). Studies on action potentials in normal human muscles. *Acta Psychiatrica Scandinavica*, *29*(2), 189-195.

Fling, B. W., Knight, C. A., & Kamen, G. (2009). Relationships between motor unit size and recruitment threshold in older adults: implications for size principle. *Experimental brain research*, *197*, 125-133.

Gabriel, D. A., Basford, J. R., & An, K. N. (2001). Neural adaptations to fatigue: implications for muscle strength and training. *Medicine and science in sports and exercise, 33*(8), 1354–1360. https://doi.org/10.1097/00005768-200108000-00017

Grgic, J., & Schoenfeld, B. J. (2018). Are the Hypertrophic Adaptations to High and Low-Load Resistance Training Muscle Fiber Type Specific?. *Frontiers in physiology, 9*, 402. https://doi.org/10.3389/fphys.2018.00402

Guo, Y., Jones, E. J., Inns, T. B., Ely, I. A., Stashuk, D. W., Wilkinson, D. J., Smith, K., Piasecki, J., Phillips, B. E., Atherton, P. J., & Piasecki, M. (2022). Neuromuscular recruitment strategies of the vastus lateralis according to sex. *Acta physiologica (Oxford, England)*, *235*(2), e13803. https://doi.org/10.1111/apha.13803

Hamilton, A. F., Jones, K. E., & Wolpert, D. M. (2004). The scaling of motor noise with muscle strength and motor unit number in humans. *Experimental brain research*, 157, 417-430.

Hatz, B. A., Frima, H., & Sommer, C. (2019). Selective fasciotomy for acute traumatic lower leg compartment syndrome: is it feasible?. *Archives of Orthopaedic and Trauma Surgery*, 139, 1755-1762.

Haynes, C. A., Tenan, M. S., Passaro, A. D., & Tweedell, A. J. (2022) Investigating Imperceptible Vibrotactile Stimulation during a Force Stability Task. https://doi.org/*10.51224/cik.2022.41*

Hendrickse, P. W., Venckunas, T., Platkevicius, J., Kairaitis, R., Kamandulis, S., Snieckus, A., Stasiulis, A., Vitkiene, J., Subocius, A., & Degens, H. (2021). Endurance training-induced increase in muscle oxidative capacity without loss of muscle mass in younger and older resistance-trained men. *European journal of applied physiology, 121*(11), 3161–3172. https://doi.org/10.1007/s00421-021-04768-4

Henneman, E., Clamann, H. P., Gillies, J. D., & Skinner, R. D. (1974). Rank order of motoneurons within a pool: law of combination. *Journal of neurophysiology*, *37*(6), 1338-1349.

Henneman, E. (1957). Relation between size of neurons and their susceptibility to discharge. *Science*, *126*(3287), 1345-1347.

Henneman, E. (1985). The size-principle: a deterministic output emerges from a set of probabilistic connections. *Journal of experimental biology*, *115*(1), 105-112.

Henneman, E., & Olson, C. B. (1965). Relations between structure and function in the design of skeletal muscles. *Journal of neurophysiology*, *28*(3), 581-598.

Herbison GJ, Jaweed MM, Ditunno JF. Muscle fiber types. Arch Phys Med Rehabil. 1982 May;63(5):227-30. PMID: 6462127.

Hughes, D. C., Ellefsen, S., & Baar, K. (2018). Adaptations to Endurance and Strength Training. *Cold Spring Harbor perspectives in medicine*, *8*(6), a029769. https://doi.org/10.1101/cshperspect.a029769

Hunter, S. K., Pereira, H. M., & Keenan, K. G. (2016). The aging neuromuscular system and motor performance. *Journal of applied physiology (Bethesda, Md. : 1985)*, *121*(4), 982–995. https://doi.org/10.1152/japplphysiol.00475.2016

Hu, X., Rymer, W. Z., & Suresh, N. L. (2014). Motor unit firing rate patterns during voluntary muscle force generation: a simulation study. *Journal of neural engineering*, *11*(2), 026015.

Inglis, J. G., & Gabriel, D. A. (2020). Sex differences in motor unit discharge rates at maximal and submaximal levels of force output. *Applied Physiology, Nutrition, and Metabolism*, *45*(11), 1197-1207.

Inglis, J. G., & Gabriel, D. A. (2021). Sex differences in the modulation of the motor unit discharge rate leads to reduced force steadiness. *Applied Physiology, Nutrition, and Metabolism*, *46*(9), 1065-1072. https://doi.org/10.1139/apnm-2020-0953

Jakobi, J. M., Haynes, E. M., & Smart, R. R. (2018). Is there sufficient evidence to explain the cause of sexually dimorphic behaviour in force steadiness?. *Applied Physiology, Nutrition, and Metabolism*, *43*(11), 1207-1214.

Jesunathadas, M., Klass, M., Duchateau, J., & Enoka, R. M. (2012). Discharge properties of motor units during steady isometric contractions performed with the dorsiflexor muscles. *Journal of Applied Physiology*, *112*(11), 1897-1905.

Johnson, M. A., Polgar, J., Weightman, D., & Appleton, D. (1973). Data on the distribution of fibre types in thirty-six human muscles: an autopsy study. Journal of the Neurological Sciences, 18(1), 111–129

Juneja, P., & Hubbard, J. B. (2018). Anatomy, bony pelvis and lower limb, tibialis Anterior Muscles.

Kakouris, N., Yener, N., & Fong, D. T. (2021). A systematic review of running-related musculoskeletal injuries in runners. *Journal of sport and health science*, *10*(5), 513-522.

Kamen, G., Sison, S. V., Du, C. C., & Patten, C. (1995). Motor unit discharge behavior in older adults during maximal-effort contractions. *Journal of applied physiology*, *79*(6), 1908-1913.

Knight, C. A., & Kamen, G. (2004). Enhanced motor unit rate coding with improvements in a force-matching task. *Journal of Electromyography and Kinesiology*, *14*(6), 619-629.

Kowalski, K. L., & Anita D, C. (2020). Force Control and Motor Unit Firing Behavior Following Mental Fatigue in Young Female and Male Adults. *Frontiers in Integrative Neuroscience*, *14*, 15.

Krans, J. L. (2010). The sliding filament theory of muscle contraction. *Nature Education*, *3*(9), 66.

Krishnan, C., & Williams, G. N. (2009). Sex Differences in Quadriceps & Hamstrings EMG-Moment Relationships. *Medicine and science in sports and exercise*, *41*(8), 1652

Kunugi, S., Holobar, A., Kodera, T., Toyoda, H., & Watanabe, K. (2021). Motor unit firing patterns on increasing force during force and position tasks. *Journal of Neurophysiology*, *126*(5), 1653-1659.

Kuo, I. Y., & Ehrlich, B. E. (2015). Signaling in muscle contraction. *Cold Spring Harbor perspectives in biology*, *7*(2), a006023.

Mattock, J., Steele, J. R., & Mickle, K. J. (2021). Lower leg muscle structure and function are altered in long-distance runners with medial tibial stress syndrome: a case control study. *Journal of Foot and Ankle Research*, *14*, 1-8.

MacIntosh BR, Gardiner PF, McComas AJ. Skeletal Muscle: Form and Function. Second. Human Kinetics, 2006.

Mear, E., Gladwell, V. F., & Pethick, J. (2022). The Effect of Breaking Up Sedentary Time with Calisthenics on Neuromuscular Function: A Preliminary Study. *International journal of environmental research and public health*, *19*(21), 14597. https://doi.org/10.3390/ijerph192114597

Mendell, L. M. (2005). The size principle: a rule describing the recruitment of motoneurons. *Journal of neurophysiology*, *93*(6), 3024-3026.

Milner-Brown, H. S., Stein, R. B., & Yemm, R. (1973). Changes in firing rate of human motor units during linearly changing voluntary contractions. *The Journal of physiology*, *230*(2), 371–390. https://doi.org/10.1113/jphysiol.1973.sp010193

Missenard, O., Mottet, D., & Perrey, S. (2009). Factors responsible for force steadiness impairment with fatigue. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *40*(6), 1019-1032.

Monster, A. W. (1979). Firing rate behavior of human motor units during isometric voluntary contraction: relation to unit size. *Brain Research*, *171*(2), 349-354.

Moritz, C. T., Barry, B. K., Pascoe, M. A., & Enoka, R. M. (2005). Discharge rate variability influences the variation in force fluctuations across the working range of a hand muscle. *Journal of neurophysiology*, *93*(5), 2449–2459. https://doi.org/10.1152/jn.01122.2004

Omar, A., Marwaha, K., & Bollu, P. C. (2017). Physiology, neuromuscular junction. In: StatPearls. StatPearls Publishing, Treasure Island (FL). PMID: 29261907.

Oomen, N. M., & van Dieen, J. H. (2017). Effects of age on force steadiness: a literature review and meta-analysis. *Ageing research reviews*, *35*, 312-321.

Park, S. H., Kwon, M., Solis, D., Lodha, N., & Christou, E. A. (2016). Motor control differs for increasing and releasing force. *Journal of neurophysiology*, *115*(6), 2924-2930.

Parra, M. E., Sterczala, A. J., Miller, J. D., Trevino, M. A., Dimmick, H. L., & Herda, T. J. (2020). Sex-related differences in motor unit firing rates and action potential amplitudes of the first dorsal interosseous during high-, but not low-intensity contractions. *Experimental Brain Research*, *238*(5), 1133-1144.

Pascoe, M. A., Holmes, M. R., Stuart, D. G., & Enoka, R. M. (2014). Discharge characteristics of motor units during long-duration contractions. *Experimental physiology*, *99*(10), 1387–1398. https://doi.org/10.1113/expphysiol.2014.078584

Patten, C., Kamen, G., & Rowland, D. M. (2001). Adaptations in maximal motor unit discharge rate to strength training in young and older adults. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *24*(4), 542-550.

Pearcey, G. E. P., Alizedah, S., Power, K. E., & Button, D. C. (2021). Chronic resistance training: is it time to rethink the time course of neural contributions to strength gain?. *European Journal of Applied Physiology*, *121*, 2413-2422.

Peng, Y. L., Tenan, M. S., & Griffin, L. (2018). Hip position and sex differences in motor unit firing patterns of the vastus medialis and vastus medialis oblique in healthy individuals. *Journal of Applied Physiology*, *124*(6), 1438-1446.

Person, R. S., & Kudina, L. P. (1972). Discharge frequency and discharge pattern of human motor units during voluntary contraction of muscle. *Electroencephalography and clinical neurophysiology*, *32*(5), 471-483.

Pesta, D. H., Angadi, S. S., Burtscher, M., & Roberts, C. K. (2013). The effects of caffeine, nicotine, ethanol, and tetrahydrocannabinol on exercise performance. *Nutrition & metabolism*, *10*, 1-15.

Piasecki, M., Ireland, A., Coulson, J., Stashuk, D. W., Hamilton-Wright, A., Swiecicka, A., ... & Jones, D. A. (2016). Motor unit number estimates and neuromuscular transmission in the tibialis anterior of master athletes: evidence that athletic older people are not spared from age-related motor unit remodeling. *Physiological reports*, 4(19), e12987.

Plotkin, D. L., Roberts, M. D., Haun, C. T., & Schoenfeld, B. J. (2021). Muscle Fiber Type Transitions with Exercise Training: Shifting Perspectives. *Sports (Basel, Switzerland)*, *9*(9), 127. https://doi.org/10.3390/sports9090127

Potvin, J. R., & Fuglevand, A. J. (2017). A motor unit-based model of muscle fatigue. *PLoS computational biology*, *13*(6), e1005581. https://doi.org/10.1371/journal.pcbi.1005581

Power, G. A., Dalton, B. H., Behm, D. G., Vandervoort, A. A., Doherty, T. J., & Rice, C. L. (2010). Motor unit number estimates in masters runners: use it or lose it?. *Medicine & Science in Sports & Exercise*, *42*(9), 1644-1650.

Power, G. A., Dalton, B. H., Behm, D. G., Doherty, T. J., Vandervoort, A. A., & Rice, C. L. (2012). Motor unit survival in lifelong runners is muscle dependent. *Medicine & Science in Sports & Exercise*, *44*(7), 1235-1242.

Pucci, A. R., Griffin, L., & Cafarelli, E. (2006). Maximal motor unit firing rates during isometric resistance training in men. *Experimental physiology*, *91*(1), 171-178.

Reed, J., & Bowen, J. D. (2008). Principles of sports rehabilitation. *The sports medicine resource manual. 1st ed. Philadelphia: Saunders*, 431-6.

Roos, M. R., Rice, C. L., Connelly, D. M., & Vandervoort, A. A. (1999). Quadriceps muscle strength, contractile properties, and motor unit firing rates in young and old men. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *22*(8), 1094-1103.

Rubinstein, S., & Kamen, G. (2005). Decreases in motor unit firing rate during sustained maximal-effort contractions in young and older adults. *Journal of Electromyography and Kinesiology*, *15*(6), 536-543.

Seyffarth, H. (1940). *The behaviour of motor-units in voluntary contractions*. Ikommisjon hos J. Dybwad.

Sica, R. E. P., & McComas, A. J. (1971). Fast and slow twitch units in a human muscle. *Journal of Neurology, Neurosurgery & Psychiatry*, *34*(2), 113-120.

Staron, R. S., Hagerman, F. C., Hikida, R. S., Murray, T. F., Hostler, D. P., Crill, M. T., ... & Toma, K. (2000). Fiber type composition of the vastus lateralis muscle of young men and women. *Journal of histochemistry & cytochemistry*, *48*(5), 623-629.

Tanji, J., & Kato, M. (1973). Recruitment of motor units in voluntary contraction of a finger muscle in man. *Experimental neurology*, *40*(3), 759-770. https://doi.org/10.1016/0014-4886(73)90110-6

Tracy, B. L., Mehoudar, P. D., & Ortega, J. D. (2007). The amplitude of force variability is correlated in the knee extensor and elbow flexor muscles. *Experimental brain research*, *176*, 448-464.

Usherwood, J. R., Channon, A. J., Myatt, J. P., Rankin, J. W. and Hubel, T. Y. (2012). The human foot and heel-sole-toe walking strategy: a mechanism enabling an inverted pendular gait with low isometric muscle force? *J. R. Soc. Interface* 9, 2396-2402.

Vila-Chã, C., Falla, D., & Farina, D. (2010). Motor unit behavior during submaximal contractions following six weeks of either endurance or strength training. *Journal of Applied Physiology*, *109*(5), 1455-1466.

Vila-Chã, C., & Falla, D. (2016). Strength training, but not endurance training, reduces motor unit discharge rate variability. *Journal of Electromyography and Kinesiology*, *26*, 88-93.

Witzemann, V. (2006). Development of the neuromuscular junction. *Cell and tissue research*, *326*, 263-271.

Webb. (2017). 6.Pages 110-139, In *Neurology for the speech-language pathologist (sixth edition)*. essay, Mosby.

Westerberg, E., Molin, C. J., Spörndly Nees, S., Widenfalk, J., & Punga, A. R. (2018). The impact of physical exercise on neuromuscular function in Myasthenia gravis patients: A single-subject design study. *Medicine*, 97(31). https://doi.org/10.1097/MD.0000000000011510

Ye, X., Beck, T. W., & Wages, N. P. (2015). Acute effects of concentric vs. eccentric exercise on force steadiness and electromyographic responses of the forearm flexors. *Journal of strength and conditioning research*, *29*(3), 604–611. https://doi.org/10.1519/JSC.0000000000000674

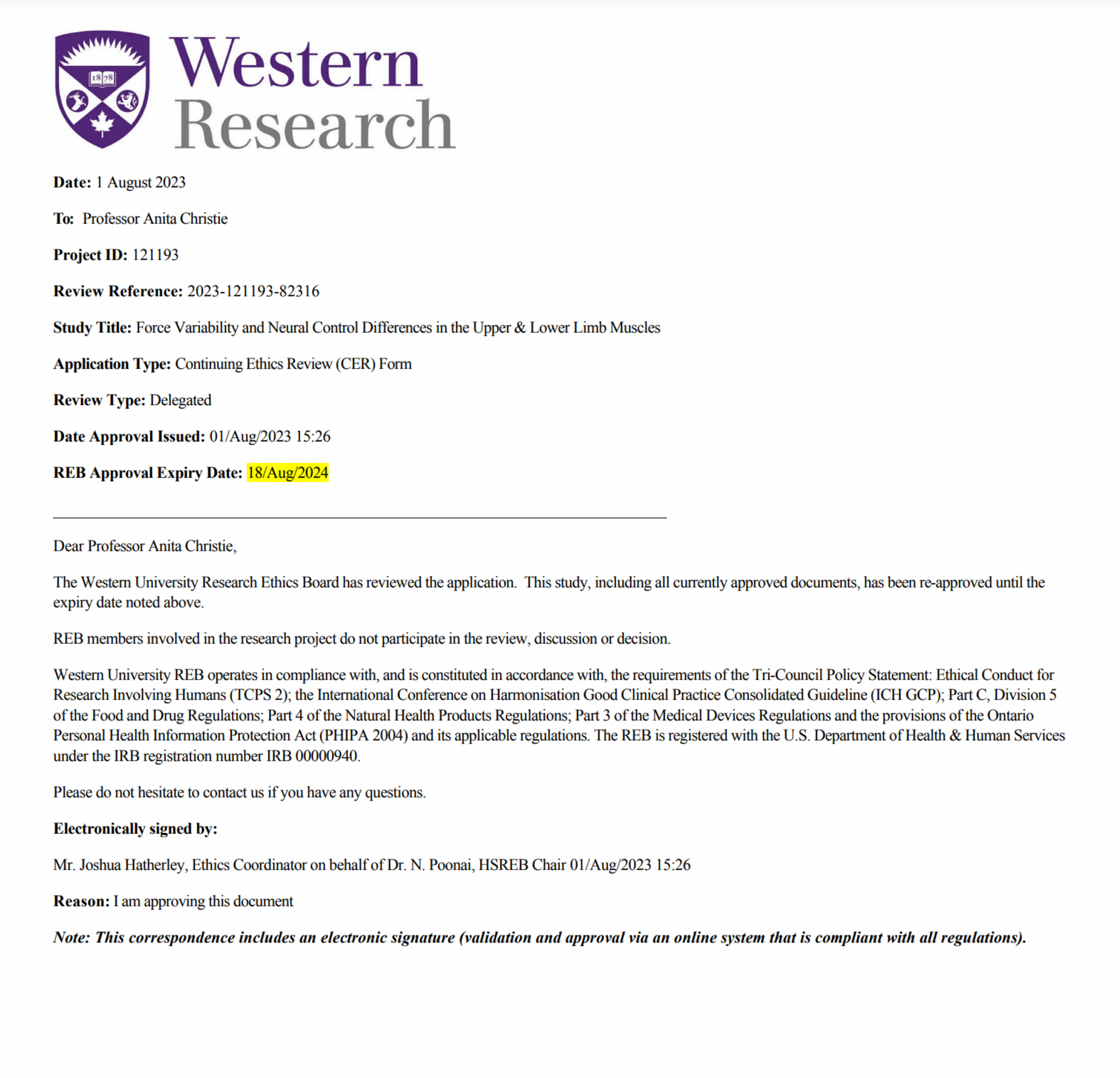
Yerdelen, D., Koç, F., & Sarica, Y. (2006). The effects of gender and age on motor unit number estimation in normal population. *Acta neurologica belgica*, *106*(1), 5.

Yoon, T., Vanden Noven, M. L., Nielson, K. A., & Hunter, S. K. (2014). Brain areas associated with force steadiness and intensity during isometric ankle dorsiflexion in men and women. *Experimental brain research*, *232*(10), 3133-3145.

Zayia, L. C., & Tadi, P. (2021). Neuroanatomy, motor neuron. In *StatPearls [Internet]*. StatPearls Publishing.

Appendices

Appendix A: Research ethics board approval



Western Research

Date: 1 August 2023

To: Professor Anita Christie

Project ID: 121193

Review Reference: 2023-121193-82316

Study Title: Force Variability and Neural Control Differences in the Upper & Lower Limb Muscles

Application Type: Continuing Ethics Review (CER) Form

Review Type: Delegated

Date Approval Issued: 01/Aug/2023 15:26

REB Approval Expiry Date: 18/Aug/2024

Dear Professor Anita Christie,

The Western University Research Ethics Board has reviewed the application. This study, including all currently approved documents, has been re-approved until the expiry date noted above.

REB members involved in the research project do not participate in the review, discussion or decision.

Western University REB operates in compliance with, and is constituted in accordance with, the requirements of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The REB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Electronically signed by:

Mr. Joshua Hatherley, Ethics Coordinator on behalf of Dr. N. Poonai, HSREB Chair 01/Aug/2023 15:26

Reason: I am approving this document

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

Curriculum Vitae

Name:	Kherto Ahmed
Post-secondary Education and Degrees:	McMaster University Hamilton, Ontario, Canada 2017-2021 BSc in Life Sciences Awards: McMaster Entrance Scholarship Dean's Honour List
	The University of Western Ontario London, Ontario, Canada 2021-2023 MSc in Kinesiology Awards: Entrance Scholarship Graduate Teaching Assistantship

Publications:

Ahmed, K., Mackinlay, J., Malhotra, K., Vijayakumar, M., Yaya, H. (2021). Investigating the Abundance and Accessibility of The New York Times Articles during two measles outbreaks and the COVID-19 pandemic. Manuscript submitted for publication.

Ahmed, K., Anning, D., Boateng, P., Jimoh, J., Mason, P., Mengesha, T., Tecle, S. (2019). Evaluating the Effectiveness of Success Beyond Limits' Graduation Model. Success Beyond Limits and Higher Education Quality Council of Ontario (HEQCO). Manuscript submitted for publication.