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Examination of Sex- and Limb-Specific Fatigue During Unilateral, Isometric Forearm Exercise

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EXAMINATION OF SEX- AND LIMB-SPECIFIC FATIGUE DURING UNILATERAL, ISOMETRIC FOREARM EXERCISE

THESIS

A thesis submitted in partial fulfillment of the
requirements for the degree of Master of Science in the
College of Education
at the University of Kentucky

By

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2021

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ABSTRACT OF THESIS

Examination of Sex- and Limb-Specific Fatigue During Unilateral, Isometric Forearm Exercise

The purpose of this study was to examine the effects of unilateral, isometric handgrip holds to failure for the dominant (Dm) and non-dominant (NDm) limb on ipsilateral ([IPS] exercised side) and contralateral ([CON] non-exercised side) performance fatigability. Twenty individuals participated in this study (Men [n =10]; Women [n = 10; Composite Demographics: Age: 22.2 years; Height: 174.4 cm; Body Mass: 75.0 kg) and completed three visits. Two, 6 s maximal voluntary isometric contractions (MVICs) for the Dm and NDm limb were performed during visit 1, followed by a familiarization of the fatigue test. Visits 2 and 3 included an isometric, handgrip hold to failure (HTF) fatigue test at 50% MVIC for either the Dm or NDm limb using a handgrip dynamometer (iWorx Systems Inc.; Dover, NH 03820). Prior to, and immediately after the HTF, a MVIC was performed on the IPS and CON sides. The fatigue test (Dm or NDm) was randomized between visits and the side tested first (IPS and CON) was randomized for pre-and post-tests, within and between each visit. The perceptual measures of Rating of Perceived Exertion (RPE) for the Active Muscle (AM) and Overall Body (O), along with the Numerical Pain Rating (NPR) for the AM and O were taken following each MVIC and the HTF. The test-retest reliability of the Dm and NDm hand pre-HTF MVIC demonstrated 'excellent' reliability (Dm: ICC = 0.936; NDm: ICC = 0.938) while the Dm limb HTF demonstrated 'fair' reliability (ICC = 0.553) with no systematic error for either the MVIC or HTF. Men and women demonstrated similar times for the HTF (Dm limb: 130.3 ± 36.8 s; NDm limb: 112.1 ± 34.3 s; $p = 0.002$), despite the men (46.07 ± 10.64 kg) demonstrating a significantly greater absolute MVIC force than women (30.52 ± 6.93 kg; $p \leq 0.001$). Performance fatiguability (decrease in exercise performance) and facilitation (increase in exercise performance) was calculated a via *a priori* planned comparisons ($\%\Delta = ((\text{pre-HTV MVIC} - \text{post-HTF MVIC}) / \text{pre-HTV MVIC})*100)$). Men, collapsed across limb, demonstrated IPS limb ($\%\Delta = 22.9 \pm 10.8\%$) performance fatiguability and CON limb facilitation ($\%\Delta = -6.1 \pm 6.9\%$) following the HTF, while women demonstrated differences in performance fatiguability between the Dm and NDm limbs in IPS (Dm: $\%\Delta = 28.0 \pm 9.4\%$; NDm: $\%\Delta = 32.3\% \pm 10.1\%$; $p = 0.027$), but no significant changes in the CON limbs (Dm: $\%\Delta = -1.6 \pm 5.7\%$; NDm: $\%\Delta = 1.7 \pm 5.9\%$). Following the HTF, men (9.2 ± 1.1) demonstrated a greater RPE-AM value than women (7.4 ± 2.2; $p = 0.031$), but the RPE-O, NPR-AM, NPR-O demonstrated no differences. The perceptual responses for the Pre-/Post-HTF in men demonstrated increases in RPE-AM and RPE-O in both limbs; women demonstrated increases in the IPS side only. The NPR-AM and NPR-O measures demonstrated increases for the men in both limbs and the women in the IPS side only. In this study, women demonstrated less absolute grip strength than men and demonstrated greater Dm limb strength than NDm grip strength while the men demonstrated no difference between limbs. Sex-specific training programming and body composition differences may have influenced this finding as well as the finding that the RPE-AM for a 50% MVIC HTF was higher for the men than women despite similar times to failure. The Dm limb was more fatigue resistant than the NDm limb, possibly due to continual favoring of the Dm limb in everyday tasks. Similar performance fatiguability in the IPS limb was demonstrated for men and women, however, the men demonstrated facilitation in the CON limb while there were no CON limb changes for the women. The finding of facilitation may be due to central factors, such as interhemispheric excitatory signaling from the ipsilateral to the contralateral hemisphere, and peripheral factors such as post activation potentiation (PAP) elicited from myosin light chain phosphorylation. The PAP phenomenon occurs more frequently in type II muscle fibers. Thus, the sex-dependent differences seen in facilitation and perceptual responses may be related to a greater proportion of type II fibers for the men compared to the women.

KEYWORDS: Neuromuscular, Facilitation, Handgrip, Fatigue, Contralateral, Sex Differences

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04/07/2021

Date

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DEDICATION

To God Almighty I dedicate this thesis, for His Glory Alone. None of this would be possible without Him. No words can describe the thankfulness I have for Your Grace.

To my parents Terry and Dawn, my siblings Crystal, Nic, and Charity. Your prayers, encouragement, and inspiration have incalculable worth beyond measure. I am eternally grateful to call you family.

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CHAPTER 1. INTRODUCTION

The nature and magnitude of fatigue across exercise modalities has been demonstrated to occur both centrally and peripherally and is commonly quantified by performance fatiguability, defined as a 'decline in an objective measure of performance over a discrete period of time' (Enoka & Duchateau 2016, pg. 3). Most commonly, fatigue is defined as an 'exercise-induced decline in maximal voluntary force' (Gandevia 2001, pg. 1725) and is often measured from changes in maximal voluntary isometric contraction (MVIC) force (Enoka & Duchateau 2016) that reflect global fatigue (i.e., including central and peripheral factors). Central fatigue commonly includes the mechanisms and processes of fatigue, proximal to the neuromuscular junction where the central nervous system modulates the drive required to produce a desired force or performance outcome based on feedback from group III/IV afferents (Davis & Bailey 1996; McMorris et al. 2018; Neltner et al. 2020). Peripheral fatigue, conversely, has been defined as mechanisms of fatigue in the working muscle, distal to the neuromuscular junction, such as ischemia and metabolic byproduct accumulation (Hureau et al. 2018; Thomas et al. 2018; Enoka & Duchateau 2016). Such effects of fatigue, which share a common point of overlap near the neuromuscular junction as metabolic byproduct elicit type III/IV afferents signaling to reduce the central drive to the muscles, has been noted to occur at different rates based on the intensity and mode of exercise (Enoka & Duchateau 2016; Neltner et al. 2020; Thomas et al. 2018). Specifically, exercise involving the activation of greater amounts of musculature, such as a bilateral leg extension, produces a reduced performance fatigability response when compared to a unilateral leg extension (Thomas et al. 2018). The fatiguing effect of this bilateral leg extension movement creates a larger homeostatic disruption from the increased muscular activation of the right and left quadriceps and possible greater physiological system distress of the cardiorespiratory system to maintain performance (Thomas et al. 2018). Unilateral leg extension creates a greater localized fatiguing response in the exercising quadricep and a lessened response of a systemic homeostatic disruption in homologous musculature but produces a greater fatiguing response in the active muscle (Thomas et al. 2018). Subsequent examination of the MVIC force, a common measure of muscular performance (Enoka & Duchateau 2016), has demonstrated greater performance fatigability following these unilateral movements than the bilateral movements, supporting this hypothesis (Neltner et al. 2020; Rattey et al. 2005; Matkowski et al. 2011; Cornwall et al. 2012; Thomas et al. 2018, Anders et al. 2020, Matkowski et al. 2011). The decrements in force production measured by MVIC force has been common in literature to quantify the combined peripheral and central factors eliciting performance fatiguability (Neyroud et al. 2016; Anders et al. 2020; Keller et al. 2020).

Examination of the systemic effect of unilateral fatigue on the force production of the contralateral, homologous muscle groups has demonstrated varying responses of no change to decreases in MVIC force (Matkowski et al. 2011; Rattey et al. 2005; Todd et al. 2003; Aboodarda et al. 2015; Halperin et al. 2014; Grabiner & Owings 1999; Kawamoto et al. 2014; Amann et al. 2013). However, there is some evidence (Neltner et al. 2020; Strang et al. 2009) of a facilitation in the MVIC force or torque in the non-exercised, contralateral, homologous muscle(s) following fatiguing, unilateral muscle actions. These differences in performance have been termed “cross-over fatigue” or “cross-facilitation” for decreases or increases in performance, respectively (Aboodarda et al. 2016; Neltner et al. 2020). No defined mechanism has been concluded to be the primary factor of these phenomenon, but rather have been suggested to be due to combination of central and peripheral factors of exercise performance modulation (Muellbacher et al. 2000; Derosière et al. 2014; Aboodarda et al. 2015; Hess et al. 1986; Neltner et al. 2020; Zijdewind & Kernell 2001; Carson et al. 2005; Matkowski et al. 2011; Cornwall et al. 2012; Halperin et al. 2015). The “cross-over” inhibition has been proposed to arise from group III/IV afferent feedback from metabolic and mechanical perturbations within the exercised ipsilateral limb (Aboodarda et al. 2015; Amann et al. 2013) This afferent feedback ultimately decreases central drive to both the exercised ipsilateral and non-exercised contralateral limb (Amann et al. 2011; Amann et al. 2013). Common fatigue elicited through the aforementioned central and peripheral mechanisms explain the decreases seen in the contralateral limb performance, but the presence of a contralateral facilitation effect in some groups (Neltner et al. 2020; Strang et al. 2009) suggests an additional mechanism may be influencing the performance of the contralateral limb following fatiguing exercise. Central factors, or factors proximal to the cortical and sub-cortical structures, of this “cross-facilitation” phenomenon have been suggested to be due to interhemispheric communication through the transcallosal connection or the mutual pathways of the exercising and non-exercising limb in the spinal cord or brain stem (Zijdewind & Kernell 2001; Hess et al. 1986; Muellbacher et al. 2000; Aboodarda 2016). Peripheral factors of this mechanism, or factors proximal to the exercising muscle and distal to the cortical processes, includes the post-activation potentiation mechanism (Stull et al. 2011; Rayment 1993; Lowey & Trybus 2010; Neltner et al. 2020; Fukutani et al. 2012; Fukutani et al. 2014; Mettler & Griffin 2012). These central and peripheral mechanisms provide evidence for the facilitation demonstrated in the contralateral, homologous, non-exercising limb through excitatory signaling ‘spilling over’ into the contralateral hemisphere providing excitation to the non-exercising muscle or through increased calcium volumes providing conformational changes through phosphorylation of myosin essential and light chain proteins, respectively (Muellbacher et al. 2000; Derosière et al. 2014; Aboodarda et al. 2015; Hess et al. 1986; Neltner et al. 2020; Zijdewind & Kernell 2001; Carson et al. 2005; Matkowski et al. 2011; Cornwall et al. 2012; Halperin et al. 2015; Stull et al. 2011; Rayment 1993; Lowey & Trybus 2010). It additionally is of importance to note that changes in performance may be influenced by the limb used for exercise performance. Differences in handgrip strength have been suggested to exist between the dominant (Dm) and non-dominant (NDm) limb (Thorngren & Werner 1979; Incel et al. 2002; Peterson et al. 1989; Bohannon et al. 2003; Kamarul et al. 2006; Bechtol et al. 1954). Specifically, the Dm hand has been suggested to produce 10% greater strength than the NDm limb (Bechtol et al. 1954). Greater Dm limb strength has been demonstrated in right limb dominant individuals, but this finding has been reduced or negated in individuals who are left limb dominant (Thorngren & Werner 1979; Incel et al. 2002; Peterson et al 1989; Bohannon et al. 2003; Kamarul et al. 2006). Continual favoring of the dominant limb to perform daily tasks has been suggested to be the principal influence on this phenomenon in right limb dominant individuals and the prevalence of right limb dominant devices negating this phenomenon in left limb dominant individuals (Gabbard et al. 1998; Helbig & Gabbard 2013; Habibu et al. 2013; Przybyla et al. 2012; Papadatou-Pastou et al. 2008). Thus, the limb dominance should also be considered in the examination of “cross-over fatigue” and “cross-over facilitation” to determine if there are differences in limb strength that influence the exercised, ipsilateral and/or non-exercised contralateral limb performance fatigability.

The nature and magnitude of exercised-induced fatigue has also been demonstrated to be sex-dependent (Martin et al. 2007; Hunter & Enoka 2001; Maughan et al. 1986; Ansdell et al. 2017; Wüst et al. 2008; Clark et al. 2004; Yoon et al. 2007). For example, performance of low intensity (20% MVIC) leg extension and forearm flexion isometric holds to failure and intermittent leg extension, forearm flexion, and handgrip holds to failure at 50% MVIC have demonstrated a reduced performance fatigability response in women compared to men (Martin et al. 2007; Hunter & Enoka 2001; Ansdell et al. 2017; Wüst et al. 2008; Clark et al. 2004; Maughan et al. 1986; Yoon et al. 2007). In addition, women have demonstrated a greater fatigue resistance compared to men, reflected by longer times to task failure for isometric leg extension holds performed at 20% of MVIC as well as the completion of more dynamic, forearm flexion repetitions to failure at 50, 60, and 70% one repetition maximum compared to men (Maughan et al. 1986). These sex-dependent fatigue responses at lower intensities (<50% MVIC) has been hypothesized to be correlated with the differences in muscle size between men and women (Monod & Scherrer 1965; Weir et al. 2006). The increased muscle mass present in men has been demonstrated to elicit greater levels of intramuscular pressure within the muscle creating blood flow alterations that may reduce the clearance of metabolic byproduct created during exercise, such as hydrogen ions (H^+), inorganic phosphate (Pi), potassium (K^+), and ammonia (Abe et al. 2003; Hicks et al. 2001; Avin et al. 2010; Shephard et al. 1988). The reduced ability to clear these metabolites may reduce the ability to produce a muscle contraction to sustain the fatiguing task, subsequently creating a greater performance fatiguability response in men than women (Abe et al. 2003; Hicks et al. 2001; Avin et al. 2010; Shephard et al. 1988). The sex differences in fatiguability have been reported to become minimized or nonexistent at as the level of intensity becomes greater, specifically when exercise is performed above a 50% MVIC threshold (Maughan et al. 1986; Hunter & Enoka 2001; Yoon et al. 2007; Ansdell et al. 2017; Sewright et al. 2008; Hicks et al. 2001). This hypothesis has been supported through examination of low intensity (25% MVIC) leg extension exercise, with and without blood flow occlusion (Yoon et al. 2007), wherein women demonstrated greater time to task failure than the men during exercise without blood flow occlusion, but these sex-differences disappeared during exercise in the occluded state. Further, the sex-dependent response may be minimized for higher intensity exercise (>80% 1RM; >50% MVIC) where no differences between men and women were reported during holds to failure and repetitions to failure for forearm flexion exercise (Clark et al. 2004; Yoon et al. 2007; Maughan et al. 1986). During performance of exercise at higher intensities, the performance fatigability response may be dictated through the inability to produce adequate levels of neural drive, demarcated as increased central fatigue, to sustain the exercise rather than through the peripheral fatigue mechanisms, such as metabolic byproduct accumulation, which may play a larger role in low intensity exercise (Davis & Bailey 1996; McMorris et al. 2018; Maughan et al. 1986; Hunter & Enoka 2001; Yoon et al. 2007; Ansdell et al. 2017; Sewright et al. 2008; Hicks et al. 2001). These studies support the existence of sex differences in performance fatiguability and support the hypothesis that due to differences in muscle mass and subsequent blood flow alterations during exercise, men may demonstrate greater levels of performance fatiguability than women during low intensity exercise and these differences may be reduced and possibly become nonexistent during high intensity exercise. Despite common differences between men and women during examination of performance fatiguability, specifically a reduced performance fatiguability and greater time to task failure in women compared to men (Martin et al. 2007; Hunter & Enoka 2001; Ansdell et al. 2017), the effect of contralateral fatigue in homologous muscle groups has not been widely examined in literature outside of a study by Martin & Rattey (2007) which demonstrated a greater effect of contralateral performance fatiguability in men than women. Thus, there is currently limited data available to describe changes in the non-exercised, contralateral limb after unilateral fatigue in men and women.

In addition to the quantification of fatigue via performance fatigability, it has been suggested that perceived fatiguability may also be quantified (Enoka & Duchateau 2016). Perceived fatiguability is defined by Enoka & Duchateau (2016) as ‘changes in sensations that regulate the integrity of the performer’ (pg. 3). Perceived fatiguability inherently requires the individual to interpret fatigue levels from the changes in homeostatic conditions following a fatiguing task but does so psychologically rather than through muscle contractility and activation levels (Enoka & Duchateau 2016). The fatigue incurred during the performance of submaximal repetitions to failure or MVIC performance is suggested to be a summation of central and peripheral factors of fatigue such as decreases in central command and the metabolite accumulation in the active muscle and alterations in blood flow, respectively (Monod & Scherrer 1965; Weir et al. 2006). The sensations elicited by fatigue may additionally impact the higher reasoning centers in the brain which dictate the task adherence through the summation of neuronal feedback provided by the group III/IV muscle afferents (O’Connor & Cook 1999; Pageaux & Gaveau 2016) as well as through feedforward pathways (Marcora & Staiano 2010). The quantification of these sensations elicited during fatiguing exercise, has been demonstrated successfully by perceptual scales such as the OMNI-RES RPE Scale (Foster et al. 2001; Sweet et al. 2004; Robertson et al. 2003).

The OMNI-RES RPE scale was specifically developed for non-steady state exercise such as resistance training (Robertson et al. 2000). The OMNI-RES scale defines perceived exertion on a scale ranging from 0 to 10 while providing visual cues to demonstrate each increasing value of a weightlifter visibly exerting greater and greater effort (Robertson et al. 2003). This scale has been shown to provide a valid and reliable quantification of the perceived exertion of an entire resistance training session, the active muscle (RPE-AM), and the overall body (RPE-O) (Robertson et al. 2003; Sweet et al. 2004). It has been reported that men and women may demonstrate different rates and levels of fatigue during exercise, depending on the mode, intensity, and duration of exercise (Cook et al. 1998; Garcin et al. 2005; Stuart et al. 2018). However, there is limited evidence examining the difference in the perceptual responses elicited during various fatiguing exercises in men and women. Stuart et al. (2018) examined the perceptual responses elicited by men and women during lumbar extension resistance exercise and demonstrated load- and sex-dependent differences in the fatigue response, as women rated perceived exertion similar to men but demonstrated a greater relative MVIC strength value. It was suggested that while men and women perceived the exertion to be similar, they experienced different levels of physiological fatigue (Stuart et al. 2018). Thus, there may be physiological differences in fatigue for men and women, although the exact mechanisms are unknown (Cook et al. 1998; Garcin et al. 2005; Stuart et al. 2018).

The perception of pain and the perception of exertion during exercise may both effectively be quantified by perceptual scales, but it is important to define the differentiation of the two measures (O'Connor & Cook 2001). Pain has been defined by The International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" (Merskey & Bogduk 2017, Online). Therefore, muscle pain, termed as an "unpleasant sensation", is considered separately from the perception of exertion or effort (Pageaux & Gaveau 2016). Furthermore, Marcora & Staiano (2010) and Pageaux & Gaveau (2016) defines the perception of effort as 'the conscious sensation of how hard, heavy, and strenuous a physical task is' (pg. 6), suggesting that the sensations are psychologically conscious in nature in relation to the physical task load the individual experiences, rather than the pain specific response from exercise (Pageaux & Gaveau 2016). As such, the use of perceptual scales must differentiate pain and exertion to effectively quantify the measure they aim to examine.

The presence of pain during various exercise modalities has been widely realized and accepted (Cook et al. 2008). Pain can be experienced during or immediately after the cessation of exercise or as a result of delayed onset muscle soreness (Miles & Clarkson 1994). This pain, although not due to a single factor, has been suggested to be due to a summation of multiple factors such as metabolic byproduct, H+ ion buildup, proteins, tissue damage, and possibly hormones (Miles & Clarkson 1994). While the presence of muscle pain is commonly experienced, the translation and quantification of this muscle pain to trainers, coaches, and practitioners has lacked substantial research between common quantification methods (Ferreira-Valente et al. 2011). A pain scale must effectively quantify changes in pain during procedures that are known to produce pain, such as exercise (Ferreira-Valente et al. 2011). Compared to other available pain scales, the Numerical Pain Rating scale (NPR) has been shown to produce a higher sensitivity to detect differences in both pain stimulus intensity and in perceptions of pain between men and women during exercise (Ferreira-Valente et al. 2011). It has, therefore, been suggested that the NPR measure of perceptual pain is both a valid and reliable measure to quantify the pain elicited through exercise performance (Cook et al. 1997; Ferreira-Valente et al. 2011).

Therefore, purpose of this study was to examine the effects of unilateral, isometric handgrip holds to failure for the Dm and NDm limb on ipsilateral ([IPS] exercised side) and contralateral ([CON] non-exercised side) performance fatigability in men and women. The specific aims of this study were to: 1) Determine the test-retest reliability for the pre-test MVIC force values and time to exhaustion for the dominant limb hold to failure; 2) determine if there are changes in the exercised ipsilateral and non-exercise contralateral limbs maximal voluntary isometric contraction (MVIC) force following unilateral, handgrip isometric holds to failure; 3) examine the perceptual responses of both perceived exertion and muscular pain in both the active muscle (AM) and overall body (O) following MVIC tests and holds to failure; and 4) examine sex-related differences in the performance fatiguability and perceptual responses for the exercised and contralateral limb after a unilateral fatigue. The hypotheses for the current study were: 1) The test-retest reliability in the pre-test MVIC force values would be in the excellent category (ICC > 0.80) but would demonstrate a learning effect from visit 1 to 2, but not from visit 2 to 3. In addition, the HTF values would demonstrate a lower reliability than the MVIC test, with ICC valued in the “fair” to “good” (ICC > 0.60) range (Cicchetti and Sparrow, 1981); 2) the women would demonstrate a longer HTF time at the relative 50% pre-HTF MVIC value than the men while demonstrating lower ratings of perceived exertion and pain; 3) the ipsilateral limb following the hold to failure would demonstrate significant performance fatiguability and the non-exercising contralateral arm would demonstrate no change or a small performance fatiguability effect due to a cross-over in fatigue response. Additionally, the Dm limb would produce a greater pre-HTF MVIC force than the NDm limb; and 4) the rating of both perceived exertion and muscular pain would increase following the HTF, specifically reflected by the greatest magnitude in the active muscle (AM) ratings. Additionally, the ratings of perceived exertion and muscular pain in the active muscle (AM) and overall (O) would both follow similar trends, such as when the active muscle (AM) rating increased, there would also be an increase in the overall (O) rating.

CHAPTER 2. LITERATURE REVIEW

2.1 Unilateral and Bilateral Fatigue

Neltner et al. (2020).

The purpose of this study was to examine the mode specific testing responses to isokinetic fatigue differences in performance fatiguability (PF) between bilateral and unilateral leg extensions. Eight male subjects (age: 22.5 ± 2.5 years) visited the lab on 4 separate occasions and performed repetitions on a leg dynamometer. The first day consisted of a familiarization session where the subjects performed submaximal and maximal, bilateral and unilateral, isometric, and isokinetic leg extensions at 180 degrees per second. Subjects warmed up by performing 5, 50% of maximum isokinetic leg extensions. Subjects then performed pre-testing with two, maximal bilateral, unilateral right, and left leg extensions at 180 degrees per second to determine peak torque (PT) values along with 2, 6 second bilateral, right, and left unilateral MVIC contractions at 135 degrees. Each subject was given 5 seconds of rest between repetitions of the same test. After pre-testing, subjects performed 50 consecutive maximal bilateral, unilateral right, or left, randomly ordered leg extensions at 180 degrees on separate days. Following each 50 repetitions, subjects completed post-testing for the unilateral and bilateral MVIC and PT, identical to the pre-testing procedures. All values used were determined using the highest value from the two MVIC tests.

The test-retest reliability was moderate/fair to good/excellent for 5 of the 6 PT and MVIC testing conditions. The bilateral task showed no significant two-way interaction but demonstrated main effects for time and testing condition. Pretest PT (236 ± 44 Nm) for bilateral fatiguing tasks were greater than post-test PT (213 ± 39 Nm). No unilateral right or left pre- and post-test PT differences were seen following bilateral testing. Bilateral pre-test PT (320 ± 59 Nm) was greater than the post-test PT (257 ± 82 Nm) following the right leg fatiguing task. Unilateral right leg testing pre-test PT (187 ± 39 Nm) was greater than the post-test PT (159 ± 41 Nm) following the right leg fatiguing task. Left leg PT testing demonstrated facilitation, as the left leg post-test PT (173 ± 32 Nm) was greater than pre-test PT (167 ± 34 Nm) following the right leg unilateral fatiguing test. PT pre- and post-testing for the right and left unilateral leg following the left leg unilateral fatiguing test demonstrated no significant differences. Pretest MVIC (291 ± 50 Nm) was greater than posttest MVIC (264 ± 52 Nm), when collapsed across fatiguing task and testing condition.

In summary, the authors state that decreases in PT were more sensitive to isokinetic fatiguing tasks than decreases in MVIC. A demonstration of facilitation in PT was seen, but not in MVIC, in the contralateral non-exercised leg following unilateral right leg fatiguing task. Bilateral fatiguing tasks resulted in decreases in bilateral, unilateral right leg, and unilateral left leg torque by 3 to 12%. Additionally, the unilateral right and left leg fatiguing tasks resulted in a decrease in bilateral torque of 3% to 20%, a 15% decrease in the unilateral right leg torque, and a 13% decrease in the unilateral left leg torque. Unilateral left and right leg fatiguing tasks resulted in 4% and 5% increases in the contralateral, non-exercising limb, respectively, producing a facilitation effect. This effect was not significant in the right unilateral leg following a left unilateral fatiguing muscle task but was significant for the left unilateral leg following right unilateral fatigue . The authors suspect this finding of increased torque may be due to a combination of central mechanisms such as reduced monosynaptic transmission via enhanced efficacy of neurotransmitters or increased myosin light chain phosphorylation through calcium ions creating post activation potentiation.

Rattey et al. (2005)

The purpose of this study was to examine the effects of voluntary muscular fatigue in a single lower limb and determine if a ‘cross-over’ of fatigue was evident in the contralateral limb. Twenty-eight subjects (13 males, 15 females, age [21±0.5 years], height [172.9±1.8 cm], mass [72.2±2.7 kg]) who classified as active, but not specifically trained, took part in this study. The subjects visited the lab for 1 session and performed standardized stimulated and voluntary contractions in the dominant limb (exercised limb) followed by the non-dominant limb (non-exercised limb) for pre-fatigued conditions. The post-fatigue conditions were randomly selected. The pre-fatigued measurements involved 6, 0.25 Hz twitches in the resting muscle evoked by stimulating the femoral nerve using adhesive electrodes placed about the medio-anterior aspect of the upper thigh directly below the inguinal fold. Following these twitches, four, 1-2 second maximal voluntary contractions (MVCs) were performed with 30 second rest periods. Following these pre-fatigue measurements, a 100-second sustained maximal isometric contraction was performed by the leg extensor muscle group of the dominant leg only. MVCs were performed on a leg dynamometer at 90° angle of the knee, with 0° being full knee extension. After completion of the 100-s sustained maximal isometric contraction, randomized leg dominance protocol was followed that was identical to the pre-fatigue protocol to examine the performance fatigability.

Prior to the fatiguing protocol there were no significant differences in the exercised and non-exercised limb maximal twitch tension, time to peak tension, and half-relaxation time.

Percent voluntary activation significant differences of the dominant and non-dominant limb were not present (91±2 and 88±2%, respectively) in the pre-fatigue condition. A significant decrease of voluntary activation was found in the dominant limb following the fatiguing protocol (91±2 to 74±3%). Voluntary activation of the non-dominant limb prior to completing the fatigue protocol was significantly higher compared to post-fatigue (88±2% to 80±3%). There were significant decreases in the dominant leg quantified by maximal voluntary force (386±16N to 321±14N) but not in the non-dominant leg (365±17N to 350±18N).

This study found that a fatiguing hold of 100-s in the dominant limb resulted in a ‘cross-over’ of fatigue to the non-dominant limb. Additionally, the measure of reduced voluntary activation and EMG in the non-dominant limb suggests that the CNS does not selectively reduce neural drive to the exercising or fatiguing musculature alone. This may be due to an overall coordination of the CNS to maintain cellular homeostasis due to anticipatory regulation. The authors suggested that the cross-over effect may be greater in lower limbs rather than upper limbs, possibly due to the necessity to maintain homeostasis to balance locomotion. In addition, it was found that minimal changes in force output was observed despite the reduced neural drive to the non-dominant limb.

Matkowski et al. (2011)

The purpose of this study was to compare the mechanisms of fatigue induced by a unilateral vs a bilateral submaximal isometric knee extension. Ten physically active male subjects (age: 25.8 ± 5.9 years; height: 179.6 ± 5.6 cm; weight: 74.1 ± 6.6 kg) reported to a lab for two visits to perform a unilateral or bilateral leg extension protocol. During session

1, subjects performed a fatiguing contraction with their non-dominant leg for the unilateral fatiguing session. Session 2 consisted of a bilateral contraction using both legs. The protocol consisted of a randomized order of: 1) Two left leg unilateral MVC force contractions with a 60 second recovery period with a doublet superimposed twitch 1.5 seconds before contraction and 1.5 seconds after contraction to assess voluntary activation level (VAL); 2) two 5-second unilateral right leg MVC assessments; 3) one MVC with the left leg muscles with a superimposed doublet 1.5 seconds before and after MVC attempts; 4) one MVC with the right leg; and 5) one bilateral MVC. These assessments were done before and after performance of the unilateral or bilateral fatiguing task of 20% MVC in a randomized order. EMG activity was recorded for the VL and RF, while superimposed twitch was performed via the femoral nerve.

Pre-MVC's showed intra-method similarities between right, left, and bilateral movements. Time to task failure for fatiguing MVC's were longer in the unilateral task (295 ± 90s) than the bilateral task (245 ± 80s) by 14%. The unilateral task performed with the left leg and did not elicit contralateral fatigue in the right leg, demonstrating no change in pre (189 ± 29 N) and post (184 ± 27 N) MVCs. During the bilateral session however, the right leg demonstrated a fatigue response of -15.2 ± 9.3%. The performance fatigue response in the left leg was greater after the unilateral fatiguing task (-36.6 ± 8.4%) than in the bilateral fatiguing task (-22.2 ± 8.5%). The bilateral MVC performance demonstrated a performance fatiguability effect following the bilateral fatiguing task (-25.8% ± 10.2) and the unilateral fatiguing task (-22.1% ± 7.8). A significant negative correlation existed for the time to task failure and MVC performance. The reduction in maximal VAL was greater following the unilateral fatiguing task (-12.9% ± 7.4) than the bilateral fatiguing task (-

6.8% ± 8.1). These results demonstrated that the time to task failure during a unilateral exercise is greater than during a bilateral exercise at the same relative force output. Additionally, the authors stated that due to a greater maximal VAL decrease during the unilateral contraction, central fatigue was greater during the unilateral contractions. The authors suggest this may be due to the total amount of exercising muscle mass and the respective metabolite concentrations influencing signaling via the group III/IV afferents. This authors stated that this study demonstrated that neuromuscular alterations exist between unilateral and bilateral movements, but more studies are needed to clarify the exact origin of the difference in fatigue mechanisms.

Cornwell et al. (2012)

The purpose of this study was to determine if the dominant limb would be more inhibited by measurement of the bilateral deficit, as the authors hypothesis suggested this may occur to reduce any disparity between each hand during a bilateral hold. Forty right-handed (19 males, 21 females) and forty left-handed (12 males, 28 females) subjects participated in this study. Subjects were declined participation if they performed regular bilateral training, were ambidextrous, or changed limb dominance as a child to prevent any of these factors from impacting their findings. During this study, EMG activity was recorded on the flexor digitorum superficialis (FDS) to quantify decreases in neural activation during bilateral and unilateral conditions. Following a two-minute rest period, subjects performed 3 MVCs for 3 seconds both unilaterally and bilaterally for each hand. These were broken into 3 distinct sets of 3 right hand, 3 left hand, and 3 bilateral for a total of 6 holds per hand. A 1-minute break was given between MVC attempts and 3-minute breaks between each set. The MVC values were determined as the peak force of each hand and was averaged across each trial. The MVC attempts were performed seated with the elbow in a 90-degree position and the hand in a semi-pronated/supinated position during the bilateral condition and with the non-exercising hand on the thigh, and relaxed, during the unilateral trials. Each subject was held in the correct anatomical position in respect to their head, neck, and shoulders, to reduce posture influences.

The results of this study showed that bilateral force deficits were not seen in the right-handed group while a small, but significant, deficit was seen in the left-handed group (-1.30±0.46%). The associated EMG responses showed a differing response, as the right-handed group showed significant facilitation (3.50±1.16%) when compared to the left-handed group (1.97±1.36%). Examination of each hand individually showed no significant decreases in force for the right or left hand for the right-handed group. A significant bilateral facilitation was seen for both hands in the right-handed group. For the left-handed group, a significant reduction in force in the left hand was seen when comparing the bilateral condition to the unilateral condition, but it was not marked by an EMG change. Despite no EMG changes in the left hand, the right hand showed a significant increase. The dominant hands demonstrated a greater force when compared to the non-dominant hand. In the right-handed group, the right hand was 10.4±2.1% stronger in the unilateral and bilateral conditions. The left-handed group showed an increase of 4.3±1.6% in the bilateral condition and 5.5±1.5% increase in the unilateral condition when comparing their left hand to their right. The differences in strength for each hand was not significant between the unilateral and bilateral conditions for the right- and left-handed groups.

After examining the differences, the authors found that 7 subjects categorized in the right-handed group were stronger in the left hand and 7 left-handed subjects were stronger in their right hand. The subjects were then reorganized into right- and left-hand strength dominance. The right-hand strength dominant group showed a 13.4±1.9% strength increase over their left hand in the unilateral hold versus a 12.0±2% increase in strength in the bilateral hold. A similar finding was seen in the left-hand strength dominant group, with 8.2±1.0% greater strength in the left hand over the right hand in the unilateral condition and a 5.9±1.5% in the bilateral condition. This left-handed strength dominance group also demonstrated a -1.0±0.4 bilateral deficit. A significant bilateral facilitation was only seen in the left-handed strength dominance in the EMG responses by 3.3±1.3% in their right hand.

This finding led the researchers to suggest that sorting of individuals into stronger hands (by use of unilateral MVC testing) may influence bilateral deficit findings. The findings in this study led the researchers to conclude that the lack of bilateral deficit may be due to co-activation of antagonist muscles providing a greater joint stability which may produce similar force outcomes despite no differences in EMG responses. As these subjects were untrained, the lack of neural adaptations to reduce coactivation in antagonist muscles were minimal and may have impacted their findings. In conclusion, the dominant hand is typically stronger than the non-dominant hand, and this difference is greater in right-handed individuals possibly due to constant favoring and use of common right-handed tools and instruments in daily living. The left-handed group was the only group to demonstrate a bilateral deficit. When the subjects were rearranged for strength dominance however, this bilateral deficit was not seen.

Unilateral and Bilateral Fatigue Summary

Performance of muscular tasks in unilateral or bilateral modes has produced differing levels of performance (force production, time to exhaustion, etc.) during initial muscular tasks and in the follow-up examination of performance fatiguability, or the decrease in muscular performance due to fatigue and the bilateral deficit (Neltner et al. 2020; Rattey et al. 2005; Matkowski et al. 2011; Cornwall et al. 2012). Neltner et al. (2020) examined the effects of performing both isokinetic and isometric leg extensions with both a bilateral and unilateral mode and the following fatigue effect. Bilateral leg extensions in an isokinetic mode demonstrated the ability to reduce the torque output in both the unilateral right and left leg by 3 to 12% (Neltner et al. 2020). This performance fatiguability was seen following left and right leg unilateral leg extensions in the ipsilateral leg (13% and 15%, respectively), but the contralateral limb demonstrated a facilitation effect of an increase in torque production of 4% in the right leg and 5% in the left leg following left unilateral and right unilateral leg extensions, respectively. Rattey et al. (2005) examined performance of fatiguing leg extension hold through both voluntary contractions and stimulated contractions via femoral nerve stimulation. A 100-second fatiguing hold in an exercising dominant leg showed a 'cross-over' of fatigue into the non-exercising non-dominant limb reflected via decreased percent voluntary activation from 88±2% to 80±3% ($P<0.01$), but this reduced neural drive did not impact the maximal voluntary force in the non-exercising, non-dominant limb (Rattey et al. 2005). Matkowski et al. (2011) examined the mechanisms of fatiguing leg extensions done bilaterally and unilaterally and found that time to task failure of a hold relative hold of 20% MVIC was longer for a unilateral muscle action (295 ± 90s) than a bilateral muscle action (245 ± 80s) by 14%. A superimposed twitch performed via the femoral nerve before and after the fatiguing leg extensions demonstrated a greater decrease in the voluntary activation level following the unilateral fatiguing task (-12.9% ± 7.4) than the bilateral fatiguing task (-6.8% ± 8.1) (Matkowski et al. 2011). The authors suggested this to be due to the greater level of central fatigue elicited by the total amount of exercising muscle mass and the respective metabolite concentrations influencing signaling via the group III/IV afferents (Matkowski et al. 2011). Cornwall et al. (2012) examined the bilateral deficit, a measure defining the reduction in bilateral force when compared to the sum of unilateral holds, which may be a measure of neural inhibition of muscle performance in homologous muscle groups, present between the dominant and non-dominant hands. No bilateral deficit was seen in untrained right hand dominant subjects, but a small but significant force decrease of 1.30±0.46% was seen in left hand dominant subjects (Cornwall et al. 2012). Cornwall et al. (2012) additionally examined the rate of force generation (RFG) and found a significant deficit in the EMG associated with the RFG of -3.48±1.57% and -2.70±1.56% in the right and left handers, respectively. This finding led the authors (Cornwall et al. 2012) to hypothesize that despite an overall force bilateral deficit only occurring in one of the hand-dominance groups, the bilateral deficit seen in the RFG EMG in both groups reflects that the neural inhibition is more present at the onset of force production. Additionally, bilateral facilitation was seen in both the right (3.50±1.16%) and left (1.97±1.36%) in EMG responses, which may suggest that neural control of muscle groups is affected by unilateral and bilateral movements by increasing, rather than decreasing, the neural drive in less trained subjects (Cornwall et al. 2012).

These studies suggest that the central nervous system (CNS) does not selectively reduce neural drive to the exercising or fatiguing muscle, possibly due to an overall coordination of the CNS to maintain cellular homeostasis due to anticipatory regulation (Rattey et al. 2005). While the fatiguing effect of muscular actions was seen following bilateral and unilateral muscle actions, facilitation was created following performance of unilateral contractions to homologous muscle groups (Neltner et al. 2020). The authors suspect this finding of increased torque may be due to a combination of central mechanisms such as reduced monosynaptic transmission via enhanced efficacy of neurotransmitters or increased myosin light chain phosphorylation through calcium ions creating post activation potentiation (Neltner et al. 2020). This effect of neural adaptation and control is similarly present in both dominant and non-dominant hands, with a greater effect seen in the inhibition of force production during the onset of force production measured by EMG, and facilitation of exercise performance in the remainder of an MVC hold in both right and left dominant hands suggesting limb dominance plays a lesser role than hypothesized (Cornwall et al. 2012). Fatiguing muscle actions performed bilaterally or unilaterally may produce differing fatigue effects which may be represented through performance fatiguability, facilitation of muscular performance, or through reduced neural drive which may not be represented in a tactile representation of performance fatiguability or facilitation (Neltner et al. 2020; Rattey et al. 2005; Matkowski et al. 2011; Cornwall et al. 2012).

2.2 Contralateral and Ipsilateral Fatigue

Amann et al. (2013)

This study examined the effects of afferent feedback associated with peripheral muscle fatigue and the inhibition of the central motor drive (CMD), to demonstrate the possible limit on endurance exercise performance. Eight recreationally active subjects volunteered for this study (Age: 24±1 year, Body mass: 83±6 kg, Height: 178±4 cm). Seven participants were right leg dominant while 1 subject was left leg dominant. Subjects performed constant-load, single-leg, knee extensor exercise to exhaustion (85% of peak power) with each leg (leg_1 and leg_2). Day 1 involved performing 60 RPM of 85% of the measured peak power to task failure, which was defined as 50 RPM or lower for at least 10 seconds in leg_1. Day 2 involved performing repetitions to failure following the same procedure as day one, on leg_2. Before and after the performance testing procedure, exercise induced quadricep fatigue was examined by reductions in potentiated quadricep twitch-force from pre- to post exercise 20 minutes before and 2 min after the testing. This was done via supramaximal magnetic femoral nerve stimulation. Day 3 examined the cross-over effect of fatigue by performing repetitions to failure on leg_1 and examining the fatigue incurred in the leg_2. The 4th and final day of testing involved performing repetitions until failure on leg_1 and immediately performing repetitions to failure on leg_2.

In spite of the fatigue induced to the quadriceps muscle, the quadriceps of the contralateral limb showed no effects of fatigue as shown by similar pre and post exercise potentiated muscle twitch, MVC force, and voluntary muscular activation. Following the performance of the repetitions to failure, the endurance time to task failure was -49±6% in the contralateral limb (Leg_2 post-trial). The potentiated muscle twitch was significantly reduced following both the performance test in days 1-3 as well as in the contralateral performance of leg_2 following leg_1 repetitions to failure. The rating of perceived exertion (RPE) increase was similar during the fatigue trials and the cross over trials. The RPE was influenced by quadriceps fatigue present in the contralateral leg, as evidenced by a 28% increase from the non-cross-over trials.

This study found that there existed reduced time to exhaustion in the contralateral limb following a fatiguing exercise performed by the other limb by ~49%. Circulatory and ventilatory responses during the exercise were within the respective maximal capacities and was suggested to be due to the muscular afferents on endurance performance. The peripheral fatigue present was suggested to provide a limiting effect and afferent feedback restricting the output of spinal motoneurons to the working skeletal muscle.

Todd et al. (2003)

The purpose of this study as to examine the cross-over effect of fatigue between elbow flexor muscles following maximal voluntary contractions (MVCs) using transcranial magnetic stimulation (TMS). Ten subjects participated in this study (3 female; 7 male; age: 38±11 years; 9 right hand, 1 left hand dominant). The subjects sat in a seated position with the elbow and shoulders flexed at 90 degrees with the forearms perpendicular to the ground and hands supinated. Each wrist was strapped in and an isometric myograph was used to measure the elbow torque, defined as force. A strain gauge was used to measure the force output and EMG was measured on the biceps brachii and brachioradialis. Electrical stimulation of the brachial plexus done via TMS placed on the motor cortex was used to produce the motor response in the aforementioned muscle groups. Subjects performed a familiarization session and two follow-up studies on different days. The first study included 20, 2-3 second MVC contractions at 1-minute intervals with 5 of the contractions stimulated via motor cortical stimulation and 5 via the brachial plexus. The subjects then performed 4 sustained MVCs with the right and left arm, alternating, with no rest between contractions. The MVCs were randomized by arm and performed to examine the cross-over effect of fatigue. The second study performed with the same participants was termed as a control for alternating protocols and included 15 brief MVCs. Motor cortical and brachial plexus stimulation was done for arm 1 for 5 contractions, and non-stimulated contractions were done for arm 2 for 5 contractions. The subjects then performed 2, 1-minute sustained MVCs with arm 1 with a stimulus. Voluntary activation was calculated during each MVC as a measurement of response to TMS and the evoked twitch value was expressed as a fraction of the voluntary force prior to stimulation.

The results of the study showed that sustained MVCs with alternation in arm use demonstrated a small, but significant, effect on the voluntary activation of limbs but did not change the voluntary force or EMG response. The voluntary force, which was relative to the brief MVC performance, declined by 35-45% of the maximal force from each sustained MVC. Differences in force output between contraction types (alternating and unilateral intermittent) existed. Voluntary force decreased from MVC 1 and 2 significantly when compared to MVC 3 and 4.

The authors surmised that a small cross-over effect was noted in the amount of central fatigue as there existed changes in voluntary activation that did not result in voluntary force changes. The voluntary force in the ipsilateral limb was similar and consistent between each protocol despite changes in rest periods from continuous and intermittent protocol. The ability of an ipsilateral side to produce similar force, despite consecutive contralateral limb performance and reduced voluntary activation, supports the hypothesis of the authors. This was surmised to be due to increased levels of adrenaline or higher levels of blood pressure aiding the muscular endurance. The amount of central fatigue inhibiting muscular performance following a contralateral contraction was reported to be minimal but did impact the level of voluntary activation as measured by superimposed twitch via TMS. This finding was greater following the alternating, continuous protocol than the intermittent protocol. The response of contraction following an electrical stimulus to the motoneurons is not reduced in relaxed contralateral muscles. This finding suggested that the cross-over effect is in a supraspinal, and possibly cortical, site.

Zijdewind & Kernell (2001)

The purpose of this study was to describe the levels of contralateral contractions demonstrated in hand muscles during unilateral voluntary activation. Five subjects (2 males; 3 females; Aged 20-25 years) participated in this study. Subjects participated in a protocol that required 5 visits, each separated by at least a week. Subjects were seated at a table with elbows placed in a slightly flexed position of 135 degrees with hands clamped in a vertical position, held in place by pressure plates and Velcro tape. The index finger was slightly abducted, with the abduction force measured at the proximal interphalangeal joint with a force transducer. The other fingers, hand, and wrist was immobilized to prevent additional abduction of the hand. EMG recordings were done via the first dorsal interosseous muscle (FDI) of each hand.

Repeated fatigue tests were done on each hand, as each subject performed 3 series of index finger abduction contractions for 4 seconds each. The first series involved 6 MVCs with the dominant hand, the second series involved 6 MVCs of the nondominant hand, and the third series involved 6 MVCs with both hands simultaneously. The first 3 MVCs of each series was performed without any electrical stimulation while the last 3 of each series was performed via interpolated twitch of the FDI. A rest period of 30 seconds was given between each MVC attempt, with the largest force value during the unilateral contraction defining the true MVC for each hand. After performance of MVCs the subjects were asked to perform 20, 40, 60, and 80% of their MVC for 6-8 seconds each. Following the MVC attempts and the force-level attempts, the subjects performed two submaximal endurance tests with their non-dominant then dominant hand. The endurance tests included a 30-second cycle of performing a 22 second hold at 30% of their MVC, a 4 second MVC, and 4 seconds of rest.

The calculated mean MVC across each MVC attempt over the course of the study (n =25) was 42.1±6.8N for the dominant hand and 41.2±7.2N for the nondominant hand. The investigators found coactivation of contralateral, homologous muscles occurring during unilateral MVC holds in 29 of the 50 attempts between subjects, determined by greater than 5% MVC activation. This effect was seen to be observed during submaximal holds as well, with an increasing degree of contralateral force production during the duration of the hold. During the unilateral MVC holds, the force increased in the contralateral limb from 9.1±6.5% to 26.0±12.1%.

As MVC duration increased, the level of contralateral co-contraction increased. The authors surmised this may be due to the increase in the excitability of the cortical pathways to the non-exercising muscle. Additionally, the coactivation of the homologous muscle group was suggested to be due to a spreading-out of facilitation occurring at both cortical and sub-cortical levels. This effect was seen to the same level for the dominant and nondominant hand, suggesting that post fatigue depression took place independently and possibly at a supraspinal level. These results were suggested to be due to possibly three different factors: Primarily, stimulation of the motor cortex ipsilateral to the target muscle which could result in a higher probability of the nontarget muscle being activated due to crossing over to contralateral motor cortex; secondly, it could be due to an increase in the interhemispheric activity due to a fatiguing activity or higher force output resulting in activity on non-target side muscles; and thirdly, it was surmised that it may be due to the shared pathways along the brain stem and/or spinal cord resulting in homologous activation. As the contralateral co-contraction decreased following a fatiguing hold in correlation with a decrease in ipsilateral MVC, the authors suggest a sharing of pathways in target and non-target muscles.

Derosière et al. (2014)

The purpose of this study was to examine the ipsilateral and contralateral activation responses of primary sensori-motor (SMI) and rostral prefrontal cortex (PFC) areas to graded levels of force production during a unilateral handgrip task. Fifteen volunteers (age: 28.0±7.5 years; height: 175.5±5.9 cm; body weight: 69.4±6.9 kg) took part in this study and were considered right-handed. Each subject performed the protocol one time and were seated at a table with their left forearm resting on a table surface held with straps to reduce movement during the isometric contractions with the right forearm. The dominant hand was held in a neutral position in the sagittal plane with a 110-degree elbow position. Subjects performed 3 MVCs for 5 seconds with 90 seconds of rest between each contraction. After this, subjects performed MVC isometric holds at 5, 10, 20, 30, 40, and 50% of MVC force, 3 times. The subjects held the aforementioned forces for 30 seconds followed by 60 seconds of rest, in a pseudorandom order. Collection of EMG data was done via electrodes places on the flexor digitorum superficialis (FDS) in the right active hand and the left passive hand. A NIRS (near-infrared spectroscopy) unit was placed over the SM1 and the rostral PFC areas using a specially designed cap during the entire study.

The results of the study showed no difference between each of the 3 trials of MVC forces (260±67.1N; 269.6±64.8N; 262.7±70.6N). Significant increases in EMG RMS values were seen in both the active and passive FDS muscles with an increase in the EMG RMS at force levels beyond 10% MVC in the active FDS and a significantly higher EMG RMS value at the 50% MVC level in the passive FDS muscle. The MVC trials showed similar cortical activation levels, which was expressed as an increase in the oxyhemoglobin and deoxyhemoglobin.

Examination of the contralateral and ipsilateral SM1 areas demonstrated significant increases in the oxyhemoglobin and significant decreases in deoxygenated hemoglobin levels with an increase in force level, but this effect was not different between brain hemispheres. Regarding the contralateral and ipsilateral rostral PFC areas, a significant interaction between force level and hemisphere was seen in the oxyhemoglobin, as a significant difference in hemisphere oxyhemoglobin was seen at the 50% MVC force level.

During this study, the cortical activation responses in the SM1 did not produce differing levels between the ipsilateral and the contralateral hemispheres at increasing levels of MVC force. Additionally, the rostral PFC activation was significantly greater in the contralateral side than the ipsilateral side during the highest force output (50% MVC), and there was a significant increase in EMG activity in the contralateral, passive arm at the

50% force MVC level. The authors suggest that the symmetrical SM1 activity was due to: 1) Symmetrical corticospinal tract (CST) activity to the contralateral and ipsilateral fibers in the CST; and 2) interhemispheric inhibition (IHI) is responsible for inhibition of mirror movements of a passive limb. There was a non-significant increase in the ipsilateral SM1 area compared to the contralateral SM1 area, possibly due to the firing of signals to the ipsilateral side which were inhibited via the IHI. When examining the rostral PFC activation, there was a significant difference in activation at the 50% MVC level between the ipsilateral and contralateral hemispheres. The possible reason for the difference in activation was suggested to be due to the visual sustained attention to the force tracing. The right-side rostral PFC area is known to be the area activated during sustained attention and may have been activated to a greater extent during more difficult tasks. In summation, the differences in contralateral and ipsilateral activation during muscle actions may be due to the ipsilateral CST and IHI in the SM1, which the latter may influence the activation in EMG responses during the higher level MVC force outputs.

Summary of Contralateral and Ipsilateral Fatigue

During performance of a unilateral muscle action, a unique phenomenon can be observed in neural responses on homologous, contralateral muscle groups (Amann et al. 2013; Todd et al. 2003; Zijdewind & Kernell 2001; Derosière et al. 2014). Following a fatiguing muscle action in a specific muscle group such as a maximal handgrip hold or leg extension, co-activation of a contralateral, homologous muscle group may result in differing effects on force production and levels of voluntary activation (Amann et al. 2013; Todd et al. 2003; Zijdewind & Kernell 2001; Derosière et al. 2014). Amann et al (2013) examined the fatiguing effects of performing high intensity (85% peak power) single-leg extensions to failure with blood flow occlusion and supramaximal magnetic femoral nerve stimulation to examine performance fatiguability. Following the fatiguing task of leg extensions in a randomized leg_1, the time to task failure in the randomized leg_2 was reduced by 49% when compared to the time to task failure when leg_2 was the first to perform the fatiguing task (Amann et al. 2013). Additionally, the performance of the fatiguing task was reflected via the O_2 uptake, CO_2 uptake, minute ventilation, heart rate, and cardiac output despite no significant differences in contralateral limb potentiated muscle twitch, MVC force, and voluntary muscle activation ($p = 0.44$; $p = 0.57$; $p = 0.89$; respectively) (Amann et al. 2013). Todd et al. (2003) examined the cross-over fatigue response from an exercising limb to the contralateral limb in elbow flexors following maximal voluntary contractions (MVCs) using transcranial magnetic stimulation (TMS) in an alternating arm protocol. The subjects demonstrated a small, but significant, effect on the voluntary activation on limbs of 7-12% but did not change the voluntary force or EMG response to sustained MVCs with alternation in arm use (Amann et al. 2013). Intrinsic hand muscles are additionally impacted by contralateral limb performance as these muscles are co-activated during performance as examined by Zijdewind & Kernell (2001). MVICs were performed using the first dorsal interosseus muscle (FDI), and despite the contralateral hand being immobilized, 29 of 50 subjects demonstrated an increase in the contralateral muscle activation during sustained MVICs of 9.1±6.5% to 26.0±12.1%, measured via EMG (Zijdewind & Kernell 2001). This value increased over the duration of the initial MVIC, but the value was decreased in follow-up MVIC holds, suggesting a sharing of neural pathways affected by fatigue in target and non-target homologous muscles (Zijdewind & Kernell 2001). Derosière et al. (2014) examined the specific areas of the brain responsible for initiating muscle actions, specifically the primary sensori-motor (SMI) and rostral prefrontal cortex (PFC) areas while performing graded levels of force production during a unilateral handgrip task. Derosière et al. (2014) found that the cortical activation responses in the SM1 did not produce differing levels between the ipsilateral and the contralateral hemispheres at increasing levels of MVC force while the rostral PFC activation was significantly greater in the contralateral side than the ipsilateral side during the highest force output (50% MVC), with a significant increase in EMG activity in the contralateral passive arm at the 50% force MVC level.

Multiple hypothesis are presented to account for the varying of responses to contralateral and ipsilateral muscle actions (Amann et al. 2013; Todd et al. 2003; Zijdewind & Kernell 2001; Derosière et al. 2014). Peripheral fatigue present may provide a limiting effect and afferent feedback restricting the output of spinal motoneurons to the working skeletal muscle (Amann et al. 2013). The ability of the ipsilateral side to produce similar force despite contralateral limb performance and reduced voluntary activation to both muscle groups supports the hypothesis of increased performance of the muscle fibers to produce force following a contralateral contraction, possibly due to increased levels of adrenaline or higher levels of blood pressure aiding in the muscular endurance (Todd et al. 2003). Examination of this cross-over affect in structures more proximal to the cortical and cerebral level suggest this may be due to the increase in the excitability of the cortical pathways to the non-exercising muscle and due to a spreading-out of facilitation occurring at both cortical and sub-cortical levels (Zijdewind & Kernell 2001). The stimulation of the motor cortex ipsilateral to the target muscle could result in a higher probability of the nontarget muscle being activated due to a crossing over to the contralateral motor cortex, increasing the interhemispheric activity due to a fatiguing activity or higher force output, resulting in activity on non-target side muscles, and due to the shared pathways along the brain stem and/or spinal cord resulting in homologous activation (Zijdewind & Kernell 2001). Symmetrical SM1 activity during muscle actions to the ipsilateral and contralateral limb may be due to symmetrical corticospinal tract (CST) activity to the contralateral and ipsilateral fibers in the CST (Derosière et al. 2014). Interhemispheric inhibition (IHI) is suggested to play a role as it is responsible for inhibition of mirror movements of a passive limb (Derosière et al. 2014). Non-significant increases in the ipsilateral SM1 area when compared to the contralateral SM1 area could possibly be due to the firing of signals to the ipsilateral side which were inhibited via the IHI (Derosière et al. 2014). The rostral PFC area, the area of the brain connected to motor areas via the cortico-cortical pathways, control the initiation and control of voluntary movements (Derosière et al. 2014). The significant difference in activation at higher MVIC force levels is possibly due to the visual sustained attention to the force tracing for which the right-side rostral PFC area is known to be the area activated (Derosière et al. 2014). The complex ability to sense and regulate muscular activity from the cerebral level to the active muscle provides insight on the varying effects of fatiguing ipsilateral muscle actions to contralateral limb performance when the contralateral limb is called upon to perform follow-up muscle actions.

2.3 Development of Fatigue and Effort Scales

Borg, G. (1970)

The purpose of this review was to examine the application of perceived exertion as a complement to physiological indicators of fatigue. Borg developed a perceptual continuum that considers the psychophysiological factors that govern the human body during increased levels of physical work. Borg examined the perceptual continuum as it relates to physical exertion in cases such as exercise, vocational efforts, and human performance; the total summation of these efforts is defined as the physical working capacity of an individual. This physical working capacity is not static in nature and can fluctuate due to a variety of factors both intrinsically and extrinsically. The changes in physical working capacity as measured by laboratory methods and instruments does not linearly change at the same rate that a subject may perceive it. Individuals react to the world as they perceive it to be, not always as how it is empirically shown to be. Due to this phenomenon, it may prove to be crucial to examine a relationship between the objective measures of physical exertion and the subjective measures as perceived by an individual. When a subject performs a work test on a cycle ergometer for example, the perceived intensity increases with the physical workload increase. This relationship is not purely linear, but rather demonstrates a non-linear relationship defined as a power function with an exponent of 1.6. These findings suggest that while perceived exertion will increase with workload increases, to maintain a consistent increase scaling in perceived exertion the workload will need to be increased by smaller and smaller intervals over the course of the exercise. For clinical and research applications, Borg developed a simple rating method using a 21-point scale which labeled each odd number from 3-19 with verbal expressions, such as light, moderate, very hard, etc. High correlations between these ratings and heart rate have been shown (r = .85). Borg developed and updated scale that consisted of 15 values between 6 – 20, thus developing the Borg 6-20 Rating of Perceived Exertion (RPE) Scale that is widely used today. It was reported that there was a linear relationship between the RPE-scale values, workload, and heart rate (r = .80). Borg also suggested that the RPE value could be multiplied by ten to provide an estimate of heart rate in middle aged individuals working at medium intensity levels. This direct relationship of heart rate to the RPE value given may not be applicable to populations that have a compromised or lowered maximal heart rate, such as older or diseased populations. RPE values may not correlate to a direct physiological underpinning in these populations as subjects may select RPE values that correspond to a heart rate higher than physiologically viable. This phenomenon suggests that RPE may be affected by the physiological capacity of an individual. In addition, it was reported that different RPE values may be selected for identical relative workloads between trained versus untrained populations. This may suggest that familiarization to exercise modalities and training status may influence perceived exertion values. Although heart rate is variable between different populations as shown above, it is currently a cost effective and simplistic measure of physiological changes in an individual. Subjects may also observe their heart rate increasing due to an increased metabolic demand in the body due to exercise, thus providing a direct physiological value to physical exertion. These findings provided additional rationale for the use of heart rate as an approximate underpinning to perceived exertion. Thus, the overall conclusion of this review was that the 6-20 RPE scale developed by Borg could be used to quantify the rating of perceived exertion due to its relationship with heart rate as a physiological underpinning.

Foster et al. (2001)

In this study, the researchers focused on evaluating the ability of the session rating of perceived exertion (RPE) method to quantitate training during non-steady state and prolonged exercise compared with an objective standard based on heart rate. The original

Borg 6-20 Rating of Perceived Exertion (RPE) scale was anchored according to the quotient of an individual's heart rate divided by 10 (i.e., 60/10 = 6 RPE). The researchers have questioned the applicability of this scale to non-steady state exercises where the heart rate can fluctuate due to the changing metabolic demands of the body. The researchers approached this problem by developing a study which existed in 2 separate but related parts. A common conditioning activity was selected that allowed for quantitative control of the exercise performed (cycle ergometry). This allowed for steady-state and interval-based exercise data to be representative of the common use of RPE in common conditioning activities. For the first part of the study, 12 well-trained, recreation level cyclists (6 males and 6 females) volunteered to undergo the exercise protocol. The second part of the study consisted of 14 members of a collegiate men's basketball team performing regular basketball activities to examine the response of heart rate and RPE in non-steady state exercise. To assess RPE in this study, the researchers used a modified 1-10 RPE scale with American idiomatic English describing each value. Subjects in part 1 of the study performed a maximal incremental exercise test on a cycle ergometer wearing a heart rate monitor. Blood lactate was analyzed for each subject at rest, at the end of each exercise stage, and at 1-, 3-, 5-, and 10-minutes post exercise. This was done to calculate the individual anaerobic threshold (IAT) on both the basis of exercise performance and blood lactate concentrations. Each subject then performed 8 randomly ordered training bouts that consisted of 30-minute steady state at a power output of 90% of IAT, 2 additional steady-state bouts at the same power output for 60- and 90-minutes, and 5 training bouts for 30-minutes that included variations in interval magnitude. Blood lactate concentrations were taken at rest and in 10-minute intervals along with RPE, and HR was recorded throughout the entire session. Session RPE was taken 30 minutes after the cessation of exercise to assess the RPE of the entire training session. The researchers used the TRIMP score method to compare the HR responses and the session RPE. This score was computed by multiplying the duration of the exercise bout by the session RPE for that bout to find the session RPE score. The summated HR zone score was calculated by separating each heart rate zone (50–60%, 60–70%, 70–80%, 80–90%, and 90–100%) and assigning a multiplier of 1, 2, 3, 4, and 5, respectively to each zone. The time in each zone was added together and this sum resulted in the summated HR zone score. During the second portion of the study, subjects performed an incremental treadmill exercise test using an Astrand protocol until volitional fatigue to determine HR_{max} and $\dot{V}O_2$ Max which were used to demarcate heart rate zones after exercise. Subjects then participated in basketball practice sessions and/or competitive matches performed at an exercise intensity and duration considered appropriate by the coaching staff, the player, and the situation. Each player wore a heart rate monitor, and each heart rate zone was separated out for duration and given the same multiplier as listed above. The subjects provided a session RPE 30 minutes after their training session and exercise score was computed by multiplying the duration of the exercise and heart rate zones by session RPE. The researchers found that there was a consistent pattern for longer intervals, more variable intervals, and longer duration steady state exercise bouts to be associated with greater evidence of psychophysiological strain, evidenced by HR and blood lactate concentrations. There were significant differences between the methods for each exercise bout, with the session RPE score consistently giving a score larger in magnitude than the summated HR zone method. A regression analysis revealed that the pattern of differences was consistent and similar to responses during steady state and interval cycle exercise observed in Part 1. Both scales provided similar responses caused by changes in intensity and duration of exercise, however, the scales cannot be interchanged due to differences in scaling. The overall consistency between the objective (summated HR zone) and subjective (session RPE) methods of monitoring training during highly disparate types of exercise suggests that the session RPE method may be useful over a very wide variety of exercise sessions. The present data provides support for the use of session RPE method as a subjective estimate of training load during non-steady state exercise, including very-high intensity interval training.

Sweet et al. (2004)

The purpose of this study was to examine the applicability of the session rating of perceived exertion (RPE) method, which was developed for aerobic training, to resistance training. Using common measurements such as heart rate or oxygen consumption to quantify resistance training is not readily viable due to the disproportionate increases in each during resistance training. These measures do not provide an accurate estimate of training load as there are short duration work periods followed by long recovery periods in most resistance training programs. This fluctuation in work performed elicits constant fluctuation of heart rate and oxygen consumption leading to difficulty in assigning workloads based on physiological variables. The use of RPE to quantify resistance training intensity has been examined previously (see Skinner et al. 1973; Foster et al. 2001) providing evidence suggesting that heart rate and RPE are well correlated during steady-state and non-steady-state exercise modalities. This study examined 10 male and 10 female volunteers who were healthy and moderately active college students, as defined by performing both aerobic and resistance training for 30 minutes a day for most days of the week. The subjects performed a graded exercise test to determine the peak $\dot{V}O_2$ and ventilatory threshold (VT-1) of each subject. The volunteers then performed 3 exercise sessions of steady-state exercise on the cycle ergometer for 30 minutes at 70%, 90%, and 110% of the VT-1 defined by their graded exercise test. Each workload was randomized in order and separated by 48 hours. Thirty minutes following exercise, the subjects gave their session RPE value for the entire exercise bout using a CR-10 RPE scale. The CR-10 scale quantifies resistance training perceived exertion using a 10-point scale. This scale uses verbal demarcations (easy, moderate, hard, etc.) to define each value and may provide a more intuitive scale for general populations. Following these procedures, the subjects performed a 1 repetition maximum (1RM) test for the bench press, lateralis pulldown, shoulder press, leg press, biceps curl, and triceps extension. The subjects then completed sessions of 2 sets x 15 reps at 50% of their 1RM. During the next session, the subjects to complete 2 sets x 10 reps at 70% of their 1RM. During the final session, the subjects to completed 2 sets x 4 reps at 90% of their 1RM. If they were not at muscle failure after the 4th repetition, the subjects were asked to complete another repetition for 5 total repetitions per set. Each exercise session was separated by 48 hours and each exercise was randomly ordered. The RPE was asked immediately following each set, and the session RPE was asked 30 minutes after the completion of exercise to prevent skewing of data for a particularly hard or easy section of the workout. The researchers also recorded a session RPE for the lifting component only (RPE-LO) due to the long rest periods possibly impacting the RPE value. The RPE for each set was averaged for each intensity and exercise to provide a mean RPE (MRPE) score. It was found that session RPE for resistance training increased from 3.8±1.6 to 5.7±1.7 to 6.3±1.4 as the intensity increased from 50%, 70%, and 90% of 1RM, respectively. The session RPE for cycling ergometry increased from 3.6±1.1 to 5.1±1.3 to 7.8±1.3 as the intensity increased from 56%, 71%, and 83% of the peak $\dot{V}O_2$, respectively. The researchers converted the 70%, 90%, and 110% of VT-1 to $\dot{V}O_2$, percentages for data analysis. The researchers also determined that the MRPE increased as weight increased for all exercises but the shoulder press, which decreased in MRPE from 70% to 90% of 1RM. Shoulder press RPE values were also consistently higher than other resistance exercises at any intensity. Repeated measures ANOVAs revealed a significant intensity effect ($p<.05$). There was a significant difference between the 50%, 70%, and 90% RPE values provided for the session RPE, MRPE, and RPE-LO in most cases, with the exception of 50% session RPE and 50% session RPE-LO, 70% MRPE and 70% session RPE-LO, and 90% MRPE and 90% session RPE-LO. The researchers suggested that the order of exercises performed could impact the RPE value of each exercise, as metabolite buildup over the training session could elicit different perceptions of effort. The researchers also suggested that RPE increases as load increases at a greater rate than the RPE increases in response to repetition increases, as the session RPE, MRPE, and RPE-LO was consistently higher for high intensity, low repetition sessions. The researchers suggested that due to these findings, using a method of RPE to measure resistance training intensity is reasonable and may allow for the athlete to view the training session globally and simplify the various physiological cues that occur into a single, quantified value.

Robertson et al. (2003)

The purpose of this study was to examine the concurrent validity of the newly developed OMNI-Resistance Exercise (OMNI-RES) scale for use in men and women during upper- and lower- body isotonic exercise (Robertson et al. 2003). The OMNI-RES scale defines levels of effort on a 1 to 10 scale and provides corresponding images of a weightlifter increasing in his level of visibly observable exertion at each value. There were 20 men and 20 women volunteers who were recreationally trained for at least 6 months prior to the start of the study. The subjects performed a 1 repetition maximum (1RM) test for the biceps curl (BC) and the leg extension (LE) to determine the maximal load that could be lifted. At the following visit, the subjects were randomly placed in one of two groups, one group performed LE and then BC and the other group performed the BC and then LE exercises. For both groups, the BC and LE exercises were performed for 3 separate sets of 4, 8, and 12 repetitions at 65% of their 1RM. The subjects were asked to provide the RPE in the active muscles (RPE-AM) after the completion of the middle (RPE-AM [mid]) and final (RPE-AM [final]) rep as well as to provide an RPE for the total body (RPE-O) after the completion of the final repetition and the recording of RPE-AM (final). The researchers found that the responses for RPE-AM ranged from 3.6-8.2 for the BC and 5.1-9.6 in the LE and the responses for RPE-O ranged from 2.4-6.7 for the BC and 4.2-7.6 for LE. There was a positive linear correlation (0.79 to 0.91) when comparing total weight lifted (Wt_{tot}) and the RPE across reps for each exercise (BC, LE) for both men and women. There were no differences in RPE values between the sexes for either exercise. The value for RPE-AM (final) was greater than RPE-O in the three sets of BC and LE. Due to their findings, the researchers suggested that the ONMI-RES scale is reliable way to measure RPE in the active muscle and the overall perceived exertion (RPE-O) in young, recreationally resistance trained individuals in either sex.

Summary of the Development of Fatigue and Effort Scales

Perceived exertion scales have been demonstrated to effectively quantify the exertion an individual experiences over the course of an exercise session (see Borg 1970; Foster et al. 2001; Sweet et al. 2004; Robertson et al. 2003). The first scale was developed by Gunnar Borg to quantify exertion over the course of an exercise session by considering the intrinsic and extrinsic factors an individual experiences (Borg, 1970) Borg developed a scale ranging from 6-20 (Borg 6-20 RPE scale) to measure perceived exertion (Borg, 1970). This scale was developed to reflect the correlation with the heart rate increases shown during an exercise bout, as each value multiplied by 10 may provide a rough estimate of an individual’s heart rate. This scale proved to be reliable and valid during steady-state aerobic exercises but was questioned for its applicability to non-steady state exercises (Foster et al. 2001). The physiological underpinning for this initial scale, heart rate, demonstrates non-linear changes during non-steady state exercise. Foster et al. (2001) observed this phenomenon and examined the correlation between the heart rate value during both steady state exercise and non-steady state exercises and the relationship of perceived exertion scores to these heart rates. A scale was used to quantify the intensity of exercise using heart rate, the Summated Heart Rate Zone scale, during both cycle ergometry and competitive basketball practices and matches (Foster et al. 2001) This scale was then compared to the measure of perceived exertion the individual experienced, the session RPE scale. The researchers suggested that due to consistency between the Summated Heart Rate Zone scale and the Session RPE scale during highly disparate types of exercise, using Session RPE to quantify perceived exertion may be valid and reliable (Foster et al. 2001) Subsequently, Sweet et al. (2004) further examined the use of Session RPE on a 1-10 scale to quantify resistance training as it relates to the overall physiological changes during exercise. To examine the validity of session RPE to quantify resistance training intensities, researchers examined the responses of subjects performing at 70%, 90%, and 110% of their ventilatory threshold. These subjects also performed resistance training exercises corresponding to 50%, 70%, and 90% of their 1 repetition maximum and were asked to rate their perceived exertion. The authors (Sweet et al. 2004) observed an increase in total RPE values at increasing workloads for both exercise modalities. It was also observed that during resistance training, exercise order, exercise intensities, and total repetitions may play a role in the perceived exertion of an individual. Sweet et al. (2004) also examined the validity of RPE-LO, or the rating of perceived exertion during the lifting only components of the overall exercise session, as rest periods comprise large portions of an overall resistance training session. This method of collecting the rating of perceived exertion was suggested to be valid due to its correlation with the session RPE observed by subjects (Sweet et al. 2004). It was suggested that collecting RPE during resistance training is valid and may provide quantification of the total physiological changes throughout increases of intensity during a resistance training session. Therefore, Robertson et al. (2003) conducted a study examining the use of a newly developed RPE scale, the OMNI-RES 1-10 scale. This scale defines the perceived exertion on a 1 to 10 scale and includes visual cues to demarcate each increasing value using a weightlifter visibly exerting more effort. Researchers collected RPE values for the active muscle (RPE-AM) and the overall body (RPE-O) to examine the validity of assessing perceived exertion in the working muscle rather than the body as a whole. The authors (Robertson et al. 2003) observed that the RPE-AM value was consistently higher than the RPE-O value, but both presented a linear correlation at all work loads. The authors suggested the RPE-AM may provide an accurate value of perceived exertion during resistance training. The articles in this section suggested that using a scale to quantify perceived exertion during resistance exercise through session RPE, overall body RPE, and active muscle RPE is valid and reliable.

2.4 Load and Intensity Effects on Perceived Exertion

Day et al. (2004)

In this study, the researchers examined the reliability of using a session rating of perceived exertion (RPE) to demarcate the differences in resistance training at the different intensities: high intensity, moderate intensity, and low. The study included 9 men (age: 24.7±3.8 yrs; body mass: 94.2±21.1 kg) and 10 women (age: 22.1±2.6 yrs; weight: 60.7±4.9 kg) who had participated in structured resistance training programs for at least 6 months prior to the start of this study. The subjects performed a 1 repetition maximum (1RM) test during the first visit and this value was used to determine the workload for the high, moderate, and low intensity training days. High intensity was defined as 90% of the 1RM value, moderate intensity was defined at 70% of the 1RM value, and low intensity was defined as 50% of the 1RM value. The subjects performed the high intensity load for 4-5 reps, the moderate intensity for 10 reps, and the low intensity was defined as 15 reps. The subjects performed 1 set of 5 different exercises at each intensity level. The exercises included the back squat, bench press, overhead press, biceps curl, and triceps pushdown. After an initial familiarization, the RPE responses were recorded on two separate days of data collection at each intensity level. Each exercise was separated by 2 minutes of rest, each exercise session was randomly ordered in intensity level, and each exercise session was separated by 48 hours. The subjects were asked their RPE both immediately after the exercise and 30 minutes post exercise on the CR-10 scale, a scale that records perceived intensity on a 1 to 10 scale with verbal cues for intensity anchoring. This method of examining RPE was used to compare the immediate rating of RPE after a working set and the exercise session as a whole. The authors reported a significant difference in the RPE values at each exercise intensity (p<.05). Across all exercises, the mean value for RPE increased as each exercise intensity increased. A within-subjects ANOVA was demonstrated no significant difference between the average RPE value recorded after each set and the overall session RPE. The researchers also discovered that individuals reported fewer repetitions at higher intensities was more difficult or required more exertion to complete than those with more repetitions at lower intensities, which may be due to a specific fatigue mechanism. The authors suggested that session RPE is a valid way of assessing perceived exertion across all exercise intensities and may be used in conjunction with post-set RPE collection.

Dias et al. (2018).

This study compared the training load and the rating of perceived exertion (RPE) in both resistance training and aerobic or endurance training. Fifty-four subjects (22 men, 32 women) who were active and recreationally trained, were placed into a resistance training (RT) or aerobic training (AT) group based on their current experience levels for each modality. Each volunteer participated in either only resistance training for an average of 200 minutes per week or only aerobic training for an average of 138 minutes per week, all for at least 3 days per week for 6 months prior to the study. The RT group consisted of 24 men and 14 women while the AT group consisted of 8 men and 8 women. The resistance training protocol required each volunteer to self-select a training load for the 45-degree leg press (LP), free weight bench press (BP), knee extension (KE), and EZ bar arm curl (AC), performed in order as listed. Subjects were asked to select a training load that they usually performed for 10 repetitions, and that corresponded to a “good workout”. Ten repetitions were performed for 3 sets of each exercise with 90 seconds of rest between each set. Forty-eight hours following the self-selected intensity training session, subjects performed a 1RM test and a 10-repetition maximum test (10RM) on separate days separated by 48 hours. This was done to compare the self-selected intensity versus the actual maximal workload. All of the exercises were performed in the same order on each day to standardize RPE responses, which were collected after the completion of each exercise using the OMNI-RES RPE scale the aerobic training group performed a fatiguing test on a treadmill for a self-selected speed and time. The intensity selected corresponded to “an exercise intensity and duration that you prefer and that you would feel happy to do regularly” (p. 773). Changes in velocity were allowed at any time, but the speedometer was blinded to the subject and was only visible to the researchers. The RPE was measured every minute using the OMNI Run/Walk RPE scale. Each subject performed the AT session until volitional failure (mean: 34.5±13.5 minutes). Forty-eight hours after the completion of this training session, subjects were asked to perform a maximal treadmill exercise test using a ramp protocol. The researchers found for the self-selected training sessions, the relative training intensity of the upper limbs (55.5-60.2% of 1RM) was higher than for lower limbs (44.2-44.9%). The self-selected mean RPE value was 7.2 for RT, while the mean RPE for AT was 6.8. No significant differences were reported in RPE across RT exercises. Each RPE value increased for each successive exercise suggesting that during RT, RPE may increase in successive sets without increases in load. The researchers found that subjects in the resistance training group chose an intensity that was below the recommended levels (43.6%-60.2% 1RM) but subjects in the aerobic training group chose an intensity that was recommended (83.9% Heart Rate Peak). The mean RPE value of 7.2 and 6.8 for RT and AT, respectively, corresponded to exercise intensities defined as “somewhat hard” to “hard” on the OMNI RPE scale. The ACSM recommends that individuals train within a range of 6-8 on the OMNI RPE scale, which corresponded to the average RPE reported by the subjects. The researchers suggested that individuals will select lower workloads (% 1RM) for resistance training than those recommended by governing bodies and will need guidance when initially learning how to resistance train. Individuals may also need familiarization to RPE scales and guidance in perceived exertion levels to maintain resistance training intensities recommended by the ACSM.

Pritchett et al. (2009)

This study examined the acute rating of perceived exertion and the session rate of perceived exertion in resistance training bouts performed to failure at low intensity (60% 1 repetition maximum [1RM]) and high intensity (90% 1 repetition maximum [1RM]). This study included 12 resistance trained males (Age: 23.8±3.1 (years); Mass: 78.8±14.5 (kg)) who had performed resistance training exercises for at least 6 weeks prior to the study. Each subject completed a 1RM test on day one of the study to provide reference for the high intensity (HI) and low intensity training (LI) loads. Each subject then completed the HI and LI training sessions in a counterbalanced order between the 2 intensities. Each session was separated by at least 24 hours. The HI and LI training session followed the same protocol and varied only in the intensity (60% or 90% of 1RM) for the overall session. During each session, the subjects completed 3 sets of 6 exercises to volitional fatigue or the point in which the individual could not complete a repetition at the required load. Each set was separated by 2-minute rest periods as well as 2-minute rest periods between each exercise. The exercise order remained fixed throughout each training session as follows: Leg Press, Bench Press, Lat Pulldown, Shoulder Press, Triceps Pushdown, and Biceps Curl. After each set was completed, the subjects reported their rating of perceived exertion (RPE) on a CR-10 RPE scale within 10 seconds of their last repetition to serve as the acute RPE value. This was done for each set of each exercise at each intensity. The session RPE was collected following the entire training session and required that each volunteer sit quietly for 30 minutes and then quantify their entire training session as a whole. During the entire training session, heart rate values were collected to provide a physiological underpinning and reference for exercise intensity as perceived through a physiological indicator. The researchers found that the LI training session elicited a significantly higher (p= 0.039) session RPE (8.8±.8) compared to the HI training session (6.3±1.2). The total work performed was higher (p= 0.043) in the LI session (17,461±4,419) than the HI session (8,658±2,255). Heart rate was also found to be higher during the LI session for the leg press (p= 0.041), the bench press (p= 0.031), the lat pulldown (p= 0.037), and the shoulder press (p= 0.046). After these exercises, there was a convergence in the heart rate values during the triceps pushdown and biceps curl exercises. This may be due to the overall increased physiological demand over the course of the training session at either intensity as the triceps pushdown and bicep curl were performed last in both training sessions. The researchers also found that the acute RPE was higher (p= 0.029) in the LI session versus the HI session across all exercises. There was a correlation between the session RPE and total work (r^2= 0.85; p= 0.029) which may suggest that total work is a better indicator and predictor of RPE increases over a training session rather than training intensity. These findings suggested that in training sessions performed until failure, total work plays a larger role in RPE changes than the exercise intensity alone. When performing repetitions to failure, subjects may perceive more effort exerted during higher repetition, lower intensity exercise. These results differ than those published by (Day et al. (2004)) in which a set number of repetitions were used at specific intensities. In the aforementioned study, it was found that higher intensity, lower repetition sets provided a higher RPE value as reported by the subjects. Thus, Pritchett et al. (2009) indicated that during the performance of repetitions to failure, an individual will perceive total work performed as a greater influence on their RPE than the specific exercise intensity.

Li et al. (2011)

This article examined the perceptual responses of grip force in males using the CR-10 Borg scale. Twenty college age male subjects (Age: 22.1±2.5 (years)) volunteered for this study. Each subject performed a power grip hold test on a hand dynamometer (TAKEI® FT5001) at four different perceived exertion levels on the CR-10 RPE scale: 2 (weak), 5 (strong), 7 (very strong), and 10 (extremely strong). Each power grip hold test was performed in a separate session and each session was separated by at least 24 hours. Each intensity level was performed with the dominant and non-dominant hand at both 90° and 180° extension of the elbow for 4 seconds and each set was separated by 5 minutes to limit the effect of fatigue. The intensity (2, 5, 7, 9), hand (dominant, non-dominant), and posture (90°, 180°) order was randomized for each subject and session. After each subject performed the power grip hold that corresponded to the specific CR-10 RPE values, the researchers recorded the force produced at each level. This portion of the study provided a force estimate that correlated to each RPE intensity on the CR-10 scale. It was hypothesized that each RPE intensity (2, 5, 7, 10) would reflect percentages of an MVIC (i.e., 20%, 50%, 70%, and 100%). After performing the power grip holds, subjects used a PEAKLIFE® FT515 handgrip to perform a 4 second hold at 10 kg and rated the CR-10 RPE value that corresponded to their level of effort. These two methods of hand grip testing were designed to mirror each other by examining the differences in the perceptual responses elicited. One test examined the handgrip force produced at a specific known CR-10 RPE value, and the other test examined the CR-10 RPE response elicited by performing a handgrip test at a known force value. The researchers found that a significant ($p<0.0001$) main effect existed for the CR-10 RPE level, hand used, and posture on the power grip force. Duncan's multiple range test results demonstrated that mean grip force at level 10 of the CR-10 RPE scale (41.9 kg) was significantly higher ($p<0.05$) than that of level 7 (32.6 kg), level 5 (24.4 kg), and level 2 (10.5 kg). Level 7 mean grip force was significantly higher ($p<0.05$) than level 5 and level 2. Level 5 mean grip force likewise demonstrated a significantly higher ($p<0.05$) value than level 2. Duncan's multiple range test also showed that the 180° elbow extension posture (28.3 kg) was significantly higher ($p<0.05$) than the 90° elbow extension posture (26.5 kg). The dominant hand (28.0 kg) demonstrated a significantly higher ($p<0.05$) force value than the non-dominant hand (26.7 kg) as well. The interaction effects of the CR-10 RPE level and hand used were significant ($p<0.0001$) and the interaction effect of CR-10 RPE levels and posture were significant ($p<0.0001$). The Pearson's correlation coefficient between the CR-10 RPE rating and grip force were shown to be 0.92 ($p<0.001$), suggesting a strong positive correlation of perceived exertion and grip force. The researchers then examined the effects during the handgrip test at 10 kg There was a significant effect of hand and posture ($p<0.05$) during this subjective rating assessment. The non-dominant hand (2.36) showed a significantly higher ($p<0.05$) CR-10 RPE value than the dominant hand (2.22) at the 10 kg level. It was also shown that the 90° posture (2.37) required a significantly higher ($p<0.01$) level of perceived exertion than the 180° posture (2.20). While looking at the force values produced at each CR-10 RPE level, the researchers converted each value into a percentage of the force value produced at the 10 CR-10 RPE level. When dividing the grip forces at levels 2, 5, and 7 by the grip force produced at level 10, the researchers found that the dominant hand produced forces of 24.7%, 56.2%, and 75.6%, respectively. The non-dominant hand produced forces of 25.6%, 60.5%, and 80.0%, respectively. These forces were all larger than the predicted force produced at each CR-10 RPE level (20% MVIC at level 2, 50% MVIC at level 5, and 70% MVIC at level 7). The researchers suggested that due to this phenomenon, individuals may exert more force than perceived. The phenomenon of the non-dominant hand producing higher force than the dominant hand at the same perceived intensity level has no clear explanation as provided by the authors and may lead to more research. This study suggests that there are no significant differences of hand and posture at low CR-10 levels, but this finding is not supported at higher CR-10 values. The researchers also suggest that there is a strong overall correlation of the perceived exertion on the CR-10 scale and the grip force values. This study suggested that individuals may produce more force than perceived when performing at a specific CR-10 RPE value and may perceive exertion levels to be higher when performing at a specific force intensity levels. This may lead individuals who prescribe training regimens to anchor according to a perceived intensity level rather than a required weight or force intensity level to maximize training intensity.

Summary of RPE and Intensity

The rating of perceived exertion (RPE) has been consistently demonstrated to increase in relation with the increased duration and intensity of exercise (Day et al. 2004; Dias et al. 2018; Pritchett et al. 2009). The RPE and intensity relationship has been examined in both anaerobic and aerobic modalities, specifically during resistance training, aerobic training via running and basketball, and isokinetic hand grip testing (Day et al. 2004; Dias et al. 2018; Pritchett et al. 2009; Li et al. 2011). Day et al. (2004) found that there was a significant increase in RPE values for increased exercise intensity. In addition, it has been demonstrated (Day et al. 2004) that the RPE taken immediately following the set of a resistance exercise was not different from the RPE of the whole training session taken 30 min after the session ended. Based on these findings, Day et al. (2004) suggested that session RPE was a valid method to determine perceived exertion responses over an exercise session. Furthermore, the authors (Day et al. 2004) reported that lower repetition, higher intensity workloads performed to a set number of repetitions was perceived as more difficult than performing higher repetition, lower intensity workloads. Thus, the authors determined the RPE was dictated the intensity of the exercise, more than the duration or volume. In contrast, Pritchett et al. (2009) found that a 60% 1RM training session elicited a significantly greater perception of effort than a 90% 1RM training session and that the total work performed was higher in a 60% 1RM training session than a 90% 1RM training session. To further support this finding, there was a strong correlation between the session RPE, and the total work performed across a training session (Pritchett et al. 2009). The authors (Pritchett et al. 2009) suggested that the total work performed was a better predictor of RPE across a training session than intensity alone. These findings, in contrast to those of Day et al. (2004) suggested that when performing repetitions to failure, the subjects perceived a lower intensity for higher repetitions to require more effort to than completing less repetitions at a higher intensity (Pritchett et al. 2009). Pritchett et al. (2009) additionally suggested that performing repetitions to failure elicits different perceptual responses than performing repetitions for a set number of repetitions across similar exercise intensities. Thus, currently there is conflicting evidence regarding the effect of intensity and volume on RPE responses reported for resistance exercise.

The use of RPE to prescribe resistance exercise has also been explored (Dias et al. 2009). Dias et al. (2009) found that individuals performing anaerobic resistance training exercises self-selected more intense workloads for their upper body limbs than for their lower body limbs and that the overall exercise intensity for anaerobic resistance training was lower than the self-selected exercise intensity for aerobic training. Although the training intensity may have been lower for anaerobic resistance training exercises, the mean RPE value for the anaerobic resistance training exercises were greater than the mean RPE value in aerobic training (Dias et a. 2009). The authors (Dias et al. 2009) suggested that self-selected anaerobic resistance training workloads are lower than self-selected aerobic training loads, possibly due to the fatigue mechanisms and perceptual responses elicited from each modality.

Li et al. (2011) assessed grip force and subjective hand exertion under handedness and postural conditions, directly examining a muscle activated for a large number of resistance exercises. These muscle groups (wrist flexors and extensors) may be a limiting component of resistance training exercises that require handgrip strength to control or maneuver weight through a specific range of motion (Li et al. 2011). Li et al. (2011)

examined the use of CR-10 RPE scale and found that the non-dominant hand produced greater force across all CR-10 RPE intensity levels when compared to the dominant hand due to an unknown phenomenon. The authors also suggested that individuals may produce more force than they perceive to when performing at a required CR-10 RPE value and may perceive their level of exertion to be greater when performing at a required intensity level (Li et al. 2011). This finding led the authors to suggest that individuals who prescribe training regimens should possibly prescribe according to a perceived intensity level rather than a required weight or force intensity level as individuals may perform different workloads for each method. (Li et al. 2011). Li et al. (2011) discovered that the perceived exertion and the overall force produced was significantly higher in the 90° elbow extension posture than the 180° elbow extension posture, suggesting that posture may impact handgrip strength. The increase in the RPE value was suggested to be due to the greater force produced in the 90° elbow extension posture (Li et al. 2011). This suggested that posture and handedness affect the amount of force that is produced in a hand grip test.

Taken together, the studies in this section suggested that RPE is influenced heavily by the intensity of a training session, the total work of a training session, and the whether the exercise is performed to failure or for a set number of repetitions. Perceived exertion levels may be important in determining the intensity of a self-selected exercise workload and may differ between aerobic and anaerobic modalities, possibly due to the manifestation of fatigue differing in the modalities. While examining the perceptual responses to fatigue in the forearms, Li et al. (2011) suggested that individuals will perform greater work when asked to complete isometric holds at a defined RPE level rather that at a specific workload. This phenomenon may suggest that individuals may perform at higher intensities when anchoring a training session via RPE values. Overall, RPE may be highly influenced due to the overall intensity and total work of a training session and using RPE to define training intensities may allow for greater work to be done over the course of a training session (Day et al. 2004; Dias et al. 2018; Pritchett et al. 2009; Li et al. 2011).

2.5 Sex Related Differences in Rating of Perceived Exertion

Cook et al. (1998)

This study examined the role of sex in the perceptions of leg muscle pain during exercise, specifically during a maximal cycle ergometry test. Twenty-six men (Age: 23.2±3.9) and 26 women (Age: 21.9±3.5) volunteered for this study. Each subject was moderately trained and reported previous experience with aerobic training and maximal exercise testing. To better examine the role of sex in this specific study, researchers matched each individual on training regimens and average weekly energy expenditure to limit differences that could influence the results of the study. Each subject performed a maximal exercise test on a cycle ergometer between 12:00 noon and 5:00 pm to limit the time of day and its effect on the testing outcome. During the maximal exercise test, the subjects were asked to press a button when the pain in their legs was “just noticeable” to demarcate the moment that the pain threshold, or the point where pain is noticeable, occurred. Each subject was asked to define their pain intensity using a modified Borg 0 to 10 RPE scale which reworded the verbal anchors to ‘pain’ rather than ‘exertion’, based on the Pain Perception Profile (Turskey, Jammer, Friedman, 1982). The rating of perceived exertion was quantified using a 6 to 20 Borg RPE Scale, and each subject was asked to demarcate their perceived exertion prior to their pain intensity. Prior to subjects reaching their pain threshold subjects were asked to define their RPE and pain intensity every minute. Once the threshold had been reached, each subject was asked for their RPE and pain intensity every 30 seconds until volitional failure occurred. During the recovery period after cessation of the test, subjects were asked to define their RPE and pain intensity every 15 seconds for 3 minutes while expiring in the mouthpiece. The researchers reported there was high variability in the pain threshold value, ranging from 24-95% of the peak power output for men and 10-90% in women. The magnitude of the group differences in measures of leg intensity at the leg muscle pain threshold were small ($d \leq 0.40$). There were main effects for sex (p= 0.009) and exercise intensity (p<.001) as well as a sex x exercise intensity interaction (p= 0.001) at power outputs that every subject was able to complete (98, 110, 122, 134, 146, and 158 watts). It was found via linear regression that differences in the pain ratings did not occur at the lower power outputs across the sexes, but as the absolute exercise intensity increased the pain ratings increased at a faster rate for women than men. These data suggested that at absolute workloads, pain was perceived to be greater in women than men. The pain responses for the relative workloads (% peak power output) indicated main effects for sex (p= 0.002) and exercise intensity (p< 0.001). A significant interaction was shown for sex x exercise intensity (p< 0.001) as well. These data suggested that when expressed via relative workloads of peak power output, women rated pain as less intense than men and the ratings of pain increased slower for women than men. When the RPE values were examined, the were main effects for sex (p=.002) and exercise intensity (p< 0.001) and a significant sex x exercise intensity interaction (p= 0.001). A linear regression analysis demonstrated that women perceived exercises to require more effort at absolute workloads compared to men. When examining RPE values to relative workloads of 60, 70, 80, 90, and 100% of peak power output, there were main effects for sex (p=.002) and exercise intensity (p<.001), but no significant sex x intensity interaction. Women also reported exercise as less effortful at every relative intensity than the men. Overall, these findings suggested that there is not a difference between men and women while examining the pain threshold, which is due largely in part to the variability in the pain thresholds. These findings also suggested that at relative workloads, women experience less muscle pain and experience less perceived exertion. At absolute workloads, women perceived pain and overall exertion to be higher, possibly due to the fact that males performed higher absolute workloads than women. The exact mechanisms underlying the differences in perceived exertion between men and women is unknown.

Garcin et al. (2005)

This study examined the effect of sex on the rating of perceived exertion (RPE) and the estimation of time limit (ETL) during runs to exhaustion at both absolute and relative workloads (Garcin, 2005). Eight male (20.7 ± 3.1 years, 62.9 ± 3.0 kg, 175.5 ± 4.1 cm) and eight female (19.2 ± 1.7 years, 50.0 ± 3.6 kg, 165.7 ± 6.9 cm) subjects who were trained for middle-distance endurance running events (800m to 10,000m) volunteered to participate in this study. Each subject participated in endurance training 3 to 5 times per week for at least 45 minutes per training session for the past 8 years. The subjects partook in a graded exercise test to determine their maximal oxygen uptake ($\dot{V}O_2$ max), the velocity associated with $\dot{V}O_2$ max (v$\dot{V}O_2$ max) and the velocity at the lactate concentration threshold (vLT). To determine these values, each individual performed a graded exercise test around a 200m indoor synthetic track performed to failure. Each individual followed an experimenter cycling at 14 km·h^{-1} and increased in speed by 1 km·h^{-1} every 3 minutes.

Between each stage, the subjects were given a 30 second rest and prompted to rate their rating of perceived exertion (RPE) using a Borg 6-20 RPE scale. Following the collection of the RPE value, each subject was asked their Estimation of Time Limit (ETL), a scale from 1 to 20 with times ranging from 16 hours to 2 minutes as to examine how much longer each individual predicts they could perform the required intensity. This method of graded exercise tests continued until each individual reached 18 $km \cdot h^{-1}$ at which point they increased their velocity 1 $km \cdot h^{-1}$ every two minutes without rest periods until the subject reached failure. The point of failure was determined at the point that the subject was running 5m or more behind the cyclist for a period of more than 100m. During this stage of the test, the subjects rated their RPE and ETL via hand signaling in which a closed fist defined a unit of 10 and an extended finger defined a unit of 1. To accurately collect this data, a second experimenter cycled alongside the subject to define the scales and collect the values reported by the subject. During the course of this run, a portable $\dot{V}O_2$ system (Cosmed®, K4b^2, Italy) was used to measure expired oxygen and inspired carbon dioxide levels. Each subject wore a heart rate monitor during their run and provided blood lactate samples (Dr Lange®, LP20, Germany) during their rest periods in addition to RPE and ETL values. After completing this run, each subject was asked to complete a run to exhaustion 48 hours later at the velocity halfway between the velocity at the $\dot{V}O_2$ max threshold and vLT defined as vΔ50. The researchers found that perceived exertion, estimated time limit, and heart rate were significantly correlated with both absolute and relative velocity ($p < 0.01$). A covariance analysis showed a significant upward slope of the regressions between RPE, ETL, heart rate, and velocity ([F (1,119) = 22.81], [F (1,119) = 12.70], [F (1,119) = 90.68], $p < 0.01$). This data suggested that for a specific absolute velocity ($km \cdot h^{-1}$) women perceived the exercise as more difficult, perceived they could endure less, and reported higher heart rate values than the men. The relationships between RPE, ETL, heart rate, and percent of $v\dot{V}O_2$ max were not significantly different between the male runners and the females ([F (1,119 = 4.89], [F (1,119) = 3.84], [F (1,119) = 6.27], $p > 0.01$). While examining a specific relative velocity, perceived exertion, estimated time limit, and HR values remained the same between the men and women. It was also found that the relationship between ETL and RPE was not significantly different between the males and females ([F (1,119) = 0.07], $p > 0.01$). The ETL values remained the same between the men and women at each RPE value. During the constant run exercise portion of this study, RPE, ETL, and heart rate were significantly correlated with the duration of exercise ($p < 0.05$). During a specific absolute time period, men perceived the exercise as more difficult and felt that they could endure for a shorter duration compared to the females. The relationships between heart rate and time period were not significantly different between the men and women ($p > 0.01$) and the heart rate remained the same between both for a given absolute and relative time period value. Similar to the incremental test, the estimated time limit values remained the same between men and women for a specific RPE value ($p > 0.01$). The $v\dot{V}O_2$ max, $v\Delta50$, maximal oxygen uptake, and vLT were significantly lower and ETL was significantly higher for the female runners compared to the males. There was no significant difference observed between men and women for the HRmax value and the percentage of $v\dot{V}O_2$ max that at the $v\Delta50$. This data led the researchers to suggest that there is a difference in relative intensities and the RPE and ETL for men and women, with women performing longer and at a perceived lower intensity. While the men performed greater absolute workloads and durations, performance differed at the relative workloads. The possible differences in the physiology of fatigue in men and women may contribute to the differences in exercise performance as demonstrated in this study.

Stuart et al. (2018)

This study examined the perceptual responses to fatigue while performing high and low intensity lumbar extension resistance training in men and women. Nine men (Age: 23.8±6.4(yrs); Height: 176.7±6.2(cm); Weight: 73.9±9.3(kg)) and eight women (Age: 21.3±0.9(yrs); Height: 170.5±6.1(cm); Weight: 65.5±10.8 (kg)) who were previously untrained in the lumbar extension participated in this study. The researchers examined the relationship between load, sex, and the fatigue response across 3 different training conditions using an ILEX® machine (MedX, Ocala, FL, USA). A fatigue response test (FRT) was performed for a heavy load (HL; 80% MVC), a light load (LL; 50% MVC), and a control (CON; no training). Each intensity was separated by at least 72 hours and the order was randomized for each subject. During the first visit, the subjects were measured for their range of motion using the ILEX® machine and performed an isometric hold at 72° (defined as full lumbar flexion) and progressing through 60°, 48°, 36°, 24°, 12°, and 0° where the subject would reach full lumbar extension. This was done to provide familiarization of the machine and methodology to the subjects, who were previously untrained in the lumbar extension. At the end of this familiarization period, subjects performed an MVC at each joint angle listed previously. Each subject provided maximal force for 3 seconds and were permitted a 10 second rest period between each angle. After this first session was complete, the subjects returned to the lab at least 72 hours later and were randomly assigned a testing condition of HL, LL, or CON. Each subject performed each intensity in a randomized order and were required to attend the lab a total of 4 times. While performing the FTR, subjects were asked to complete repetitions through the full range of motion as measured previously until failure. Repetitions were performed at a set rate of 2 seconds concentric and 4 seconds eccentric with visual time feedback and verbal encouragement. When subjects began to fatigue, they were allowed to increase repetition duration but could not perform repetitions faster than what was previously determined. Subjects performed at each intensity until volitional exhaustion prevented a full concentric phase movement. Immediately following the failed repetition due to fatigue, each participant performed an MVC at each joint angle mentioned previously (72°, 60°, 48°, 36°, 24°, 12°, and 0°) to examine the change in force production. The researchers discovered a difference in the time-under-load (TUL) between the HL and LL conditions, and required a rest period of 120 seconds for the HL and 30 seconds for the LL to provide similar total time while seated in the dynamometer. For the CON conditions, subjects were seated in the dynamometer for 3 minutes (the average time to complete the fatiguing repetitions and rest periods stated previously for HL and LL) before performing the MVC at each joint angle. Immediately after performing the repetitions to failure and prior to the MVC measurement, subjects were asked for their rating of perceived exertion for effort (RPE-E) and discomfort (RPE-D) using the Borg 1-10 scale to determine the perceptual responses elicited during the fatiguing task. The mixed model ANOVA showed no significant effects for condition in the pre-MVC force ($p=0.342$) or interaction effects for condition x group ($p=0.217$). There was a significant effect for group ($p=0.005$; Males: 373.1±20.7; Females: 274.3±22). When examining absolute fatigue, there was a significant effect for condition ($p<0.001$), group ($p=0.012$) and condition x group ($p=0.011$). A post hoc comparison revealed significant differences between the CON and both the HL (p<0.001) and LL (p<0.001) conditions, as well as between the HL and LL (p=0.001). The absolute changes in MVC for men in the CON, HL, and LL (5.59±20.7; -77.1±41.9; -128.8±41.4; Nm, respectively) were greater than for women (-2.55±25.5; -32.6±39.4; -70.7±29.6 Nm; respectively). Each group demonstrated a decrease in MVC following an exercise bout, while the CON condition demonstrated a small increase in men and a small decrease in women. There was a significant effect by condition (p<0.001) when examining relative fatigue, but not for group (p=0.160) or condition x group (p=0.068). The relative changes in the MVC for men in the CON, HL, and LL (1.3±5.9; -21.3±9.8; -33.3±9.9 %, respectively) were shown to be greater than in women (-0.5±9.7; -10.6±14.0; -25.9±8.4 %, respectively). Similar to the absolute changes, each group had a relative decrease in MVC for each condition, with the CON condition providing a slight increase in men and a slight decrease in women. There was a significant effect for condition (p<0.001) but not group (p=0.076) or condition x group (p=0.103) for the TUL. A Wilcoxon signed ranked test revealed a significant difference between condition for RPE-D (Males: [HL:6.33±0.71; LL:8.0±0.71]; Females: [HL:6.25±0.71; LL:8.25±0.71]; p<0.001; Z=-3.568), while a Mann Whitney U test did not reveal a significant difference between each sex for either HL (Z=-0.264; p=.791) or LL (Z=-0.742; p=0.458). The measured RPE-E values reached maximal (10 out of 10) at the moment of failure to complete the concentric phase of the repetition in both men and women and no statistical tests were run using this data. Due to these findings, the researchers suggested that there are load-dependent differences and sex-based differences in fatigue responses during lumbar extension exercise performed until failure. The recorded perceived intensity and discomfort were higher for LL than HH, but were not different between men and women, while the measure of physiological fatigue (MVC changes pre/post) were greater for men than women. This study suggested than men and women perceived lumbar extension exercise to require similar levels of exertion and discomfort despite different levels of physiological fatigue at failure. This study also demonstrated that women are able to perform higher MVC values after a fatiguing work bout and may either recover from fatigue at a quicker rate than men or experience less drastic decreases in force production after a fatiguing bout. The researchers suggest that since women may not incur the same degree of fatigue as males while performing similar protocols, women may require higher repetitions or higher relative loads to elicit similar training responses in men. The authors suggest that although fatigue responses to resistance training differ between men and women, the differences in recovery are not clear and may be affected by changes in the training volume women may perform to elicit similar adaptations as men.

Summary of Sex Related Differences in Rating of Perceived Exertion

It has been reported that men and women may demonstrate different rates and levels of fatigue during exercise, depending on the mode, intensity, and during of the exercise (Cook et al. (1998); Garcin et al. (2005); Stuart et al. (2018). However, there is limited evidence examining the difference in the perceptual responses elicited during various fatiguing exercises in men and women. Cook et al. (1998), Garcin et al. (2005), and Stuart et al. (2018) examined the differences of perceived exertion required to complete cycle ergometry, high intensity running, and resistance training in men and women, respectively.

During cycle ergometry at relative workloads of each subject’s peak power, women rated pain as less intense, and pain increased at a slower rate than the men (Cook et al.

1998). Conversely, the women perceived that absolute workloads required more exertion and elicited a greater pain response than in the men (Cook et al. 1998). This phenomenon may be due to the men performing higher absolute workloads than women during the testing (Cook et al. 1998). These data corresponded with the findings of Garcin et al. (2005) during high intensity running to failure. When performed across a specific absolute time period, men perceived the running as more difficult and estimated that they could endure the exercise for a shorter duration than the women (Garcin et al. 2005). During these tests, there was a correlation in the time to exhaustion and the RPE values in both men and women without a significant difference between the groups, validating the scale and providing reference to the exertion level between the groups (Garcin et al. 2005). The absolute exercise intensity for the run, the vΔ50, was lower in women than in men and at a specific absolute exercise intensity, women perceived exertion to be higher (Garcin et al. 2005). This finding was consistent with the findings of Cook et al. (1998), suggesting that in both aerobic cycle ergometry and aerobic running exercises women performed lower absolute workloads and found the absolute workloads to elicit a greater RPE value. Relative workloads for men and women elicit a different response, however, as women rate their perceived exertion and muscular pain as lower, while estimating a longer time to failure in these aerobic modalities (Cook et al. 1998; Garcin et al. 2005).

Stuart et al. (2018) examined the perceptual responses elicited by men and women during lumbar extension resistance exercise. For both MVIC and holds performed at specific intensities until failure on a dynamometer, there were load-dependent and sex-dependent differences in fatigue response (Stuart et al. 2018). Across both groups, there was a greater RPE response during the low load exercise than the high load exercise, possibly due to the greater total work performed at the lower load (Stuart et al 2018). Stuart et al. (2018) examined the decrease in MVIC after performing the repetitions to failure at various intensities and found that women were able to perform a higher MVIC value after their fatiguing work bout than men. Despite this difference in post-performance MVIC, there were no differences shown between men and women in lumbar extension RPE values. This suggested that while men and women perceived the exertion to be similar, they experienced different levels of physiological fatigue (Stuart et al. 2018).

The perceived exertion data collected by Cook et al. (1998), Garcin et al. (2005), and Stuart et al. (2018) suggested physiological differences in fatigue exist for both men and women although the exact mechanisms are unknown. This difference in performance and perceived exertion during fatiguing exercises at both relative and absolute workloads lend support for the implementation of different training prescription for men and women (Stuart et al. 2018). During both aerobic and anerobic exercises, men were able to complete greater absolute workloads while fatiguing at a faster rate than women (Cook et al. 1998; Garcin et al. 2005; Stuart et al. 2018). Despite performing lower absolute workloads than men, women were able to perform longer, with less perceived exertion, and were able to mitigate the fatigue response more efficiently than males (Cook et al. 1998; Garcin et al. 2005; Stuart et al. 2018).

CHAPTER 3. METHODS

3.1 Experimental Approach and Design

This study used an experimental, randomized crossover design to examine the effects of unilateral forearm muscle fatigue during handgrip holds to failure (HTF) for the dominant (Dm) and non-dominant (NDm) limb on ipsilateral (IPS = exercised side) and contralateral (CON = non-exercised side) performance fatigability and the associated perceptual responses. The subjects visited the lab a total of three times, with at least 24 hours separating each visit. During visit 1, the subjects completed a familiarization of the MVIC and fatigue tests, including 2-4, 6 second MVICs using a handgrip dynamometer and a familiarization for the HTF fatigue tests. During visits 2 and 3, the subjects performed a single, randomized, Dm or NDm, handgrip HTF at 50% of the MVIC force. Prior to, and immediately after the HTF, a MVIC was performed on the IPS and CON sides. The fatigue test (Dm or NDm) was randomized between visits and the side tested first (IPS and CON) was randomized for pre-and post-tests within each visit. Each subject provided RPE values according to the OMNI-RES RPE scale for the overall sensations of exertion in the entire body (RPE-O), and for active muscle specific exertion (RPE-AM) in the forearms. Additionally, the muscular specific pain was measured on the Numerical Pain Rating scale for the overall sensations of pain in the entire body (NPR-O), and for active muscle specific pain (NPR-AM) in the forearms immediately after the measurement of the OMNI-RES RPE values.

3.2 Subjects

Ten men (Age: 22.6 yrs; Height: 182.0 cm; Weight: 82.9 kg) and 10 women (Age: 21.7; Height: 166.8 cm; Weight: 67.1 kg) between 18 and 35 years of age were recruited for this study. The subjects were familiar with resistance training exercise and had been resistance training at least 3 times per week for the past year. In addition, subjects were only included if they had no known cardiovascular, metabolic, or musculoskeletal diseases or disorders, particularly in the shoulder, arm, elbow, forearm, or wrist. The subjects were asked to maintain their current level of physical activity, but to abstain from upper body resistance exercise at least 24 hours prior to their testing session. Subjects were only included if they meet the criteria above regarding age, training status, and health history. All of the subjects completed a health history questionnaire and signed a written informed consent document before participation in this study. This study was approved by the University's Institutional Review Board for Human Subjects.

3.3 Description of Instruments, Measurements, and/or Apparatus

The instruments for this study included the handgrip dynamometer (iWorx Systems Inc.; Dover, NH 03820), OMNI-RES RPE scale and the Numerical Pain Rating scale (NPR), which were both a 0-10 category scale. The handgrip dynamometer was used to determine the absolute grip strength of the subjects and to examine the time to failure for the HTF. The OMNI-RES RPE scale was used to define the perceived exertion across the Dm and NDm HTF trials performed in the study. This RPE scale was developed to measure the perceived intensity during resistance training exercises and has been shown to be valid and reliable relative to the original Borg 6-20 perceived intensity scale for aerobic training (Borg 1970; Foster et al. 2001; Sweet et al. 2004; Robertson et al. 2003). The NPR scale has been shown effectively quantify both pain stimulus intensity and perceptions of pain between men and women during exercise and is a valid and reliable measure to quantify elicited pain during muscular exercise (Ferreira-Valente et al. 2011).

3.4 Procedures

3.4.1 Maximal Voluntary Isometric Contraction Handgrip Force and Hold to Failure

During visits 1-3 of this study, the subjects performed 2-4, 6 sec pre-HTF MVIC with the IPS and CON side using a handgrip dynamometer (FT-220 hand dynamometer, iWorks, Dover, NH 03820). The handgrip MVIC holds and HTF were performed in a 90° forearm flexion position with the hand supinated (Richards et al. 1996; Alkurdi et al. 2010). Only two MVIC tests were performed per hand if the MVIC force (kg) values are within 5% of one another. Additional MVIC tests were performed until two values were recorded that did not differ by greater than 5% (Clark et al. 2005; Yoon et al. 2007). All of the subjects obtained 2 MVIC values within 5% of one another within 4 tests. The highest instantaneous force value for 2 of the 2-4 tests was used as the pre-HTF MVIC value. The pre-HTF MVIC values for visits 1-3 were used to determine reliability of the measure. The pre-HTF MVIC values measured for visit 2 and 3 were used to examine performance fatigability. A 5-min rest was provided after the MVIC tests. The subjects then performed a single, fatiguing HTF for the Dm or NDm hand at 50% of the IPS MVIC force until volitional fatigue or until the force dropped by greater than 5% of the target force for more than 5 seconds. Immediately following the HTF, the post-HTF MVIC force was determined for the IPS and CON hands. The HTF test (Dm or NDm) was randomized between visits 2 and 3 and the side tested first (IPS and CON) was randomized for pre-and post-HTF tests within each visit. The highest instantaneous force value for the IPS and CON MVIC as well as the total time for the HTF at 50% of MVIC were recorded and used in subsequent analyses. The performance fatigability was defined as a percent change (%Δ) from the pre-test to the post-test MVC values.

3.5 Perceptual Scales

Following the performance of the handgrip MVC tests and handgrip HTF at 50% MVIC force, the ratings of perceived exertion and physical pain were measured via the OMNI-RES RPE scale and the Numerical Pain Rating (NPR) Scale, respectively. The measurement of the rating of perceived exertion in the active muscle(s) (RPE-AM) was recorded within 10 sec after the completion of the pre- and post-HTF MVIC tests and after the 50% MVIC HTF on the OMNI-RES scale (Robertson et al. 2003). Immediately following the assessment of RPE-AM, the RPE of the overall body (RPE-O) was assessed (Robertson et al. 2003). Following the assessment of the RPE, the NPR scale was used to assess the muscular pain involved in the active muscle (NPR-AM) and the overall body (NPR-O).

To establish high and low anchors to the perceptual scales, the subjects performed a visual-cognitive procedure following the warm-up and prior to the completion of each trial (Robertson et al. 2003). The subjects were asked to envision an intensity that requires a level of physical exertion that corresponded to the exertion intensity to the visually depicted weightlifter on the bottom (0 rating) and the apex (10 rating) of the OMNI-RES scale (Robertson et al. 2003). The subjects were encouraged to recall the exertion required to perform their lowest and greatest intensity resistance training exercise to assist in their

RPE estimation (Robertson et al. 2003). To provide anchoring for the NPR scale, the subjects were encouraged to recollect the greatest pain experienced during physical exercise (10 rating) and the lowest pain experienced during physical exercise (0 rating).

The following scaling and perceived exertion definitions were read prior to the RPE OMNI-RES: Perception of physical exertion was defined as the "the conscious sensation of how hard, heavy, and strenuous a physical task is" (Marcora & Staiano 2010 (380)) (Noble and Robertson, 1996; Pageaux & Gaveau 2016 (pg. 3)). The following instructions were read prior to each testing session:

> "Instructions: We would like you to use these pictures to describe how your body feels during weightlifting exercise (showed subject the OMNI-RES). You are going to perform resistance exercises using your upper body. Please look at the person at the bottom of the scale who is performing a repetition using a light weight. If you feel like this person when you are lifting weights the exertion will be EXTREMELY EASY. In this case, you would respond with the number zero. Now look at the person at the top of the scale who is barely able to perform a repetition using a very heavy weight. If you feel like this person when you are lifting weights the exertion will be EXTREMELY HARD. In this case, you would respond with the number 10. If you feel somewhere in between Extremely Easy (0) and Extremely Hard (10), then give a number between 0 and 10. We will ask you to give a number that describes how your active muscles feel and then a number that describes how your whole body feels. Remember, there are no right or wrong numbers. Your number can change as you lift weights. Use both the pictures and

> the words to help select the numbers. Use any of the numbers to describe how you feel when lifting weights." (Robertson et al. 2003 (pg. 336)).

Pain intensity was assessed using a 0-10 category scale, the NPR Scale. This scale provides a range of scores equally separated on a visual analog scale increasing from left to right from 0 to 10, with the number 0, 5, and 10 placed along the line. As the numerical values increase, the shading of the line in which the numbers reside is gradually darkened from pure white to pitch black. Below the scale, there is a verbal anchor of "No Pain" placed at 0, "Moderate Pain" at 5, and "Worst Possible Pain" at 10. The individual perceptual anchoring was done via a visual-cognitive procedure as described above (Robertson et al. 2003). The following instructions were read prior to the administration of the NPR Scale:

> Instructions: "The scale before you contains the numbers 0 to 10 (Showed the NPRS). You will use this scale to assess the perceptions of pain in your muscles during the exercise test. For this task, pain is defined as the intensity of hurt that you feel in your muscles only. Do not underestimate or overestimate the degree of hurt you feel, just try to estimate it as honestly and objectively as possible. The numbers on the scale represent a range of pain intensity from "No pain" (number 0) to "Worst Possible Pain" (number 10). When you feel no pain in your muscles, you should respond with the number 0. If you feel extremely strong pain that is almost unbearable, you should respond with the number 10. Following the completion of the set, you will be asked to rate the feelings of pain in your muscles. When rating these pain sensations, be sure to attend only to the specific sensations in exact muscle the researcher inquiries about, and not report other pains you may

> be feeling (e.g., shin abrasion pain). It is very important that your ratings of pain intensity reflect only the degree of hurt you are feeling in the muscle. Do not use your ratings as an expression of fatigue (i.e., inability of the muscle to produce force) or exertion (i.e., how much effort you are putting into performing the exercise).” (O’Connor & Cook 2001 (pg. 1047-1048)[adapted]).

3.6 Statistical Analyses

The reliability of the pre-fatigue MVICs was examined separately for the Dm and NDm limb using intra-class correlation coefficients ($ICC_{2,1}$), standard errors of the measurement (SEM), and coefficients of variation (CoV) (Weir 2005). The range of ICC values for categorizing into reliability descriptors were set at: “excellent” (ICC = 0.75 – 1.00), “good” (ICC = 0.60 – 0.74), “fair” (0.40 – 0.59), and ‘poor’ (< 0.40) (Cicchetti and Sparrow, 1981). The reliability of the HTF time, measured during the familiarization and either visit 2 or 3, was determined from a subset of subjects (n = 17; Men: n = 10; Women: n = 7) for the Dm hand only. In addition, analyses were performed to examine the handgrip MVIC kg values for the IPS and CON sides as well as time to failure at 50% MVIC for the Dm and NDm condition. The perception of exertion and pain were also examined using the ONMI-RES RPE and NPR scales, respectively. The time for the HTF was examined using a 2 (condition [Dm, NDm] x 2 (sex [men, women]) mixed model ANOVA. A 2 (condition [Dm, NDm]) x 2 (sex [men, women]) x 2 (side [IPS, CON]) x 2 (time [pre-HTF, post-HTF]) mixed model ANOVA was used to examine the MVIC kg force. Separate, 2(Condition [Dm, NDm]) x 2(Sex [men, women]) mixed model ANOVAs were used to examine the RPE-AM, RPE-O, NPR-AM, and NPR-O responses immediately after the HTF. *A priori* planned comparisons of the performance fatigability (%Δ = ((pre-HTV

MVIC – post-HTF MVIC) / pre-HTV MVIC)*100)) following the HTF between men and women were examined based on the 2 (condition [Dm, NDm]) x 2 (sex [men, women]) x 2 (side [IPS, CON]) x 2 (time [pre-HTF, post-HTF]) mixed model ANOVA used to examine the MVIC kg force. Separate, 2 (condition [Dm, NDm]) x 2 (sex [men, women]) x 2(time [pre-HTF, post-HTF]) x 2(Side [IPS, CON]) mixed model ANOVAs were used to examine the RPE-OMNI-RES and NPR scale responses for the active muscle and overall body. Follow up analyses consisted of 3-, and 2-way mixed model and repeated measure ANOVAs and pairwise comparisons. The 95% confidence intervals for mean comparisons were constructed and measures of effect size were calculated using partial eta squared and Cohen's *d*. The alpha level was set at $p \leq 0.05$ for all analyses. Analyses were performed using IBM SPSS Statistics 24 software (IMB SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel®.

CHAPTER 4. RESULTS

4.1 Reliability – Pre-HTF and HTF Time

The descriptive characteristics of the subjects are presented in Table 4.1. The reliability of the pre-HTF MVIC force (kg) was examined separately for the Dm and NDm limb, across visits 1-3. There was no systematic error ($F(2,38) = 0.129$; $p = 0.879$; $p\eta^2 = 0.007$) for the pre-HTF MVIC in the dominant limb and the MVIC demonstrated “excellent” test-retest reliability (ICC = 0.936; $p < 0.001$; 95% CI [0.871, 0.972]). The SEM was 2.7 kg with an MD of 7.6 kg, and a CoV of 6.6% (Table 4.2.). There was no systematic error ($F(2,38) = 0.403$; $p = 0.671$; $p\eta^2 = 0.021$) for the pre-HTF MVIC in the non-dominant limb and the MVIC demonstrated “excellent” test-retest reliability (ICC = 0.938; $p < 0.001$; 95% CI [0.876, 0.973]). The SEM was 3.0 kg with an MD of 8.3 kg, and a CoV of 7.4% (Table 4.2.).

A subset of subjects (Men: n=10; Women: n=7) were used to examine the reliability of the time to task failure for the HTF of the dominant limb. Each HTF was completed twice for the dominant limb, during visit 1 and either visit 2 or 3. There was no systematic error ($F(1,16) = 0.007$; $p = 0.936$; $p\eta^2 = 0.000$) and the HTF of the dominant limb demonstrated “fair” test-retest reliability (ICC = 0.553; $p = 0.011$; 95% CI [0.099, 0.813]). The SEM was 46.6 seconds with an MD of 129.1 seconds, and a CoV of 36.2% (Table 4.3.).

4.2 Hold to Failure – Time to Failure

There was no 2(condition: Dm vs NDm) x 2(sex: men vs women) significant interaction ($F(1,18) = 1.940$; $p = 0.181$; $p\eta^2 = 0.097$) and no main effect for sex ($F(1,18) =$

0.620; $p = 0.441$, $p\eta^2 = 0.033$), but there was a main effect for condition ($F(1,18) = 12.638$; $p = 0.002$; $p\eta^2 = 0.412$) for the total time for the HTF. The mean time (collapsed across sex) for Dm limb HTF (130.3 ± 36.8 seconds) was significantly longer ($p = 0.002$; mean diff = 18.3 ± 23.52s; 95% CI = 7.5s – 29.0s; *d* = 0.50) than the NDm limb HTF (112.1 ± 34.3 seconds) (Table 4.4.).

4.3 MVIC Force

A four-way mixed model ANOVA of 2(Condition: Dm vs NDm) x 2(Side: IPS vs CON) x 2(Time: Pre vs Post) x 2(Sex: Men vs Women) demonstrated no significant interactions for condition x side x time x sex ($F(1,18) = 1.316$, $p = 0.259$, $p\eta^2 = 0.070$), condition x side x time ($F(1,18) = 1.413$, $p = 0.250$, $p\eta^2 = 0.073$), side x time x sex ($F(1,18) = 3.309$, $p = 0.086$, $p\eta^2 = 0.155$), or condition x time x sex ($F(1,18) = 0.410$, $p = 0.530$, $p\eta^2 = 0.022$), but a significant interaction for condition x side x sex ($F(1,18) = 4.511$, $p = 0.048$, $p\eta^2 = 0.200$). Additionally, there were no significant interactions for condition x sex ($F(1,18) = 0.822$, $p = 0.376$, $p\eta^2 = 0.044$), side x sex ($F(1,18) = 2.147$, $p = 0.160$, $p\eta^2 = 0.107$), condition x side ($F(1,18) = 1.888$, $p = 0.186$, $p\eta^2 = 0.095$), condition x time ($F(1,18) = 0.368$, $p = 0.552$, $p\eta^2 = 0.020$), or time x sex ($F,18) = 0.586$, $p = 0.454$, $p\eta^2 = 0.032$), but there was a significant interaction for side x time ($F(1,18) = 162.697$, $p \leq 0.001$, $p\eta^2 = 0.900$). There was also a main effect for sex ($F(1,18) = 22.626$, $p < 0.001$, $p\eta^2 = 0.557$) that indicated the MVIC was greater ($p \leq 0.001$, mean diff: 15.552 ± 3.269) for the men (46.07 ± 10.64 kg; 95% CI [41.214, 50.928]) than the women (30.52 ± 6.93 kg; 95% CI [25.662, 35.376]), when collapsed across condition, side, and sex. Because all four factors were involved in an interaction, the model was decomposed with separate 2(Condition: Dm vs NDm) x 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the men and women.

The follow-up three-way repeated measures ANOVA of 2(Condition: Dm vs NDm) x 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the men (n =10) demonstrated no significant 3-way interaction (F(1,9) = 1.498, p = 0.252, $p\eta^2 = 0.143$) or 2-way interactions for condition x side (F(1,9) = 0.189, p = 0.674, $p\eta^2 = 0.021$) or condition x time (F(1,9) = 0.000, p = 0.986, $p\eta^2 = 0.000$). There was a significant interaction for side x time (F(1,9) = 76.2, $p \leq 0.001$, $p\eta^2 = 0.000$). The IPS pre-HTF MVIC force (collapsed across condition) (48.4 ± 9.0 kg) was greater than (t = 6.891; $p \leq 0.001$; mean diff: 10.7 ± 5.0; 95% CI [7.2, 14.2]; *d* = 0.99) the IPS post-HTF MVIC (37.6 ± 10.2 kg) (%Δ = 22.9 ± 10.8%). The CON pre-HTF MVIC (47.9 ± 9.5 kg) was less than (t = -2.676; p = 0.025; mean diff: -2.8 ± 3.0; 95% CI [-4.7, -0.4]; *d* = -0.29) the CON post-HTF MVIC (50.4 ± 8.7 kg) (%Δ = -6.1 ± 6.9%). There was no difference (t = 0.726; p = 0.486; mean diff: 0.5 ± 2.1; 95% CI [-1.0, 2.0]; *d* = 0.05) between the IPS pre-HTF MVIC and the CON pre-HTF MVIC, but the IPS post-HTF MVIC was less than (t = -8.822; $p \leq 0.001$; mean diff: -12.1 ± 4.6; 95% CI [-16.1, -9.5]; *d* = -1.13) the CON post-HTF MVIC (Figure 4.1).

The follow-up three-way repeated measures ANOVA of 2(Condition: Dm vs NDm) x 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the women (n = 10) demonstrated no significant 3-way (F(1,9) = 0.002, p = 0.968, $p\eta^2 = 0.000$) or 2-way condition x time (F(1,9) = 4.774, p = 0.057, $p\eta^2 = 0.347$) interactions. However, there were significant 2-way interactions for side x time (F(1,9) = 98.631, $p \leq 0.001$, $p\eta^2 = 0.916$) and condition x side (F(1,9) = 12.003, p = 0.007, $p\eta^2 = 0.571$). Because all three factors were involved in an interaction, the model was decomposed with separate 2(Side: IPS vs CON) x 2(Time: Pre vs Post) repeated measures ANOVAs for the Dm and NDm limb.

The follow-up two-way repeated measure ANOVA of 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the Dm limb demonstrated a significant interaction (F(1,9) = 79.975, $p \leq 0.001$, $p\eta^2 = 0.899$). The IPS pre-HTF MVIC (34.1 ± 5.0 kg) was greater than (t = 7.424; $p \leq 0.001$; mean diff: 9.7 ± 4.1; 95% CI [6.7, 12.6]; *d* = 1.43) the IPS post-HTF MVIC (24.4 ± 4.3 kg) (%Δ = 28.0 ± 9.4%), but the CON pre-HTF MVIC (31.6 ± 6.7 kg) was not different (t = -0.619; p = 0.551; mean diff: -0.33 ± 1.7; 95% CI [-1.6, 0.9]; *d* = -0.05) from the CON post-HTF MVIC (32.0 ± 5.9 kg) (%Δ = -1.6 ± 5.7%). The IPS (i.e., Dm limb) pre-HTF MVIC was greater than (t = 2.575; p = 0.030; mean diff: 2.4 ± 3.0; 95% CI [0.297, 4.59]; *d* = 0.41) the CON (i.e., NDm limb) pre-HTF MVIC. In addition, the IPS post-HTF MVIC was less than (t = -5.829; $p \leq 0.001$; mean diff: -7.55 ± 4.09; 95% CI [-10.48, -4.62]; *d* = -1.2) the CON post-HTF (Figure 4.2).

A follow-up two-way repeated measure ANOVA of 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the NDm limb demonstrated a significant interaction (F(1,9) = 99.91, $p \leq 0.001$, $p\eta^2 = 0.917$). The IPS pre-HTF MVIC (32.3 ± 6.5 kg) was greater than (t = 7.073; $p \leq 0.001$; mean diff: 10.61 ± 4.74; 95% CI [7.21, 13.998]; *d* = 1.38) the IPS post-HTF MVIC (21.7 ± 4.6 kg) (%Δ = 32.3% ± 10.1%). The CON pre-HTF MVIC (34.3 ± 5.6 kg) was not different from (t = 0.939; p = 0.373; mean diff: 0.64 ± 2.16; 95% CI [-0.91, 2.19]; *d* = 0.12) the CON post-HTF MVIC (33.7 ± 5.3 kg) (%Δ = 1.7 ± 5.9%). The IPS (i.e., NDm limb) pre-HTF MVIC was less than (t = -2.537; $p \leq 0.001$; mean diff: -1.95 ± 2.43; 95% CI [-3.69, -0.219]; *d* = -0.33) the CON (i.e., Dm limb) pre-HTF MVIC. In addition, the IPS post-HTF MVIC was less than (t = -16.25; $p \leq 0.001$; mean diff: -11.92 ± 2.32; 95% CI [-13.57, -10.26]; *d* = -1.54) the CON post-HTF (Figure 4.3).

4.4 Performance Fatigability

The *a priori* planned comparisons for the performance fatigability indicated that there was no difference in the %Δ between the men (22.9 ± 10.8%; collapsed across Dm and NDm HTF condition) and the women (28.0 ± 9.4%) for the IPS side, Dm HTF condition (t = -1.12; p = 0.277; mean diff: -5.1 ± -4.55; 95% CI [-14.65, 4.55]; *d* = -0.50) or between the men (22.9 ± 10.9%; collapsed across Dm and NDm HTF condition) and the women (32.3 ± 10.1%) for the IPS side, NDm HTF condition (t = -2.01; p = 0.060; mean diff: -9.43 ± -4.70; 95% CI [-19.29, 0.44]; *d* = -0.69). The Dm and NDm HTF condition on the IPS side for women demonstrated differences in performance fatiguability (t = -2.634; p = 0.027; mean diff: -4.33 ± -5.20 ; 95% CI [-8.05, -0.61]; *d* = -0.44). In addition, for the %Δ on the non-exercised, CON side, there was no difference between the men (-6.1 ± 6.9%; collapsed across Dm and NDm HTF condition) and the women (-1.57 ± 5.74%) in the Dm condition (t = -1.62; p = 0.123; mean diff: -4.65 ± 2.87; 95% CI [-10.69, 1.39]; *d* = 0.10). Alternatively, the men (-6.1 ± 6.9%) demonstrated a greater %Δ (facilitation of the CON limb) compared to the women (1.7 ± 5.9%)) in the NDm condition (t = -2.72; p = 0.014; mean diff: -7.90 ± 2.90; 95% CI [-13.998, -1.80]; *d* = -0.23).

4.5 Perceptual Responses

4.5.1 *Hold to Failure*

Separate 2-way repeated measures ANOVA of 2(Condition: Dm vs NDm) x 2(Sex: M vs W) were used to examine the RPE-AM, RPE-O, NPR-AM, and NPR-O responses immediately after the HTF. For the RPE-AM, there was no significant interaction for condition x sex (F(1,18) = 0.000, p = 1.000, $p\eta^2 = 0.000$) or main effect for condition (F(1,18) = 0.367, p = 0.522, $p\eta^2 = 0.000$), but there was a main effect for sex (F(1,18) =

5.497, p = 0.031, pη^2 = 0.234). The RPE-AM was greater (mean diff = 1.8 ± 2.9; 95% CI [0.19, 3.41]; *d* = 0.94) for the men (9.2 ± 1.1) compared to the women (7.4 ± 2.2) (Table 4.5.).

The RPE-O measures demonstrated no significant interaction for condition x sex (F(1,18) = 0.422, p = 0.524, pη^2 = 0.023) and no significant main effects for condition (F(1,18) = 0.152, p = 0.701, pη^2 = 0.008) or sex (F(1,18) = 0.472, p = 0.501, pη^2 = 0.026). The RPE-O, collapsed across sex and condition, was 3.0 ± 2.2 (Table 4.5.).

The NPR-AM measures demonstrated no significant interaction for condition x sex (F(1,18) = 0.476, p = 0.499, pη^2 = 0.026) and no significant main effects for condition (F(1,18) = 0.053, p = 0.821, pη^2 = 0.003) or sex (F(1,18) = 0.644, p = 0.433, pη^2 = 0.035). The NPR-AM, collapsed across sex and condition, was 4.8 ± 2.6 (Table 4.5.).

The NPR-O measures demonstrated no significant interaction for condition x sex (F(1,18) = 0.031, p = 0.862, pη^2 = 0.002) and no significant main effect for condition (F(1,18) = 0.031, p = 0.862, pη^2 = 0.002), or sex (F(1,18) = 0.116, p = 0.737, pη^2 = 0.006). The NPR-O, collapsed across sex and condition, was 1.2 ± 1.7 (Table 4.5.).

4.5.2 *Pre- and Post-MVIC*

4.5.2.1 RPE-AM

The four-way mixed model ANOVA indicated no significant 2(Condition: Dm vs NDm) x 2(Side: IPS vs CON) x 2(Time: Pre vs Post) x 2(Sex: Men vs Women) interaction (F(1,18) = 0.095, p = 0.762, pη^2 = 0.005) and no significant interactions for condition x side x time (F(1,18) = 0.307, p = 0.587, pη^2 = 0.017), condition x time x sex (F(1,18) = 1.023, p = 0.325, pη^2 = 0.054), or condition x side x sex (F(1,18) = 0.774, p = 0.391, pη^2 =

0.041). There was a significant interaction for side x time x sex (F(1,18) = 8.566, p = 0.009, $p\eta^2 = 0.322$).

The follow-up analyses indicated significant interactions for side x time (F(1,18) = 17.407, p = 0.001, $p\eta^2 = 0.492$) and side by sex (F(1,18) = 9.722, p = 0.006, $p\eta^2 = 0.351$) but not for time x sex (F(1,18) = 0.724, p = 0.406, $p\eta^2 = 0.039$). The follow-up analyses included separate 2-way repeated measures ANOVAs for 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the men and women.

A 2-way repeated measures ANOVA of 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the men (n=10) demonstrated no significant 2-way interaction for side x time (F(1,9) = 0.625, p = 0.804, $p\eta^2 = 0.393$. No main effect was demonstrated for side (F(1,9) = 1.550, p = 0.245, $p\eta^2 = 0.147$), but a main effect was demonstrated for time (F(1,9) = 14.778, p = 0.004, $p\eta^2 = 0.622$). The Post-HTF RPE-AM (6.8 ± 2.1) was greater than (t = -3.844; p = 0.004; mean diff: -0.85 ± 0.70; 95% CI [-1.35, -0.35]; *d* = 0.39) the Pre-HTF RPE-AM (5.9 ± 2.1).

A 2-way repeated measures ANOVA of 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the women (n=10) demonstrated a significant 2-way interaction for side x time (F(1,9) = 24.347, p = 0.001, $p\eta^2 = 0.730$). The IPS Post-HTF RPE-AM (6.2 ± 2.6) was greater than (t = -4.045; p = 0.003; mean diff: -2.70 ± 2.11; 95% CI [-4.21, -1.19]; *d* = -0.86) the IPS Pre-HTF RPE-AM (3.5 ± 3.1). The CON Pre-HTF RPE-AM (3.4 ± 3.0) was not different from (t = 0.429; p = 0.678; mean diff: 0.15 ± 0.35; 95% CI [-0.64, 0.94]; *d* = 0.05) the CON Post-HTF RPE-AM (3.3 ± 2.8). The IPS Pre-HTF RPE-AM was not different than (t = 0.318; p = 0.758; mean diff: 0.05 ± 0.50; 95% CI [-0.31, 0.41]; *d* = 0.02) the CON Pre-HTF RPE-AM. The IPS Post-HTF RPE-AM was greater than (t = 5.209; p = 0.001; mean diff: 2.90 ± 1.76; 95% CI [1.64, 4.16]; *d* = 0.95) the CON Pre-HTF RPE-AM.

4.5.2.2 RPE-O

A four-way mixed model ANOVA of 2(Condition: Dm vs NDm) x 2(Side: IPS vs CON) x 2(Time: Pre vs Post) x 2(Sex: Men vs Women) for the RPE-O responses demonstrated no significant interactions for condition x side x time x sex (F(1,18) = 0.365, p = 0.553, $p\eta^2 = 0.020$), condition x side x time (F(1,18) = 0.822, p = 0.376, $p\eta^2 = 0.044$), side x time x sex (F(1,18) = 4.130, p = 0.057, $p\eta^2 = 0.187$), condition x side x sex (F(1,18) = 1.108, p = 0.307, $p\eta^2 = 0.058$), and condition x time x sex (F(1,18) = 0.034, p = 0.856, $p\eta^2 = 0.002$. Additionally, no significant interactions were shown for condition x time (F(1,18) = 1.216, p = 0.285, $p\eta^2 = 0.063$), condition x side (F(1,18) = 1.508, p = 0.235, $p\eta^2 = 0.077$, time x sex (F(1,18) = 0.176, p = 0.679, $p\eta^2 = 0.010$), and condition x sex (F(1,18) = 0.029, p = 0.866, $p\eta^2 = 0.002$), but side x time (F(1,18) = 13.054, p = 0.002, $p\eta^2 = 0.420$) and side x sex (F(1,18) = 4.976, p = 0.039, $p\eta^2 = 0.217$) demonstrated a significant interaction. Because all side, time, and sex were all involved in an interaction, the model was decomposed with separate 2-way repeated measures ANOVAs for 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the men and women.

A 2-way repeated measures ANOVA of 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the men (n=10) demonstrated no significant 2-way interaction for side x time (F(1,9) = 1.830, p = 0.209, $p\eta^2 = 0.169$. There was no main effect for side (F(1,9) = 3.645, p = 0.089, $p\eta^2 = 0.288$), but there was a main effect for time (F(1,9) = 7.979, p = 0.020, $p\eta^2 = 0.470$). The Post-HTF RPE-O (collapsed across side) (1.6 ± 1.3) was greater than (t =

2.83; $p \leq 0.002$; mean diff: 0.63 ± 0.70; 95% CI [0.12,1.13]; *d* = 0.56) the Pre-HTF RPE-O (1.0 ± 0.8).

A 2-way repeated measures ANOVA of 2(Side: IPS vs CON) x 2(Time: Pre vs Post) for the women (n=10) demonstrated a significant 2-way interaction for side x time (F(1,9) = 12.097, p = 0.007, $p\eta^2 = 0.573$. The IPS Post-HTF RPE-O (2.0 ± 1.8) was greater than (t = 2.482; p = 0.035; mean diff: 1.45 ± 1.85; 95% CI [0.13,2.77]; *d* = 0.97) the IPS Pre-HTF RPE-O (0.5 ± 0.6). The CON Post-HTF RPE-O (0.7 ± 1.0) was not different than (t = 0.712; p = 0.494; mean diff: 0.20 ± 0.89; 95% CI [0.44, 0.84]; *d* = 0.25) the CON Pre-HTF RPE-O (0.5 ± 0.5). The IPS Pre-HTF RPE-O was not different than (t = 0.00; p = 1.00; mean diff: 0.00 ± 0.41; 95% CI [-0.29, 0.29]; *d* = 0.00) the CON Pre-HTF RPE-O. The IPS Post-HTF RPE-O was greater than (t = 3.727; p = 0.005; mean diff: 1.25 ± 1.06; 95% CI [0.49, 2.01]; *d* = 0.81) the CON Post-HTF RPE-O.

4.5.2.3 NPR-AM

A four-way mixed model ANOVA of 2(Condition: Dm vs NDm) x 2(Side: IPS vs CON) x 2(Time: Pre vs Post) x 2(Sex: Men vs Women) for NPR-AM responses demonstrated no significant interactions for condition x side x time x sex (F(1,18) = 0.005, p = 0.945, $p\eta^2 = 0.000$), condition x side x time (F(1,18) = 0.403, p = 0.534, $p\eta^2 = 0.022$), side x time x sex (F(1,18) = 3.180, p = 0.091, $p\eta^2 = 0.150$), condition x time x sex (F(1,18) = 0.226, p = 0.640, $p\eta^2 = 0.012$), or condition x side x sex (F(1,18) = 1.346, p = 0.261, $p\eta^2 = 0.070$). No significant two-way interactions were shown for condition x time (F(1,18) = 0.731, p = 0.404, $p\eta^2 = 0.039$), condition x side (F(1,18) = 0.116, p = 0.737, $p\eta^2 = 0.006$), time x sex (F(1,18) = 0.218, p = 0.646, $p\eta^2 = 0.012$), side x sex (F(1,18) = 4.019, p = 0.060, $p\eta^2 = 0.183$), and condition x sex (F(1,18) = 0.235, p = 0.633, $p\eta^2 = 0.013$), but there was a significant interaction for side x time (F(1,18) = 9.674, p = 0.006, pη^2 = 0.350). The follow-up pairwise comparisons (collapsed across condition and sex) indicated that the IPS Post-HTF NPR-AM (3.5 ± 2.4) was greater than (t = 4.828; p ≤ 0.001; mean diff: 2.33 ± 2.15; 95% CI [1.32,3.33,]; *d* = 1.05) the IPS Pre-HTF NPR-AM (1.2 ± 1.1), however the CON Post-HTF NPR-AM (1.8 ± 1.9) was not different from (t = -1.22; p = 0.238; mean diff: -0.45 ± 1.65; 95% CI [-1.22, 0.32]; *d* = 0.29) the CON Pre-HTF NPR-AM (1.3 ± 1.2). The IPS Pre-HTF NPR-AM was not different from (t = -1.06; p = 0.301; mean diff: -0.15 ± 0.63; 95% CI [-0.45, 0.15]; *d* = -0.13) the CON Pre-HTF NPR-AM. The IPS Post-HTF NPR-AM was greater than (t = 2.919; p = 0.009; mean diff: 1.73 ± 2.64; 95% CI [0.49, 2.96]; *d* = 0.75) the CON Post-HTF NPR-AM.

4.5.2.4 NPR-O

A four-way mixed model ANOVA of 2(Condition: Dm vs NDm) x 2(Side: IPS vs CON) x 2(Time: Pre vs Post) x 2(Sex: Men vs Women) for NPR-AM responses demonstrated no significant interactions for condition x side x time x sex (F(1,18) = 2.151, p = 0.160, pη^2 = 0.107), condition x side x time (F(1,18) = 0.630, p = 0.438, pη^2 = 0.002), side x time x sex (F(1,18) = 0.630, p = 0.548, pη^2 = 0.034), condition x time x sex (F(1,18) = 2.874, p = 0.188, pη^2 = 0.094), or condition x side x sex (F(1,18) = 1.271, p = 0.274, pη^2 = 0.066). In addition, there were no significant interactions for condition x time (F(1,18) = 0.023, p = 0.881, pη^2 = 0.001), condition x side (F(1,18) = 0.051, p = 0.824, pη^2 = 0.003), time x sex (F(1,18) = 0.886, p = 0.359, pη^2 = 0.047), side x sex (F(1,18) = 0.224, p = 0.641, pη^2 = 0.012), and condition x sex (F(1,18) = 0.648, p = 0.431, pη^2 = 0.035). There was a significant side x time (F(1,18) = 9.101, p = 0.007, pη^2 = 0.336) interaction. The follow-up pairwise comparisons (collapsed across condition and sex) indicated that the IPS Post-HTF

NPR-O (0.8 ± 1.1) was greater than (t = 2.81; p = 0.011; mean diff: 0.60 ± 0.95; 95% CI [0.15,1.05]; *d* = 0.67) the IPS Pre-HTF NPR-O (0.2 ± 0.4), however the CON Post-HTF NPR-O (0.3 ± 0.6) was not different from (t = 1.31; p = 0.204; mean diff: 0.13 ± 0.43; 95% CI [-0.07,0.32]; *d* = 0.25) the CON Pre-HTF NPR-O (0.2 ± 0.4). The IPS Pre-HTF NPR-O was not different from (t = -1.00; p = 0.330; mean diff: -0.03 ± 011; 95% CI [-0.08, 0.03]; *d* = -0.07) the CON Pre-HTF NPR-O. The IPS Post-HTF NPR-O was greater than (t = 2.93; p = 0.009; mean diff: 0.45 ± 0.69; 95% CI [0.129, 0.771]; *d* = 0.48) the CON Post-HTF NPR-O.

Table 4.1. Individual and composite subject anthropometric characteristics (age, height, and weight) and limb dominance.

Subject	**Age (years)**	**Height (cm)**	**Body Mass (kg)**	**Hand Dominance**
1 (W)	27	165.9	66.0	R
5 (W)	21	163.0	65.3	R
7 (W)	22	167.5	51.4	R
8 (W)	18	176.1	62.0	R
9 (W)	18	172.0	67.9	R
10 (W)	21	161.0	61.2	R
11 (W)	19	168.7	60.2	R
12 (W)	25	163.0	99.7	R
20 (W)	18	159.6	60.4	R
22 W)	28	170.8	76.7	R
Mean	**21.7**	**166.8**	**67.1**	
SD	**3.8**	**5.3**	**13.2**	
3 (M)	30	172.0	77.1	R
6 (M)	20	186.8	94.6	R
13 (M)	21	184.3	71.5	R
14 (M)	20	189.4	93.8	R
15 (M)	28	177.8	78.0	L
16 (M)	25	179.7	65.8	R
17 (M)	19	177.1	74.4	R
18 (M)	21	190.6	117.4	R
19 (M)	22	188.5	82.5	L
21 (M)	20	174.0	74.0	L
Mean	**22.6**	**182.0***	**82.9***	
SD	**3.8**	**6.8**	**15.2**	
Composite				
Mean	**22.2**	**174.4**	**75.0**	
SD	**3.7**	**9.8**	**16.0**	

* indicates the mean for the men was significantly greater than the women.

Table 4.2. Individual and composite pre-hold to failure maximal voluntary isometric contraction (MVIC) values (kg) for the dominant (Dm) and Non-Dominant (NDm) limbs and reliability analyses for Visits 1-3.

Subjects	**Visit 1 Dm MVC**	**Visit 2 Dm MVC**	**Visit 3 Dm MVC**	**Visit 1 NDm MVC**	**Visit 2 NDm MVC**	**Visit 3 NDm MVC**
1(W)	32.4	34.0	36.8	35.6	33.1	35.3
3 (M)	36.9	37.7	31.9	37.8	43.9	33.9
5(W)	30.6	36.1	34.7	25.8	29.3	31.0
6 (M)	58.8	60.3	63.6	64.1	60.5	64.6
7 (W)	25.9	28.2	27.0	25.7	25.7	25.6
8 (W)	36.6	37.7	34.6	28.3	35.7	37.5
9 (W)	40.3	43.1	41.1	40.6	41.7	45.6
10 (W)	30.6	26.9	30.1	21.4	24.1	23.2
11 (W)	34.1	32.3	33.0	29.4	29.2	28.4
12 (W)	36.0	32.5	33.9	32.8	30.5	32.6
13 (M)	57.6	46.9	49.2	60.0	49.0	55.6
14 (M)	59.5	61.1	62.1	57.4	57.3	52.0
15 (M)	49.3	53.1	55.9	57.8	50.8	52.8
16 (M)	41.4	37.0	40.6	39.6	38.0	42.0
17 (M)	51.7	47.9	50.5	49.8	46.2	49.1
18 (M)	55.2	55.0	51.1	52.5	54.5	57.5
19 (M)	37.7	45.0	45.6	41.0	38.2	41.9
20 (W)	31.5	30.3	27.2	27.0	27.3	25.0
21 (M)	39.9	37.1	33.1	42.7	35.0	36.9
22 (W)	45.3	43.6	40.6	38.9	42.8	36.2
Mean	**41.6**	**41.3**	**41.1**	**40.4**	**39.6**	**40.3**
(SD)	**10.4**	**10.2**	**11.1**	**12.8**	**10.8**	**11.8**
ICC		**0.936**			**0.938**	
SEM		**2.7 kg**			**3.0 kg**	
CoV		**6.6%**			**7.4%**	
MD		**7.6 kg**			**8.3 kg**	

ICC = intraclass correlation coefficient, SEM = standard error of the measurement, CoV = coefficient of variation, MD = minimal difference

Table 4.3. Individual and composite dominant (Dm) limb Hold to Failure (HTF) values (seconds) and reliability for Visits 1-3 for a subset of subjects (n=17).

Subjects	Dm HTF 1	Dm HTF 2
3 (M)	185	154
5 (W)	154	159
6 (M)	86	126
8 (W)	95	115
9 (W)	79	86
10 (W)	97	111
12 (W)	103	113
13 (M)	103	112
14 (M)	53	89
15 (M)	60	113
16 (M)	108	131
17 (M)	122	140
18 (M)	72	120
19 (M)	106	87
20 (W)	447	207
21 (M)	178	207
22 (W)	132	132
Mean	**128.2**	**129.5**
(SD)	**90.1**	**35.7**
ICC	**0.553**	
SEM	**46.6 sec**	
CoV	**36.2%**	
MD	**129.1 sec**	

ICC = intraclass correlation coefficient, SEM = standard error of the measurement, CoV = coefficient of variation,
MD = minimal difference

Table 4.4. Individual and composite dominant limb (Dm) and nondominant (NDm) hold to failure (HTF) time (seconds) for all subjects (n = 20).

Subjects	**Dm HTF**	**NDm HTF**
1(W)	91	93
3 (M)	154	154
5(W)	159	150
6 (M)	126	81
7 (W)	148	137
8 (W)	115	92
9 (W)	74	79
10 (W)	111	92
11 (W)	177	182
12 (W)	113	111
13 (M)	112	72
14 (M)	89	72
15 (M)	113	99
16 (M)	131	103
17 (M)	140	151
18 (M)	120	62
19 (M)	87	93
20 (W)	207	154
21 (M)	207	138
22 (W)	132	126
Mean	**130.3***	**112.1**
(SD)	**36.8**	**34.3**

*indicates the Dm HTF was significantly longer than the NDm HTF

Table 4.5. Individual and composite hold to failure (HTF) perceptual responses for Rating of Perceived Exertion – Active Muscle (RPE-AM), Rating of Perceived Exertion – Overall (RPE-O), Numerical Pain Rating – Active Muscle (NPR-AM), Numerical Pain Rating – Overall (NPR-O) collapsed across the dominant (Dm) and nondominant (NDm) limbs.

Subjects	**HTF RPE-AM**	**HTF RPE-O**	**HTF NPR-AM**	**HTF NPR-O**
1 (W)	10.0	6.0	7.5	2.5
5 (W)	10.0	6.0	8.5	6.0
7 (W)	7.0	5.5	4.5	1.0
8 (W)	4.5	1.0	3.5	0.0
9 (W)	4.0	1.5	3.5	2.0
10 (W)	6.5	1.0	5.5	0.5
11 (W)	6.5	3.0	3.5	0.0
12 (W)	9.0	2.0	1.5	0.0
20 (W)	6.5	2.5	0.0	0.0
22 (W)	9.5	5.0	5.0	1.0
Mean	**7.4**	**3.4**	**4.3**	**1.3**
(SD)	**2.2**	**2.1**	**2.5**	**1.9**
3 (M)	8.5	4.0	7.0	3.0
6 (M)	9.5	3.0	3.5	0.5
13 (M)	10	1.5	7.5	1.0
14 (M)	10	1.5	6.0	1.0
15(M)	10	3.5	0.0	0.0
16 (M)	10	2.0	7.5	0.5
17 (M)	10	7.0	7.0	4.0
18(M)	7.5	0.0	5.5	0.0
19 (M)	7.5	0.0	5.5	0.0
21 (M)	8.5	4.5	2.5	0.5
Mean	**9.2***	**2.7**	**5.2**	**1.1**
(SD)	**1.1**	**2.2**	**2.5**	**1.4**
Composite				

Table 4.5 (continued)				
Mean	**7.9**	**3.0**	**4.6**	**1.2**
(SD)	**2.2**	**2.0**	**2.4**	**1.5**

*indicates the mean for the men was significantly greater than the women. See Results for full ANOVA decomposition (pg. 80).

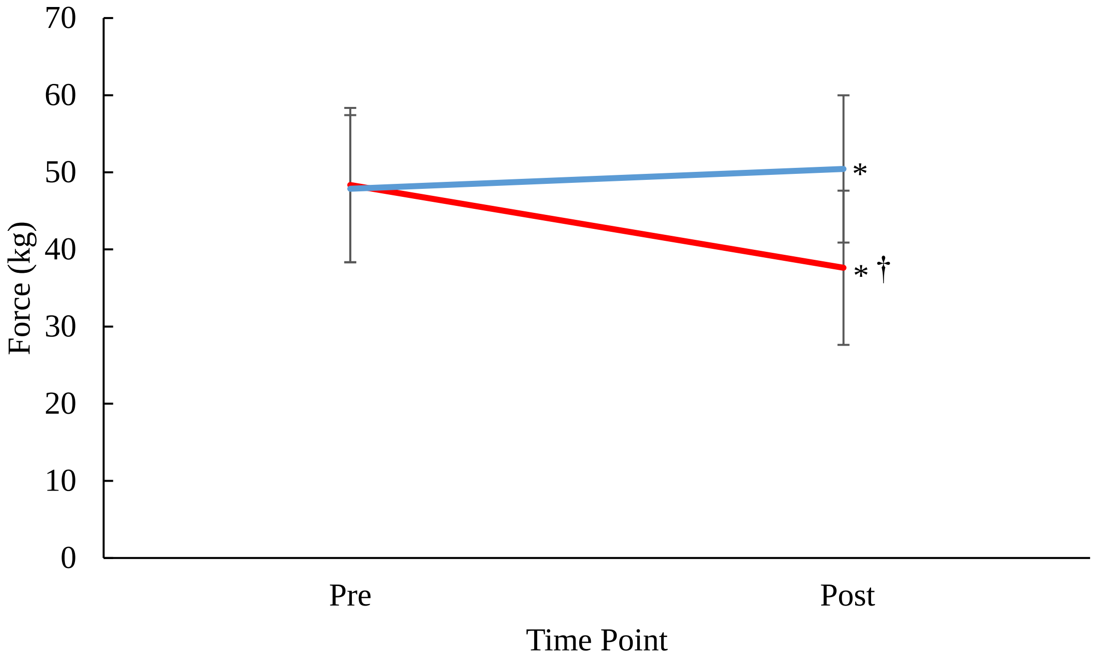

Figure 4.1. The mean maximal voluntary isometric contraction force (MVIC) in kilograms (kg) pre- and post-handgrip hold to failure (HTF) for the men in the ipsilateral limb (red) and contralateral limb (blue) with respect the HTF limb (collapsed across condition). An asterisk (*) indicates that data point was significantly different from pre-test MVIC force for the respective side. A † indicates the ipsilateral (Dm) post-test MVIC force was significantly less than the contralateral (NDm) post-test MVIC force. See Results for full ANOVA decomposition (pg. 77).

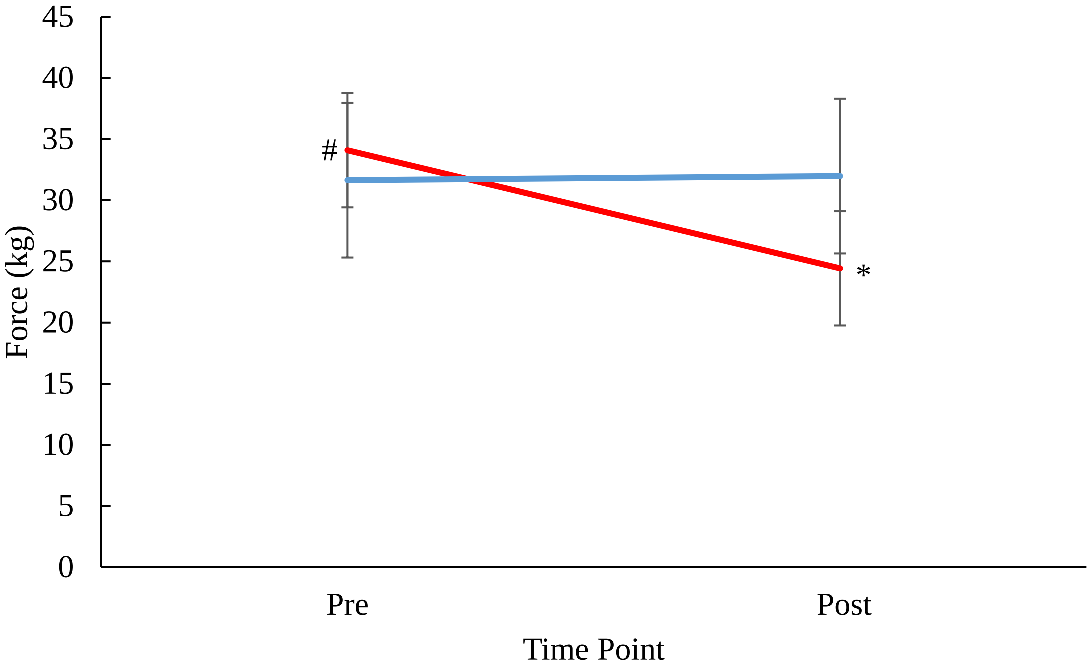

Figure 4.2. The mean maximal voluntary isometric contraction force (MVIC) in kilograms (kg) pre- and post-handgrip hold to failure (HTF) of the dominant (Dm) limb for the women in the ipsilateral limb (red) and contralateral limb (blue) with respect the HTF limb. An asterisk (*) indicates that data point was significantly less than the pre-test MVIC force for the respective side. A number sign (#) indicates the ipsilateral (Dm) pre-test MVIC force was significantly greater than the contralateral (NDm) side. See Results for full ANOVA decomposition (pg. 78).

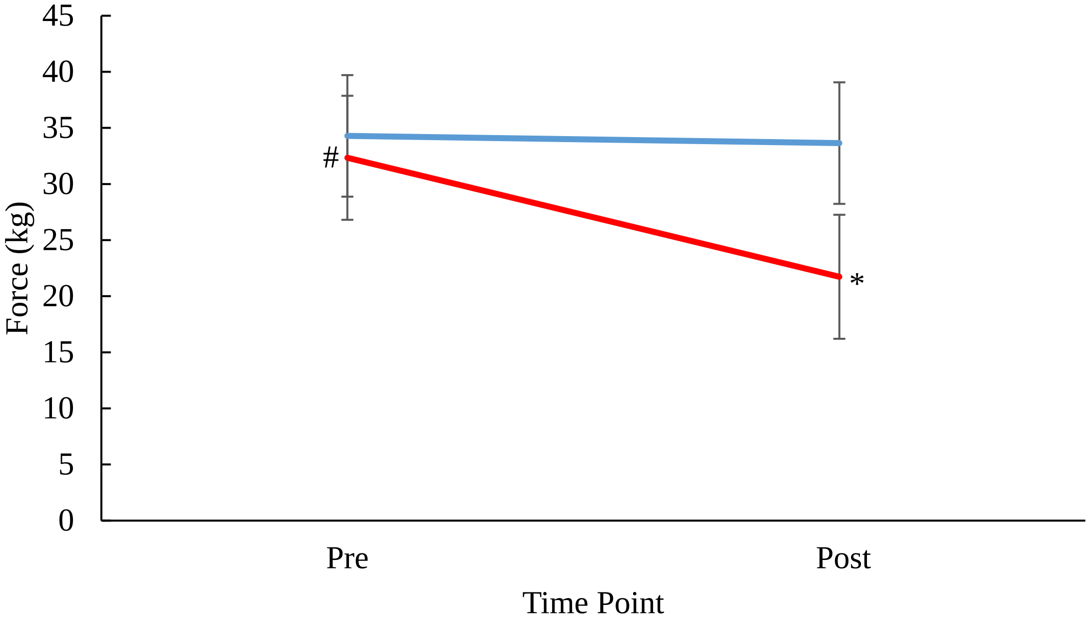

Figure 4.3. The mean maximal voluntary isometric contraction force (MVIC) in kilograms (kg) pre- and post-handgrip hold to failure (HTF) of the nondominant (NDm) limb for the women in the ipsilateral limb (red) and contralateral limb (blue) with respect the HTF limb. An asterisk (*) indicates that data point is significantly different from pre-test MVIC force for the respective side. A number sign (#) indicates the ipsilateral (NDm) pre-test MVIC force was significantly less than the contralateral (Dm) side. See Results for full ANOVA decomposition (pg. 78).

CHAPTER 5. DISCUSSION

5.1 Reliability: Maximum Voluntary Isometric Contractions and Isometric Handgrip Hold to Failure

The test-retest reliability was examined for the Dm and NDm pre-HTF MVIC force, measured during visits 1-3. In this study, the Dm and NDm limbs demonstrated “excellent” test-retest reliability (ICC = 0.936 and 0.938, respectively) for the pre-HTF MVIC force. These ICC values were consistent with the ICC values previously reported (Baldwin et al. 2013; Innes et al. 1999; Essendrop et al. 2001) for handgrip test-retest reliability (ICC = 0.930 to 0.980). It has been reported (Hamilton et al. 1994) that the MVIC reliability is relatively robust to variations in the method in which the MVIC force was determined during handgrip holds. Specifically, ICC values of 0.930 or higher were reported when the MVIC force was taken from a single trial, the mean score of two or three trials, or the highest score of three trials. The current study supported the reliability of the MVIC force selected from the highest of 2 similar (within 5%) trials. Furthermore, the hypothesis that there would be a learning effect from visit 1 to visit 2 was not supported. There was no systemic variability between visits 1 through 3 (Table 4.2.). Thus, the current finding indicated that a familiarization may not be necessary for the reliable measurement of MVIC handgrip force.

The Dm limb HTF demonstrated “fair” test-retest reliability (ICC = 0.553), with no systematic variability. Generally, time trial performance and time to exhaustion have demonstrated lower levels and a wider range of test-retest reliability ICC values (0.54 – 0.99) (Mutchler et al. 2015; Moreau et al. 2001) compared to the test-retest of MVIC force (0.93 – 0.98) (Baldwin et al. 2013; Innes et al. 1999; Essendrop et al. 2001). The ICC for the HTF in this study was just below or within the range reported for sustained, fatiguing isometric holds for the hip (ICC = 0.60 to 0.89) and lower back musculature (ICC = 0.54 to 0.99) (Mutchler et al. 2015; Moreau et al. 2001). Thus, the results of this study demonstrate that the pre-HTF MVIC testing produced "excellent" reliability of MVIC force values, but examination of time to failure during a 50% MVIC handgrip hold demonstrated "fair" reliability.

5.2 Absolute Strength: Sex- and Limb-Dependent Responses

In this study, the absolute MVIC force was greater for the men (46.07 ± 10.64 kg) compared to the women (30.52 ± 6.93 kg). These findings were consistent with previous studies that have demonstrated greater absolute strength for men compared to women (Leyk et al. 2007; Kamarul et al. 2006; Massy-Westropp et al. 2011; Trampisch et al. 2012). Interestingly, the women, but not the men, demonstrated greater MVIC force for the Dm limb compared to the NDm limb, consistent with the findings of Thorngren & Werner (1979). Specifically, Thorngren & Werner (1979) investigated the mean maximal grip strength between men and women's Dm and NDm hand across age groups, demonstrating a significant ratio of 1.10 ± 0.08 from the Dm to the NDm hand for women and a nonsignificant ratio of 1.05 ± 0.08 for the men in the age group represented in this study (18-30 yrs). Previous studies have demonstrated differing effects in limb dominance on handgrip strength (Thorngren & Werner 1979; Incel et al. 2002; Peterson et al. 1989; Bohannon et al. 2003; Kamarul et al. 2006). Peterson et al. (1989) examined the 10% rule, a hypothesis that the dominant limb produces 10% more grip strength than the nondominant limb (Bechtol et al. 1954), but this effect was suggested to be minimized in left limb dominant individuals as no difference was found in grip strength. To this point, Bohannon et al. (2003) reported that greater grip strength was demonstrated in the Dm limb, however, left limb dominant individuals were less likely to show significant grip strength differences between limbs. In the present study, there were three left limb dominant individuals, all of whom were men. This may, in part, explain the lack of mean differences between the Dm and NDm limbs for the men. It is also possible that the greater absolute strength for the men compared to the women, and limb dependent strength in the women, but not the men, were due to the differences in training background and sex-specific factors between women and men. Although women generally demonstrate about two-thirds the absolute strength of men, when expressed relative to bodyweight or fat-free weight, lower body strength is similar between men and women, but greater differences are still noted for the upper body (Halloway et al. 1998). This has been suggested to be due to sex-related differences in body composition and fat-free body mass distribution as women tend to demonstrate lower muscle mass above the waist (Bishop et al. 1987) compared to men, who tend to have broader shoulders relative to their hips and, thus, are able to support more muscle mass in the upper body. However, there are no sex differences in upper-body strength when strength is expressed relative to muscle cross-sectional area (Castro et al. 1995; Miller et al. 1992). Additionally, it has been reported that the general focus of training programming tends to differ between men and women (Kraemer et al. 2001). These differences in training program focus (i.e., more holistic strength and fitness outcomes in women compared to men) have been reported to produce lesser absolute upper body strength development in women (Kraemer et al. 2001). Upper body specific training exercises, more common in programming by men, require repeated activation of the handgrip muscles to perform dumbbell and free-weight exercises, such as the biceps curl (i.e., forearm flexion), resulting in additional strength outcomes that may affect absolute grip strength (Chilibeck et al. 1998; Myer et al. 2006). The additional focus of upper body training with unilateral or bilateral movements in men may reduce MVIC force production differences in the Dm and NDm limb. When the training programs are similar, however, women have demonstrated relative increases in strength at the same or greater rates than men, but the effect of reduced absolute body strength has reflected lower baseline neuromuscular activation levels in women compared to men (Myer et al. 2006). Thus, the training programming and sex-specific physiological differences may contribute to the findings demonstrated in this study where men produce greater absolute grip strength compared to women, but only the women demonstrated greater strength in the Dm compared to NDm limb.

5.3 Isometric, Unilateral Handgrip Holds to Failure: Performance Fatiguability of the IPS Side

There were no differences between men and women in the 50% MVIC HTF time, however, the Dm limb demonstrated a greater time to task failure (130.3 ± 36.8 sec) compared to the NDm limb (112.1 ± 34.3 sec). The differences in fatigue resistance between the Dm and NDm limb may be attributed to activities of daily living wherein individuals will favor their Dm limb rather than their NDm limb. Repeated use of the Dm limb to perform sustained, lower intensity activities such as carrying groceries may elicit performance outcomes in muscle endurance observed in the current study. This hypothesis is supported by Habibu et al. (2013), who suggest that frequent and continuous favoring of the Dm limb may result in greater performance outcomes compared to the NDm limb. The subconscious decision to favor the Dm limb, in conjunction with the right-hand dominance bias of our cultural environment in the development of ergonomics support this hypothesis despite the differences in occurrence of right- and left-hand dominant individuals (Gabbard et al. 1998; Helbig & Gabbard 2013; Przybyla et al. 2012; Papadatou-Pastou et al. 2008).

Previously, women have been reported to be more fatigue resistant than men, which is evidenced by longer times to task failure and/or lesser degrees of performance fatiguability (Martin et al. 2007; Hunter & Enoka 2001; Ansdell et al. 2017; Wüst et al. 2008; Clark et al. 2004; Maughan et al. 1986; Yoon et al. 2007). Specifically, women have demonstrated longer times to task failure for isometric leg extension holds performed at 20% of MVIC as well as the completion of more dynamic, forearm flexion repetitions to failure at 50, 60, and 70% one repetition maximum compared to men (Maughan et al. 1986). Similar findings were reported (Yoon et al. 2007) during forearm flexion exercise at 20% MVIC, as women demonstrated a greater time to failure than men (17.0 ± 8.7 minutes; 10.6 ± 8.7 minutes; respectively). Furthermore, Ansdell et al. (2017) demonstrated that women (937 ± 525 seconds) had a greater time to task failure for intermittent leg extension holds performed at 50% MVIC compared to men (397 ± 153 seconds) and a lower performance fatiguability response (24% ± 1%; 34% ± 8%; respectively). At 30% MVIC, the women (15% ± 16%) demonstrated a lower performance fatiguability response compared to the men (32 ± 15%) for an intermittent forearm flexion hold task for 30 minutes (Ansdell et al. 2017). It has also been reported (Hunter et al. 2009) that women (408 ± 205 seconds) demonstrated a longer time to task failure than men (297 ± 57 seconds) for intermittent, isometric, handgrip holds at 50% MVIC performed to failure. Based on this evidence, we hypothesized that the women would be more fatigue resistant than the men and sustain the HTF at 50% MVIC longer with a lesser degree of performance fatiguability. Our hypothesis was not supported and instead the time to task failure for the unilateral, isometric HTF was not different between the men and women and there were no sex differences in performance fatigability for the exercised, IPS side. The 23% (collapsed across Dm and NDm limb) decrease in MVIC force for the men and the 28% to 32% (Dm and NDm, respectively) decreases in MVIC force for the women were similar to the magnitude of the performance fatiguability (16% to 39%) of values previously reported for bilateral and unilateral isometric muscle actions of the leg extensors following intermittent, sustained, dynamic, or isometric fatigue at 20% to 50% MVIC or one repetition maximum intensity (Martin et al. 2007; Hunter & Enoka 2001; Ansdell et al. 2017). Thus, the current findings showed no difference between the men and the women in HTF time or performance fatigability that may be related to the relative intensity (50% MVIC) and the mode (i.e., isometric, intermittent isometric, or dynamic) of the fatiguing task.

There is some evidence (Maughan et al. 1986; Hunter & Enoka 2001; Yoon et al. 2007; Ansdell et al. 2017; Sewright et al. 2008; Hicks et al. 2001) that sex-differences in fatigability become smaller or are not present for fatiguing isometric exercise performed at intensities that are greater than or equal to 50% MVIC. The greater fatigue resistance reported for the women compared to the men at lower intensities (<50% MVIC) has been suggested to be related to muscle size and blood flow alterations that occur due to increased intramuscular pressure during exercise (Monod & Scherrer 1965; Weir et al. 2006). That is, typically, men have more muscle mass than women and generate higher levels of intramuscular pressure which limits metabolic byproduct clearance and expedites the deleterious effects of hydrogen ions (H^+), inorganic phosphate (Pi), potassium (K^+), and ammonia on the skeletal muscle contractile process (Abe et al. 2003; Hicks et al. 2001; Avin et al. 2010; Shephard et al. 1988). These differences in muscle size and the subsequent alterations in blood flow between men and women may be more important at lower versus higher intensities as well as sustained isometric versus intermittent isometric muscle actions (Hanson et al. 2020; Suga et al. 2010; Proctor et al. 2001; Neyberg et al. 2017). To this point, women have demonstrated a greater time to failure during performance of leg extensions at 25% MVIC with no occlusion of blood flow compared to men (214 ± 20.5 s; 169.1 ± 20.5 s: respectively), but this difference was negated during occlusion of blood flow (women: 179.6 ± 19.6 s; men: 165.2 ± 19.6 s) (Clark et al. 2004). Yoon et al. (2007) demonstrated sustained, isometric forearm flexion holds at 80% MVIC did not elicit differing time to fatigue in men (25.0 ± 6.5 s) and women (24.3 ± 6.6 s). Similarly, isometric holds of 80% and 50% MVIC demonstrated no differences in time to failure between men and women (80%: 20 ± 10 s vs 17 ± 8 s; 50%: 53 ± 12; 59 ± 15; respectively), similar to repetitions to failure at 90% and 80% 1 repetition maximum for forearm flexion exercise (90%: 3.5 ± 1.9 reps vs 3.7 ± 2.2 reps; 80%: 8.0 ± 2.6 reps vs 9.1 ± 4.5 reps; respectively) (Maughan et al. 1986). It is possible that the isometric HTF, performed at 50% MVIC in the current study, was at an intensity high enough to cause increases in intramuscular pressure for both the men and the women that occluded blood flow within the muscle and created similar performance limitations.

The fatigue elicited following isometric, unilateral holds to failure, reflected by a decrease in the amount of volitional force produced, has been suggested to be due to both peripheral and central mechanisms (Davis & Bailey 1996; Doix et al. 2013; McMorris et al. 2018; Neltner et al. 2020). Peripheral fatigue is, in part, elicited from the production of metabolic byproducts within the working muscle that inhibit the ability of the musculature to contract (Amann et al. 2011; Halperin et al. 2014; Knuth et al. 2006; Fitts 2008). The local effect of the metabolic byproducts (i.e., H+, Pi, K+, and ammonia) may cause this reduced muscle fiber contractility response (Halperin et al. 2014; Knuth et al. 2006; Fitts 2008). To this point, it has been demonstrated that accumulation of H^+ reduces the force produced by cross bridges and the myofibrillar sensitivity to calcium (Halperin et al. 2014; Knuth et al. 2006; Fitts 2008). These same byproducts may elicit a neuromuscular response from metaboreceptors within the centrally projected type III/IV afferents that lead to attenuations in neural activity (Amann et al. 2011; Amann et al. 2013). Specifically, type III/IV afferents relate a signal to the central nervous system, reducing the central drive to the working muscle(s) (Amann et al. 2011; Amann et al. 2013). Thus, the performance fatigability from the HTF at 50% MVIC demonstrated in this study was likely mediated by both peripheral and central factors that limited the contractility of the muscle and/or a decreased central drive to the exercising limb from group III/IV afferent feedback.

The signaling produced by the type III/IV afferents elicit fatigue sensations in the higher reasoning centers of the brain, dictating the task adherence through summation of this neuronal feedback and feedforward pathways (O'Connor & Cook 1999, Pageaux & Gaveau 2016; Marcora & Staiano 2010). Previous investigators (Stuart et al. 2018; Hunter et al. 2009) have demonstrated that men and women reported similar RPE values (at or near RPE max), despite a greater time to task failure and lower performance fatigability for women compared to men. Evidence by Stuart et al. (2018) supported this point, as greater relative performance fatiguability following 80% and 50% MVIC lumbar extensions to failure existed in men (-21.3% ± 9.8%; -33.3% ± 9.9%, respectively) than women (-10.6% ± 14.0%; -25.9 % ± 8.4%; respectively), despite identical ratings of perceived exertion (RPE = 10) for men and women. Hunter et al. (2009) found additional evidence for this claim, as intermittent, isometric, handgrip holds at 50% MVIC performed to failure demonstrated a longer time to task failure for women (408 ± 205 seconds) than men (297 ± 57 seconds), despite no differences in the RPE between men and women after reaching failure (9.7 ± 0.6; 9.6 ± 0.9; respectively). Hunter et al. (2004) examined intermittent elbow flexor holds to failure in men and women at 50% of their MVIC and found that despite no difference in the starting RPE (Men: 1.4 ± 0.8; Women: 1.4 ± 1.0) or end point RPE (Men: 9.8 ± 0.6; Women: 9.9 ± 0.3) at the cessation of the performance, the rise in RPE during the exercise was slower for women, as women (1,408 ± 1,133 seconds) performed longer than men (513 ± 194 seconds). In the current study, the RPE-AM was greater in the men (9.2 ± 1.1) than the women (7.4 ± 2.2) following the HTF, despite no difference in the time to exhaustion. The lower RPE-AM response in women following a relative 50% MVIC HTF when compared to men, despite similar fatigue response at the same relative workloads, suggested differences in the perceptual response to fatigue. This may be explained by sex-dependent characteristics of muscle fiber type distribution patterns. It has been suggested that women have a greater number (Bajek et al. 2000) or area of type 1 muscle fibers compared to men (70-75%; 54-58%; respectively) (Thorstensson & Carlson 1987; Mannion et al. 1997). These type I muscle fibers have a greater oxidative capacity and fatigue resistance, when compared to type II muscle fibers (Bajek et al. 2000; Westerblad et al. 2010). The type II muscle fibers demonstrate greater rates of crossbridge cycling as their ability to utilize ATP more rapidly allows this phenomenon (Westerblad et al. 2010). This disparity in the amount of type I and type II between men and women may reflect different mechanisms of fatigue and subsequently the perception of effort. Differences in the high intensity and low intensity exercise and the associated fatigue responses support this finding, as the high intensity (< 50% MVIC) exercise fatigue is suggested to develop in regard to central factors, such as the decrease in number and discharge of motor units, and low intensity (>50% MVIC) fatigue may be mediated peripherally as a result of the metabolite byproducts (Boyas & Guével 2011; Gandevia et al. 2001; Stuart et al. 2018). The afferent signaling elicited by these byproducts may produce the differences in the RPE reported by men and women as the relative intensity of 50% MVIC is directly between maximal effort (100%) and rest (0%). It is possible that the relative contribution of central and peripheral factors of fatigue to the RPE differs between men in women. However, the relative contribution of these central and peripheral factors could not be fully delineated in this study.

As men did not perform the 50% MVIC HTF for a significantly different length of time than women, the greater number and area of type II fibers in men may have resulted in greater metabolite accumulation during the same period of time, resulting in a greater afferent group III/IV feedback and level of perceived exertion. As stated previously, the greater amount of muscle mass in men and blood flow alterations that occur due to increased intramuscular pressure during exercise influences the metabolite clearance that may occur to a greater extent at lower intensities than higher intensities (Monod & Scherrer 1965; Weir et al. 2006; Hanson et al. 2020; Suga et al. 2010; Proctor et al. 2001; Neyberg et al. 2017). In addition, the demonstration of greater perceived exertion during the 50% MVIC HTF task in the men than the women despite no differences in HTF time suggests greater musculature activation was elicited by the men to sustain the hold. Performance of a horizontal handgrip hold has been demonstrated to activate greater amounts of accessory musculature such as the supraspinatus, infraspinatus, teres minor, and the posterior deltoid, than during a handgrip hold in a vertical position, as measured by EMG (Rudroff et al. 2007). The activation may be due to the increased external rotation required to maintain a supinated handgrip position (Rudroff et al. 2007). This hypothesis is supported by Le Bozec & Bouisset (2004), as the ability to perform a 75% MVIC pushing task was mediated by the postural muscles of the pelvis. In addition, examination of handgrip position (neutral, supinated, and pronated) on the steadiness of force production between men and women demonstrated that men produced more stable force production in all positions between 25-75% MVIC force, possibly due the greater absolute force production due to greater muscle mass and activation of accessory muscles in men compared to women (Brown et al. 2010; Bishop et al. 1987; Halloway et al. 1998). It is possible that during the 50% MVIC HTF, a greater activation of accessory muscles may have provided additional increases in force production to maintain the hold, at the cost of producing greater volumes of metabolite accumulation in conjunction with the recruitment of greater absolute volume of type II muscle fibers eliciting subsequently greater metabolite accumulation which may in turn elicit greater type III/IV afferent feedback for the men relative to the women (Thorstensson & Carlson 1987; Mannion et al. 1997; Bajek et al. 2000; Westerblad et al. 2010; Boyas & Guével 2011; Gandevia et al. 2001; Stuart et al. 2018). The greater volumes of type II muscle fibers and increased recruitment of accessory muscles to perform the 50% MVIC HTF and the subsequent increases in metabolite accumulation may help explain the increased perceived exertion was seen in the men despite similar times to failure

(Thorstensson & Carlson 1987; Mannion et al. 1997; Bajek et al. 2000; Westerblad et al. 2010; Boyas & Guével 2011; Gandevia et al. 2001; Stuart et al. 2018).

There were no differences in the NPR-AM and NPR-O pain measures between men and women following a relative 50% MVIC HTF in this study. Poudevigne et al. (2002) demonstrated no differences in the pain elicited for men and women following eccentric forearm flexor exercise at 80%, 100%, and 120% MVIC, while Cook et al. (1998) demonstrated conflicting evidence for cycling exercise at peak power, where associated pain ratings were lower in women (5.5 ± 2.9) than men (8.5 ± 2.3). Conversely, when performing isometric holds at 25% MVIC to failure, sustained for 2 minutes, and at 80% MVIC to failure in the forearm flexion task, there was a greater reported pain response for women than for men (Bement et al. 2008). The conflicting evidence regarding pain ratings in men and women mirror difficulties in the examination of sex differences in pain (Greenspan et al. 2007). Suggestions have been made for these findings on both the psychological and physiological level. Physiological evidence for the pain ratings has been difficult to measure, but one hypothesis for the sex differences in the perception of pain is due to the NMDA receptors (Klepstad et al. 1990; Fillingim et al. 2009; Dong et al. 2007; LeResche et al. 1997; McRoberts et al. 2007; Herrero et al. 2000). The NMDA receptors are expressed in the dorsal horn and sustained activation from NMDA and glutamate enhances the nociceptive response (Fillingim et al. 2007). The NMDA receptors are widely involved in the processing of afferent signals to the brain, and estrogenic presence enhances the excitability of these receptors, possibly contributing to a greater central sensitization in women than men (Herrero et al. 2000; Fillingim & Ness 2000). In addition, inherent psycho-social factors associated with pain response suggests that masculine gender norms have been associated with increased tolerance to pain, while feminine norms accept pain and are more receptive to quantifying their pain response (Myers et al. 2003; Unruh 1996; Fillingim et al. 2009). In support of this hypothesis, anecdotal evidence in the current study demonstrated that a statement by the investigator that the quantification of pain and exertion at lower or higher levels does not correlate with weakness or strength in physical or mental status was helpful to subjects unfamiliar with perceptual scales. The demonstration of no differences in the NPR-AM and NPR-O between men and women in this study suggested that these potential physiological and psychological factors did not differentially influence men and women in their assessment of pain.

5.4 Contralateral Limb Responses to Fatiguing, Isometric, Unilateral Handgrip Holds

In the current study, there was a facilitation (6% increase) in force in the CON limb following the 50% MVIC HTF for the men, but no change in CON limb force for the women. Previous literature has demonstrated no change, decreases, or increases in force for the non-exercised, CON limb (Grabiner & Owings 1999; Kawamoto et al. 2014; Amann et al. 2013; Neltner et al. 2020; Strang et al. 2009). Unilateral fatiguing tasks have been reported most frequently to cause no change (Grabiner & Owings 1999; Kawamoto et al. 2014; Amann et al. 2013) or decreases (Todd et al. 2003; Aboodarda et al. 2015; Halperin et al. 2014) in force production of the non-exercise CON limb that have been attributed to the "cross-over" inhibitory phenomenon (Aboodarda et al. 2015). This "cross-over" inhibition is thought to be caused by group III/IV afferent feedback of metabolic and mechanical perturbations from the exercised limb (Amann et al. 2013). This afferent feedback in turn leads to central fatigue by limiting central drive to both the IPS and CON limbs (Amann et al. 2013). However, the presence and magnitude of this "cross-over" inhibitory effect may be related to the mode and intensity of the fatiguing task (Grabiner & Owings 1999; Kawamoto et al. 2014; Amann et al. 2013; Neltner et al. 2020; Strang et al. 2009).

The CON limb facilitation demonstrated for the men in this study was consistent with the findings of Neltner et al. (2020), where 4 to 5% increases in torque were demonstrated in the non-exercised CON limb following unilateral, dynamic leg extensions. Strang et al. (2009) also reported a significant increase in the quadricep force of the CON limb of 13.38%, and a nonsignificant increase of 2.69% in the CON limb hamstring following fatiguing, dynamic leg extension exercise. The facilitation of force/ torque in the CON limb demonstrated in these studies may be due to a combination of central mechanisms that lead to increased central (i.e., cortical) drive to the non-exercise CON limb (Aboodarda et al. 2016). Changes in the cortical-spinal pathways may be responsible for the increase in performance in the contralateral limb, defined as “cross-facilitation” (Aboodarda et al. 2015; Neltner et al. 2020). Contralateral activation has been reported in homologous intrinsic muscle groups of the hand during the performance of unilateral exercise at intensities of 20-40% MVIC in tonic pinch grips (Liepert et al. 2001) and greater than or equal to 50% MVIC in isometric thumb abductions (Muellbacher et al. 2000; Derosière et al. 2014; Aboodarda et al. 2016; Derosière et al. 2014). This contralateral activation may have been produced via excitatory signaling through the transcallosal connection or shared pathways in the brain stem or spinal cord, influencing both hemispheres of the brain and subsequent exercised IPS and non-exercised CON muscle groups (Zijdewind & Kernell 2001; Hess et al. 1986; Muellbacher et al. 2000; Aboodarda 2016). Interhemispheric inhibition (IHI) is a mechanism in which this shared excitatory signaling pathway is inhibited to prevent mirror movements in a CON limb during a unilateral task (Derosière et al. 2014; Carson et al. 2005). Depolarized inhibitory neurons at the cortical level signal further depolarization in the distal decussating pyramidal neurons which project to the homologous, contralateral muscle fibers (Derosière et al. 2014; Carson et al. 2005). Despite the presence of this IHI, muscle actions at higher intensities have been demonstrated to decrease its inhibitory effects (Muellbacher et al. 2000; Derosière et al. 2014; Aboodarda et al. 2015; Hess et al. 1986). Higher intensity muscle actions will elicit excitatory signaling in the trans-colossal fibers, mediated by the collaterals of corticospinal neurons via the corpus collosum, producing the cross-facilitation effect despite inhibitory signaling in the interneurons (Derosière et al. 2014; Carson et al. 2005). The activation of additional brain regions from this excitatory signaling may subsequently elicit greater motor evoked potential (MEP) amplitude, as amplitude is contingent upon the balance of both the excitation and inhibition of supraspinal and spinal anatomy leading to increased neural drive to the muscle (Gandevia et al. 1990; Aboodarda et al. 2016). During fatiguing muscle actions, increased neural drive, regulated by the motor cortex to compensate for the decreased spinal motoneuron excitability elicited by fatiguing muscle actions, may produce these greater force productions associated with facilitation (Neltner et al. 2020; Aboodarda et al. 2015). Thus, the results of the current study in conjunction with others (Neltner et al. 2020; Rattey et al. 2005; Matkowski et al. 2011; Cornwall et al. 2012), suggested that the central nervous system does not selectively control neural drive to the exercising muscle only, possibly to provide overall coordination to maintain cellular homeostasis due to anticipatory regulation between shared neural networks of the IPS and CON limbs (Halperin et al. 2015).

In the current study, the hypothesis that the non-exercising contralateral limb would demonstrate no change or a small performance fatiguability effect due to a cross-over in fatigue response, was not supported in the men. The 50% MVIC HTF was at an intensity similar to or greater than the intensity demonstrated to produce a sum of excitatory signaling that is greater than the inhibitory signaling from IHI eliciting activation at the cortical level, leading to activation in the non-exercising CON limb (Muellbacher et al. 2000; Derosière et al. 2014; Aboodarda et al. 2015; Hess et al. 1986; Neltner et al. 2020). The effect of this signaling may have additionally increased the neural drive to compensate for the reduction in the spinal motoneuron activity following the fatiguing HTF and may have produced this facilitation that was demonstrated in the men (Neltner et al. 2020; Aboodarda et al. 2015). The cross-over facilitation effect may have been elicited by a combination of these central mechanisms, however, the lack of change for the women suggested an alternative mechanism may help further explain these findings.

The facilitation demonstrated from the men, but not the women, may also be the result of a combination of central and peripheral mechanisms related to post-activation potentiation (PAP). During unilateral muscle actions, the increased neural drive to the exercised muscle travels through crossed and shared neural pathways of the IPS and CON homologous muscles during exercise performance. It has been reported that this shared pathway results in a 10-15% activation in the homologous, non-exercised CON muscle (Nyberg-Hansen & Rinvik 1963; Phillips & Porter 1964; Neltner et al. 2020). This CON limb activation during IPS exercise may lead to increased myosin light chain phosphorylation through calcium ions eliciting a PAP response (Rassier and MacIntosh, 2000). Two protein subunits which wrap themselves around the myosin rod region that connect the myosin head to the thick filament, termed the essential light chain and regulatory light chain, provide a type of mechanical support to the myosin rod region (Stull et al. 2011; Rayment 1993; Lowey & Trybus 2010). Calcium release to the sarcomeres may phosphorylate the essential and regulatory light chains, resulting in a movement in the myosin head closer to the actin filament subsequently resulting in a greater number of possible cross-bridge formations or increased cycling rates (Stull et al. 2011; Rayment 1993; Lowey & Trybus 2010). The PAP phenomenon has been demonstrated in plantar flexion muscles following various 6-second MVIC intensities of 40, 60, 80, and 100%, with the 80% MVIC increasing force production by 6.1 ± 5.5% and 100% MVIC increasing force production by 7.4 ± 6.8% (Fukutani et al. 2012), which was similar to the 6.1 ± 6.9% increase in the CON limb MIVIC force demonstrated for the men in the current study. Fukutani et al. (2014) demonstrated similar findings in the thumb adductor muscles, as performance of 10-second MVICs at 20, 40, and 60% significantly increased the PAP effect in the MVIC torque production and demonstrated greater PAP effects for each increasing intensity. Mettler & Griffin (2012) supported these findings, as the potentiation effect of performing 25%, 50%, and 100% MVIC in the adductor pollicis muscle increased as the intensity of the hold increased. The subjects in the current study performed a 50% MVIC HTF at a similar intensity to these aforementioned studies, suggesting that PAP may have played a role in the facilitation effect seen in the men (Fukutani et al. 2012; Fukutani et al. 2014; Mettler & Griffin 2012). The PAP phenomenon and its subsequent effect on force generation has been suggested to occur during tasks that require smaller motor units, similar to the handgrip muscles used in the current study (Sale, 2004; Sonne et al. 2015). In addition to motor unit size, the muscle fiber type may impact the PAP phenomenon (Sale

2002; Sweeney et al. 1993). Type II fibers have been suggested to demonstrate a greater PAP response as the phosphorylation of myosin regulatory light chains occurs more rapidly in these fibers (Sale 2002; Sweeney et al. 1993). In a study conducted by Gervasi et al. (2018), following a 40-minute run at the lactate threshold, the countermovement jump height increased and subjects subsequently recruited greater numbers of type II fibers to perform the movement. The men in the current study demonstrated a CON facilitation effect while the women demonstrated no significant change, possibly due to the differences in muscle fiber type distributions between men and women (Thorstensson & Carlson 1987; Mannion et al. 1997; Bajek et al. 2000). It is possible the men in the current study possessed a greater number of type II muscle fibers that are more sensitive to the mechanisms associated with the PAP phenomenon and may explain the sex-differences in CON limb MVIC force production. (Thorstensson & Carlson 1987; Mannion et al. 1997; Bajek et al. 2000). Thus, it is hypothesized that the central factors of shared neural pathways and the interhemispheric influence of excitatory and inhibitory signaling may have produced a ‘cross-facilitation’ effect that was demonstrated in the current study, however, a greater emphasis is placed upon the peripheral influence of the post-activation phenomenon.

The demonstrated CON facilitation in the men and no change demonstrated in the women was reflected through perception quantification. Men demonstrated an increase in the RPE-AM elicited by an MVIC performed prior to, and following, the HTF collapsed across the IPS and CON side, from 5.9 ± 2.1 to 6.8 ± 2.1, respectively. This change was demonstrated in the RPE-O, as the men increased from 1.0 ± 0.8 to 1.6 ± 1.3, respectively. The women demonstrated no differences in the RPE-AM (3.4 ± 2.8; 3.3 ± 2.8; respectively) and RPE-O (0.5 ± 0.5; 0.7 ± 1.0; respectively) in the CON limb subsequently elicited from an MVIC prior to and following the HTF. Amann et al. (2013) demonstrated a similar finding in contralateral limb RPE following a leg extension exercise, as the CON limb RPE demonstrated a greater RPE response at the start point of exercise following IPS limb performance. Elmer et al. (2013) demonstrated a similar finding with the change in RPE following a unilateral cycling exercise, as the non-exercising CON limb increased in RPE and did not differ from the exercising, IPS limb (19.3 ± 0.2; 19.6 ± 0.1; respectively) following a 10-minute time trial. The similar IPS and CON limb RPE increases in the men and not the women support the hypothesis that the greater volume of metabolite accumulation in the men due to increased type II muscle fibers and greater accessory muscle activation for the men (Monod & Scherrer 1965; Weir et al. 2006; Hanson et al. 2020; Suga et al. 2010; Proctor et al. 2001; Neyberg et al. 2017; Thorstensson & Carlson 1987; Mannion et al. 1997; Bajek et al. 2000; Westerblad et al. 2010; Boyas & Guével 2011; Gandevia et al. 2001; Stuart et al. 2018). These factors may have led to increased afferent signaling for the men, which produced an increased level of perceived exertion systemically, raising the baseline exertion level of a non-exercising muscle group in the men and not the women (Amann et al. 2013).

5.5 Limitations

This study examined the performance fatigability of the handgrip and forearm muscles in the exercised, IPS limb and non-exercised, CON limb following unilateral HTF. During the course of data collection in this study, the handgrip dynamometer demonstrated a maximal value of measurement of 36 PSI. This force output, when translated to kg using the calibration procedure of placing a 20.412 kg plate on the bulb, was roughly 65 kg. This force output was achieved by 2 of the first 4 subjects, subsequently ‘maxing out’ the machine and forcing recruitment of less-trained men or men that may produce a lower absolute force value. While recruitment of subjects who were adequately trained to perform the study was achieved, the demonstrated facilitation effect may have been different if men with higher force production and greater training background were recruited.

A second limitation of this study involved the size of the dynamometer handgrip bulb, which was ~16 cm in circumference and ~11 cm in length. Hand size was not measured in this study, but anecdotal evidence provided by subjects demonstrated a greater force value was correlated with larger hand size. Despite differing training backgrounds between subjects in terms of their preference for bilateral or unilateral training and the prevalence of heavy handgrip loading such as deadlifting in their programming, hand size anecdotally played a role in force production. In addition to the hand size providing differences in force production, subjects were instructed to grip the bulb in a modified manner than what may be inherently performed. Subjects were instructed to wrap the fingers around the bulb using the distal, middle, and proximal phalanx to produce force rather than the distal end of the distal phalanx, near the fingertip. Performing this method to produce handgrip force eliminated the impact of various fingernail lengths and inconsistencies in the placement of the fingertip on force production.

This study was also limited by a lack of measures to distinguish central and peripheral factors of fatigue. This study did not examine the metabolic byproduct accumulation, neuromuscular responses, or fiber type distribution patterns of the subjects. These measures may explain the mechanisms underlying the responses observed in the current study and may better inform future studies examining the fatigue response in the CON and IPS limb following a unilateral, isometric HTF in both men and women.

5.6 Summary

The results of this study demonstrated that performance of pre-HTF MVIC testing across each visit produced ‘excellent’ reliability in addition to ‘fair’ reliability in the HTF. Following unilateral, isometric handgrip holds to failure, sex-dependent differences were demonstrated in the IPS and CON limb performance fatiguability and perceptual responses. The mean absolute grip strength produced by MVIC holds was greater in the men (46.07 ± 10.64 kg) than the women (30.52 ± 6.93 kg) and was suggested to be due to training programming and sex-specific physiology, such as increased muscle distribution above the waist in men (Halloway et al. 1998; Bishop et al. 1987; Castro et al. 1995; Miller et al. 1992; Kraemer et al. 2001; Chilibeck et al. 1998; Myer et al. 2006). Despite the differences in absolute grip strength, the isometric handgrip HTF time was not different between the men and women at the same relative intensity of 50% MVIC but demonstrated differences in handedness, as the Dm limb (130.3 ± 36.8 seconds) demonstrated a greater fatigue resistance than the NDm limb (112.1 ± 34.3 seconds). The similar times demonstrated in the HTF did not produce similar perceptual responses, as the men (9.2 ± 1.1) reported greater a RPE-AM value than the women (7.4 ± 2.2). This finding is hypothesized to be due to greater type II muscle fiber distribution and/or additional accessory muscle recruitment in men compared to women, which may have resulted in increased afferent signaling (Thorstensson & Carlson 1987; Mannion et al. 1997; Bajek et al. 2000; Westerblad et al. 2010; Boyas & Guével 2011; Gandevia et al. 2001; Stuart et al. 2018).

Similar performance fatiguability was demonstrated in the IPS limb following the HTF in both men (22.9 ± 10.8%) and women, however, this effect was demonstrated to be greater in the NDm limb (32.3 ± 10.1%) in women than the Dm limb (28.0 ± 9.4%)(p =

0.027). The limb dependent performance fatigability for the women may have been related to the greater absolute strength in the Dm limb relative to the NDm limb. Interestingly, CON limb facilitation was demonstrated in the men (-6.1 ± 6.9%), but not the women. The existence of such a phenomenon may be due to central factors of facilitation such as shared neural pathways at the cortical and spinal cord levels and the summation of excitatory and inhibitory signaling eliciting interhemispheric influences. However, as this facilitation was not demonstrated for the women, it is hypothesized that the peripheral PAP phenomenon may have played a larger role as it is demonstrated more frequently in type II muscle fibers (Neltner et al. 2020; Rattey et al. 2005; Matkowski et al. 2011; Cornwall et al. 2012; Thorstensson & Carlson 1987; Mannion et al. 1997; Bajek et al. 2000; Stull et al. 2011; Rayment 1993; Lowey & Trybus 2010). Isometric, unilateral handgrip holds to failure therefore have been demonstrated to produce reliable measures of MVIC forces across multiple visits, while producing sex-dependent responses in handedness, force production in the CON limb, and perceptual responses in the active muscle. This study additionally demonstrated that isometric holds to failure produced a CON limb facilitation effect in men and not women, despite similar times to failure during a relative 50% MVIC hold.

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VITA

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EDUCATION

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Thesis: *Examination of Sex- and Limb-Specific Fatigue During Unilateral, Isometric Forearm Exercise*

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Assistant Manager and Sales Associate at Pecatonica Hardware	**2016-Present**
Tutor at the University of Kentucky CATS Center	**2018-2019**
University of Kentucky Resident Advisor	**2017-2018**
University of Kentucky KHP LLP Peer Mentor	**2016-2017**
Facilities Assistant at the Johnson Center	**2016-2017**

Scholastic and Professional Honors

Kinesiology and Health Promotion Research Award	**2020-2021**
College of Education Dean’s List	**2015-2021**
University of Kentucky Heritage Scholarship	**2015-2019**

PUBLICATIONS

1. Dinyer, T. K., Soucie, E. P., Succi, P. J., **Voskuil, C. C.**, Byrd, M. T., & Bergstrom, H. C. Interlimb Muscular Performance and Neuromuscular Fatigue are not Sex-Dependent During Low-Load Fatiguing Bilateral Leg Extension Exercise. *NueroSports*, Vol. 1, Article 7. April 2021.
2. Succi, P.J., Dinyer, T.K., Byrd, M.T., Souci, E.P., **Voskuil, C.C.**, and Bergstrom, H.C. Test-retest reliability of critical power, critical heart rate, time to exhaustion, and average heart rate during cycle ergometry. *Journal of Science in Sport and Exercise Online*, April 2021.

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1. **Voskuil, C.C.**, Dinyer, T.K., Succi, P.J., Bryd, M.T., Garver, J.G., Rickard, A.J., Miller, W.M., Burns, S., Bergstrom, H.C. Affective and Perceptual Responses During a 4-week Low- Vs. High-load Resistance Training Intervention. (Accepted for presentation at American College of Sports Medicine National Conference, 2021).

2. **Voskuil, C. C.**, Dinyer, T. K., Succi, P. J., Abel, M. G., Campbell, M. S., Bergstrom, H. C. Unilateral Muscular Fatigue from Handgrip Holds on Ipsilateral and Contralateral Performance Fatigability. (Accepted for Presentation at the National Strength and Conditioning Annual Convention, 2021).

3. **Voskuil, C. C.**, Dinyer, T. K., Succi, P. J., Byrd, M. T., Garver, M. J., Rickard, A. J., Miller, W. M., Burns, S., Soucie, E. P., & Bergstrom, H. C. Acute and early-phase perceptual response to 30% 1RM training to failure in untrained women. (Presented at the National Strength and Conditioning Annual Convention, 2020, Online).

4. Dinyer, T. K., Succi, P. J., **Voskuil, C. C.**, Soucie, E. P., Clasey, J. L., Abel, M. G., Butterfield, T. A., Bergstrom, H. C. Load-, but not Sex-, Dependent Responses in Leg Extension Performance Fatigability around the Critical Load. (Accepted for Presentation at the National Strength and Conditioning Annual Convention, 2021).

5. Dinyer, T.K., Soucie, E.P., Succi, P.J., **Voskuil, C.C.**, Byrd, M.T., Bergstrom, H.C. Inter- and Intra-individual Differences in Neuromuscular Responses during Submaximal Leg Extension Exercise. (Accepted for Presentation at American College of Sports Medicine National Conference, May 2021).

6. Succi, P. J., Dinyer, T.K., **Voskuil, C. C.**, Byrd, M. T., Bergstrom, H. C. Time Course of Changes in Physiological and Perceptual Responses during Incremental versus Constant Power Exercise. (Accepted for Presentation at the National Strength and Conditioning Annual Convention, 2021).

7. Succi, P.J., Dinyer, T.K., **Voskuil, C.C.**, Byrd, M.T., Bergstrom, H.C. Inter- And Intra-individual Vo_2 Responses Above Critical Power. (Accepted for Presentation at American College of Sports Medicine National Conference, May 2021).

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1. **Voskuil, C.C.**, Dinyer, T.K., Succi, P.J., Byrd, M.T., Garver, M.J., Rickard, A.J., Miller, W.M., Burns, S., & Bergstrom, H.C. Affective responses to performing repetitions to failure at 30% versus 80% one-repetition maximum in untrained women. (Presented at the Southeast American College of Sports Medicine Regional Chapter Convention, 2021, Virtual).

2. **Voskuil, C. C.**, Dinyer, T. K., Byrd, M. T., Vesotsky, A. N., Succi, P. J., & Bergstrom, H. C. Linear and nonlinear modeling of critical resistance. (Presented at the Southeast American College of Sports Medicine Regional Chapter Convention, 2020, Jacksonville, FL).

3. Dinyer, T.K., Soucie, E.P., Succi, P.J., **Voskuil, C.C.**, Byrd, M.T., & Bergstrom, H.C. Inter- and intra-individual differences in neuromuscular responses during submaximal leg extension exercise. Presented at the Southeast American College of Sports Medicine Regional Chapter Convention, 2021, Virtual).

4. Succi, P.J., Dinyer, T.K., **Voskuil, C.C.**, Byrd, M.T., & Bergstrom, H.C. Inter- and Intra-Individual O_2 Responses Above Critical Power. (Presented at the Southeast American College of Sports Medicine Regional Chapter Convention, 2021, Virtual).

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7. Dinyer, T. K., Byrd, M. T., Succi, P. J., **Voskuil, C. C.**, & Bergstrom, H. C. Sex-related differences in neuromuscular responses during exercise performed below

and above critical resistance. (Presented at the Southeast American College of Sports Medicine Regional Chapter Convention, 2020, Jacksonville, FL).

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