ARE SEX DIFFERENCES IN FORCE STEADINESS DUE TO DISSIMILAR MOTOR UNIT ACTIVITY BETWEEN MEN AND WOMEN?

by

Ruth Emily Brown

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Abstract

Force steadiness (FS) is the ability to maintain a constant isometric contraction around a given force level and is expressed as the coefficient of variation (CV) of force. Although it has recently been shown that men are steadier than women in the elbow flexor muscles, the primary mechanism for this difference has yet to be determined. Motor unit activity is thought to influence FS, in particular motor unit discharge rate variability (MUDRV). The purpose of this thesis was to determine if motor unit activity differs between men and women, and if this is a possible mechanism to explain sex differences in FS. Eight young men (25 ± 3.6 years) and 11 young women (21.2 ± 3.2 years) performed a 7.5 second steady isometric elbow flexion contraction in the neutral wrist position at 5%, 10%, 25% and 50% of maximum voluntary contraction (MVC). Single motor unit activity, force, and surface electromyography (EMG) were measured simultaneously during the 7.5s contraction from the short head (SH) and long head (LH) of the biceps brachii (BB) of the left, non-dominant arm. Results indicate that men were significantly ($p < 0.05$) stronger than women as well as steadier at all force levels. Motor unit discharge rate (MUDR) and surface EMG did not differ between men and women at the same relative force levels. However, women exhibited greater MUDRV than men ($p = 0.02$). When data for men and women were combined, significant relationships were observed between CV of force with MVC ($r^2 = 0.42$) ($p < 0.001$), CV of force with MUDR ($r^2 = 0.05$) ($p = 0.01$), but CV of force and MUDRV were not related. When men and women were assessed independently, there was no relationship between FS and MVC, MUDR, or MUDRV for men, yet significant relationships were observed between FS and MVC ($r^2 = 0.35$) ($p < 0.001$) and FS and MUDR ($r^2 = 0.25$) ($p < 0.001$) for women. Partial correlations revealed that maximum strength (-0.71) and MUDR (-0.37) contribute the most to FS. Although MUDRV was greater in

women than men during isometric elbow flexion, MUDRV does not appear to be a factor contributing to FS in young adults. Maximum strength seems to be the largest contributor to sex differences in FS, in that the weaker the muscle the less steady it is.

Preface

This study was approved by the UBC Clinical Research Ethics Board. Effects of Caffeine on Standing: H09-02470.

Chapter 3 is based on work conducted in the neuromuscular physiology laboratory at the University of British Columbia Okanagan by Dr. Jennifer M. Jakobi, Nikki Karn, Olga Theou, and Ruth E. Brown. Dr. Jakobi was responsible for contributing to the overall concept and design of the study, writing process, technical assistance, equipment acquisition, and funding for the study. Nikki Karn and Olga Theou assisted with data collection. I contributed to the overall concept and design of the study, data collection and analysis, and writing.

A version of chapter 3 has been published in abstract form. Ruth E. Brown, Nikki Karn, and Jennifer M. Jakobi. (2010) Influence of Motor Unit Activity on Sex Differences in Force Steadiness. Med Sci Sports Exerc. Volume 43: Supplement 5. I was responsible for the data collection and analysis, and formatting of the abstract.

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List of Abbreviations

BB: biceps brachii

BR: brachioradialis

CV: coefficient of variation

EMG: electromyography

FS: force steadiness

LH: long head of the biceps brachii

MUDR: motor unit discharge rate

MUDRV: motor unit discharge rate variability

MVC: maximum voluntary contraction

SH: short head of the biceps brachii

WF: wrist flexors

Glossary

Absolute Strength: The maximum force a person can exert with all or part of the body, irrespective of body size or muscle size.

Action Potential: an electrical impulse that travels along nerve and muscle fibres.

Afferent: A term used to describe a pathway that travels from a sensory receptor to the central nervous system.

Alpha Motor Neuron: Large lower motor cells of the brainstem and spinal cord that innervate extrafusal muscle fibres.

Coefficient of Variation: A statistical measure indicating the amount of variability. It is assessed by dividing each individual sample's standard deviation from the individuals' mean.

Efferent: A term used to describe a pathway that travels from the central nervous system to an effector (ie. muscle).

Electromyography: The electrical activity of muscles that is measuredwith electrodes placed on the skin surface.

Force Steadiness: the ability to maintain an isometric contraction around a given force level. Often expressed as the coefficient of variation of force, which has an inverse relationship to force steadiness (ie. as coefficient of variation decreases, force steadiness increases).

Ia afferent: a neuron that transmits information regarding length and rate of length change from the spindle apparatus of the intrafusal fibre of skeletal muscles to the motor nucleus in the ventral spinal cord.

Ib afferent: A neuron that transmits information regarding tension from the Golgi tendon organ in the aponeurotic region of the musculotendinous junction to the motor nucleus in the ventral spinal cord.

II afferent: A neuron that transmits information regarding length change from the spindle apparatus of the intrafusal fibre of the skeletal muscles to the motor nucleus in the ventral spinal cord.

Isometric Contraction: Muscle contraction without shortening or change in distance between its origin and insertion.

Lateral corticospinal tract: Bundle of neurons originating in the primary cortical neurons in the brain that travel down the spinal cord to the motor nuclei in the contralateral ventral horn.

Maximum Voluntary Contraction: When an individual attempts to voluntarily contract a muscle while producing as much force as possible. When a contraction is maximal all available motor units should be active and discharging at the optimal rate.

Motor Unit: A single motoneuron and all the muscles fibres it innervates.

Motor Unit Discharge Rate: The frequency at which a motor neuron discharges action potentials.

Motor Unit Discharge Rate Variability: The temporal consistency in which a motor neuron discharges action potentials. Often expressed as the coefficient of variation of motor unit discharge rate.

Motor Unit Recruitment: A force grading mechanism by which additional motor units are activated in response to an increase in force demand.

Neutral Forearm Position: An anatomical position in which the forearm is half-way between palm-up and palm-down. The palm is faced medially.

Relative Force Level: A measure of force at a given percentage of an individual's maximum force.

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Dedication

To Josh… the love of my life and the most patient person I know

Chapter 1: Literature Review

1.1 Organization of Voluntary Movement

When a human being attempts to conduct a voluntary movement, the process of information transmission starts in the brain and descends to the level of the muscle. Signals from the primary motor cortex are first sent down the lateral corticospinal tract to the grey matter in the ventral horn of the spinal cord. Multiple excitatory and inhibitory electrochemical inputs converge on the cell bodies of alpha motor neurons that lie in the ventral grey matter. If the membrane potential of the cell body of the neuron reaches threshold, an action potential will occur and travel along the axon of the motor neuron. As the action potential descends closer to the muscle, the axon splits and each branch divides further, so that one motor neuron can innervate multiple muscle fibres (Figure 1.1)

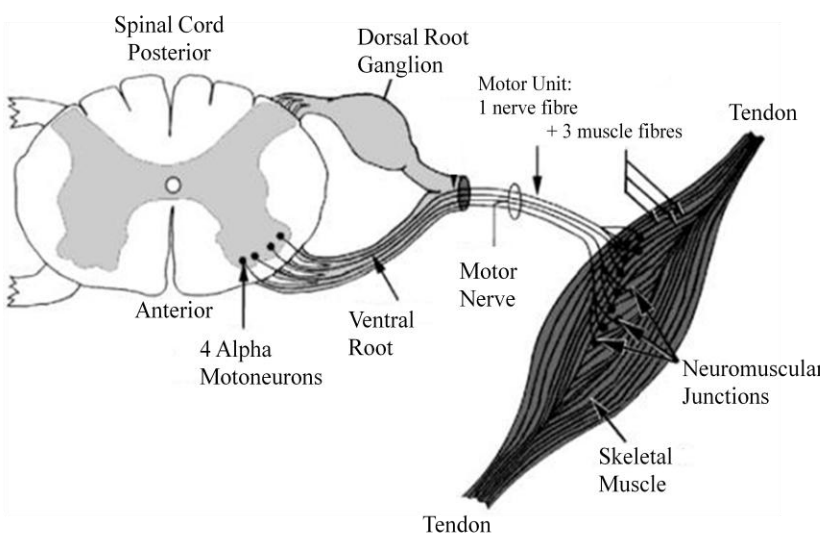

Figure 1.1. Signal transmission from the level of the spinal cord to the muscle. Excitatory and inhibitory signals converge on motoneurons in the grey matter of the ventral horn of the spinal cord. If threshold is reached an action potential will descend along an alpha motoneuron whose axon will branch out in multiple directions when it reaches close proximity to the muscle. A single motoneuron can innervate several to thousands of muscle fibres within the same muscle.

The single alpha motor neuron and all of the muscle fibres that are innervated is called a motor unit. Where the nerve branch and muscle fibre meet is called the neuromuscular junction. The synapse is the area between the nerve and muscle fibre where the pre-synaptic membrane of the nerve releases the neurotransmitter acetylcholine. Acetylcholine crosses the synaptic cleft and attaches to receptors on the post-synaptic membrane of the muscle fibre, where the signal continues down a series of transverse tubules within the muscle. Ultimately calcium is released from the sarcoplasmic reticulum to initiate cross-bridge formation and a muscle contraction occurs (McComas, 1996).

Muscle spindles and golgi tendon organs both influence the motoneuron to adjust its MUDR to control force output. Muscle spindles are surrounded by extrafusal muscle fibres that are innervated by the alpha motor neuron. They detect and are very sensitive to the length of the muscle fibres during contraction and send excitatory impulses to motoneurons via group 1a afferent axons. Muscle spindles are innervated by gamma motor neurons, which have small diameter axons that originate in the ventral horn of the spinal cord. These efferent neurons help maintain optimal sensitivity of the spindle at all muscle lengths. Adjustments in gamma motor neuron activation enable the spindle to continuously monitor the length of the muscles that contain them (McArdle, Katch & Katch, 2001). Golgi tendon organs are found at the musculotendinous junction and detect changes in tension when the muscle fibre contracts. Sensory signals are sent to the spinal cord via group 1b afferent axons that are inhibitory to motoneurons of the same muscle, and excitatory to antagonist muscles. Golgi tendon organs act as a protective mechanism to ensure that the muscle is not stretched to the point of damage (McComas, 1996).

1.2 Motor Unit Characteristics

As previously mentioned, an alpha motor neuron and all the muscle fibres that it innervates is collectively referred to as a motor unit. Although one alpha motor neuron can innervate up to several hundred fibres within a muscle, the muscle fibres can only be innervated by one alpha motor neuron within a motor unit. The motor unit is said to be the final functional unit of force production (Kandell, Schwartz & Jessell, 2000). The motor neuron pool is the term used to describe a group of motor units that belong to the same muscle (McArdle, Katch & Katch, 2001). A motor neuron pool has both slow (type I) and fast (type IIa and IIb) twitch motor units, although a motor unit itself contains only one specific muscle fibre type (McArdle, Katch & Katch, 2001). Type I motor units innervate slow twitch muscle fibres, which generate a low amount of force, have a slow contraction time, and are resistant to fatigue. Type II motor units innervate fast twitch muscle fibres that are capable of producing greater force than slow twitch fibres, have a faster contraction time, but are more easily fatigable. The functional ability of the motor unit is a reflection of its nerve to muscle fibre ratio (McArdle, Katch & Katch, 2001). A motor neuron that innervates a small number of muscle fibres typically plays a role in precise fine skilled movements. For example, motor units of the external eye muscles have about nine muscle fibres per motor unit (Feinstein, Lindegard, Nyman &Wohlfart, 1955). Muscles that require gross or powerful movements, such as the medial gastrocnemius (1934 muscles fibres/unit) and BB muscle (1433 fibres/unit) have a much higher muscle fibre to nerve ratio (Feinstein, Lindegard et al., 1955; Miller, MacDougall, Tarnopolsky & Sale, 1993).

1.3 Force Production and Movement Control

There are two mechanisms by which motor units can increase force production; motor unit recruitment and MUDR. The first method, motor unit recruitment, occurs when an increase in force is required. To increase force the nervous system will recruit additional motor units, and increase the MUDR of already active units (Adrian & Bronk, 1929). The process with which motor units are recruited is not random but according to the size of the motor unit. The size principle - according to Henneman who originally proposed this theory (Henneman, 1957) - states that motor units are recruited in an orderly manner. The smaller, low threshold units are recruited first and as force increases larger high threshold units are recruited. Motor unit recruitment is associated with a curvilinear increase in force. When force begins to increase the smaller low threshold motor units turn on first, so force is increased at a slower rate. As force continues to increase the larger, high velocity conduction motor units begin to fire so the rate of force production increases. The second method of increasing force is by modulating the MUDR (the rate at which the motor unit discharges an action potential). When an alpha motor neuron fires and the signal reaches the neuromuscular junction, all of the muscle fibres within the unit will contract simultaneously or not contract at all; this is referred to as the all-or-none principle (Adrian, 1914). Motor unit discharge rate does not increase linearly with increased force production; rather it has been shown to increase in an S-shape manner (de Luca and Erim, 1994; Kanosue, Yoshida, Akazawa, & Fujii, 1979) (Figure 1.2).

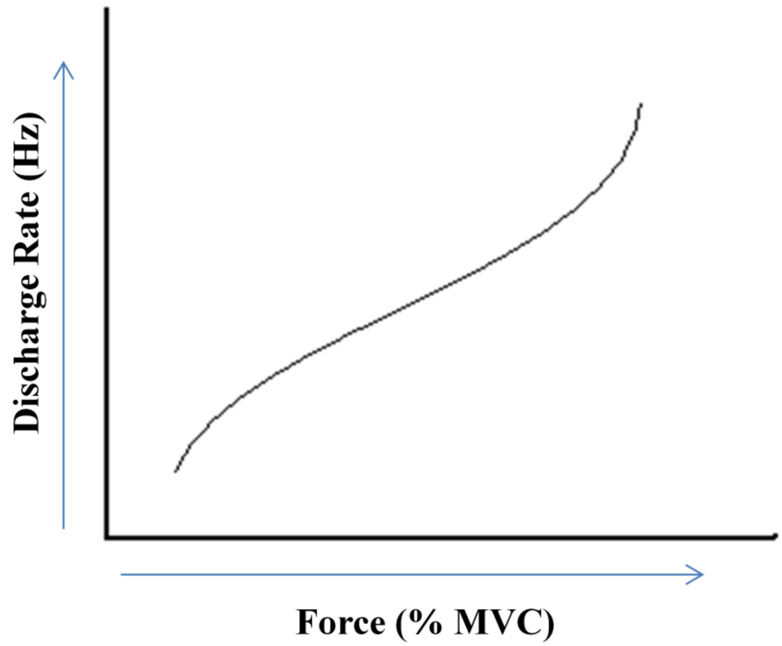

Figure 1.2. Model representing a non-linear increase in motor unit discharge rate with a linear increase in force. The figure is depicting four different motor units that were recruited at different times with a linear increase in force production. The change in MUDR is high during initial force production, begins to level off at intermediate force levels, and rises again at high force levels. Hz, hertz; %, percent; MVC, maximum voluntary contraction.

Initially MUDR increases sharply at the beginning of force production due to the minimal number of motor units recruited. At intermediate force levels the increase in the rate of discharge slows as recruitment of additional motor units becomes the dominant mechanism of increasing force of a muscle. As the muscle approaches maximal force all motor units will be active, therefore the MUDR will again increase to produce greater force (de Luca, Le Fever, McCue & Xenakis, 1982). A property of MUDR that is often studied with respect to force control is MUDRV. Motor unit discharge rate variability is the temporal consistency in which an action potential fires. Simply put, it is a measure of how consistently or regularly an action potential discharges over a period of time. It is often expressed as a percentage in relative terms as the CV of MUDR (standard deviation divided by mean MUDR). It is related to movement control (Moritz, Barry, Pascoe & Enoka, 2003) and has been typically reported as a constant value that ranges between 10-20% as muscle force increases (Nordstrom, Fuglevand & Enoka, 1992).

Certain tasks require a muscle to maintain a given load at a constant force level. When a person attempts to maintain a certain level of strength over time, force is not held constant but fluctuates around a given force level. Force fluctuations, often termed FS, is the ability to maintain a constant isometric contraction around a given force level and is a measure of how the neuromuscular system controls force output. It is often expressed in relative terms as the CV of force (standard deviation divided by mean force). Force steadiness has been studied in different populations and has been found to differ depending on a variety of factors, such as the muscle group investigated, age, sex, and intensity of contraction. For example, isometric FS declines in older adults compared with younger adults in the first dorsal interosseus muscle (Laidlaw et al. 2000), tibialis anterior (Dewhurst et al. 2007), and quadriceps of older adults with a history of falling (Carville et al. 2007); but no differences were observed between young and old adults in grip force variability (Cole & Beck, 1994) or index finger abduction force (Erim, Beg, Burke & de Luca, 1999). With respect to sex differences, women are less steady than men in the elbow flexors and this was associated with muscle strength being less in women (Brown, Edwards & Jakobi, 2010), or due to gender-dependent force control mechanisms whereby women experience less afferent feedback than men when producing a constant force (Svendson & Madeleine, 2010). The relationship between FS and intensity of contraction (% MVC) is not linear but operates as a U-shape function (Danion & Gallea, 2004; Slifkin & Newell, 1999;

Tracy & Enoka, 2002). Coefficient of variation of force is highest (least steady) at low and high force levels and isometric contractions produced at intermediate force levels have the lowest CV of force (most steady) (Figure 1.3).

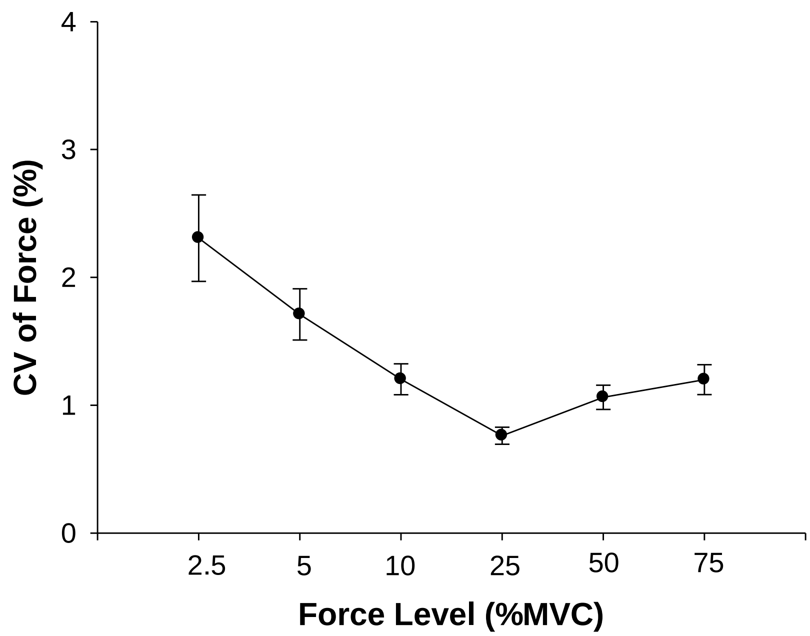

Figure 1.3. Relationship between force and coefficient of variation of force. CV is highest (least steady) at low and high force levels and is lowest (most steady) at intermediate force levels. Unpublished observations from Brown, Edwards and Jakobi, 2010. CV, coefficient of variation; %, percent; MVC, maximum voluntary contraction.

This U-shape function is proposed to be due to the dual contribution of both motor unit recruitment and MUDR as control mechanisms at intermediate force levels. Motor unit recruitment is the dominant mechanism for increasing force production at low forces levels, and when force approaches maximum strength all motor units should be recruited so MUDR is primarily responsible for increases in force (Slifkin & Newell, 1999).

Functionally, a decrease in FS may lead to a decrease in motor performance (Keen et al. 1994). Carville et al. (2007) found that young adults and old adults who did not have a history of falling were similar in strength and FS of the quadriceps. However, older adults with a history of falling were both weaker and less steady compared to healthy young adults. Seynnes et al. (2005), measured FS in the quadriceps of older women and found that FS is an independent predictor of some functional tasks e.g., chair rise time and stair-climbing power. An investigation by Svendson and Madeleine (2010) found that men had greater absolute variability of force (standard deviation of force) in the elbow flexors, but when force was normalized to MVC, men had a lower CV of force (greater FS) compared to women. They proposed that the central nervous system of females may not allow appropriate adaptation to changes in sensory afferent feedback, which may increase the risk of muscle overload and damage in women.

It has been suggested that one of the key mechanisms that contribute to FS is motor unit activity (Enoka, Christou, Hunter, Kornatz, Semmler, Taylor & Tracy, 2003). Two properties of motor unit activity that have been investigated with respect to FS are MUDR and MUDRV (Patten & Kamen, 2000). As mentioned, MUDR is the frequency at which a motor unit discharges an action potential. To investigate the characteristics of motor units that may contribute to FS across a wide range of force levels, Taylor, Christou and Enoka (2003) compared experimental and simulated contractions of the index finger. They concluded that there is not one single factor that is responsible for force fluctuations, and that a decrease in FS may be due to a) organization of the motor unit pool, b) recruitment and MUDR properties of the motor units, or c) the activation pattern of the motor-unit population (Taylor et al. 2003). However, several studies have concluded that MUDRV is the main contributor to FS. Motor unit discharge rate variability was found to be the critical factor that best predicted differences in FS between young and old adults in the first dorsal interosseous muscle (Moritz, Barry, Pascoe & Enoka, 2003; Laidlaw, Bilodeau & Enoka, 2000). Tracy, Maluf, Stephenson, Hunter and Enoka (2005) found that as MUDRV increased, FS decreased across a wide range of muscle forces in the first dorsal interosseous muscle.

1.4 Contribution of Elbow Flexor Muscles to Movement

To produce isometric elbow flexion when the forearm is in a neutral position, the muscles that primarily contribute to force production are the brachialis, brachioradialis (BR) and BB (Buchanan, Rovai & Rymer, 1989). The BB is a large muscle that is located on the anterior surface of the arm. It is a bi-compartmental muscle that includes a LH and a SH (Figure 1.4).

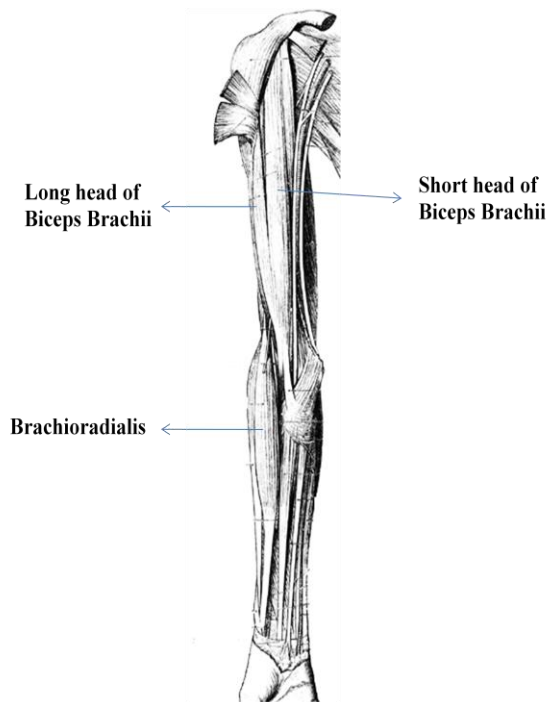

Figure 1.4. Diagram of the Elbow Flexor Muscles. The LH originates from a tubercle above the glenoid cavity of the scapula and inserts on the radial tuberosity of the radius. The origin of the SH is the coracoid process of the scapula and it inserts on the bicipital aponeurosis. The BR originates at the lateral border of the distal end of the humerus and inserts superior to the styloid process of the radius. LH, long head; SH, short head; BR, brachioradialis.

The LH originates from a tubercle above the glenoid cavity of the scapula and inserts on the radial tuberosity of the radius. The origin of the SH is the coracoid process of the scapula and it inserts on the bicipital aponeurosis. The role of the BB is to flex the forearm at the elbow joint, supinate the forearm at the radioulnar joint, and flex the arm at the shoulder joint (Tortota, 2005). The BR flexes the forearm at the elbow joint. Its origin is the lateral border of the distal end of the humerus and it inserts superior to the styloid process of the radius. In addition to elbow flexion it supinates and pronates the forearm to a neutral position at the radioulnar joints (Tortora, 2005). Motor unit activity of the BB is position dependent and differs between the two heads. Harwood, Edwards and Jakobi (2010) reported that the SH of the biceps experienced a higher MUDR in the supinated forearm position compared to neutral and pronated during isometric elbow flexion at a low force level. The SH also had a higher MUDR compared to the LH, and exhibited greater MUDRV in the pronated position compared to neutral and supinated. There was no position dependency for MUDR or MUDRV in the LH (Harwood et al. 2010). Force steadiness during isometric elbow flexion has also shown to be position dependent, as well as differ between men and women (Brown et al. 2010). It is possible that men and women differ in FS of the elbow flexors due to differences in motor unit activity of the BB; however, this has not been investigated.

1.5 Sex Differences in Force Production and Neuromuscular Function

Although men and women have comparable anatomy, differences in neuromuscular function have been observed. One of the most obvious differences between men and women is that men tend to be able to produce greater muscular force. Miller, Macdougall, Tarnopolsky and Sale (1993) investigated mechanisms of strength differences between men and women in the BB and vastus lateralis. They suggested that men were stronger in both muscles due to a larger cross sectional area of muscle, and larger muscle fibres. However, a review by Jones, Bishop, Woods and Green (2008) suggested that the relationship between muscle force and muscle cross-sectional area is not consistent and mechanisms of strength warrant further investigation.

It is well established that women are less fatigable than men during prolonged isometric contractions. For example, Hunter, Griffith, Schlachter and Kufahl (2009) found that men reached fatigue faster in the handgrip muscles than women. Time to failure was suggested to be a function of rate of increased muscle activity and perceived exertion, and was not due to differences in blood flow (post-contraction hyperaemia or vascular conductance of the forearm) between men and women. When men and women were matched for strength in the elbow flexors there was no difference in time to fatigue during a sustained submaximal contraction. Despite similarity in time to task failure men displayed a greater rate of increase in muscle activity and women experienced a greater rate of EMG burst activity during the sustained contraction (Hunter, Critchlow, Shin & Enoka, 2004). However, when men and women performed intermittent submaximal contractions of the elbow flexors to fatigue men were more fatigable than women. Due to men having a greater increase in rate of muscle activity during the fatiguing contraction it was concluded that men require a more rapid increase in descending drive to maintain a similar force level (Hunter et al. 2004).

Sex differences in muscle activity have been observed in other studies as well. For example, overall muscle activity in the upper and lower limbs was shown to be greater in women compared to men during a task of daily living (Harwood, Edwards & Jakobi, 2008). Women also exhibited greater muscle activity in the BB during tasks of daily living throughout a 10-hour recording (Kern, Semmler & Enoka, 2001). Since fibre-type distribution is similar between men and women, this increased muscle activity is likely due to muscle strength, muscle mass, or endurance capacity (Kern et al. 2001). In addition to sex differences in muscle activity, women and men have also shown differences in mechanomyography of the elbow flexors, which is the mechanical counterpart of myoelectrical activity and reflects the motor unit activation strategy in force production (Nonaka, Mita, Akataki, Watakabe & Itoh, 2006). Females exhibited higher mechanomyography per cross sectional area compared to men, which the author's speculated may be due to a lower motor unit firing rate in females. In addition to sex differences in muscle activity and mechanomyography of the elbow flexors, men have also been found to produce steadier isometric contractions than women when maintaining constant elbow flexion force (Brown et al. 2010; Svendsen & Madeleine, 2010). However, due to the limited number of studies investigating this phenomenon, the precise mechanism of sex-dependent force fluctuations in the elbow flexors remains unknown.

1.6 Summary of Literature

Although there are discrepancies in the literature regarding the primary mechanism underlying FS of a muscle, it is evident that motor unit activity plays a role. Several studies have suggested that MUDRV may be the best predictor of force variability during isometric contractions. It is apparent that men and women differ physiologically in many aspects of movement and force control. Sex differences in FS have been observed in the elbow flexors, but motor unit activity was not recorded in these studies. If motor unit activity is a key component to FS, it seems likely that men and women would differ in motor unit characteristics as steadiness differs between sexes. To date motor unit activity has not been measured in men and women to investigate sex-differences in FS.

Chapter 2: Purpose, Objectives and Hypotheses

2.1 Purpose

The purpose of the thesis study is to examine mechanisms that contribute to sex differences in force steadiness of the elbow flexors. Specifically, motor unit discharge rate and discharge rate variability will be evaluated simultaneously with force steadiness over a range of contraction levels. Force steadiness and motor unit activity will be compared between men and women.

2.2 Objectives

1. To record motor unit discharge rate and discharge rate variability in the biceps brachii of men and women.

2. To evaluate force steadiness of the elbow flexors in men and women across a range of muscle forces.

3. To determine the relationship between motor unit activity and force steadiness of the elbow flexors in men and women.

2.3 Research Hypotheses

1. Men and women will produce similar motor unit discharge rates at the same relative force levels, but women will exhibit greater motor unit discharge rate variability relative to men.

2. Men will produce steadier isometric contractions than women at all measured force levels.

3. Women will have greater motor unit discharge rate variability than men, which will be the primary mechanism contributing to sex differences in force steadiness of the elbow flexors.

Chapter 3: Manuscript

3.1 Introduction: Background and Motivation

When force is exerted at a given intensity, the force produced does not remain constant but fluctuates around an intended value. These force fluctuations, commonly referred to as FS, represent the ability to maintain a constant isometric contraction around a given force level. It can be expressed in absolute terms as the standard deviation of force, but is often expressed in relative terms as the CV of force. Force steadiness has been examined in a variety of contexts and has shown to differ depending on age (Laidlaw, Bilodeau & Enoak, 2000), contraction type (Mottram, Jakobi, Semmler & Enoka, 2005), contraction intensity (Danion & Gallea, 2004), physical status of an individual (Enoka, Christou, Hunter, Kornatz, Semmler, Taylor & Tracy, 2003), arousal level (Christou, Jakobi, Critchlow, Fleshner and Enoka, 2004), environment (Dewhurst, Graven-Nielsen, De Vito, & Farina, 2007) and sex (Brown, Edwards & Jakobi, 2010).

Most studies that have investigated the mechanisms that underlie FS have compared younger and older adults (Christou et al. 2004; Taylor et al. 2005). These mechanisms have been investigated with both experimental and simulated contractions (Taylor, Christou & Enoka, 2003). Motor unit activity has been found to have a significant contribution to fluctuations in force. There is evidence that force fluctuations arise as a consequence of MUDRV in older adults, particularly at low force levels. For example, Laidlaw, Bilodeau and Enoka (2000) found that young adults were steadier than older adults in the first dorsal interosseous muscle due to older adults having greater MUDRV during isometric contractions. Similarly, MUDRV was reported as the factor that best predicted a motor unit model of force fluctuations in a hand muscle (Moritz, Barry, Pascoe & Enoka, 2005). The contribution of MUDRV was greatest at low force levels (2-5% MVC). However, older adults exhibited greater variability in MUDR than young adults across a wide range of muscle forces in the first dorsal interosseous (Tracy, Maluf, Stephenson, Hunter & Enoka, 2005). This increased variability was correlated with the decrease in FS seen in older adults (Tracy et al. 2005). Although a decline in steadiness has been readily observed in older adults and is likely a function of MUDRV, Sosnoff and Newell (2006) found that steadiness may also be related to absolute strength. Older adults were less steady than young adults during index finger abduction. However, when absolute strength was co-varied, there was no age difference in FS, indicating that strength is a better function of FS than chronological age.

Although FS between men and women has not been as well investigated as it has between young and old, studies have consistently reported women to be less steady than men in the elbow flexors (Brown, Edwards & Jakobi, 2010; Svendsen & Madeleine, 2010) and the first dorsal interosseous muscle (Cristou, Jakobi, Critchlow, Fleshner & Enoka, 2004). However, the underlying mechanism for this is still not clear. Research indicates that absolute strength is a factor in reduced FS for isometric elbow flexion in women (Brown, Edwards & Jakobi, 2010) - men were stronger than women, as well as steadier in the neutral, supinated and pronated positions of the forearm from 2.5-75% MVC. However, force was the only physiological variable recorded in that study. Another study investigating sex-related differences in force control of the elbow flexors proposed that men were steadier than women due to sex-dependent force control mechanisms (Svendson & Madeleine, 2010). They suggested that men had elevated activity of the BB compared with women and that muscle activation may be different between sex. Moreover, during pinch grip tasks women have exhibited greater force fluctuations in the first dorsal interosseous than men. Though, subjects in these studies were presented with noxious stimuli that increased cognitive and physiological arousal levels, which were associated with the decrease in FS (Christou, Jakobi, Critchlow, Fleshner & Enoka, 2004; Noteboom, Fleshner & Enoka, 2001). Women also exhibited greater 1-to 2-Hz oscillations in force during the steady-state contractions, which was suggested to be due to a reduced ability to modulate descending drive (Christou et al. 2004). The ability of women to produce steady isometric contractions is of interest since FS has been shown to predict functional ability in older women (Seynnes, Hue, Garrendes, Colson, Bernard, Legros & Fiatarone Singh, 2005).

Differences in FS between men and women have been observed, yet it is clear that the mechanisms for these differences are unknown. It is evident that absolute strength or sex-dependent control mechanisms play a role in these differences; however, due to the strong evidence that motor unit activity influences FS between young and old adults, it is possible that motor unit activity is also a factor in sex differences in FS. To date, MUDR and MUDRV have not been compared between men and women. Yet, men and women differ on other neuromuscular factors, such as EMG burst activity (Harwood, Edwards & Jakobi, 2008), neuromuscular activation (Clark, Collier, Manini & Ploutz-Synyder, 2005), mechanomyography (Nonaka, Mita, Akataki, Watakabe & Itoh, 2006), electromechanical response times (Bell & Jacobs, 1986) and fatigue (Hunter, Griffith, Schlachter & Kufahl, 2009). Therefore, the purpose of this study was to compare motor unit activity (MUDR and MUDRV) between men and women and to investigate possible mechanisms for sex differences in FS of the elbow flexors.

3.2 Methodology

The participants in this study were eight young men and 11 young women. All subjects were right hand dominant, free of neurological disease, and were not participating in any upper limb training regimes (eg. weight training) and were not fine motor skill trained (eg. sewing or musicians). Female participants were tested only during the follicular phase of the menstrual cycle, as hormones during the luteal phase have been found to decrease maximal force production (Sarwar, Niclos & Rutherford, 1996). Subjects were not regular caffeine consumers; they drank on average one cup of coffee or less per day and were told to refrain from any caffeine use 48 hours prior to experimentation. Informed written consent was obtained prior to participation for all subjects. The procedures in this study were approved by the University of British Columbia Clinical Research Ethics Board and conformed to the declaration of Helsinki.

3.2.1 Experimental Setup and Procedures

Subjects visited the laboratory for one or two occasions for an experimental session that began between 7:00 a.m. and 11:00 a.m. They were seated in a custom-made chair (Don Clarke, University of Windsor; Harwood, Edwards and Jakobi, 2010) that was adjusted for height so that hip and knee angle were at 90°. The left arm was also flexed at 90°, and the left shoulder abducted 15°. The left elbow rested in a padded elbow support while the forearm lay on a horizontal arm rest in a neutral position. The arm rest was adjusted to individual arm length so that the hand grasped the handle of the wrist apparatus. Underneath the wrist apparatus was a MLP-150 linear calibrated force transducer (68 kg) with a sensitivity of 266 N/mV (Transducer Techniques, Temecula, CA) that measured force applied by the elbow flexors (see experimental set-up, Figure 3.1). Visual feedback of force was provided with a 19- inch computer monitor (1280 x 1024 resolution) placed one metre in front of the subject 15° below eye level. Visual feedback gain was determined by a measure of the screen parameters coupled with the linear transducer output. The feedback each subject received was 22 pixels/Newton. The y-axis of the computer screen was adjusted to ensure the visual feedback gain was constant for all force levels. (experimental set-up Figure 3.1)

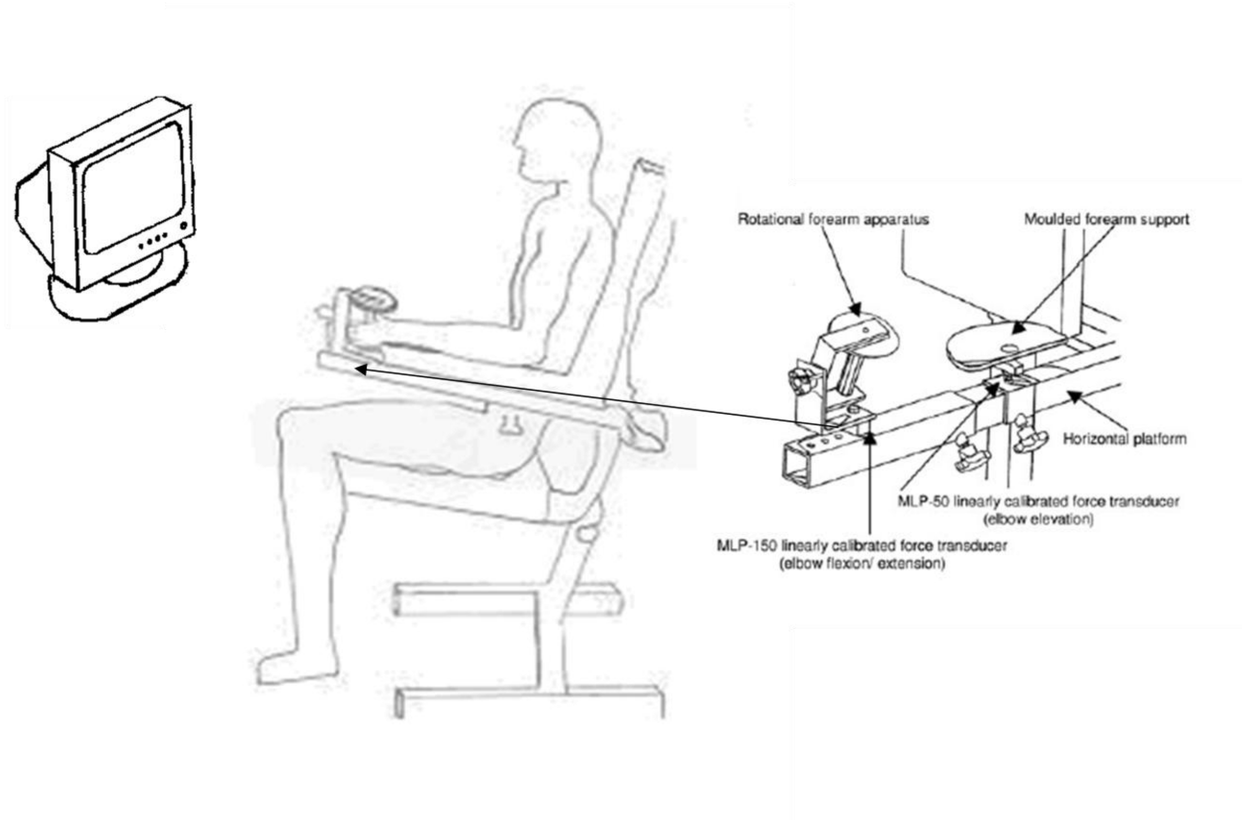

Figure 3.1. Experimental set-up. The left panel is a diagram of how a subject would sit during the experiment, one metre in front of a computer monitor. Elbow, hips and knees were flexed at 90°, and left shoulder was abducted at 15°. The forearm was placed in a neutral position. The right panel is a diagram of the arm apparatus. Adapted from Harwood, Edwards and Jakobi, 2010.

The subject's skin was exfoliated with 70% isopropyl alcohol pads and low friction cleansing pads. Bipolar surface electrodes were placed over the muscle belly of the SH of the BB, LH of the BB, BR and WF muscles to record surface EMG during the steadiness task. Fine wires were inserted into the SH and LH of the BB for single motor unit recordings. Subjects performed three elbow flexion MVC while the wrist was maintained in a neutral position. Each contraction was held for 3-5 seconds while the same experimenter verbally encouraged the participant to produce as much force as possible. One minute of rest was given between contractions to prevent fatigue. Relative submaximal force levels of 5, 10, 25, and 50% MVC were calculated based on the highest maximal force attained and used to determine target force levels for the sub-maximal FS task. Subjects were given a practice session at 25% MVC to ensure they understood the task. The task involved the subject gradually increasing force over 8 seconds to a target line, holding a relative force at a target line as steady as possible for 7.5 seconds, and a gradual ramp down of force over another 8 seconds, as previously described (Brown, Edwards and Jakobi, 2010). Each of the four force levels were targeted two to three times, and the order was randomized for each subject. Approximately 30 seconds of rest were given after contractions held at 5% and 10% MVC, and 60 seconds of rest were given after contractions that were held at 25% and 50% MVC to prevent fatigue. Force, surface EMG and motor unit activity were simultaneously recorded during the 8 second ramp up phase, the 7.5 second steady force phase, and the 8 second ramp down phase. The motor unit wires were moved within the muscle at least once to ensure recording of multiple motor units from the same muscle.

Elbow flexion force was recorded with a MLP-150 linear calibrated force transducer (68 kg) (Transducer Techniques, Temecula, CA) with a sensitivity of 266 N/mV that was oriented below the mainupulandum (Figure 3.1). Force signals for isometric elbow flexion in the neutral forearm position were sampled at 1100 Hz, collected (Coulbourn, Allentown, PA) and converted from an analog to digital format by a 16-bit 1401 plus A/D converter (CED, Cambridge, England). Average force, standard deviation of force, and CV of force (SD/mean) were determined for the approximate 7.5s steady contraction phase.

Bipolar surface electrodes (4mm Ag/AgCl) were placed over the muscle belly of the SH, LH, BR and WF muscles. Palpation, visual inspection, and functional movements, such as elbow flexion, extension and rotation were used to determine proper placement. The inter-electrode distance between the pairs of electrodes was approximately 1 centimetre. Ground electrodes were placed over the acromion process of the scapula for the SH and LH of the BB, the lateral epicondyle for the BR, and the medial epicondyle for the WF. The signal from the surface EMG electrodes was amplified 1000 times with an isolated bioamplifier (Coulbourn Electronic, Allentown, Pennsylvania), band-pass filtered (8Hz – 1kHz) (Coulbourn, Allentown, Pennsylvania), sampled at 1111 Hz (1401, CED, Cambridge, England) and converted from analog to digital format (CED, Cambridge, England). The signal was rectified and the integrated EMG was averaged for 0.5s windows over the 7.5s steady phase. Surface EMG at each force level was expressed relative to the maximal EMG (muscle activity recorded during MVC) recorded for each muscle to allow for comparison between subjects and muscles (Spike 2 version 6, CED, Cambridge, England).

A fine wire unit was threaded through a one-inch long 25 gauge hypodermic needle that was inserted into the muscle belly of both the SH and LH of the BB to record single motor unit activity. Each unit consisted of three fine wires (California Fine Wire, Grover Beach, California) (25-50 μm diameter) manually glued together at the tip. All wires were sterilized in an autoclave prior to use. One wire unit was placed between the pair of surface electrodes on the SH, and one unit was inserted between the pair of surface electrodes on the LH. When the needle was penetrated into the muscle approximately 2.5 centimetres, it was withdrawn and the wires remained in the muscle. A ground electrode was placed over the medial end of the clavicle for the SH, and on the lateral end of the clavicle for the LH. The end of the wire opposite to that inside the muscle was connected to a custom-made pre-amplifier that amplified the signal 10 times (Don Clarke, University of Windsor). The motor unit signal was sampled at a rate of 16 666 Hz, amplified (100-1000 times) and band-pass filtered (8Hz – 1kHz) (Coulbourn, Allentown, Pennsylvania). Intramuscular EMG was converted from analog to digital format by a 16-bit A/D coverter (1401 plus, CED, Cambridge, England).

Offline analysis of single motor units was conducted with a customized software package (Spike 2 version 6.0, CED, Cambridge, England). To identify motor units, a template matching algorithm was used that discriminated motor units based on shape and firing frequency. To ensure proper classification of motor units, visual inspection of each action potential was conducted to ensure it belonged within a train of action potentials. An action potential train was defined as a continuous discharge of six or more action potentials. All motor units analyzed correspond to the reported area of steadiness for the 7.5second submaximal contraction. Motor unit discharge rate and MUDRV was analyzed using a custom software package (Spike 2 version 6.0). Motor unit discharge rate was calculated as the firing frequency (Hz) of a motor unit train over a given time period. Motor unit discharge rate variability was expressed as the CV of MUDR (standard deviation of the discharge rate divided by the mean discharge rate multiplied by 100).

3.2.2 Statistical Analysis

All statistical analyses were conducted with Statistical Package for Social Sciences (SPSS) version 16.0. A 2-way univariate analysis of variance (ANOVA) compared strength between men and women. Coefficient of variation of force (FS) was evaluated with a 2 (sex) x 4 (force level) repeated measures ANOVA. A 2 (sex) x 4 (muscle) x 4 (force level) repeated measures ANOVA was used to determine differences in the dependent variable of surface EMG. Motor unit discharge rate and MUDRV were assessed separately with a 2 (sex) x 2 (muscle; SH and LH) x 4 (force level) univariate ANOVA. Standard multiple linear regression analysis was used to examine the relationship between the dependent variable of FS and the independent variables of MVC, MUDR, and MUDRV. Probability for significance was set to an Alpha level of 0.05. All in-text data and tables are presented as mean ± standard deviation (SD), and figures are presented as mean ± standard error (SE).

3.3 Results

Age, height and weight of the subjects are presented in Table 3.1. Men and women did not differ in age ($p > 0.05$) but men were heavier as well as taller than women ($p < 0.001$). As expected, men (264.9 ± 41.8 N) were stronger than women (142.7 ± 18.6 N) ($p < 0.001$) (Table 3.1).

Table 3.1. Subject characteristics.

	Men	**Women**
Age (years)	25.0 ± 3.6	21.2 ± 3.2
Height (cm)	182.4 ± 5.5	165.3 ± 6.4 *
Weight (kg)	86.6 ± 16.2	58.2 ± 5.8 *
MVC (N)	264.9 ± 41.8	142.7 ± 18.6 *

Men and women were similar in age, but men were taller and heavier than women. *, women less than men ($p < 0.05$). cm, centimetres; kg, kilograms; N, Newtons

3.3.1 Force and Muscle Activity

The 2 (sex) x 4 (force level) repeated measures ANOVA for FS revealed a significant 2-way interaction for the between-subjects factors of sex and force level ($p < 0.001$). The CV of force was greater in women compared to men at all force levels, indicating that men were steadier than women ($p < 0.001$) (Figure 3.2).

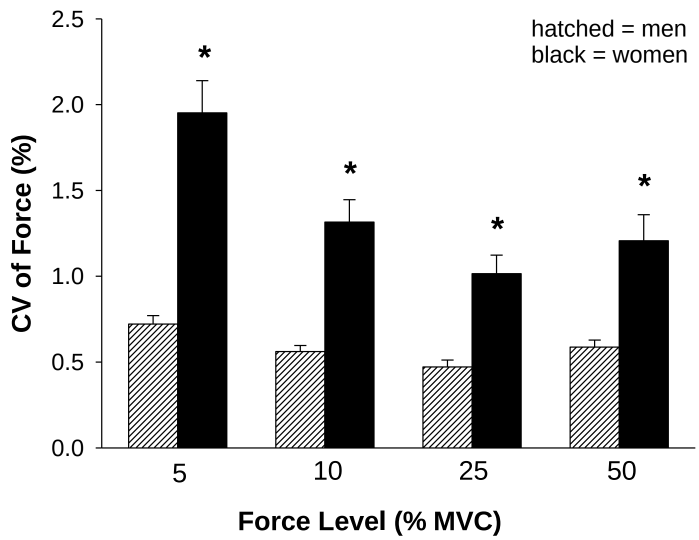

Figure 3.2. Sex differences in coefficient of variation of force. Coefficient of variation of force for men (hatched bars) and women (black bars) at the four submaximal force levels. Women had a higher coefficient of variation of force (were less steady) than men at all force levels. *, significantly less than men ($p > 0.05$). CV, coefficient of variation; %, percent; MVC, maximal voluntary contraction; hatched bars, men; black bars, women.

There was no 3-way interaction between force level (5%, 10%, 25% and 50% MVC), sex (men and women), and muscle (SH, LH, BR and WF) for normalized surface EMG ($p = 0.55$).

There were also no significant 2-way interactions [(force level x sex $p = 0.52$) (muscle x sex $p = 0.15$) (muscle x force level $p = 0.09$)]. There was no between-subjects factor for sex ($p = 0.30$) and no main effect for muscle ($p = 0.20$). Therefore, normalized surface EMG did not differ between muscle, or men and women. As expected there was a main effect for force level ($p < 0.001$). The average normalized surface EMG at 5% MVC (3.35 %) was lower compared to 10% MVC (5.87 %), 25% MVC (15.63 %) and 50% MVC (40. 66 %) ($p < 0.001$). At 10% MVC, surface EMG was lower compared to 25% and 50% MVC ($p < 0.001$) and 25% MVC was lower than 50% MVC ($p < 0.001$).

3.3.2 Motor Unit Activity

A total of 331 motor units were recorded. The number of motor units recorded in men (164) was similar to women (167) ($p > 0.05$). There was a similar number of motor units recorded between the SH (161) and the LH (170) ($p > 0.05$). The number of motor units recorded between the four submaximal force levels were also similar at 5% (89), 10% (75), 25% (88), and 50% MVC (79) ($p > 0.05$). The number of motor units, MUDR, and MUDRV for sex, BB compartment, and force level are presented in Table 3.2. A representative raw data figure depicting a force tracing with its associated motor unit recording for a woman is presented in Figure 3.3.

Table 3.2. Motor unit discharge rate and motor unit discharge rate variability for sex, biceps brachii compartment, and force level.

	Men				**Women**			
	SH		**LH**		**SH**		**LH**	
%MVC	MUDR (Hz)	MUDRV (%)	MUDR (Hz)	MUDRV (%)	MUDR (Hz)	MUDRV (%)	MUDR (Hz)	MUDRV (%)
5	11.3	10.4	11.3	10.5	12.2	11.2	11.6	12.3
10	12.4	10.4	14.0	10.2	14.5	9.7	13.7	10.2
25	16.5	12.7	16.5	12.6	16.4	13.1	17.3	13.5
50	21.4	11.5	23.0	12.1	20.8	12.9	22.7	14.3

LH, long head; SH, short head; MUDR, motor unit discharge rate; MUDRV, motor unit discharge rate variability; %, percent; Hz, Hertz.

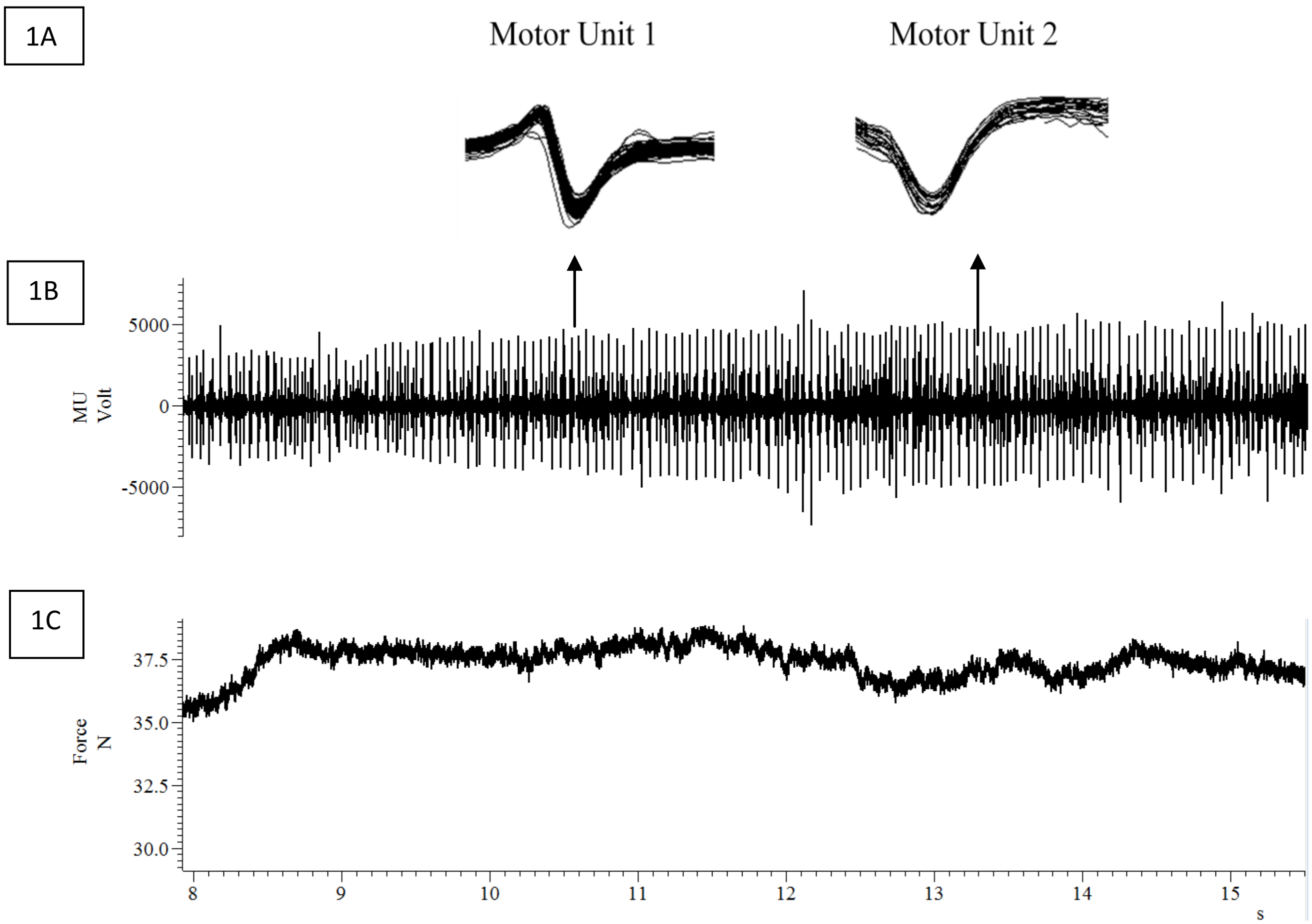

Figure 3.3. Representative Raw Data Figure. Representative recording of a 25% MVC force steadiness trial for a young female. Panel A identifies two single motor unit action potentials recorded from the 7.5sec contraction. Motor unit train one was composed of 125 spikes with a MUDR of 19.75 Hz and MUDRV of 9.4%. Motor unit train two was composed of 26 spikes with a MUDR of 16.53 Hz and a MUDRV of 15.6%. Panel B depicts the train of action potentials recorded from the steady state phase. Panel C is the steady phase where MUDR and MUDRV were calculated for the constant 25% force. The ramp up and ramp down portion of the contraction is not shown, as MUDR and MUDRV were not compared relative to steadiness for these aspects of the contraction. MVC, maximum voluntary contraction; MUDR, motor unit discharge rate; Hz, Hertz; MUDRV, motor unit discharge rate variability; %, percent; MU, motor unit; N, Newtons.

The 3-way interaction between sex (men and women), force level (5%, 10%, 25% and 50% MVC) and muscle (SH and LH) for MUDR was non-significant (p = 0.29). There were also no significant 2-way interactions for MUDR [(sex x muscle p = 0.52) (sex x force level p = 0.95) (force level x muscle p = 0.74)]. Men (15.78 Hz) had a similar average MUDR compared to women (16.29 Hz) (p = 0.14). The only significant main effect was for force level (p < 0.001). Average MUDR was lowest at 5% MVC compared to 10%, 25%, and 50% (p < 0.001). At 10% MVC, MUDR was lower compared to 25% and 50% MVC (p < 0.001) and 25% MVC was lower compared to 50% MVC (p < 0.001) (Figure 3.4).

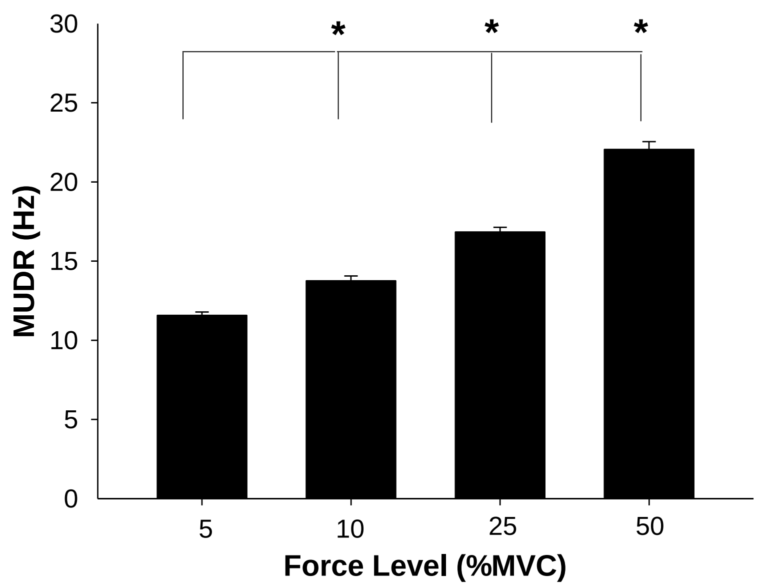

Figure 3.4. Differences in motor unit discharge rate across force levels. *, greater than previous force level (p < 0.05). MUDR, motor unit discharge rate; Hz, Hertz; %, percent; MVC, maximal voluntary contraction.

The 3-way interaction between sex (men and women), force level (5%, 10%, 25% and 50% MVC) and muscle (SH and LH) for MUDRV was non-significant (p = 0.87). All 2-way interactions were also non-significant [(sex x muscle $p = 0.14$) (sex x force level $p = 0.47$) (muscle x force level $p = 0.65$)]. Although there was a non-significant main effect for muscle ($p = 0.13$), there was a significant main effect for sex ($p = 0.02$) (Figure 3.5) and force level ($p < 0.001$) (Figure 3.6). Overall, women (12.1%) had a significantly higher CV of MUDR compared to men (11.3%). Therefore women had greater MUDRV than men. The average MUDRV at 5% MVC (11.05%) and 10% MVC (10.17%) were similar ($p = 0.09$), but were significantly less variable compared to 25% MVC (12.82%) and 50% MVC (12.68%) ($p < 0.001$). Motor unit discharge rate variability at 25% and 50% MVC did not differ significantly ($p = 0.79$).

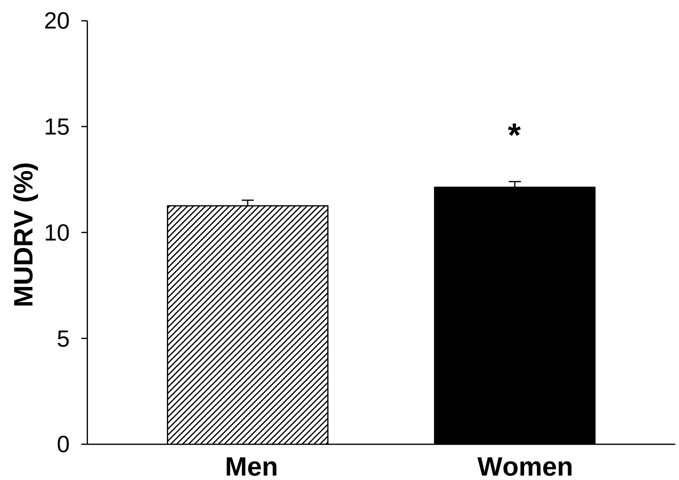

Figure 3.5. Sex differences in motor unit discharge rate variability. Women had higher MUDRV than men. *, greater than men ($p < 0.05$). MUDRV, motor unit discharge rate variability; %, percent; hatched bar, men; black bar, women.

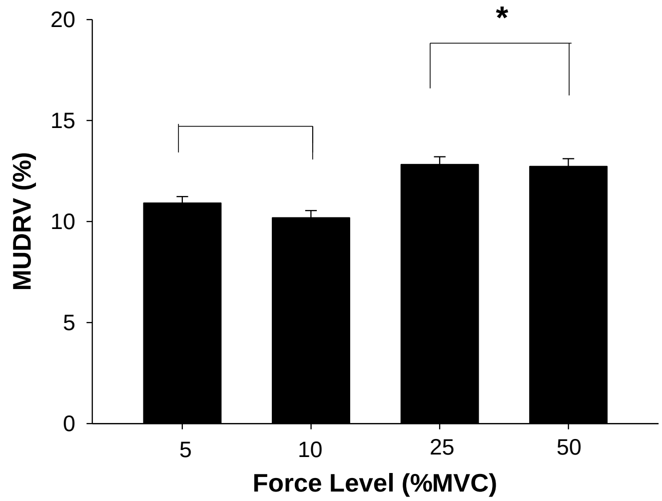

Figure 3.6. Difference in motor unit discharge rate variability across four submaximal force levels. At 25% and 50% MVC MUDRV was higher compared to 5% and 10% MVC. *, greater MUDRV ($p < 0.05$). MUDRV, motor unit discharge rate variability; %, percent; MVC, maximum voluntary contraction.

Multiple linear regression analysis probed the relationship between FS and MVC, MUDR, and MUDRV. When the data for men and women was combined, CV of force had a moderate correlation with MVC ($r^2 = 0.42$) ($p < 0.001$) (Figure 3.7). Therefore, as MVC (or absolute strength) increases, CV of force decreases (FS increases). However, when the relationship between CV of force and MVC was assessed separately for men and women, there was no relationship between CV of force and MVC for men ($r^2 = 0.009$) ($p = 0.49$), yet there was still a moderate and significant relationship for women ($r^2 = 0.35$) ($p < 0.001$). There was a small but significant correlation between CV of force and MUDR when the data for men and women was combined ($r^2 = 0.05$) ($p = 0.02$) (Figure 3.8). Similar to MVC, as MUDR increases, CV of force decreases (FS increases). However, when the relationship between CV of force and MUDR was examined for men and women separately, this relationship was significant for women ($r^2 = 0.25$) ($p < 0.001$) but not men ($r^2 = 0.04$) ($p = 0.18$). The correlation between MUDRV and CV of force was not statistically significant when the motor units for men and women were combined ($r^2 = 0.003$) ($p = 0.58$), or assessed separately for men ($r^2 = 0.05$) ($p = 0.30$) and women ($r^2 = 0.02$) ($p = 0.30$). Therefore, there seems to be no relationship between MUDRV and force steadiness. For all motor units combined, CV of force was well predicted by MVC, MUDR, and MUDRV ($r = 0.78$; $r^2 = 0.53$). Partial correlations showed that MVC (-0.71) and MUDR (-0.37) contributed the most to CV of force when all other variables were controlled for ($p < 0.001$).

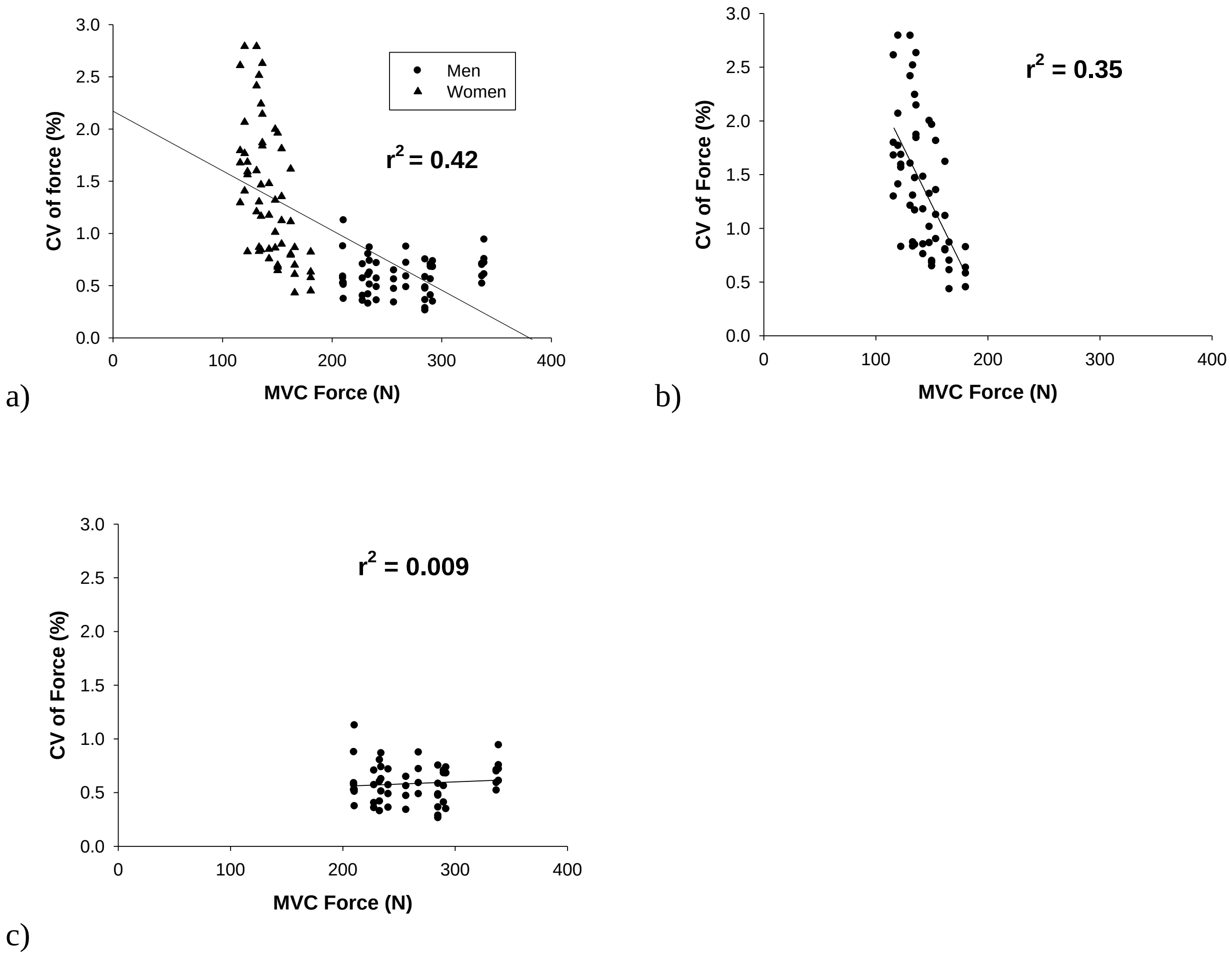

Figure 3.7. Relationship between MVC and CV of force for a) men and women b) men and c) women. a) There is a moderate, significant correlation between MVC and CV of force for men and women ($p < 0.001$). Therefore, as MVC increases, CV of force decreases (FS increases). b) There is a non-significant correlation between MVC and CV of force for men ($p = 0.49$). c) There is a significant correlation between MVC and CV of force for women ($p < 0.001$). FS, force steadiness; CV, coefficient of variation; %, percent; MVC, maximum voluntary contraction; N, Newtons; circles, men; triangles, women.

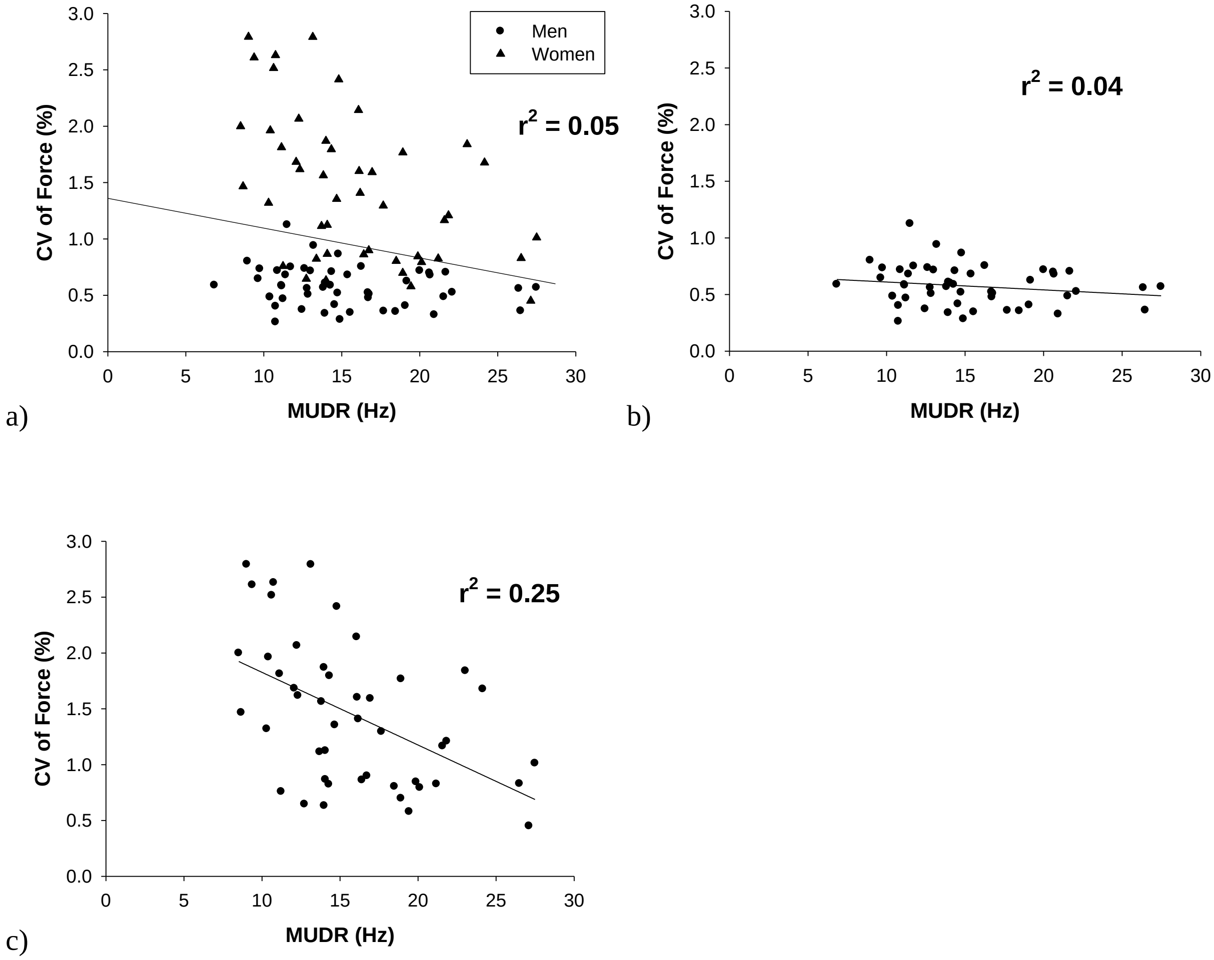

Figure 3.8. Relationship between MUDR and CV of force for a) men and women b) men and c) women. a) There is a small, significant correlation between MUDR and CV of force ($p = 0.02$) for men and women. Therefore, as MUDR increases, CV of force decreases (FS increases). b) There is a non-significant correlation between MUDR and CV of force for men ($p = 0.18$). c) In women there is a small significant correlation between MUDR and CV of force. FS, force steadiness; CV, coefficient of variation; %, percent; MUDR, motor unit discharge rate; Hz, Hertz; circles, men; triangles, women.

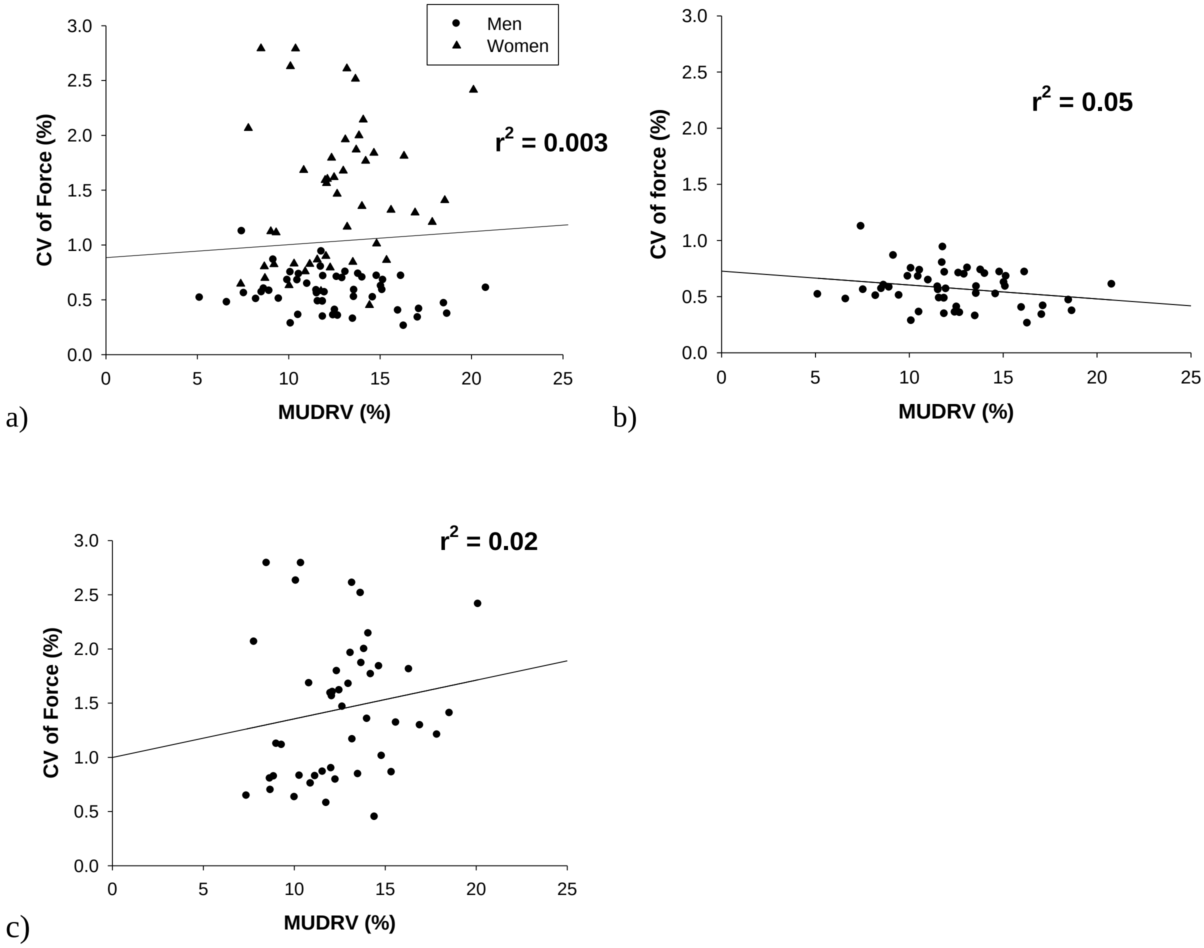

Figure 3.9. Relationship between MUDRV and CV of force for a) men and women b) men and c) women. a) There is a non-significant correlation between MUDRV and CV of force ($p = 0.58$). Therefore, there is no relationship between MUDRV and FS. b) There is a non-significant correlation between MUDRV and CV of force men. c) There is a non-significant correlation between MUDRV and CV of force for women. FS, force steadiness; CV, coefficient of variation; %, percent; MUDRV, motor unit discharge rate variability; circles, men; triangles, women.

3.4 Discussion

The purpose of this thesis was to compare MUDR and MUDRV between young men and women during sustained isometric elbow flexion across a range of force levels. The main findings were a) men were stronger than women, b) men were steadier than women in the 5-50% MVC range, c) men and women produced similar MUDR at the same relative force levels, d) women had greater MUDRV at the same relative force levels as men, and e) MVC was strongly correlated with FS in women, whereas MUDRV was not. Therefore, strength is a better predictor of sex differences in FS of the elbow flexors than MUDRV.

The finding that men were stronger than women is consistent with the literature regarding strength differences between men and women (Brown et al. 2009; Brown et al. 2010). Women tend to have less lean tissue mass than men in their upper body, as well as smaller cross-sectional area of muscle. It has been reported that the smaller cross-sectional area of muscle in women is due to smaller muscle fibres compared to men; no difference in fibre number between sexes was observed (Miller et al. 1993; Alway, Grumbt, Gonyea & Stay-Gundersen, 1989). Accordingly, muscle cross-sectional area is thought to be one of the main factors that contribute to force production in both the upper and lower limb muscles of men and women (Kanehisa et al. 1994). Although twitch interpolation was not utilized in the present study, it is unlikely that women produced less strength due to lower activation of available motor units. Men and women have been observed to produce similar muscle activation in the tibialis anterior (Brown, Bruce & Jakobi, 2009), and elbow flexors and knee extensors (Belanger & McComas, 1981). In addition, subjects were given three attempts at MVC in the current study along with verbal encouragement. As a result, the differences in strength observed between men and women are unlikely to result from a lower voluntary drive in women. In support of this was a lack of difference observed in surface EMG between men and women. As well, the amount of EMG that contributed to elbow flexion force in the LH of the biceps, SH of the biceps, BR, and WF muscles was similar between sexes. The LH, SH, and BR are the main contributors to isometric elbow flexion when the forearm is in a neutral position (Buchanan et al. 1989). The capacity of the BB and BR to contribute to elbow flexion force in the neutral forearm position is similar, despite differences in muscle architecture (Murray, Buchanan & Delp, 2000). The surface EMG in the present study indicates that these muscles contributed similarly to elbow flexion, and these contributions were not sex-specific. Previously we have observed no difference in EMG between young men and women at 15% elbow flexion MVC in the neutral position (Brown, Uniat, Bigsby, Binsted & Jakobi, unpublished observations, 2010). In addition, there were no sex differences in muscle activity of the triceps brachii (antagonist muscle), and triceps muscle activity was significantly less than the elbow flexors for both men and women ($p < 0.05$). Subjects were similar in age, strength and physical activity status as the current study.

To date, this is the first study to compare MUDR and MUDRV between men and women. Although men produced steadier isometric contractions than women, MUDR did not differ between sexes. This result is similar to those that report young adults are steadier than old adults but produce similar MUDR (Laidlaw et al. 2000; Semmler, Steege, Kornatz & Enoka, 2000). With all motor units combined, MUDR was significantly correlated with CV of force. However, when men and women were assessed separately, this relationship was significant only for women, not for men. Therefore, as MUDR increases CV of force decreases (increased FS). This correlation likely occurred due to the fact that as force level increased, so did MUDR, as well as FS. Therefore, it is unlikely that MUDR contributed to differences in FS between men and women in the current study.

A novel finding of this study is that men and women differed in MUDRV. As previously mentioned, MUDRV is the regularity with which motor neurons discharge action potentials. Greater MUDRV in women could be a likely explanation for decreased steadiness compared to men, as several studies have shown that a decline of steadiness in older adults is explained by a higher degree of variability in MUDR (Laidlaw et al. 2000; Enoka et al. 2003; Mortiz et al. 2005; Tracy et al. 2005). Laidlaw et al. (2000) proposed that greater MUDRV in the first dorsal interosseous of older adults was a result of either changes in transmission efficacy over corticospinal and reflex pathways (the contributors to the synaptic input to motoneurons) or differences in biophysical properties of motoneurons. Although these neuronal properties are suggested to change as a function of aging, there is evidence that women have smaller diameter axons in the pyramidal tract than men (Souma, Goto, Goto, Chiba & Ishida, 2008), smaller diameter motoneurons between C5 and L3 of the spinal cord (Yuan, Goto, Akita, Goto & Jin, 2000), as well as smaller diameter axons of the corticospinal tract in the lumbar area. Studies that report high MUDRV were comparative between young and old adults. It is well known that reorganization of the neuromuscular system is a consequence of aging (Rice, 2000), where decreased signal transmission efficacy over neural pathways, and altered biophysical properties of motoneurons are suggestive factors contributing to increased MUDRV (Laidlaw et al. 2000). Therefore, the mechanisms that contribute to greater MUDRV in older adults may not be comparable to the factors that cause higher MUDRV in young women. More research should be conducted to find the precise mechanism(s) that explain a greater MUDRV in young women compared to young men.

Although women had greater MUDRV than men in the current study, according to correlation analyses MUDRV was not a contributing factor to sex differences in FS. It is possible that MUDRV is a mechanism of FS that is more important in older individuals than young. For example, Tracy et al. (2005) found that the relationship between FS and MUDRV was significant for older adults in the first dorsal interosseous ($r^2 = 0.30$) but not for younger adults ($r^2 = 0.06$). This is similar to the current study in that young adults did not show any relationship between CV of force and MUDRV ($r^2 = 0.003$) in the elbow flexors. The majority of studies that report a strong relationship between MUDRV and FS have been conducted in the first dorsal interosseous, which is a small distal muscle of the hand (Tracy, 2005; Laidlaw et al. 2000; Moritz et al. 2005). The primary mechanisms in which small distal muscles and large proximal muscles increase force production are known to differ. For example, small distal muscles, such as the first dorsal interosseous, increase force production primarily by MUDR modulation, while larger more proximal muscles, such as the BB, rely more on motor unit recruitment (Seki & Narusawa, 1996). Thus it is possible that MUDR and MUDRV may not be a primary contributing factor to maintaining force control in the elbow flexors. This is supported by the low correlation between MUDRV and FS in the current study. To date this is the first investigation to assess FS and motor unit activity simultaneously in the BB.

Although sex differences in MUDRV were observed, the difference in variability between men and women was not as great as differences in variability typically observed between young and old. For example, the average amount of MUDRV in men in the present study was 11.3% and 12.1% for women. Harwood et al. (2010) reported that at 10% MVC, young men had a MUDRV of 5%, while old men exhibited a variability of 11% for isometric elbow flexion in the neutral position. Similarly, a nearly two-fold increase in variability was observed in old adults (28%) compared to young adults (15%) in the first dorsal intersseous at 5% MVC (Laidlaw et al. 2000). Tracy (2005) reported less of a difference in MUDRV between young (17.5%) and old (21.5%) in the first dorsal interosseous over a range of muscle forces; however, there was no difference in absolute strength, and FS only differed between 0 and 5% MVC. It is possible that women in this study were "too steady" for MUDRV to influence FS. For example, there may be an unknown threshold of MUDRV that needs to be met to influence FS. It is possible that women in the current study did not reach this threshold, despite being less steady than men. Although studies indicate that MUDRV increases with age and has been linked to decreased FS (Enoka et al. 2003), there is little FS research done on middle-aged adults. Thus, it is not possible to estimate when a decline in FS really begins across the life span.

Individuals who are stronger have been reported to maintain steadier contractions than weaker individuals. Sosnoff and Newell (2006) suggested that absolute strength is a better predictor of FS than age. In the current study, men were significantly stronger than women. The moderately strong correlation ($r^2 = 0.42$) between MVC and CV of force for men and women combined, the moderately strong correlation ($r^2 = 0.35$) between MVC and FS for women, as well as the partial correlation between MVC and FS (-0.71), suggests that absolute strength is a stronger determinant of sex differences in FS than MUDRV. A relationship between absolute strength and FS has been reported in other studies as well (Brown et al. 2010; Sosnoff & Newell, 2006). A simulation study by Hamilton, Jones and Wolpert (2004) supports this theory. They found that proximal muscles produce a higher absolute force than distal muscles of the upper limb, and that a higher force was correlated with lower CV of force. A relationship between number of motor units in a muscle and absolute strength of a muscle was also found in that a greater number of motor units lead to greater strength output. In addition to having fewer motor units, they suggested that weaker muscles also produce higher MUDRs than stronger muscles at the same relative force levels. Thus, it was suggested that weaker muscles with higher firing rates produce more noise within the muscle, which ultimately leads to greater force variability (Hamilton et al. 2004). If this theory is true, it would mean that women are weaker than men partly due to fewer numbers of motor units. Motor unit number estimation between men and women is not well established. Miller et al. (1993) estimated motor unit numbers in an upper limb and lower limb muscle of young males and females. Males had a greater number of motor units than women in the biceps (126 vs. 110), and vastus medialis (282 vs. 229) although these differences did not reach statistical significance. It is clear that not enough evidence exists to make a definitive statement about motor unit number and activity in men and women.

With respect to weaker muscles having a higher relative MUDR (Hamilton et al. 2004), women in the present study were weaker than men, yet expressed similar rates of discharge at the same relative force levels. There was a trend towards women having approximately a 9.7% higher MUDR than men at all measured force levels (5% MVC, women 4% higher; 10% MVC, women 5% higher; 25% MVC, women 3% higher; 50% MVC, women 2% higher). According to the findings of Hamilton et al. (2004) the weaker muscle and higher MUDR of women in this study would be two mechanisms responsible for the sex differences observed in FS. Although weaker muscles in old men have been associated with a lower MUDR due to less absolute force production, it is also likely due to altered muscle contractile properties caused by aging (Connelly, Rice, Roos & Vandervoort, 1999). For that reason, the mechanisms underlying motor unit activity during force production may not be comparable between young women and old adults. Therefore, differences in FS between young men and women may be due to a unique combination of factors than those that cause differences in FS between young and old adults.

Several other mechanisms beyond high MUDRV and low absolute strength have been proposed to cause a decrease in FS. Although these variables were not assessed in the present study, their potential as possible mechanisms underlying sex differences in FS should be acknowledged. Motor unit synchronization occurs when motoneurons receive common input from branched corticospinal projections that results in pairs of motor units discharging action potentials at relatively the same time. A simulation study by Yao, Fuglevand and Enoka (2000) showed that increased rates of motor unit synchrony during isometric contractions in the first dorsal interosseous led to decreased FS. Common input to the motoneuron pool has also been shown to cause 1-2 Hz frequency oscillations in mean MUDR during sustained isometric contractions of the first dorsal interosseous (Lowery & Erim, 2005). Low frequency (0-2 Hz) oscillations in MUDR are associated with 1-2 Hz frequency oscillations in force (Vaillancourt, Larsson & Newell, 2002). These low frequency oscillations were higher in young women than young men in the first dorsal interosseous muscle, and were proposed to be the factor that caused women to be less steady than men during a pinch-grip task (Christou et al. 2004). If women have greater low frequency MUDR modulation resulting in increased motor unit synchronization relative to men, this would contribute to sex-related steadiness. To date, however, neither common input nor motor unit synchrony has been assessed between sexes.

Co-activation of the agonist and antagonist muscle is often seen when a task requires precision or joint stability. Co-activation has shown to be a contributing factor to age-related decreases in FS in the tibialis anterior muscle (Patten & Kamen, 2000), but did not influence FS between young and old adults in the first dorsal interosseous (Burnett, Laidlaw & Enoka, 2000). Although co-activation of the antagonist muscle (triceps brachii) was not measured in this study, data from our laboratory suggests that young men and women do not differ in triceps bachii muscle activity during sustained isometric elbow flexion (Brown et al. 2010 – unpublished observations). Thus, muscle co-activation is likely a minimal factor in decreased FS in women compared to men in the elbow flexors.

In conclusion, young men are steadier than young women during isometric elbow flexion at a range of force levels between 5-50% maximum strength. It is likely that there is not one single mechanism alone that can explain these differences. It seems that maximum strength contributes the most to FS; in that the stronger an individual is the steadier they will be able to maintain an isometric contraction. Although higher MUDR was associated with increased FS, men and women in this study produced similar MUDRs. Therefore MUDR was not a factor that influenced sex differences in force steadiness in the present study. Women did exhibit greater MUDRV than men. In older adults, this is considered to be a key mechanism that leads to greater force variability. However, MUDRV may not play as an important role in young adults. Results from this study indicate that absolute strength is the primary factor that influences isometric force control of the elbow flexors between men and women; however, there is still little understood about sex differences in motoneuron output. This area should be further investigated to gain a better understanding of differences in movement control between men and women.

Chapter 4: Conclusions

4.1 Conclusions about Objectives and Hypotheses

Overall the objectives of this study were met. Motor unit discharge rate and MUDRV were recorded from the biceps in men and women. The hypothesis that MUDR would be similar between sexes and that MUDRV would be higher for women was accepted. Force steadiness of the elbow flexors was evaluated in men and women across a range of muscle forces. The hypothesis that men would be steadier than women between 5% and 50% MVC was accepted. The relationship between motor unit activity and FS of the elbow flexors in men and women was determined. The hypothesis that higher MUDRV in women would be the primary mechanism underlying sex differences in FS was refuted. Although women did exhibit greater MUDRV than men, there was no relationship between MUDRV and FS.

4.2 Implications

It is evident from other studies as well as the current investigation that men and women differ in their ability to maintain a constant isometric contraction. This may have implications for movement control in young women. For example, women may be at a disadvantage compared to men at tasks that require steady control of muscles, such as during the shooting component in a biathlon race, or painting. This may have implications for older women as well. Studies investigating FS between young and old adults generally find that steadiness declines in older adults. If young women are less steady than young men, it is likely that older women will be less steady than old men. Since FS has been shown to have functional implications, such as predicting stair-climbing power and chair-rise time (Seynnes et al. 2005), these abilities may show a greater decline in older women than men. Therefore, if absolute strength is a primary mechanism that contributes to FS, young adults, but especially women, should be encouraged to strength train to preserve muscle strength as they age. Particularly since older adults who are put on strength-training protocols have been shown to increase FS in the quadriceps (Tracy, Byrnes & Enoka, 2004; Hortobagyi, Tunnel, Moody, Beam & De Vita, 2001). Another implication is that investigators studying motor unit activity or FS should test either men or women, or test for sex differences first before collapsing data between sexes.

4.3 Strengths and Limitations

The major methodological strength of the current study was the subject exclusion criteria and the effort made to control for extraneous variables. For example, all subjects were recreationally active and none were on any training regimen of the upper limbs, as strength training has been shown to influence motor unit activity (Yao et al. 2000; Patten & Kamen, 2000). All of the women in the study were tested in the follicular phase of the menstrual cycle because force production declines during the luteal phase (Sarwar, Niclos & Rutherford, 1996). All the participants were right-hand dominant, so measurements were taken from the left upper-limb to account for any training effect of the right limb on hand-dominance. Subjects were told to refrain from any caffeine consumption 48 hours prior to experimentation, as preliminary data in our laboratory suggest that caffeine may influence FS. As well, individuals were chosen to participate if they consumed one cup of coffee or less in an average day to prevent any physiological effects from the 48 hour withdrawal before participation. Therefore, any differences observed between men and women in the current study are likely due to real physiological differences and not variation in subject characteristics. The physiological strength of this study is that it is the first to assess MUDR and MUDRV between men and women, and also to relate these measurements to sex differences in FS.

One limitation of this study is that surface EMG was not recorded from the triceps brachii, the antagonist muscle to the BB. This would have given an indication of the amount of co-activation between the two muscles, which has been shown to influence FS. Motor unit synchronization was also not assessed in this study. Greater motor unit synchronization has been shown to cause an increase in force variability. Motor unit synchrony has yet to be assessed between men and women, making it impossible to conclude if it was a factor that led to sex differences in FS in the current study. Another limitation was that steadiness was not measured beyond 50% MVC. Since the neuromuscular strategies for force control differ at higher force levels than lower and intermediate levels, it would be interesting to determine if men and women control force in the same manner at these higher force levels.

4.4 Future Directions

Future research should compare motor unit synchronization between men and women to see if greater force variability in women is partially due to a higher amount of motor unit synchronization. Since strength seems to be an important predictor of force variability, future studies of FS should also test men and women who are matched for strength. Finally, FS should be measured between old men and old women. Given that muscle mass declines more in old women than old men, it is of interest to see if older women also decline more in steadiness than older men. This may have functional implications for movement control in the elderly.

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