Sex-Based Differences in the Response of Resistance-Trained Male and Female Athletes to Resistance Exercise

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Statement of Authenticity

This work, to the best of my knowledge and belief, is original work except where otherwise acknowledged. I hereby declare that I have not previously submitted this content, either in full or in part, for a degree at this or any other institution.

Emily Kate Ellis Metcalf

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List of Abbreviations

½ RT	Half relaxation time
1-RM	1-repetition maximum
AEMG	Average of rectified EMG
ANOVA	Analysis of variance
BW	Bodyweight
DeoxyHb	Deoxygenated haemoglobin
FF	Free-flow (normal blood flow) muscle conditions
I	Ischaemic muscle conditions
IP	Immediately post exercise
MAP	Mean arterial pressure
MVIC	Maximal voluntary isometric contraction
MVT	Maximal voluntary torque
M-wave	Muscle compound action potential
NvRTD	Normalised voluntary rate of torque development
PDT	Peak dynamic torque
PDTL5	Peak dynamic torque of the last 5 reps
POMS	Profile of mood states
PT	Potentiated twitch
RER	Rate of EMG rise
RMS	Root mean square
RPE	Rating of perceived exertion
sEMG	Surface electromyogram

TPT	Time to peak twitch
TSI	Tissue saturation index
T_{sup}	Superimposed twitch
VA	Voluntary activation
VL	Vastus lateralis
VM	Vastus medialis
vRTD	Voluntary rate of torque development

Abstract

Previous research on novice athletes has indicated between-sex differences in fatigability during low-intensity contractions. These studies are limited in their application, as they utilise single limb, single contraction type exercises. However, it is currently unclear whether these differences extend to resistance-trained athletes, particularly after a full-body resistance training session.

The aim of this thesis was to observe the between-sex differences in muscle fatigability of resistance-trained male and female athletes. The pilot study was developed to establish whether the previously observed between-sex differences in the muscular fatigability of novice athletes extends to resistance-trained athletes. This study used a heavy knee extensor resistance exercise session, and found females had less muscular fatigue than males. Despite both sexes experiencing reductions in maximal voluntary torque, only males had reductions in rate of torque development even when between-sex differences in strength were corrected for. The results of this study informed the main study of this thesis, aimed to expose resistance-trained athletes to a 'real world' full-body resistance exercise session, and assess whether the between-sex differences observed in the pilot study continue to be present. Additionally, a longer period of assessment was included in the main study, to examine not only the immediate fatigue but also the recovery of the athletes following the session. This main study found both male and female athletes fatigued similarly after the full-body resistance exercise session, and all measurements had returned to baseline levels at 24 hours post exercise completion.

The results of this study indicate between-sex differences can be observed in resistance-trained athletes when they are exposed to significant and localised fatigue. However, in the context of a full-body training session, these differences are no longer observed.

Chapter 1: Introduction

1.1 Background

Historically, resistance exercise prescription guidelines for female athletes in a competitive performance setting have not been informed by sex-specific research. This may partly be explained by the significant underrepresentation of females (only 37% of participants) in health trials (1); additionally, only 13% of studies analyse their data specific to sex (2). From this, a lack of knowledge is available to inform the understanding of female biology and physiology (3), leaving exercise professionals to adapt or follow male-centric research findings. This practice can lead to poorly informed exercise prescriptions, hindering their effectiveness. The differences between males and females also expand beyond the purely physical, as for example post-learning stress enhanced memory has been observed in males, but not females (4). Due to the lack of knowledge on both the physiological and psychological differences between males and females, the question is raised whether generalising the results of studies using male participants to females is appropriate, and truly evidence-based practice. Due to the current lack of knowledge and research on female athletes, particularly well-trained and competitive female athletes, there is a clear requirement for sex-based research to inform effective training for both sexes.

It has been found that males and females exhibit differences in their muscular fatigability following isometric and dynamic contractions, where fatigability is defined by reductions in maximal voluntary torque and rate of torque development (5). Females have displayed a longer time to task failure in both sustained and dynamic tasks across a range of contraction intensities and muscle groups (6). These between-sex differences in fatigability can be explained via a range of factors such as greater perfusion to active muscle and the increased utilisation of oxidative metabolism in females (7, 8), the greater strength and muscle mass typically observed in males (9, 10), in addition to differences in muscle contractility and central motor output (11).

Previous research has examined sex-based differences in fatigability of untrained individuals, typically through investigating the contributions of both central motor output (i.e. muscle activation, voluntary activation) and muscle contractility (i.e. electrically evoked twitch responses of the muscle) (7, 8, 12, 13). Studies on sex-based differences in novices found that impaired central motor output was a contributor to greater muscle fatigability in males than females (8), with males exhibiting greater reduction in the voluntary activation of ankle dorsiflexors (8) and knee extensors (12, 14) compared with females. Males also exhibit greater reductions in evoked twitches of the elbow flexor muscles compared to females (15), suggesting that factors associated with the contractility of muscle (i.e. perfusion, fibre type, predominant energy system usage) influence between-sex differences in muscle fatigability. However in trained males, central motor output was well maintained after resistance exercise despite reductions in quadriceps twitch amplitude of up to 70% from baseline values (16). This resilience in central motor output was thought to be explained by the significant adaptations in the central nervous system (17) exhibited by trained individuals such as increased supraspinal drive and greater input-output responses at the level of the α-motoneuron (18-20). It is unclear, as a result of this increased resilience in central motor output with training, whether similar sex-based differences will be observed in trained individuals as it has been in novices. While sex-based differences in the muscle fatigability of novices can be primarily explained by both muscle contractility and central motor output reductions, it is likely any differences in fatigability observed after resistance exercise in trained males and females are explained by greater reductions in muscle contractility as opposed to central motor output due to the adaptations acquired through training.

The current body of research is difficult to translate into practice as studies typically use a fixed contraction intensity for the exercise bout (e.g. 20 or 80% of maximal strength), or an isolated concentric or eccentric only movement (8, 12, 14). No study has yet examined the sex-based differences in muscular fatigability following resistance exercise sessions that resemble traditional prescriptions, such as using a range of contraction intensities, contraction types, and active muscle groups. While it has been suggested that muscle perfusion and oxygenation may be a factor in between-sex differences in the muscle fatigability of novices, its impact in trained athletes has not yet been examined. Moreover,

no study has yet examined whether the between-sex differences in muscle fatigability observed in novice athletes extends to trained males and females, or whether their trained status alters this discrepancy.

1.2 Overview of Thesis

To address gaps in the current literature and to better inform clinical practice, this thesis was designed to examine the existence of sex-based differences in the fatigability of resistance-trained male and female athletes. It did so in two contexts, single limb exercise at a variety of intensities, and a full-body resistance training session which utilised a variety of contraction types, intensities, and active muscle groups. The pilot study focused on single limb exercise, and observed between-sex differences in muscle fatigability, particularly muscle contractility, in resistance-trained male and female athletes. The main study of this thesis utilised a full-body resistance exercise session, expanding the examination to a training session which replicated a real-world prescription provided for professional sports teams as part of their strength and conditioning programs. This progression increased the external validity of this full-body session study. In addition, the saturation of oxygen and deoxyhaemoglobin measures were examined in these athletes, as previous studies on novice athletes (6-8) indicated that this parameter may provide some understanding of sex-based differences in fatigability.

Chapter 2: Literature Review

This chapter serves to examine the current climate of sex-specific research in the area of sport and exercise science. Following this, a summary of the most relevant and appropriate resistance training studies which have compared male and female athletes has been included. To conclude this chapter, an in-depth examination of the differences between sexes regarding physiology and anatomy is included, with explanations on how these impact differences in performance.

2.1 Sex Bias in Health Research

Published research in the sector of health, particularly the field of sport and exercise science, is dominated with male participants. Females are significantly underrepresented in health trials (1), comprising only 37% of participants, and only 13% of studies analysed their data specific to sex (2). The lack of female participation in health science research compromises our understanding of the unique intricacies of female biology and physiology (3). Overgeneralisation of results from male-based research may be harmful for females – with an example being 'abnormal' presentations of conditions such as coronary artery disease leading to delayed diagnosis, which in some cases can become life threatening (1, 21). Another example of detriment arising from the overgeneralisation of results is the recommendation of aspirin to reduce the incidence of coronary heart disease. A protective effect was discovered in men - however, regular aspirin usage may actually increase the risk of bleeding events for females (22). The differences between males and females also expands beyond the purely physical: Cahill (4) found that post-learning stress enhanced memory in males, but not females. These examples, albeit not specific to sport and exercise science, illustrate not only the differences in anatomy and physiology between males and females, but also highlight potential risks involved in the overgeneralisation of results.

On average males and females have similar participation rates in physical activity, as is the case in Australia (23). Given the lack of data available for female athletes, especially those that are resistance-trained (2), sourcing well-trained female participants is more difficult than similarly trained males. This may be due to females tending towards other forms of physical activity (23). It has also been argued that females, due to their fluctuating hormone levels, introduce possible confounding factors to research which may decrease the homogeneity of the sample (24). Controlling for the variability in the female hormonal cycle, which can be inconsistent, can create an increased complication that can make research logistically difficult.

It is possible that the lack of female participants in sport science and health research is due to a smaller number of suitable participants, or due to the hormone cycle introducing unwanted complications and variables.

2.2 Fatigue and Resistance Exercise Prescription

Muscular fatigue is defined as the reduced ability of the muscle to produce muscular force or power; influenced by both 'central' or neural components, and 'peripheral' or muscular components, it is reversible with rest (25, 26). The type of fatigue is denoted by its location relative to the neuromuscular junction (25, 27, 28). Central components of fatigue consist of factors within the central nervous system and thus before the neuromuscular junction, which can impact the voluntary drive to motoneurons (25, 27). Central fatigue occurs when there is a decrease in voluntary drive to the motoneurons, resulting in a measurable reduction in force (25). Central fatigue can be further broken down in to supra-spinal and spinal mechanisms. Supra-spinal factors decease the excitability of the motor cortex, while spinal factors consist of feedback from the muscle spindles, Golgi-tendon organ, group III and IV afferents that impact the excitability of motorneurons, and α-motoneuron excitability (27). Peripheral components of fatigue consist of factors below the neuromuscular junction and within the muscle fibre. Peripheral fatigue thus occurs when there is a reduced capacity to propagate action potentials, and the inability to trigger excitation-contraction coupling resulting in a muscular contraction (29). The concentrations and locations of certain ions are altered

following exercise, which in turn results in peripheral muscle fatigue. Excitability of the muscle is reduced by increased extra-cellular K^+ ions, as K^+ efflux is inhibited, in turn reducing the ability of the muscle to repolarise (30, 31), as well as the accumulation of H^+ ions. The impaired release of Ca^{2+} from the sarcoplasmic reticulum is a contributor to peripheral muscle fatigue, as the excitation-contraction coupling process relies on this release (30). Alterations in the balance of ions in the sarcoplasmic reticulum disrupts the flow of Ca^{2+}, another factor required for excitation-contraction coupling and contraction (31, 32).

Consideration of the magnitude and type of muscle fatigue plays an important role in the prescription and scheduling of exercise for athletes. Optimising athlete development and performance requires an exercise prescription strategy that carefully balances performance and stress to the body, with periods of recovery and regeneration to mitigate the risk of performance inhibiting fatigue (33). Accumulating fatigue through a high volume of high intensity training without appropriate recovery periods will have a negative impact on athlete performance (34).

Training to fatigue can be employed as a stimulus in exercise prescription. It is thought by some to be the most influential factor in enhancing training outcomes (35-37). Training to failure, whether at high or low intensity, has been found to increase muscle protein synthesis (38), however, a delicate balance between fatigue and recovery must be created. Too little or too much fatigue, and the athlete will not reap any performance benefits. There are multiple ways in which an optimal level of fatigue may be elicited. Some studies employ a 'no rest' protocol, where each set is performed back to back without inter-set rest periods. This methodology has been found to improve dynamic strength in novice athletes to a greater extent than the comparison 'rest' group (35). Another method used to produce fatigue within a training session is training to repetition failure, when the athlete can no longer perform the task or exercise. This latter methodology has been shown to foster greater improvements in both strength and power in trained individuals when compared with a group who performed exercise sessions of equal volume and intensity, but with assigned rest periods (36). From these studies it may be inferred that

employing some form of fatigue-inducing exercise, whether it be through manipulation of rest periods or training to repetition failure, can be beneficial for athletes regardless of training status.

Excessive muscle fatigue of the athlete can be detrimental to performance (39), and there is no linear relationship between exercising to fatigue and performance improvement, particularly as the physiological response to training has individual variability (40). Without appropriate rest and recovery periods, athletes and coaches will notice a sacrifice in performance, motivation, and adaptation due to over training (41, 42). Aside from its use as a training stimulus to elicit maximal improvements in performance, fatigue should also be considered as an influential element in the prescription and scheduling of exercise within the context of a training week or cycle. Optimal athlete development and performance requires an exercise prescription strategy that carefully balances stress or fatigue with recovery (43). Understanding the location and magnitude of fatigue plays a role in the scheduling of exercise, as each type is elicited by differing exercise intensities or durations, and has differing recovery rates. Typically central or nervous system fatigue is associated with fast recovery times, whereas peripheral or muscle fatigue can take hours or longer to fully recover (44). It is the responsibility of the coach to ensure adequate fatiguing stimulus and recovery to elicit meaningful increases in performance, without negatively impacting the wellbeing of the athlete.

Due to the delicate balance of fatigue and recovery required for optimal athlete performance, it is important to assess sex-based differences in the response of athletes to exercise. Differing amounts of muscle fatigue may result from identical exercise sessions for males and females, and thus result in differing amounts of improvement. To optimise athletic performance of both males and females, the responses of the athletes to a real-world resistance training session should be assessed, to determine whether sex-specific training guidelines are required.

2.3 Resistance Training Studies

Table 1 below summarises published articles which have compared the responses of male and female athletes to resistance exercise.

Table 1: Summary of resistance training studies in literature.

Reference	Subjects	Aim	Method	Findings
7. Maughan R, Harmon M, Leiper J, Sale D, Delman A. Endurance capacity of untrained males and females in isometric and dynamic muscular contractions. European Journal of Applied Physiology and Occupational Physiology. 1986;55(4):395-400.	25 males 25 females Untrained athletes	This study aimed to compare muscle fatigue response of untrained males and females in both upper and lower body resistance exercises.	**Isometric Leg Extension** Performed a maximal isometric leg extension, 3 attempts allowed. After 10min rest, subjects performed isometric contractions at 80, 50, and 20% MVC. Always performed in same order, 5 min rest allowed between each. **Bilateral Elbow Flexion** 1RM weight was determined. 5 separate occasions (>48hrs between) reps of concentric contraction to failure at 90, 80, 70, 60, and 50% of 1RM, with tests performed in random order.	**Isometric Leg Extension** There were no sex-based differences in time to task failure at 80% or 50% of MVC, however females had a greater time to failure at 20% of MVC. **Bilateral Elbow Flexion** At 90% and 80% of 1RM there was no difference between males and females. At 70%, 60% and 50% females were able to complete more contractions than males. The authors believe greater sex-differences in dynamic force production lie in the differences in muscle fibre composition (greater proportion of Type 1 in females than males). The muscle fibre differences may also then be linked to metabolic differences, such as greater oxidative energy system usage which reduces production of metabolites such as acid which can inhibit muscle contractility. Differences at low forces could be explained by greater muscle blood flow in females (lower force output = less restriction on blood vessels).

Reference	Subjects	Aim	Method	Findings
8. Russ DW, Kent-Braun JA. Sex differences in human skeletal muscle fatigue are eliminated under ischemic conditions. J Appl Physiol. 2003;94(6):2414-22.	8 males 8 females Similarly active	Compare male and female responses to two circulatory conditions: free flow (normal circulation) and ischaemia.	Ischaemic conditions (I) achieved using pneumatic thigh cuff. Stimulated peroneal nerve, force measured using force transducer. Each protocol involved 4 mins of 5s MVIC, 5s rest. At the end of mins 1, 2, and 3 a single stimulus was delivered at rest. A 50 Hz train was delivered during final MVIC. Immediately after final MVIC, a single pulse, a 50 Hz train, and a 10 Hz train were delivered in that order. In I condition thigh cuff was immediately released following 10 Hz train. Same sequence was delivered at 2, 5, and 10 mins post protocol. At 10 mins post a 50 Hz train was also delivered during an MVIC. All participants performed both protocols.	Males exhibited greater fatigue than females in the normal blood flow (FF) condition, but not the I condition. No significant effects of sex were found for stimulated force. Men experienced greater decline in central activation in FF, but not I condition. No sex-based differences in peripheral activation. Authors concluded between-sex differences in muscle fatigue are blood flow related, and a central activation was more impaired in males which was a primary contributor to greater fatigue in males compared to females.

Reference	Subjects	Aim	Method	Findings
14. Hunter SK, Critchlow A, Shin I-S, Enoka RM. Fatigability of the elbow flexor muscles for a sustained submaximal contraction is similar in men and women matched for strength. J Appl Physiol. 2004;96(1):195-202.	10 males 10 females Strength matched	Compare time to task failure for sustained isometric submaximal contraction of elbow flexors in strength matched males and females.	Individual MVCs and targets determined prior to fatiguing task. Subject instructed to maintain contraction of elbow flexor muscles @ 20% of MVC. Fatigue was determined as when torque declined by 10% of the target 20% value for longer than 5s, or when the subject lifted the elbow off support for longer than 5s. Strong verbal encouragement given. RPE assessed at 30s intervals during fatiguing task.	Time to task failure was similar between males and females in strength matched group. For all subjects, females were weaker than males and had longer time to task failure. No association between performance and day of menstrual cycle for females. MAP, HR, and RPE values were similar between males and females throughout the fatiguing trial. Females had greater bursts of EMG activity during contraction, however no correlation found between this and time to task failure. Females also had less AEMG (smaller %) throughout contraction and a reduced rate of increase. Strength-matched males and females experienced similar cardiovascular adjustments. EMG activity differed between the sexes. Males and females achieved similar time to fatigue with varying strategies of activating the motor neuron pool.

Reference	Subjects	Aim	Method	Findings
12. Hunter SK, Critchlow A, Shin I-S, Enoka RM. Men are more fatigable than strength-matched women when performing intermittent submaximal contractions. J Appl Physiol. 2004;96(6):2125-32.	10 males 10 females Strength matched	Compare time to task failure for intermittent submaximal contractions of elbow flexors in strength matched males and females.	Individual MVCs and targets determined prior to fatiguing task. Intermittent isometric contractions @ 50% MVC, contraction for 6s and rest for 4s. Once every minute, MVC performed during 6s contraction period. Fatigue was determined as when torque declined by 10% of the 50% target values for longer than 5s, or when subject lifted elbow off support for longer than 5s. Strong verbal encouragement given. RPE assessed at 30s intervals during fatiguing task.	Time to task failure was longer for females compared to males (7/10 pairs showed this, 3/10 had similar time to fatigue). No association between performance and day of menstrual cycle for females. Rates of increase in mean arterial pressure (MAP), HR, and RPE were less for females. Similar values at task failure. Authors suggest females had more efficient clearance of metabolites during rest period, diminish metaboreflex which increases MAP. AEMG and amplitude of torque fluctuations differed between males and females. Females had less AEMG for elbow flexor muscles during contractions and task failure, less fluctuation in vertical torque at task failure. Authors suggest males required greater rate of descending drive, seen in EMG activity, to maintain similar torque as strength-matched females.

Reference	Subjects	Aim	Method	Findings
13. Yoon T, Delap BS, Griffith EE, Hunter SK. Mechanisms of fatigue differ after low- and high-force fatiguing contractions in men and women. Muscle & Nerve. 2007;36(4):515-24.	9 males 9 females Similarly active	Compare time to task failure and voluntary activation of males and females for sustained isometric contraction performed at a low and high intensity with the elbow flexor muscles.	Each session followed this structure: determination of supramaximal electrical stimulation, assessment of MVC torque and VA, performed MVC, brief submaximal isometric contractions to determine EMG force and voluntary activation torque relations, performed fatiguing contraction at either 20% or 80% of MVC, immediately followed by twitch contraction, a recovery MVC, and another twitch contraction. Maintain an isometric contraction at 20% or 80% of previously determined MVC until failure (order randomised) determined as force decline by 10% for 3-5s. Force output measured via a dynamometer strapped to the arm, elbow joint set so forearm was horizontal to the floor. Electrical stimulation used to assess VA, stimulating cathode on biceps brachii, anode on bicipital tendon. Included control twitch. EMG used to assess muscle activity in biceps brachii, brachioradialis, triceps brachii. HR and BP monitored via automated beat-by-beat blood pressure monitor.	Males had shorter time to task failure than females in 20% MVC, however males and females had similar times in the 80% task. Decline in MVC torque was greater for females than males in 20% contraction, however was similar in 80% task. Voluntary activation declined similarly for males and females in both the 20% and 80% tasks. Control twitch amplitude indicates similar magnitude of peripheral fatigue in both tasks for both males and females. Rate of change in MAP was the single predictor of time to failure for the 20% MVC fatiguing contraction, with MAP increasing more for males than females and at a greater rate of increase. 80% recordings were poor and not analysed. HR increases were similar and there was no impact on time to task failure etc. RPE values were similar, however rate of increase in RPE was more gradual for females than males.

Reference	Subjects	Aim	Method	Findings
11. Lee A, Baxter J, Eischer C, Gage M, Hunter SK, Yoon T. Sex differences in neuromuscular function after repeated eccentric contractions of the knee extensor muscles. Eur J Appl Physiol. 2017;117(6):1119-30.	13 males 13 females Recreationally active	Examine mechanisms for reductions in force and power during and up to 48 hours after maximal eccentric contractions of knee extensors.	Performed 150 maximal effort eccentric contractions (5 sets of 30) with the knee extensor muscles at 60° s^{-1}. MVIC and MVCC were performed before and after the 150 eccentric contractions. The MVCCs involved a set of two isokinetic contractions at 60° s^{-1} and sets of isotonic contractions performed at seven different resistance loads (1 N m, 10, 20, 30, 40, 50, and 60% MVIC). Electrical stimulation was used during the MVICs and at rest to determine changes in voluntary activation and contractile properties.	There were no sex-related differences in either muscle soreness, the reduction of maximal isometric strength, or recovery of peak power up to 48 hrs after repeated maximal eccentric contractions. Both reductions in voluntary activation and contractile function were associated with the reductions in MVIC torque immediately after the termination of the eccentric contraction exercise. The loss in MVIC torque at 48 hours post was primarily due to central mechanisms, because voluntary activation was reduced and the resting twitch amplitude had recovered to baseline levels.

This table summarises the available published studies examining the muscle fatigue responses to resistance training sessions. All studies utilised single muscle group, single contraction type exercises. The majority of studies also used novice participants, with the exception being the most recent study by Lee *et al.* (11) using recreationally active participants. No studies were found that compared the muscle fatigue response of resistance-trained male and female athletes. From these studies, it can be determined that isometric contractions at high intensity, e.g. 80% of MVC, lead to similar fatigue responses in males and females (7, 13), isometric contractions at moderate intensity, e.g. 50% of MVC, lead to inconsistent differences in the muscle fatigue response of males and females (7, 12), and isometric contractions at low intensity, e.g. 20% of MVC, consistently showed a longer time to task failure for female athletes (7, 13, 14). Intermittent concentric contractions of the upper limb showed no differences in time to task failure of males and females at high intensities, 80%-90%, and longer time to task failure for females at lower intensities, 50-70% (7). Eccentric contractions of the knee extensors found no differences in muscle fatigue responses between the sexes at any intensity (11). When an ischaemic condition was compared with a normal blood flow condition, it was determined that males experience greater fatigue in normal flow conditions, but these differences disappear in an ischaemic condition (8).

From these results it is likely that blood flow plays a primary role in the sex-based differences in muscular fatigue. An artificially induced ischaemic condition mitigated differences between the sexes (8), and a similar response is seen when isometric contractions are performed at high intensity (7, 13). During lower intensity or intermittent contractions, more optimal blood flow can be achieved, possibly due to less pressure on the blood vessels which would otherwise partially occlude blood flow, and thus between-sex differences are observed (7, 11-14). While this theory may explain between-sex differences in muscle fatigability, no study has directly examined muscle blood flow to determine whether it plays a significant role in between-sex differences in fatigability. Additionally, these studies were performed on novices or recreationally trained athletes. It is unclear whether these differences would extend to resistance-trained athletes, as training causes adaptations in the muscles and nervous system. With additional muscle bulk in both sexes as a result of resistance training, it is unclear whether

the hypothesis that greater muscle bulk places pressure on blood vessels and reduces blood flow more in males will still result in meaningful differences between the sexes in muscle fatigue response.

The possible reasoning behind observed sex-based differences in muscle fatigue response to resistance exercise are detailed below, particularly differences in muscle anatomy, primary energy system utilisation, muscular perfusion, and central motor output between the sexes.

2.4 Muscle Composition Differences Between the Sexes

Males and females typically differ in both the volume and composition of skeletal muscle, although these differences vary with training status. In an analysis of 468 healthy males and females, it was found that on average males have greater absolute (33 kg versus 21 kg) and relative (38.4% versus 30.6%) skeletal muscle mass than females (9). Muscle biopsies from novice athletes indicate that while the number of type I and type II fibres do not differ between male and females, males generally have a greater area (%) and fibre size of type II muscle fibres than females, while females have a greater area (%) of type I fibres (45, 46). It is well established that a common adaptation following resistance exercise is increased muscle fibre cross sectional area, or hypertrophy (47). Type II muscle fibres adapt most readily to resistance training, exhibiting greater hypertrophy over type I fibres (48-50). Male and female athletes have shown a similar percentage increase in muscle size in response to resistance training, however absolute increases in muscle cross sectional area are greater in males (51, 52).

Although the absolute and relative masses of muscle are different between sexes, male and female athletes have similar proportions of the number of type I and type II muscle fibres. Male athletes have a greater % area of type II muscle fibres, and female athletes have a greater % area of type I muscle fibres, regardless of training status.

2.5 Energy System Differences Between the Sexes

Energy systems run in conjunction with each other to provide energy for working muscle (53). Sex-based differences in primary substrate utilisation have been found, as males and females utilise different substrates for the majority of their energy production during exercise, and this is true in both trained and untrained athletes (54). Males have a greater *in vivo* glycolytic rate than females, while females rely predominantly on fat oxidation to produce energy during exercise (46, 54-57).

It has been postulated that the differences in energy production and metabolic waste products may partially explain the greater acidosis found in males after isometric exercises of the ankle dorsiflexors (55, 56) and contractions of the finger flexor muscles (58). Greater acidosis is not always linked, however, to greater fatigue in males (55). One study comparing recreational athletes after a sprint cycling protocol found glycogen reduction was 42% less, and lactate content was 20% lower, in type I muscle fibres in females than males (59). A similar study with sprint cycling in physically active males and females found less accumulation of ATP breakdown products alongside other metabolites in females, hypothesising that a smaller reduction of ATP in females than males post exercise was due to faster recovery of ATP (60). Both studies performed by Esbjörnsson-Liljedahl *et al.* above however do not note any sex-based differences in fatigue and recovery, and thus is it not known whether the measured differences in metabolism impacted fatigue variables.

While it is known that in males the post exercise variables mentioned above such as greater acidosis, greater reduction in ATP levels, and greater lactate content are generally related to a faster time to fatigue compared to females, this is not always the case. Even when a distinctive sex-based difference is found in the muscle, this does not always translate to differences in performance.

2.6 Muscle Perfusion Differences Between the Sexes

In a study of fatigability differences between the sexes in novice athletes (8), one explanation provided for the differences in fatigability of males and females was muscular perfusion. The athletes were exposed to two blood flow conditions, free flow and ischaemia. Sex-based differences in time to fatigue were seen in the free flow conditions, however these were mitigated in the ischaemic condition. This led researchers to propose that muscular perfusion has a significant impact on differences of the fatigability of muscle between sexes.

Females have greater capillarisation within the muscle in comparison to males (61) which allows for greater blood flow within the muscle. Additionally, male athletes often have greater skeletal muscle mass and produce larger amounts of torque during exercise; these two factors possibly contribute to greater localised blood flow occlusion in males when compared with female athletes (7). Poor muscular perfusion can mean decreased time to fatigue due to reduced oxygen delivery to the muscle, and inhibition of metabolic waste product removal, both of which impede muscular contraction (8, 62). When the less optimal muscle perfusion in males is coupled with the greater production of metabolites (see 2.5 Energy System Differences Between the Sexes), greater fatigability is seen.

2.7 Central Motor Output Differences Between the Sexes

As with other factors that contribute to the sex-based differences in fatigability, muscle group specific central motor output differences have been observed in novices. Supraspinal fatigue is an elemental of central fatigue, and is due to reduced output from the motor cortex (25). Males were found to have greater reduction of their voluntary activation in the ankle dorsiflexors than females (8), with similar findings in the knee extensors (63). These greater reductions in voluntary activation of males were further associated with a larger decrease in force output than females. In the elbow flexors however, there was no difference in supraspinal fatigue, however males exhibited greater overall muscular fatigue (15). These results lead to the conclusion that the impact of central motor ouput and supraspinal fatigue is dependant on the fatiguing muscles.

Another between-sex difference in central motor output has been observed, particularly peripheral afferent feedback. This mechanism is related to the greater muscle ischaemia and metabolite accumulation in men, associated with their greater reliance on glycolysis for energy production. The group III and IV muscle afferents are sensitive to the ischaemia and metabolite accumulation, and thus depress cortical excitation (55, 64-66). This as a result may lead to greater reductions in voluntary activation in males, however research is not conclusive on this link (6).

Given that the above studies were all performed on novices, it is unclear whether these sex-based differences will present in trained athletes. With training comes adaptations of the nervous system (17), namely increased supraspinal drive and greater input-output responses at the level of the α-motoneuron (18-20). Indeed, a study on trained males found that even when reductions in quadriceps twitch amplitude of up to 70% were experienced, central motor output was maintained (16). However, this study was performed solely on trained male athletes, and involved a single limb, single contraction type exercise session.

Current research does not offer insight into whether the resilience in central motor output observed in trained male athletes despite significant muscular fatigue will persist to trained female athletes. Additionally, with the differing influence of voluntary activation on fatigue and performance between the upper and lower limbs, it is unclear whether differences will be present following a full-body resistance training session.

2.8 Summary

At present, there is a lack of high-quality research examining the fatigue response of well-trained female athletes following resistance training. It is well established that the appropriate balance of fatigue and recovery can elicit a training effect in well-trained athletes, however too much may lead to diminution in performance and mood. There are significant anatomical and physiological differences between the sexes, specifically in muscle composition, muscle metabolism, perfusion, and central motor output. Females

have proportionately less muscle, with greater cross-sectional area of type I fibres, and less cross-sectional area of type II fibres in comparison to males. Males rely more on glycolysis for energy production, whereas females rely more heavily on lipid oxidation. As a result, females tend to have less build-up of metabolites following exercise. Less muscle mass and thus pressure on the blood vessels, coupled with greater capillarisation has led to better perfusion to the working muscle in females. In a study on novices, females were found to be more fatigue resistant than males in free flow conditions, whereas fatigue response was the same in ischaemic conditions. It is likely a combination of the energy system and muscle perfusion differences that lead to this sex-based difference in the fatigue response. Finally, central motor output changes observed in both novices and trained individuals found males experienced a greater reduction in voluntary activation following an exercise session.

From these observations in the literature, it is clear there are many differences already observed between males and females, both novice and trained. Some of these observations have been found to impact differing fatigue responses, however evidence in trained individuals is scarce. It is necessary to examine sex-based differences in fatigue of trained individuals further to strengthen the findings and correlations between the anatomical and physiological differences, and performance outcomes.

Chapter 3: Summary of Pilot Study on Between-Sex Differences Following Leg Extension Task

Supervisor Statement

The data in this chapter was collected prior to the commencement of Emily Metcalf's Master of Research, and served as the pilot data for her main study.

Emily was responsible for:

- Analysis of the data
- Lead author on the published manuscript associated with the data (Appendix 1).

I confirm that the content in this thesis pertaining to the data collected for this chapter is entirely the result of Emily's data analysis and writing. The final published manuscript provides a contrast to the contributions provided by myself and the co-author Dr. Mandy Hagstrom.

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3.1 Objectives

When improving the performance of trained individuals, appropriate balance of stress must be maintained to allow maximal improvement for the athlete. Thus, understanding both the demands of training and the response of the athlete is important when designing an effective program. Studies on novice athletes have indicated the presence of sex-based differences in the fatigue response. A pilot study was developed as a part of this thesis to establish whether there was any merit in assessing sex-based differences in the fatigue response of well-trained athletes, and thus whether it is necessary to develop future research that is both relevant and supports practical applications.

3.2 Method

3.2.1 Subjects

Eight resistance-trained males (mean ± SD; age 26 ± 5 years, height 1.77 ± 0.07 m, weight 78.2 ± 8.7 kg) and eight resistance-trained females (mean ± SD; age 25 ± 3 years, height 1.62 ± 0.06 m, weight 68.2 ± 3.0 kg) voluntarily participated in this study after providing informed written consent.

All participants had a minimum of three years of resistance training experience (≥ 3 sessions/week for majority of the year), with regular performance of both upper and lower body resistance exercises. The participants were all familiar with the exercise task, knee extension, however none reported weekly performance of the movement.

All procedures in this study were approved by the Western Sydney University Human Research Ethics Committee, and were conducted in accordance with the Declaration of Helsinki.

3.2.2 Experimental Design

Participants made two preliminary visits to the laboratory, 24 to 48 hours apart, for familiarisation with the femoral nerve stimulation protocol, and the unilateral maximal isometric testing of the knee extensors (first visit), in addition to a dynamic 1-repetition maximum (1-RM) knee extension test (second visit; Iso-lateral knee extension, Life Fitness, Sydney, AUS). During the familiarisation sessions, participants were also informed of the pre-test nutrition and exercise guidelines, which required the athletes to abstain from alcohol (24 hours prior to testing) and caffeine (12 hours prior to testing) consumption, and resistance or strenuous aerobic exercise for the legs (48 hours prior to testing).

The experimental session occurred between 5 and 7 days after the second familiarisation visit. Pre-workout nutrition was standardised among the participants, with a beverage

consisting of 0.3 g·kg^{-1}BW of 60% maltodextrin and 40% whey protein isolate provided to the participants to be consumed 1 hour prior to testing. Maximal voluntary isometric contractions (MVIC) of the knee extensors of the right leg were performed before and after each experimental training session on an isokinetic dynamometer (KinCom 125, Version 5.32, Chattanooga, USA). Participants were tested in a seated position, with their hip and knee joints flexed to 90° and 75° respectively. The centre of rotation of the lever arm was aligned with the sagittal plane axis of the knee joint. The lever arm of the dynamometer was firmly attached to the lower leg, 2-3cm superior to the lateral malleolus. Straps were also placed diagonally across the trunk to minimise excessive movement by the participant during all MVICs. Torque output signals were continuously sampled at 1000 Hz (Powerlab, ADI Instruments, Sydney, Australia), and a low pass filter was applied at 10 Hz. Torque signals were calibrated in the resting test position for each participant's limb weight after all straps were secured, and a pre-determined calibration factor was applied to the obtained signals for conversion of the recorded voltage to torque (N·m).

Before pre-training MVICs were performed, participants completed a series of sub-maximal isometric knee extension efforts at 25, 50, and 75% of their perceived maximal effort. Following this, two MVICs were performed, with 2 minutes rest allowed between efforts. Participants were instructed to perform the MVIC as fast and forcefully as possible, maintaining this effort until the tester could see a plateau or reduction in force output. Surface electromyograms (sEMG) were recorded continuously from the vastus medialis (VM) and vastus lateralis (VL) muscles during the MVICs. Femoral nerve stimulation (see 3.2.5 Femoral Nerve Stimulation) was applied during and approximately 2-3 seconds after each MVIC. Strong verbal encouragement was provided by the tester during all MVICs to aid in ensuring a true maximal effort by the participant. The post-training MVICs were performed within 1-1.5 minutes after completion of the exercise protocol.

3.2.3 Exercise Session

Knee extension range of motion for each repetition was standardised for each participant. The starting position was set from a seated position on the knee extension machine where

the participant was reclined so the lower limb was vertical, and the knee joint angle was at 110° of flexion. End range of motion was set to where the lower limb was approximately parallel to the floor, which was just before terminal knee extension.

The resistance exercise session was designed to accrue volume across a range of high intensity contractions based on the previously measured 1-RM (average male 1-RM was 40.3 ± 8.3kg, average female 1-RM was 21.3 ± 4.5kg), and was designed to be similar to a strength session in clinical practice. The session began with a warm up set of 10 self-paced, unweighted repetitions, followed by a similar set at 40% of the individuals 1-RM, during which the aforementioned range of motion was established. The working sets are as detailed in Table 2 below:

Table 2: Leg extension exercise session.

Sets	**Reps**	**Intensity (% of 1-RM)**
1	10	60
2	5	80
1	5	85
1	3	87.5
1	2	90
2	Repetition Failure	80

The final 2 sets performed at 80% of 1-RM were performed until repetition failure, when the participant was no longer able to reach the minimum range of motion. Participants were instructed to perform 1.5-2 minutes rest between sets, and to perform each contraction with an as explosive as possible contraction phase, and a controlled lowering of 1.5-2 seconds.

The angle at the knee joint was continuously monitored at 1000 Hz (10 Hz low pass filter) from a single axis electrogoniometer (ADI Instruments, Sydney, Australia). Knee joint angle was then continuously monitored during the extensions to determine successful repetitions which passed through the correct range of motion.

3.2.4 Surface Electromyography

sEMG was recorded from the VM and VL, using paired Ag/AgCl surface electrodes (Maxsensor Medimax Global, Australia). The electrodes (10 mm contact diameter, 10 mm inter-electrode distance) were placed in a bipolar configuration parallel to the direction of the muscle fibres. The skin was carefully prepared by shaving any excess hair, lightly abraded with fine sandpaper, and finally cleaned with an isopropyl alcohol swab. The inferior VM electrode was placed 3-4 cm superior to the lateral aspect of the patella, and the inferior VL electrode was placed 8-12 cm superior to the lateral aspect of the patella. A reference electrode was placed on the right patella.

sEMG signals were recorded using the ML138 Octal BioAmp (common mode rejection ratio > 85 dB at 50 Hz, input impedance 200 MΩ) with 16-bit analog-to-digital conversion, sampled at 4,000 Hz (ADI Instrument, Sydney, AUS). Raw signals were filtered with a fourth-order Bessel filter between 20 and 500 Hz, and subsequently smoothed for analysis using a 50 ms-mean-square calculation (RMS).

3.2.5 Femoral Nerve Stimulation

A 5 x 9 cm custom-made electrode constructed of aluminium foil and conduction gel was taped to the lateral aspect of the hip, equidistant between the iliac crest and greater trochanter, acting as an anode. A cathodal probe was then used to identify the location of the femoral nerve in the participant. The probe was moved around the femoral triangle, applied with firm pressure and using a stimulus intensity of 30 mA until the largest muscle compound action potential (M-wave) was elicited from both the VM and VL recording sites. When the femoral nerve was located, this area was marked with a felt-tip pen, and

a 2 cm diameter Ag/AgCl surface electrode was adhered in replacement of the cathodal probe.

Stimulations applied during MVIC testing were supramaximal doublets applied to the femoral nerve (200 μs square pulses) at 100 Hz and 10 Hz by a high voltage (400 V) constant current stimulator (Digitimer DS7AH; Digitimer, Hertfordshire, UK). Stimulation intensity was determined by progressively increasing the current in 10 mA increments until plateaus were observed in both the twitch amplitude and M-wave response to the 10 Hz doublet stimulation. Supramaximal stimulation for testing was calculated by increasing the final intensity at which the muscle response of the participant plateaued to 130% (intensity range for testing ranged from 80 to 190 mA).

During each MVIC, two superimposed doublets (100 Hz and 10 Hz) were applied to the femoral nerve when the tester determined torque had reached a visible plateau. A 1.5 s time period was used between applied doublets. The resting potentiated twitches were evoked by delivering another two doublets (100 Hz and 10 Hz) to the resting muscle, with the first stimulation in the doublet sequence delivered 2 to 3 s post contraction. Doublets were applied in random order between all measurements. Another study (16) which used a similar methodology found dependant variables were not influenced by the order of doublet stimulation.

3.2.6 MVIC Data Processing

Contraction onset for voluntary torque and resting potentiated twitches were identified with an automated algorithm in LabChart as the point after which torque exceeded the baseline by 2.5 N·m and 1 N·m respectively. VL and VM onsets were visually determined (67). The torque recordings were then used to analyse:

1. The maximal voluntary torque during contraction prior to the first instance of stimulation (MVT, N·m);
2. Rate of voluntary torque development (vRTD) calculated as the average slope of the torque-time curve (Δtorque/Δtime) in the following time periods 0-25 ms

($vRTD_{25}$), 0-50 ms ($vRTD_{50}$), 0-75 ms ($vRTD_{75}$), and 0-100 ms ($vRTD_{100}$) following contraction onset; and

3. The maximum voluntary RTD ($vRTD_{max}$) was determined as the greatest average 10 ms slope during the first 100 ms of the contraction.

All vRTD measures were normalised to the corresponding MVT to control for between-sex differences in strength.

Voluntary activation (VA) was calculated from the 10 Hz (VA_{10}) and 100 Hz (VA_{100}) stimulations using the superimposed twitch technique (68) according to the following formula (69):

$$VA(\%) = 100 - \left(D \times \frac{\left(\frac{T_{sup}}{MVT}\right)}{PT} \right) \times 100$$

where D is the difference between the torque level just before the superimposed twitch (T_{sup}) and the maximum torque recorded during the twitch, MVT is the maximal voluntary torque during the entire contraction (not including the twitch response), and PT is the maximal amplitude of the resting potentiated twitch (PT_{10} and PT_{100}). The following variables were calculated:

1. The time-to-peak twitch (TPT_{10} and TPT_{100}); and
2. The half relaxation time (1/2RT10 and 1/2RT100) calculated as the time from the peak amplitude until 50% of the maximal amplitude had been reached.

All sEMG variables during maximal contractions were normalised to the first respective M-waves elicited during 10 Hz stimulation applied to each contraction for data analysis (EMG/M, %). sEMG recordings were used to analyse the following variables from each MVT measurement:

1. The electrically evoked M-wave from the first response to the 10 Hz doublet, calculated from the peak-to-peak amplitude of the VL and VM sEMG raw signal elicited during contraction;

2. The maximal amplitude of the VL (VL_{MAX}) and VM (VM_{MAX}) sEMG signal during MVTs based on processing the greatest average 250 ms RMS value;
3. The rate of sEMG rise for VL and VM (VL_{RER} and VM_{RER}) were calculated from the average slope of the RMS sEMG-time curve during the time periods 0-25, 0-50, and 0-75 ms post contraction onset; and
4. The maximal rate of sEMG rise for VL (VL_{RERmax}) and VM (VM_{RERmax}) calculated from the greatest 10 ms slope of the RMS EMG-time curve throughout the first 200 ms of the contraction.

3.2.7 Statistical Analysis

Analysis of variance (ANOVA) procedures were performed using IBM SPSS to examine the changes in the dependant variables over time (from pre to post measurements) and compare these changes between the sexes. When a significant main effect was observed, post-hoc tests with Bonferroni's correction were applied to identify differences. Unless otherwise stated data are mean ± SD. Statistical significance was defined as $p \leq 0.05$.

3.3 Results

3.3.1 Maximal Voluntary Torque and Voluntary Rate of Torque Development

Males and females exhibited similar reductions in maximal voluntary torque from baseline measurements of 245.5 ± 31.9 N·m and 180.6 ± 32.0 N·m respectively, with an average reduction of 26.3 ± 12.5% ($p < 0.001$).

Between-sex differences in reductions of vRTD and NvRTD were also observed, as indicated in Figure 1 below.

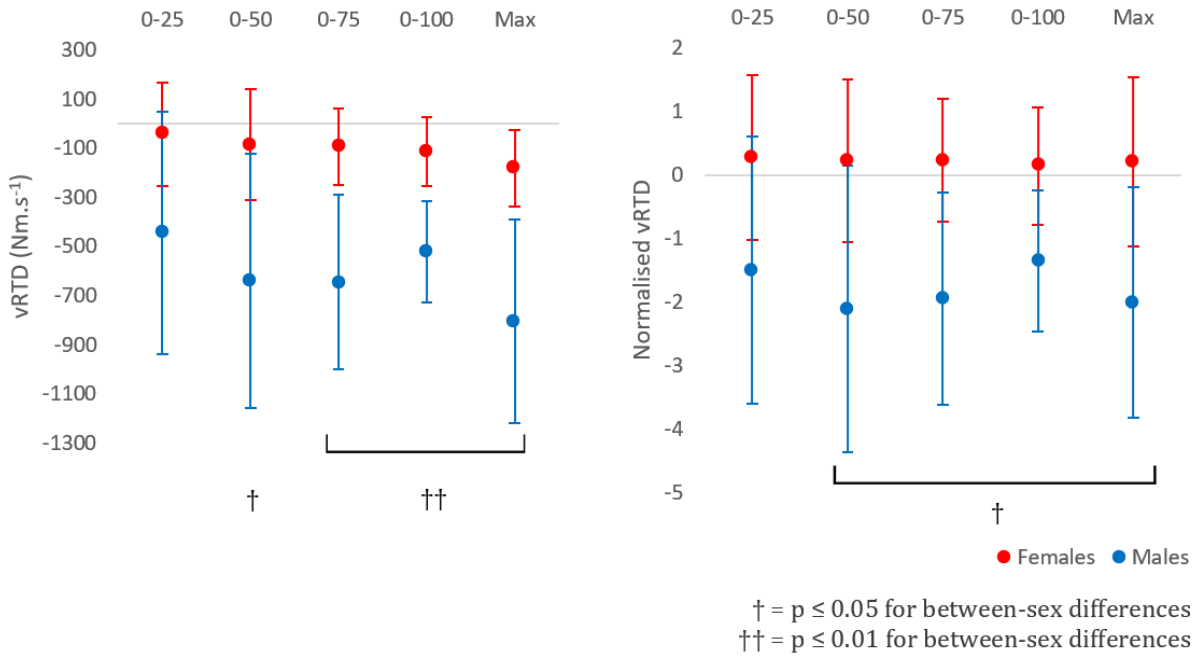

Figure 1: Changes (Post – Pre) Reductions in voluntary (vRTD) and normalised voluntary rate of torque development (NvRTD) for males and females following a knee extension task. Data are mean ± SD.

Similar reductions in maximal voluntary torque from baseline values were seen in both males and females, with changes of 254.5 ± 31.9 N·m and 180.6 ± 32.0 N·m respectively, and an average reduction of 26.3 ± 12.5% ($p<0.001$). Differences between the sexes were observed for reduction in vRTD however, at the time intervals of 0-50, 0-75, and 0-100 ms after contraction onset in addition to vRTD max (Figure 1; $p < 0.05$). Males displayed an average reduction of between 446.5 and 806.3 $N \cdot m \cdot s^{-1}$ ($p < 0.05$) after exercise in vRTD measures, while females did not display a reduction from pre-exercise values.

NvRTD data also showed between-sex differences at the time intervals of 0-50, 0-75, and 0-100 ms post contraction onset ($p < 0.05$), alongside NvRTDmax ($p = 0.014$). No reductions from baseline were observed in females for these variables. For males, NvRTD was reduced between 26.3 to 35.4% in time intervals from 0-50 ms to 0-100 ms post contraction onset, and reductions of 25.4 ± 14.5% for NvRTD max.

3.3.2 Central Motor Output

No changes were observed for VA_{10} (males -1.6 ± 5.1%, females 0.7 ± 4.85%), VA_{100} (1.8 ± 8.7, females 8.3 ± 11.1) or VL and VM max% for either sex over time.

Males and females displayed similar reductions in VL sEMG at the time intervals of 0-25 ms ($p = 0.032$) and 0-50 ms ($p = 0.002$) of between 7.9 and 16.44%.s^{-1} (Table 3). Similar reductions for both sexes were also observed for VM sEMG at the time intervals of 0-25 ms and 0-50 ms of between 2.6 and 10.6%.s^{-1} ($p < 0.05$). Between sex differences in VL_{RERmax} were observed ($p = 0.02$), with females exhibiting no change, while males decreased an average of 82.5 ± 72.1%.s^{-1} from baseline measures (Table 3).

Table 3: Changes (Post-Pre) in rate of EMG rise for VM and VL at 0-25, 0-50, 0-75, and 0-100 ms post contraction onset, and maximal rate of EMG rise following a knee extension task. Data are mean ± SD.

Muscle	Sex	0.25 ms (%.s^{-1})	0-50 ms (%.s^{-1})	0-75 ms (%.s^{-1})	0-100 ms (%.s^{-1})	RER_{max} (%.s^{-1})
VL	Male	-10.6 ± 21.5*	-12.8 ± 18.4**	-0.2 ± 25.4	5.7 ± 18.3	-82.5 ± 72.1*†
	Female	-7.9 ± 4.3*	-16.4 ± 11**	-14.8 ± 16.9	-11.2 ± 13.1	-7.8 ± 39.1
VM	Male	-10.6 ± 14.7*	-9.3 ± 15.3	-0.9 ± 11.3	5.6 ± 7.3	16 ± 61.7
	Female	-2.6 ± 8*	-5.8 ± 8.5*	-9.1 ± 10.8	-6.2 ± 7.5	-31.3 ± 31.9

* = $p \leq 0.05$ from pre-exercise

** = $p \leq 0.01$ from pre-exercise

† = $p \leq 0.05$ for between-sex difference

3.3.3 Muscle Contractility

Maximal twitch amplitudes measured at 10 Hz (males -56 ± 28 N·m, females -35.1 ± 8.1 N·m) and 100 Hz (males -46.8 ± 26.2 N·m, females -17.3 ± 5.8) were reduced for both sexes from baseline measures ($p < 0.001$, Table 4), although the reduction for males was greater than females at 100 Hz and similar at 10 Hz. No changes were observed for ½ RT and TPT (Table 4) for either sex.

Table 4: Changes (Post-Pre) after the exercise session for measures of time-to-peak twitch (TPT, ms), 1/2 relaxation time (1/2 RT, ms), and peak amplitude of the resting twitches (PT, N·m) measured with 10 Hz and 100 Hz stimulation frequencies following a knee extension task. Data are mean ± SD.

Doublet	Sex	TPT (ms)	½ RT (ms)	PT (N·m)
10 Hz	Male	0.003 ± 0.02	0.02 ± 0.03	-56.0 ± 28.0***
	Female	-0.002 ± 0.003	-0.02 ± 0.05	-35.1 ± 8.1***
100Hz	Male	-0.002 ± 0.01	0.02 ± 0.03	-46.8 ± 26.2***†
	Female	-0.01 ± 0.01	0.004 ± 0.04	-17.3 ± 5.8***

*** = $p < 0.001$ from pre-exercise

† = $p \leq 0.05$ for between-sex interaction

Declines in rate of twitch development were observed for both sexes (Table 5), with greater reductions observed for males (i.e. maximum rate of twitch development, -49.9± 22.8% for males, -31.5 ± 14.0% for females, $p = 0.01$). VL and VM M-waves were 8.4 ± 2.5 mV and 16.4 ± 4.4 mV respectively at baseline, and remained unchanged after the exercise session.

Table 5: Change (Post-Pre) in rate of maximal potentiated twitch development (N·m.s^{-1}) measured with 10 Hz and 100 Hz stimulation frequencies following a knee extension task. Data are mean ± SD.

Doublet	Sex	0-25 ms (N·m.s^{-1})	0-50 ms (N·m.s^{-1})	0-75 ms (N·m.s^{-1})	0-100 ms (N·m.s^{-1})	Max (N·m.s^{-1})
10 Hz	Male	-229.4 ± 160.2*	-483.4 ± 234.7*	-467.5 ± 218.5*	-360.9 ± 155.9*	-778.7 ± 377.9*†
	Female	-279.3 ± 91.5*	-318.2 ± 81.0*	-247.5 ± 88.6*	-233.2 ± 68.5*	-430.2 ± 116.3*
100 Hz	Male	-258.8 ± 175.4*	-533.5 ± 311.3*†	-577.6 ± 318.2*††	-469.5 ± 264.8*†	-880.4 ± 531.8*†
	Female	-257.7 ± 129.7*	-263.3 ± 118.1*	-213.5 ± 89.0*	-188.5 ± 54.2*	-340.3 ± 176.4*

* = $p < 0.05$ from pre-exercise

† = $p \leq 0.05$ for between-sex interaction

†† = $p \leq 0.01$ for between-sex interaction

3.4 Summary of Pilot Study

This pilot study is the first study to assess between-sex differences in the fatigability of experienced, resistance-trained individuals following a resistance training session. The primary finding of this study was that when compared to trained females, trained males exhibited greater declines in absolute and relative voluntary rate of torque development. No between-sex differences were observed for declines in maximal voluntary torque. The greater reductions in voluntary rate of torque development appear to be explained by larger reductions in muscle contractility for males when compared to females. A novel finding of this pilot study was that females maintained their voluntary rate of torque development following the leg-extension session, despite reductions in maximal strength, early rates of muscle activation, and muscle contractility. These findings suggest that females are less fatigable than males when exposed to the same exercise stimulus.

This method was limited in its application. The exercise task was selected to elicit muscle fatigue exclusively in the quadriceps. Single exercise, single muscle group training methods are not commonly applied in practice for resistance-trained athletes. Additionally, fatigue was only measured immediately post the exercise session. The brevity of the fatigue response measurements in this pilot study do not serve to inform how a training session would impact both training and performance within a realistic training week, rather that purely an isolated session.

The results of this pilot study informed the development of a full-body resistance training session, with fatigue assessed at multiple time points up to 48 hours post exercise session. This model was then applied to the main study of this thesis, with the objective to create a methodology that would be externally valid.

Chapter 4: Main Study Assessing Between-Sex Differences Following a Full Body Training Session

Supervisor Statement

For the main experimental study in the thesis Emily was responsible for:

- Study design
- Methodology development
- Ethics application
- Participant recruitment
- Data collection
- Data processing
- Statistical analysis.

All writing pertaining to the data from this study is solely the work of Emily.

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4.1 Objectives

The pilot study indicated that the sex-based differences in fatigue already seen in novices, were also present in trained individuals. However, the pilot study was not designed to be externally valid, and thus the primary study of this thesis was designed. The primary study utilised a full-body resistance training session, which had been designed through consultation with strength and conditioning coaches of professional sporting teams, to allow the results to be applicable to clinical practice. Additionally, the testing period was extended to cover follow-up assessments at 1 hour, 24 hours, and 48 hours following the conclusion of the training session. This enabled assessment of fatigue over a longer period, and thus allowed the research to examine the timing of training sessions and competition in the context of a training week.

The primary objective of the study was to examine the fatigue responses of well-trained male and female athletes for up to 48 hours post training, and compare these between the sexes. The secondary objective of this study was to determine whether there was any link between muscle oxygenation and blood flow, and the fatigue response of the athletes. Previous research (8) suggested that females may have greater blood flow to their skeletal muscles in comparison to males, and thus the inclusion of direct measurements of muscle oxygenation and deoxyhaemoglobin levels to the primary study enabled examination of this relationship.

4.2 Method

4.2.1 Subjects

Eight well-trained males (mean ± SD, age 25.5 ± 6 years, height 1.79 ± .05 m, weight 86.4 ± 9.8 kg) and eight well-trained females (mean ± SD, age 25.6 ± 6 years, height 1.68 ± .06 m, weight 71 ± 8.6 kg) volunteered to participate in this study. The subjects in this study voluntarily provided informed written consent (Appendix 4). Performance indicators were detailed in the inclusion criteria for this study (Appendices 2 and 3) to ensure the participants were well-trained and thus suited for the study as training age does not always indicate training status. This study was approved by the local institution's Human Research Ethics Committee (approval number H12614) and was conducted in accordance within the guidelines of the Declaration of Helsinki.

The inclusion criteria for this study were as follows:

- Regular resistance exercise during the past two or more years of both the upper body and lower body for at least three or more sessions per week for the majority of the training year.
- Males must be able to complete 1 RM lifts which satisfy the following criteria: 1x bodyweight bench press and 1.5x bodyweight back squat.
- Females must be able to complete 1 RM lifts which satisfy the following criteria: 0.85x bodyweight bench press and 1.2x bodyweight back squat.
- Within the ages of 18 and 45 years old.

The exclusion criteria were as follows:

- Following completion of Exercise and Sport Science Australia (ESSA) health screening, participant is determined to be 'high risk'.
- Recent injuries which effect the participant's ability to exercise and provide maximal effort during MVIC contractions.

4.2.2 Experimental Design

This study involved four total visits to the laboratory. The first visit involved a familiarisation session, completed approximately a week prior to the testing period, in which participants were introduced to the femoral nerve stimulation protocol, the exercise task, and performance expectations. The following three sessions were used to assess the participants' fatigue and recovery by testing them before, and up to two days after a full-body exercise session. The full-body exercise session was designed following consultation with professional netball and basketball team strength and conditioning coaches to ensure the external validity of this study.

The first testing session involved maximal voluntary isometric contractions (MVICs) immediately prior to, immediately post, and one hour post a full-body exercise session, the structure of which is detailed in 4.2.3 Exercise Session. The participant also performed a leg extension task during the full-body training session and all subsequent testing sessions with a near-infrared spectroscopy (NIRS) probe adhered to the skin superior to the muscle belly of the rectus femoris. The second and third testing sessions which occurred at 24 and 48 hours post the full-body training session involved the performance of two MVICs with nerve stimulation, alongside 2x10 leg extensions with the aforementioned NIRS probe monitoring the saturation of oxygen and deoxyhaemoglobin levels in the rectus femoris.

Post-workout nutrition was standardised among all participants and provided by the investigators. Participants were provided with a beverage consisting of $0.4 g.kg^{-1}$BW protein and $0.5 g.kg^{-1}$BW maltodextrin. Post-workout nutrition was provided following the testing session immediately post workout.

All maximal voluntary isometric contractions (MVC) and leg extensions were performed on a Biodex seated dynamometer (Biodex Medical Systems, New York, United States of America). At each testing time-point, participants were asked to fill out a Profile of Mood States (POMS) questionnaire, and rate their quadricep soreness at rest (passive), and at

full contraction (active) on a 10-point scale. The duration of the exercise session was recorded for each individual and used alongside a Rate of Perceived Exertion (RPE) rating on a 10-point scale to calculate workload (time (min) x RPE).

4.2.3 Exercise Session

After pre-training MVC testing was completed, participants underwent a full-body resistance training session.

Participants completed a full-body training session, designed after discussion with strength and conditioning coaches of representative netball and basketball teams. Participants selected individualised weights in the 4-6 RM movements, and the power movements were calculated as a percentage of bodyweight. Participants determined their own warm up sets, with 1.5-2 minutes rest between working sets. The duration of the session was approximately 1 hour. The layout of the session is as detailed in Table 6:

Table 6: Full-body resistance training exercise session.

Exercise	Intensity	Sets x Reps
Leg Extension	60 deg.sec^{-1} concentric 600 deg.sec^{-1} eccentric	2 x 10
Rack Pull	4-6 RM	4 x 4-6
Bench Press off Pins	4-6 RM	4 x 4-6
Barbell Row	4-6 RM	4 x 4-6
Hang Power Clean	50% BW	4 x 4-6
DB Snatch	25% BW (males) 20% BW (females)	4 x 5/arm
Leg Extension	60 deg.sec^{-1} concentric 600 deg.sec^{-1} eccentric	2x10

The dumbbell snatch weight was calculated differently between the sexes due to the difference in distribution of weight between males and females. Females, on average, have a higher percentage of fat mass in comparison to males (70), which means their total weight is not as conducive to power production as males. The different calculations for males and females were thus determined to maintain similar effort. The repetitions and weights achieved for each set of each exercise were recorded for all participants (Appendix 6).

The training session prescribed in this study was designed following consultation with Australian netball and basketball strength and conditioning coaches. It included heavy pure strength movements with restricted range (rack pull, barbell row, pin bench) in combination with power movements (hang power clean and dumbbell snatch). This session also contained an appropriate amount of volume and intensity to elicit strength benefits when prescribed four times per week (71-73).

4.2.4 Surface Electromyography

Paired Ag/AgCl surface electrodes (Kendall, ADIinstruments, Australia) were used to record sEMG from the VL and VM. Following careful skin preparation (shaving excess hair, gentle abrasion with fine sandpaper, and cleaning the skin with isopropyl alcohol swabs), electrodes were placed in a bipolar configuration parallel to the direction of the muscle fibres. The locations of each electrode were marked with a skin safe marker to ensure consistent placement throughout all trials. The inferior VM electrode was placed 3-4cm superior to the medial border of the patella, with the superior electrode placed adjacent and parallel to the direction of the muscle fibres. The inferior VL electrode was placed 8-12cm superior to the lateral aspect of the patella, on the body of VL. The superior VL electrode was placed 5-10cm above this, closer to the origin of VL. A reference electrode was placed on a bony surface, either the right patella or the lateral surface of the tibia.

sEMG signals were recorded using the ML138 Octal BioAmp (common mode rejection ration > 85 dB at 50 Hz, input impedance 200 MΩ) with 16-bit analog-to-digital conversion, sampled at 4,000 Hz (ADI Instruments, Sydney, Australia). Raw signals were filtered with a fourth-order Bessel filter between 20 and 500 Hz, and subsequently smoothed for analysis using a 50 ms mean-square calculation (RMS).

4.2.5 Femoral Nerve Stimulation

A 5 x 5 cm electrode constructed of aluminium foil and conduction gel was taped equidistant between the iliac crest and greater trochanter on the lateral aspect of the hip to act as an anode. To locate the femoral nerve for cathodal stimulation, a rubber insulated portable probe was used. The probe was moved around the femoral triangle using a stimulus intensity of 40mA until the largest muscle compound action potential (M-wave) was elicited by both the VM and VL, alongside visual confirmation of the entire quadriceps group contracting. Once the femoral nerve was located, the skin was marked with a skin safe marker and an Ag/AgCl electrode (3M, Australia) was applied.

The femoral nerve was stimulated during MVIC testing using a 10Hz doublet by a high voltage (400 V) constant current stimulator (Digitimer DS7AH; Digitimer, Hertfordshire, UK). The participant's individual threshold was identified at the beginning of each testing session by increasing the current by 10mA increments until a plateau in twitch amplitude and M-waves were achieved. From this, a supramaximal stimulation was calculated by increasing the current to 125% of the individual's threshold.

During MVC testing, the participant was instructed to perform an isometric quadriceps contraction as 'hard and fast as possible'. The investigator delivered a doublet to the femoral nerve when torque had reached a visible plateau. The individual was then asked to relax, and a second doublet was delivered to the femoral nerve 2-3 seconds post contraction to determine the resting potentiated twitch of the quadricep.

4.2.6 Near-Infrared Spectroscopy (NIRS)

Saturation of oxygen (%) and deoxyhaemoglobin measurements were taken from the rectus femoris during leg extensions using a NIRS device (MoorVMS-NIRS, Moor Instruments, Axminster, United Kingdom). Testing at all time points involved the placement of a surface probe on the muscle belly with a 30mm inter-probe distance, sampled at 10 Hz with a low pass filter set to 5 Hz. The probes were adhered to the skin with double-sided adhesive tape, and additionally secured with skin-safe tape (3M Transpore Surgical Tape).

4.2.7 MVIC Data Processing

An automated algorithm was applied to the voluntary torque and potentiated twitch data which indicated the point at which torque exceeded the baseline readings by 2 N·m to identify contraction onset for both voluntary torque and resting evoked twitches. VL and VM muscle onset was then calculated to be 100ms before the previously calculated contraction onset.

Torque data was then used to determine:

1. The maximal voluntary torque during contraction prior to the first instance of stimulation (MVT, N·m)
2. Rate of voluntary torque development (vRTD) calculated as the average slope of the torque-time curve (Δtorque/Δtime) in the following time periods 0-25 ms, 0-50 ms, and 0-100 ms following contraction onset
3. The maximum voluntary RTD ($vRTD_{max}$) was determined as the greatest average 10 ms slope during the first 100 ms of the contraction.

All vRTD measures were also normalised to their corresponding MVT to control for strength differences between the subjects.

In addition to the maximal amplitude of the potentiated twitch (PT), the time to peak twitch (TPT) and half relaxation time ($^{1}/_{2}$RT) which is the time from maximal amplitude until 50% of the maximal amplitude had been reached were calculated.

Voluntary activation (VA) was estimated using the superimposed twitch technique (68) using the following formula (69):

$$VA(\%) = 100 - \left(D \times \frac{\left(\frac{T_{sup}}{MVT}\right)}{PT} \right) \times 100$$

where D is the difference between the maximum torque recorded during the twitch and the torque level immediately prior to the superimposed twitch ($Tsup$), MVT is the maximal voluntary torque prior to the first instance of stimulation, and PT is the maximal amplitude to the resting potentiated twitch.

All sEMG variables during maximal contractions were normalised to the respective M-waves elicited in each contraction for data analysis (EMG/M, %). sEMG recordings were used to analyse the following variables from each MVT measurement:

1. The electrically evoked M-wave from the first response to the doublet, calculated from the peak-to-peak amplitude of the VL and VM sEMG raw signal elicited during contraction;
2. The maximal amplitude of the VL (VL Max Amplitude) and VM (VM Max Amplitude) sEMG signal during MVTs based on processing the greatest average 250 ms RMS value;
3. The rate of sEMG rise for VL and VM (VL_{RER} and VM_{RER}) were calculated from the average slope of the RMS sEMG-time curve during the time periods 0-25, 0-50, and 0-100 ms post contraction onset; and
4. The maximal rate of sEMG rise for VL (VL RER_{max}) and VM (VM RER_{max}) calculated from the greatest 10 ms slope of the RMS EMG-time curve throughout the first 200 ms of the contraction.

4.2.8 NIRS and Knee Extension Data Processing

A low frequency 5Hz filter was applied to the saturation of oxygen and deoxyhaemoglobin measurements recorded during the leg extension sets performed at each testing time point. The peak dynamic torque (PDT) and the average peak dynamic torque for the last 5 reps of each set (PDTL5) were recorded. Additionally, baseline measures were taken for the oxygen saturation (TSI) and deoxyhaemoglobin levels (DeoxyHb) from the 5 seconds prior to the set of leg extensions beginning. These scores were compared to an average value recorded for each measure in during the last 5 reps of each set, with a change score (baseline – average during last 5) recorded for both oxygen saturation and deoxyhaemoglobin. Average cyclic maximum EMG from VM and VL were also recorded for the last 5 reps of each set.

4.2.9 Perceptual Fatigue Measures

Each individual completed a POMS form and quadricep soreness scores, both active and passive, at the beginning of each testing session (Appendix 5). Following the completion of the exercise session they were also asked to provide an RPE score for the session (Appendix 7). POMS scores were totalled and quadricep soreness scores recorded for each participant at each testing time point. The duration of the exercise session in minutes was also multiplied with the RPE score to provide a workload score for each participant.

4.2.10 Statistical Analysis

An analysis of variance (ANOVA) was used to examine changes in the dependant variables over time, and compare these changes between the sexes. When a significant time effect was observed, post-hoc tests with Bonferroni's correction were applied to identify differences between the sexes. Unless otherwise stated data are mean ± SD. Statistical significance was defined as $p \leq 0.05$.

4.3 Results

4.3.1 Workload and Perception of Fatigue

No between-sex difference was observed for the calculated session workload (males 302.1 ± 80.5; females 333.7 ± 151.2). A time effect was observed for POMS scores (Table 7), with a significant average increase of 5 ± 5 points from Pre to Post exercise session ($p \leq 0.05$). However, POMS scores returned to baseline levels from 1Hr onwards. A time effect was also observed for active quadricep soreness scores ($p \leq 0.001$, Table 7), however scores only increased significantly by the 1 Hr time point by 2 ± 2 from pre-exercise ($p = 0.008$). Scores returned to baseline values by the 24 Hr time point. No time effect was observed for passive quadricep soreness scores (Table 7). No time by sex interaction was observed for POMS, as well as active and passive quad soreness scores.

Table 7: Perceptual fatigue scores for males and females before and following a full-body resistance training session. Data are mean ± SD.

Variable	Sex	Pre	IP	1 Hr	24 Hr	48 Hr
POMS	Male	4 ± 3	7 ± 4*	5 ± 4	3 ± 2	1 ± 2
	Female	2 ± 2	8 ± 4*	3 ± 2	2 ± 2	2 ± 3
Quad Soreness Active	Male	2 ± 2	2 ± 2	3 ± 1*	1 ± 1	1 ± 1
	Female	0 ± 0	2 ± 2	2 ± 1*	0 ± 0	0 ± 0
Quad Soreness Passive	Male	2 ± 2	2 ± 2	3 ± 1	1 ± 1	1 ± 1
	Female	0 ± 0	2 ± 2	2 ± 1	0 ± 0	0 ± 0

* = $p \leq 0.05$ from pre- exercise

4.3.2 Maximal Voluntary Torque and Voluntary Rate of Torque Development

Similar reductions in maximal voluntary torque over time were observed for both sexes (-28.6 ± 31.7 N·m) from pre to post full-body training session (p = 0.035, Table 8). Maximal voluntary torque values returned to baseline measures from the 1 Hr time point onwards. No time by sex interaction was observed for maximal voluntary torque. No time effect was observed for vRTD (Table 8). When vRTD values were normalised for maximal voluntary torque at each time point, NvRTD, again no time effect was observed (Table 9).

Table 8: Maximal voluntary torque (MVT) and voluntary rate of torque development (vRTD) for males and females before and following a full-body resistance training session. Data are mean ± SD.

Variable	Sex	Pre	IP	1Hr	24 Hr	48 Hr
MVT (N·m)	Male	254.5 ± 58.5	222.4 ± 31.9*	239.4 ± 60.1	234.7 ± 60.7	250.3 ± 51.4
	Female	192.8 ± 31.9	168.7 ± 23.4*	173.1 ± 24.6	175.5 ± 33.5	184.8 ± 34.1
vRTD 0-25 ($N \cdot m.s^{-1}$)	Male	827.4 ± 303.2	844.2 ± 425.5	636.2 ± 324.3	839.8 ± 389.3	970.9 ± 523.4
	Female	575.6 ± 155.0	433.7 ± 148.9	437.3 ± 177.9	544.8 ± 152.6	446.3 ± 155.2
vRTD 0-50 ($N \cdot m.s^{-1}$)	Male	1134.5 ± 334.5	1111.4 ± 447.9	915.2 ± 392.2	1113.2 ± 426.9	1253.8 ± 503.4
	Female	786.2 ± 182.2	607.7 ± 179.7	618.4 ± 159.3	738.0 ± 189.2	635.1 ± 184.5
vRTD 0-100 ($N \cdot m.s^{-1}$)	Male	1730.1 ± 256.1	1621.9 ± 463.3	1515.5 ± 337.3	1644.0 ± 382.7	1759.2 ± 434.5
	Female	1165.6 ± 257.9	968.5 ± 234.3	1012.2 ± 214.4	1075.0 ± 252.5	1026.0 ± 227.3
vRTD Max ($N \cdot m.s^{-1}$)	Male	1332.2 ± 255.1	1231.7 ± 352.8	1128.1 ± 326.7	1228.9 ± 323.6	1336.2 ± 347.7
	Female	922.7 ± 200.0	745.1 ± 182.2	770.7 ± 195.1	853.3 ± 181.7	790.3 ± 179.1

* = $p \leq 0.05$ from pre-exercise

Table 9: Normalised voluntary rate of torque development (NvRTD) values for males and females before and following a full-body resistance training session. Data are mean ± SD.

Variable	Sex	Pre	IP	1 Hr	24 Hr	48 Hr
NvRTD 0-25 ($N \cdot m.s^{-1}$)	Male	3.5 ± 1.6	3.8 ± 2.0	2.9 ± 1.5	3.9 ± 1.8	2.9 ± 2.0
	Female	3.0 ± 0.8	2.6 ± 0.8	2.6 ± 0.7	3.1 ± 0.9	2.6 ± 0.9
NvRTD 0-50 ($N \cdot m.s^{-1}$)	Male	4.7 ± 1.8	5.0 ± 2.1	4.2 ± 2.0	4.9 ± 1.9	5.0 ± 1.8
	Female	4.1 ± 0.9	3.6 ± 0.9	3.6 ± 0.9	4.2 ± 1.0	3.6 ± 1.0
NvRTD 0-100 ($N \cdot m.s^{-1}$)	Male	5.4 ± 1.4	5.5 ± 1.5	5.1 ± 1.8	5.5 ± 1.5	5.4 ± 1.1
	Female	4.8 ± 0.8	4.4 ± 0.8	4.5 ± 1.1	4.9 ± 0.8	4.5 ± 0.9
NvRTD Max ($N \cdot m.s^{-1}$)	Male	7.1 ± 1.6	7.3 ± 2.0	6.7 ± 2.1	6.7 ± 2.0	7.1 ± 1.5
	Female	6.1 ± 0.9	5.7 ± 0.9	5.9 ± 1.1	6.2 ± 1.2	5.8 ± 1.1

* = $p \leq 0.05$ from pre- exercise

4.3.3 Central Motor Output

There was no time effect for VA for either sex (Table 10). No time effect was observed for VM (Table 10) and VL (Table 11) 0-25, 0-50, 0-100, or max measurements. No time effect was observed for VM (Table 10) and VL (Table 11) MMax, or EMG maximal amplitude. A time effect was observed for VL 0-100 ($p = 0.007$), however post-hoc testing with Bonferroni's correction indicated the study was underpowered to detect a significant difference. A trend was observed that the values at the 24 hours post exercise session were lower in comparison to pre and immediately post exercise values. VL EMG maximal amplitude also showed a time effect ($p = 0.033$), with values at 24 hours post exercise reduced compared to baseline ($p = 0.017$). All other time points were not significantly different to baseline.

Table 10: Voluntary activation (VA), VM rate of EMG rise (RER), and VL RER values for males and females before and following a full-body resistance training session. Data are mean ± SD

Variable		Sex	Pre	IP	1 Hr	24 Hr	48 Hr
VA (%)		Male	92.8 ± 3.8	92.1 ± 4.2	91.5 ± 4.2	92.3 ± 4.9	92.0 ± 3.5
		Female	97.5 ± 1.8	97.1 ± 2.4	95.7 ± 3.4	96.2 ± 2.7	96.0 ± 2.5
VM	0-25 ms ($\%.s^{-1}$)	Male	107.4 ± 36.9	100.8 ± 38.5	101.5 ± 47.1	87.0 ± 31.0	107.9 ± 42.6
		Female	75.0 ± 34.4	52.1 ± 23.9	63.2 ± 25.3	63.5 ± 29.6	65.3 ± 42.0
	0-50 ms ($\%.s^{-1}$)	Male	98.6 ± 36.7	93.0 ± 18.4	106.1 ± 87.8	82.7 ± 55.3	102.6 ± 52.4
		Female	73.2 ± 30.3	53.1 ± 24.2	69.5 ± 23.0	67.1 ± 30.0	68.4 ± 40.6
	0-100 ms ($\%.s^{-1}$)	Male	46.2 ± 34.1	48.1 ± 35.1	53.8 ± 68.3	39.0 ± 56.5	51.0 ± 36.9
		Female	51.2 ± 28.8	44.5 ± 23.0	50.0 ± 25.3	49.3 ± 22.2	52.0 ± 32.5
	RER_{max} ($\%.s^{-1}$)	Male	137.1 ± 46.5	143.3 ± 53.0	158.3 ± 154.0	138.6 ± 86.3	154.2 ± 65.6
		Female	117.5 ± 55.0	94.3 ± 34.3	103.6 ± 34.2	104.2 ± 36.0	117.6 ± 57.2
	MMax (mV)	Male	11.1 ± 6.0	10.4 ± 5.9	9.5 ± 5.3	12.0 ± 6.7	11.0 ± 6.0
		Female	8.3 ± 2.1	8.8 ± 2.1	8.3 ± 2.0	9.5 ± 1.9	7.1 ± 1.8
	Max Amplitude (mV)	Male	9.2 ± 2.5	9.9 ± 2.9	11.8 ± 10.5	16.4 ± 18.6	10.4 ± 2.1
		Female	10.4 ± 3.5	8.6 ± 3.1	10.1 ± 4.7	8.6 ± 2.6	10.3 ± 3.7

Table 11: VL rate of EMG rise (RER) values for males and females before and following a full-body resistance training session. Data are mean ± SD.

Variable		Sex	Pre	IP	1 Hr	24 Hr	48 Hr
VL	0-25 ms (%.s^{-1})	Male	96.1 ± 28.8	105.3 ± 32.0	94.2 ± 38.7	85.2 ± 29.6	99.0 ± 27.2
		Female	78.2 ± 40.5	86.5 ± 51.3	77.5 ± 53.4	61.4 ± 36.0	56.5 ± 34.9
	0-50 ms (%.s^{-1})	Male	79.6 ± 22.8	79.8 ± 16.4	70.4 ± 28.7	65.7 ± 25.8	76.3 ± 22.2
		Female	68.2 ± 31.1	79.2 ± 45.3	69.1 ± 47.0	55.9 ± 64.8	55.8 ± 28.5
	0-100 ms (%.s^{-1})	Male	34.2 ± 18.0	36.5 ± 16.8	22.5 ± 21.2	16.6 ± 23.5	20.9 ± 14.8
		Female	51.1 ± 32.7	50.9 ± 36.0	41.4 ± 27.5	33.0 ± 23.7	41.2 ± 21.1
	RER_{max} (%.s^{-1})	Male	124.1 ± 29.0	131.1 ± 32.3	118.0 ± 36.6	108.9 ± 37.0	117.7 ± 30.1
		Female	122.0 ± 30.6	118.6 ± 60.8	105.5 ± 57.2	86.1 ± 49.9	97.0 ± 38.5
	MMax (mV)	Male	13.6 ± 3.9	12.3 ± 3.7	12.0 ± 4.1	13.6 ± 3.4	13.2 ± 2.7
		Female	11.2 ± 4.8	10.6 ± 4.5	11.0 ± 4.7	12.0 ± 3.7	12.0 ± 4.0
	Max Amplitude (mV)	Male	10.0 ± 2.1	10.2 ± 1.4	9.9 ± 1.8	8.6 ± 2.1*	9.4 ± 1.7
		Female	11.3 ± 5.6	10.7 ± 6.4	10.4 ± 6.5	7.4 ± 3.8*	8.8 ± 2.5

* = $p \leq 0.05$ from baseline

4.3.4 Muscle Contractility

Potentiated twitch (PT) amplitudes showed a time effect ($p \leq 0.001$), with changes similar between sexes (Table 12). Values post-exercise and 1Hr were significantly reduced from baseline measures ($p \leq 0.002$) by an average of 17.7 and 15.8 N·m respectively. PT returned to baseline values by the 24 Hr time point. No time effect was observed for ½ RT or TPT (Table 12).

Table 12: Potentiated twitch (PT), 1/2 relaxation time (1/2 RT), and time to peak twitch (TPT) for males and females before and following a full-body resistance training session. Data are mean ± SD.

Variable	Sex	Pre	IP	1 Hr	24 Hr	48 Hr
PT (N·m)	Male	105.1 ± 13.9	84.1 ± 14.7**	87.9 ± 11.3***	106.0 ± 16.8	102.4 ± 14.4
	Female	73.6 ± 11.9	59.3 ± 11.4**	59.2 ± 10.4***	66.2 ± 9.9	67.6 ± 11.8
½RT (ms)	Male	87.5 ± 23.5	88.9 ± 18.2	91.6 ± 35.0	96.4 ± 42.4	76.3 ± 12.5
	Female	84.3 ± 5.1	99.8 ± 24.2	84.6 ± 7.4	86.4 ± 7.9	88.4 ± 6.3
TPT (ms)	Male	172.9 ± 4.4	168.1 ± 19.8	169.0 ± 5.7	174.8 ± 4.7	174.0 ± 7.4
	Female	174.8 ± 3.0	175.3 ± 4.8	172.3 ± 6.6	173 ± 6.4	174.3 ± 7.0

** = $p \leq 0.01$ from baseline

*** = $p \leq 0.001$ from baseline

4.3.5 Muscle Oxygenation and Deoxyhaemoglobin

No time effect was observed for the changes (Baseline – Average of Last 5 Reps) in tissue oxygen saturation (TSI) and Deoxyhaemoglobin (DeOxyHb) measurements for either sex (Figure 2). However, significant differences were noted between each sex at every time point for change in DeOxyHb, with males increasing by an average 58.7 ± 49.5, and females increasing by an average of 8.1 ± 10.7 ($p \leq 0.05$). A similar relationship was seen for changes in TSI, however significant differences between the sexes were only seen at the Post, 1Hr, and 24Hr time points ($p \leq 0.05$), with an average reduction of 6.6 ± 4.6% for females and 18.9 ± 13.4% for males.

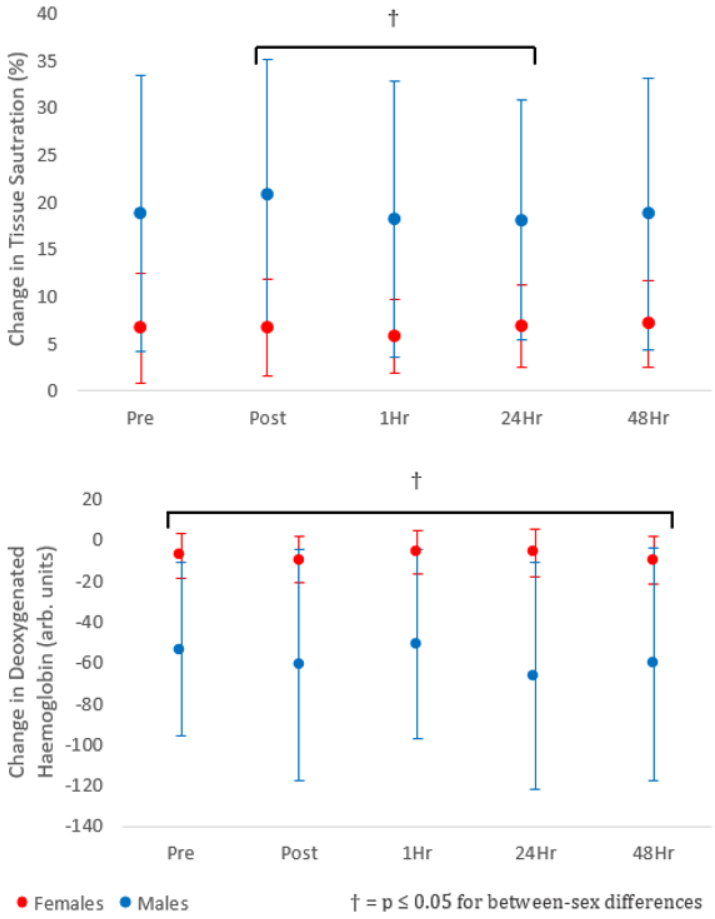

Figure 2: Changes (baseline - average of the last 5 repetitions) in tissue saturation (%) and deoxygenated haemoglobin (arb. units) for males and females before and following a full-body resistance training session. Data are mean ± SD.

4.3.6 Dynamic Strength

A time effect was observed for PDT ($p = 0.042$), with an average reduction of 12.1 ± 13.8 N·m from baseline at the 1 Hr post exercise time point. PDT values returned to baseline levels at the 24 Hr time point. No time effect was observed for PDTL5 ($p > 0.05$).

Table 13: Peak dynamic torque (PDT) and peak dynamic torque of last 5 repetitions (PDTL5) of males and females before and following a full-body resistance training session. Data are mean ± SD.

Variable	Sex	Pre	IP	1 Hr	24 Hr	48 Hr
PDT (N·m)	Male	229.3 ± 29.7	228.7 ± 33.8	217.5 ± 29.1*	221.3 ± 26.6	231.9 ± 28.6
	Female	176.3 ± 26.8	174.4 ± 22.8	163.9 ± 20.0*	161.7 ± 22.4	167.8 ± 24.5
PDTL5 (N·m)	Male	190.0 ± 20.6	201.5 ± 32.3	166.5 ± 47.9	180.1 ± 43.2	201.7 ± 31.0
	Female	145.7 ± 21.3	143.8 ± 21.2	142.2 ± 20.9	141.8 ± 22.2	143.7 ± 21.0

* = $p \leq 0.05$ from baseline

4.4 Summary of Main Study

This study was unique in its examination and comparison of the acute and chronic recovery of well-trained male and female athletes following an externally valid full-body training session. This study was also the first to utilise NIRS to measure muscle oxygenation and DeoxyHb as an indirect estimate of muscular perfusion in order to examine its role in differing muscle fatigue responses between the sexes. The main finding of this study was that while the exercise session induced significant muscular fatigue, indicated by losses in maximal voluntary torque and potentiated twitch, values returned to baseline levels after 24 hrs of rest. A novel finding of this study was that all changes were similar over time for both sexes, thus indicating similar responses to the exercise session.

The assessment of muscular perfusion and its role in sex-based differences in fatigue was a key objective of this study. It has been suggested previously (6, 8) that blood flow within the muscle is a between-sex anatomical difference which can manifest as an observable performance differences between the sexes. NIRS was used to measure oxygen saturation and deoxyhaemoglobin levels in the rectus femoris during exercise at each time point in this study, acting as an indirect estimation of muscle perfusion. The change (pre-post) in deoxygenated haemoglobin at all time points, and oxygen saturation (at immediately post, 1Hr, and 24Hr time points) showed significant between-sex differences. The male participants experienced greater reductions in oxygen saturation and greater increases in deoxygenated haemoglobin than the female participants at the abovementioned time points. However, there was no time effect for either variable. Additionally, despite acute differences in oxygenation and deoxyhaemoglobin at testing time points being observed, this was not associated with sex-based differences in the change of dynamic torque (peak dynamic torque – torque of the last five reps). These results indicate that although there were acute differences in muscle oxygenation and deoxygenated haemoglobin, there was no chronic effect, and the acute differences did not manifest as sex-based differences in performance.

Maximal voluntary torque reduced significantly from pre- to post-exercise, however scores returned to baseline measures at 1Hr post exercise session for both sexes. Rate of torque development, both absolute and relative to maximal voluntary torque of each time point, did not change for either sex over the course of the testing period. The finding was expected in females due to the pilot study results, however was unexpected in males. Therefore, while maximal strength decreased following exercise, power (determined by the surrogate measure of rate of torque development) was not inhibited by performing a full-body exercise session. Dynamic strength, measured during the leg extensions at each testing time point, only showed a reduction at the 1Hr time point but recovered to baseline levels by 24 hours post exercise. Resting potentiated twitch was reduced immediately following and 1Hr post exercise. The reductions in maximal voluntary torque and maximal dynamic strength are likely explained by losses in muscle contractility of the athletes. It is unlikely that central motor output impacted the loss of maximal voluntary torque, as no change was seen in voluntary activation and VM sEMG measurements, with no consistent change observed for VL sEMG measurements. These findings suggest that males and females experienced similar levels of fatigue, both muscular and perceptual, from the full-body exercise session.

While no between-sex differences were observed in perceptual measures (POMS, active quadricep soreness, and dynamic quadricep soreness), these values did indicate a time effect. POMS scores peaked immediately following exercise, however returned to baseline values at 1Hr post. Quadricep soreness scores peaked slightly later at 1Hr post exercise, however, also returned to baseline values at 24Hr post. The post-exercise nutrition and mandatory stretching of the gluteals, quadriceps, and hamstrings implemented immediately following the conclusion of the full-body training session were used to not just enhance recovery, with scores returning to baseline earlier than in previous similar studies on trained male cohorts (74), but also mitigate the potential impact of passive muscle stiffness which may otherwise heighten muscle soreness scores after exercise (75, 76). It must be recalled that questionnaires such as the POMS, while providing useful information, are subjective in terms of athlete perception. As a result, questionnaire data can be subject to inaccuracies and scores may be manipulated to provide a more desirable result in the athlete's eyes (77). It appears from the data gathered that a similar

perception of workload was undertaken by both sexes, and perceptually the athletes felt recovered by the 24Hr post exercise testing session.

In conclusion, following an appropriately fatiguing and externally valid full-body exercise session, the athletes in this study experienced muscular fatigue as indicated by reductions in maximal voluntary torque and potentiated twitch, alongside increases in perceptual fatigue as indicated by POMS and active quadricep soreness values. All values, both of muscular and perceptual fatigue, returned to baseline values by 24 hours post exercise session, and thus it can be assumed that the athletes were both physically and mentally recovered by this point. Unlike in the pilot study, no time by sex interaction was observed for any measurements in the study. It is assumed from this that the male and female athletes fatigued and recovered similarly in response to the full-body training session.

Chapter 5: General Discussion

5.1 Summary of Findings

The two studies included in this thesis present differing results with regards to the presence of a sex-based differences in the muscle fatigability of well-trained male and female athletes. The pilot study (Chapter 3) examined the athlete response to a fatiguing knee extension task. This study found between-sex differences in the changes of absolute and relative rate of torque development, which was primarily explained by greater losses of muscle contractility in male athletes. The main study (Chapter 4) examined the athlete response to a full-body training session over a 3-day period. This study did not find any sex-based differences in muscle fatigability. Reductions in maximal voluntary torque post exercise were seen in both studies, however rate of torque development was reduced for males in the knee extension study only. Both studies found no reduction in voluntary activation, with some reductions in EMG and other central motor output measurements. It is hypothesised that potentiated twitch, a measurement of muscle contractility, is the primary explanation for reductions in maximal voluntary torque for both studies due to the resistance-trained participants.

As stated above, declines in maximal voluntary torque were observed in both studies post-exercise, and are likely explained by reductions in muscle contractility. No reductions were observed for either sex in the pilot study and main study for measures of central motor output, namely voluntary activation and normalised quadriceps surface electromyograms, and these findings were consistent in the main study. These findings contrast previous research which found greater reductions in voluntary activation of novice male participants (11, 63). Following the pilot study it was proposed that perhaps the inclusion of a full-body resistance training session may exacerbate a between-sex difference in central motor output, as seen in a study by Marshall *et al.* (74) where declines in voluntary activation of trained males and decreases up approximately 50% of quadriceps potentiated twitch were observed, however this was not the case in the main study. Whether this is due to only an average approximate decrease of 20% of quadriceps

potentiated twitch for both sexes immediately following the session, or simply the variability of a new participant group is unclear.

5.2 The Disagreement Between the Pilot Study and Main Study

The primary disagreement between the pilot study and the main study of this thesis is the presence of between-sex differences in muscle fatigability. In the pilot study, males experienced reductions in both absolute and relative voluntary rate of torque development while females did not. In the main study both sexes did not experience reductions in absolute and relative voluntary rate of torque development, and no values changed differently between males and females over time. The pilot study found males experienced greater muscle fatigability, and this was primarily explained by greater losses in muscle contractility in males than females. The main study found no between-sex differences in fatigability, both perceptual and muscular.

Greater capillarisation (61) and smaller muscle mass (9), leading to improved muscle blood flow in females has been hypothesised as a main influencing factor on between-sex differences of muscle fatigue by the current body of literature (6, 8), and thus it was deemed necessary to examine in this thesis. They were speculated to be a cause of the between-sex differences in muscle fatigability observed in the pilot study. When deoxygenated haemoglobin and tissue saturation were assessed with NIRS during the main study, significant between sex differences were observed at multiple time points. Males had greater increases in deoxyhaemoglobin at all time points, and greater decreases in tissue saturation at the immediately post, 1 hour post, and 24 hours post time points. However, these differences did not manifest in differences in performance outcomes, such as the reduction of maximal voluntary torque or dynamic strength. Additionally, exercise did not appear to alter this relationship, with the changes in deoxygenated haemoglobin and tissue saturation staying consistently different between the sexes at all time points before and after the full-body resistance training session. It is possible that these measures, acting as an estimate of muscle perfusion, offer only a short-term (i.e. within-session) impact on performance. As explored in previous research, studies which utilise low intensity contractions exacerbate the impact muscle perfusion

has on muscle fatigability, thus resulting in between-sex differences (7, 8, 13). However, in a real-word scenario with the allowance of recovery time, these measures no longer hold the same impact as has been previously suggested.

The lack of between-sex differences in muscle fatigue within the main study of this thesis, in stark comparison to the current literature describing differences observed in novice athletes and the results of the pilot study, likely stems from the exercise modalities employed. Previous research, including the pilot study, has utilised single limb, single muscle group, single contraction type fatiguing exercises (7, 8, 11, 13, 14, 26). The theory which may explain this discrepancy is that during the low-intensity contractions, the greater capillarisation and less muscle mass of females is advantageous in clearing metabolites and delivering oxygenated blood to the muscle. However, during high-intensity contractions there is greater pressure on the blood vessels for both sexes and the anatomical advantages of females begin to disappear, as was seen in the ischaemic condition of Russ and Kent-Braun's 2003 study (8). Despite these observations in novices the pilot study, which contained high intensity contractions, showed between-sex differences in fatigability. Perhaps training status played a role in this distinction from what has been observed in the literature, with the athletes more accustomed to high intensity repetitions. In the main study however, where no between-sex differences were observed, it is possible this may be due to the rest periods prescribed and a wider variety of muscles were targeted by the prescribed exercises rather than a quadricep focused fatiguing protocol. Rest periods may play a part in the presence of between-sex differences in fatigue, as another study which did not observe between-sex differences had similar rest periods to the main study (11), while one study which did detect differences had little to no rest time (12). It is possible that these rest periods allow the blood flow to resume as normal, rectifying any acute advantages females may have had in preservation of blood flow due to their anatomy over males. Thus, between-sex differences that are regularly seen in deliberate fatigue of a single muscle group were not observed in the externally valid full-body resistance training session. It is hypothesised this result is due to a more varied and less quadricep focused exercise session with extended, but still externally valid, rest periods.

The maintenance of the rate of torque development in only females in the presence of significant reductions in maximal voluntary torque was a novel finding in the pilot study, however this response was seen in both sexes in the main study. The between-sex difference for declines in both absolute and relative rate of torque development in the pilot study can be attributed to greater losses in both muscle contractility and maximal rate of early muscle activation experienced by the males. Greater declines in relative rate of torque development for males in the pilot study were present even when the between-sex differences in absolute muscle strength were controlled for, which is often thought to be (combined with muscle mass) a primary reason for the greater fatigability of males. The between-sex differences in contractility observed in this study support similar findings in untrained males and females (8, 11), and extends these findings to trained individuals.

In the pilot study, between-sex differences in loss of muscle contractility were observed. Some of the mechanisms thought to explain the resistance to muscle contractility loss during and after exercise in females are greater muscle perfusion and lipid metabolism (6, 78). Greater capillarization in the vastus lateralis of females (61) combined with hormonally mediated vasodilation (79) allows increased perfusion and thus delivery of oxygen to the working muscle in addition to increased clearance of metabolites (e.g. H^+) which may otherwise impede muscular contraction (6). Between-sex differences in fatigability have been eliminated through occlusion of blood flow to the muscle (8), illustrating the relationship between muscle perfusion and fatigability. In addition to perfusion differences, females have greater lipid oxidation than males at the same relative exercise intensity, with males also exhibiting higher in-vivo glycolysis (61, 78). For females, the reliance on lipid metabolism during exercise contributes to a smaller production of metabolites that can inhibit muscle contraction (8, 56, 62, 80), which is thought to facilitate faster recovery of maximal force and power (6). Despite these anatomical and physiological differences which would assumedly contribute to greater fatigue resistance in females, as it did in the pilot study, no between-sex differences were observed in the main study. It is likely that the design of the full-body training session, a mixture of strength and power movements with utilisation of both the upper body and lower body, did not create the same localised fatigue in the tested quadriceps muscle. As

a result, it may be speculated that blood flow was not as occluded to the quadriceps as it would be in a knee extension task, and thus male athletes were able to clear metabolites and deliver oxygen to the working muscle.

5.3 The Relevance of These Findings to Exercise Prescription

While the pilot study was a controlled and deliberately manufactured environment in which to assess the possibility of between-sex differences in muscle fatigability, the main study expanded on this concept and utilised a 'real-world' exercise session. The full-body training session employed in the main study allows the results to become more applicable to clinical practice and allows practitioners to inform their exercise prescription.

As discussed previously, the pilot study displayed between-sex differences in muscle fatigability of resistance-trained athletes, while the main study did not. It is speculated that this discrepancy between the results of the two studies included in this thesis stems from the exercise modalities employed. Localised muscle fatigue, as created in the leg extension protocol of the pilot study, exacerbates the anatomical and physiological differences between the sexes and thus results in differences in muscle fatigability. The structure of the full-body, multi-limb resistance training session of the main study allowed for more dispersed muscular fatigue and hence no between-sex differences in fatigability were observed. A resistance exercise session of greater intensity and volume may allow between-sex differences in both muscle perfusion and metabolism to manifest in greater reductions of central motor output and muscle contractility, thus creating significant between-sex differences in fatigability over a longer period. However, one must be careful in examining such a scenario, as it is possible to lose sight of what is externally valid and relevant to practice. If a between-sex difference is only seen when deliberately manufactured, and it disappears when participants are exposed to a session that is performed regularly in practice, it indicates that perhaps the differences observed in previous research do not translate to real-world practice.

From the results of the main study, it can be determined that resistance-trained athletes of both sexes recover by 24 hours post exercise. Prescribing a full-body exercise session within the context of a training week will not impact performance on the next day. Athletes may have fully recovered between the 1 hour and 24 hours post exercise time points, however this was not assessed in this study.

Chapter 6: General Conclusion

6.1 Summary

The aim of this thesis was to observe the between-sex differences in muscle fatigability of resistance-trained male and female athletes. The pilot study (Chapter 3) exposed the resistance-trained athletes to a knee extension task at varying intensities of individual 1 repetition maximums. The physiological response of the athletes was assessed immediately prior to and following the knee extension task, with males exhibiting greater muscle fatigability than females. This is most evident in greater reductions of rate of torque development for males, even when between-sex differences in strength were controlled for.

In response to the findings of the pilot study, the main study was designed (Chapter 4) and required the resistance-trained males and females to complete a full-body resistance training session. The session was modelled to be as close to a 'real world' full-body training session as possible, and the testing period was extended to 48 hours post exercise session to gather a broader understanding of the fatigue and recovery profiles of the athletes. Additionally, perceptual measures of mood and muscle soreness were included in the main study to assess perceptual fatigue. The main study did not find any between-sex differences in muscle fatigability, or in the reductions in performance. It is likely that observed between-sex differences have occurred due to the anatomical advantages females have over males, with greater capillarisation and less muscle mass allowing for more optimal blood flow, bringing with it better oxygenated blood delivery and clearance of metabolites. The lack of between-sex differences in the main study have been attributed to the more varied exercises prescribed within the session, as well as rest times allowing males to recover and diminishing any previous advantages females would have.

6.2 Originality of Research

This thesis is unique in its studies of the between-sex differences in fatigability of resistance-trained male and female athletes, as all other previous studies have examined novices only. The pilot study was the first study to examine between-sex differences in resistance-trained athletes following a resistance training session (81). A novel finding of this study was that females, despite significant reductions in maximal torque, were able to maintain their rate of torque development while males were not. The main study of this thesis builds on the pilot study and was the first study to analyse between-sex differences in resistance-trained athletes following a 'real world' full-body resistance training session, and was also unique in including comparisons up to 48 hours post exercise completion. A novel finding of this study, and contradictory to the pilot study, was that no between-sex differences were found in perceptual fatigue or muscle fatigability.

In addition to being innovative in its assessment of between-sex differences in the fatigability of resistance-trained athletes, this study is also the first to use NIRS and thus muscle oxygenation as a measure to compare between-sex differences in said athletes. It has been speculated that muscle oxygenation and blood flow may play a role in the observed differences in fatigability of novice athletes, however it was not previously directly measured. It is interesting to note that despite acute differences between the sexes within the exercise, with rest and a full-body training session context the impact of muscle oxygenation is negated.

6.3 Practical Applications, Limitations, and Future Directions

The design of the main study of this thesis makes it easily applicable to practice. The results of this study suggest there are no differences in the responses of male and female athletes following a resistance-exercise session that could be prescribed within the context of a training week. Both males and females were recovered by 24 hours post exercise session.

The main study, although estimations were measured, did not directly measure blood flow. As a result, the relationship between blood flow and fatigue can only be inferred in this study, and not directly examined. While inclusion and exclusion criteria were designed to ensure the athletes were well-trained, the participants of both studies came from a wide background of resistance training modalities. This variation within the sample could possibly influence results, and thus future research may include an introductory training cycle to reduce the variability within the participant group. Additionally, both studies assessed fatigue in the quadricep as a sample of muscle fatigue, meaning the response of the whole body and other muscle groups was not examined. This is an area that could be further explored in future research to examine whether the response seen in the lower body examined in this thesis will extend to the upper body. Future research may also examine the fatigue response throughout a more accurate training week, with multiple sessions dispersed throughout the week to assess whether this manifests in any between-sex differences.

6.4 Conclusion

The outcomes of the research within this thesis expand the currently available literature on between-sex differences in fatigability by assessing resistance-trained athletes. During a single limb, single contraction type exercise session, between-sex differences in muscle fatigability were observed immediately following the session. However, when athletes were exposed to a full-body resistance training session, these previously observed between-sex differences did not arise, despite acute differences in muscle perfusion estimates. Further examination in more contexts such as multi-session training weeks or examining the upper limb muscles may offer further useful information regarding between-sex differences in muscle fatigability.

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Appendices

Appendix 1: Published Article of Pilot Study

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ORIGINAL ARTICLE

Trained females exhibit less fatigability than trained males after a heavy knee extensor resistance exercise session

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Abstract

Purpose We examined differences between trained males and females in measures of muscular fatigability and central motor output after a resistance exercise session.

Methods Sixteen trained males ($n=8$) and females ($n=8$) participated in the study. Knee extensor maximal torque and rate of torque development were measured before and after the exercise session, and the twitch interpolation technique was used during the maximal efforts to derive measures of voluntary activation and muscle contractility by supramaximal stimulation of the femoral nerve using 10 and 100 Hz doublets. Surface electromyograms were recorded during all maximal efforts to examine maximal and rate of quadriceps muscle activation.

Results After exercise, maximal torque was reduced for both sexes by $26.3 \pm 12.5\%$ ($p<0.001$). Absolute and relative vRTD was reduced only for males after exercise ($p<0.05$). The early (0–50 ms) rate of muscle activation rise was similarly reduced for both sexes between 2.6 and 16.4% s^{-1} ($p<0.01$), but males experienced an average decrease of $82.5 \pm 72.1\%$ s^{-1} for the maximal rate of muscle activation compared to no change for females ($p=0.02$). Males had greater reductions ($p<0.05$) for maximal twitch amplitudes and rate of twitch development ($-51.1 \pm 21.5\%$ and $-49.9 \pm 22.8\%$, respectively) compared to females ($-35.8 \pm 13.7\%$ and $-31.5 \pm 14.0\%$, respectively).

Conclusions These findings suggest that trained females are resistant to reductions in rapid torque development, despite similar reductions in maximal torque, after resistance exercise, with this result explained by better-maintained muscle contractility and maximal rate of muscle activation compared to males.

Keywords Fatigue · Exercise · Sex · Resistance · Physiology

Abbreviations

1-RM	1-repetition maximum strength test
½ RT	Half relaxation time
ANOVA	Analysis of variance
β	Beta, representing the estimate for type II experimental error
BW	Bodyweight
d	Cohen's effect size
MVC	Maximal voluntary isometric contraction
MVT	Maximal voluntary torque
M-wave	Muscle compound action potential
RER	Rate of EMG rise
sEMG	Surface electromyogram
TPT	Time to peak twitch
VA	Voluntary activation
VL	Vastus lateralis
VM	Vastus medialis
vRTD	Voluntary rate of torque development

Introduction

At present, between-sex differences in many physiological responses to exercise are unknown.

Specifically, there is a paucity of information regarding between-sex differences in muscular fatigability following an acute resistance exercise session in trained individuals. It is believed males and females exhibit differences in muscular fatigability following isometric and dynamic contractions,

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where fatigability may be defined by reductions in maximal voluntary torque and rate of torque development (Vøllestad 1997). Females appear to display longer time to exhaustion in both sustained and dynamic tasks across a range of contraction intensities and muscle groups (Hunter 2014). This between-sex difference in fatigability is explained via a number of factors such as greater perfusion to active muscle and increased utilisation of oxidative metabolism in females (Maughan et al. 1986; Russ and Kent-Braun 2003), the greater strength and muscle mass typically observed in males (Janssen et al. 2000; Miller et al. 1993), in addition to differences in muscle contractility and central motor output (Lee et al. 2017). The translation of these experimental findings to clinical practice to inform resistance exercise prescription for males and females is difficult. Studies typically use a fixed contraction intensity for the exercise bout (e.g. 20 or 80% maximal strength), or an isolated concentric or eccentric only movement (Hunter et al. 2004a, b; Russ and Kent-Braun 2003). No study has examined the sex-based differences in fatigability following a resistance exercise prescription typically used in a training environment that involves a range of contraction intensities and combination of both concentric and eccentric movements. Moreover, no study has examined whether between-sex differences in fatigability exist in trained males and females.

To our knowledge, previous research has only examined sex-based differences in fatigability of untrained individuals, with mechanistic measures typically investigating the contributions of muscle contractility (i.e. electrically evoked twitch responses of muscle) and central motor output (i.e. muscle activation, voluntary activation) (Hunter et al. 2004b; Maughan et al. 1986; Russ and Kent-Braun 2003; Yoon et al. 2007). For example, males exhibit greater reductions in evoked twitches of the elbow flexor muscles compared to females (Hunter et al. 2006a), suggesting that factors associated with the contractility of muscle (i.e. perfusion, fiber type) influence between-sex differences in fatigability. Studies on sex-based differences have also identified measures of central motor output as a contributor to the greater fatigability in males than females (Russ and Kent-Braun 2003), with males exhibiting greater reductions in voluntary activation of the ankle dorsiflexors (Russ and Kent-Braun 2003) and knee extensors compared to females (Hunter et al. 2004a, b). It is unclear whether similar between-sex differences for reductions in muscle contractility and measures of central motor output will be observed in resistance trained males and females.

In trained males central motor output, as measured from both voluntary activation and changes in the normalized rate of rise in muscle activity, was well maintained after isometric leg extension contractions despite reductions in quadriceps twitch amplitude of up to 70% from baseline values (Marshall et al. 2015). This resilience in central motor output despite a large loss of muscle contractility was thought to be explained by the adaptations in the central nervous system (Carroll et al. 2002) exhibited by trained individuals such as increased supraspinal drive and greater input–output responses at the level of the α-motoneuron (Aargaard et al. 2002; Ekblom 2010; Vila-Chã et al. 2012). It is unclear whether any sex-based differences in central motor output will be observed in trained individuals. While it appears trained males are resistant to reductions in central motor output following single limb exercise (Marshall et al. 2015), this has not been examined in trained females. Therefore any differences in fatigability (i.e. reductions in maximal and rate of torque) observed after resistance exercise in trained males and females may only be explained by greater reductions in muscle contractility as opposed to central motor output.

The purpose of this study was to examine changes in fatigability and concomitant measures of muscle contractility and central motor output after a leg extension focused resistance exercise session in trained males and females. We hypothesized that reductions in maximal force and rate of force development would be greater in resistance trained males, and that these reductions would be associated with a larger reduction in evoked twitches from the quadriceps as an estimate of muscle contractility. Similar to previous reports in trained males, we also hypothesized that resistance trained females would exhibit no reductions in central motor output after a session of single-limb resistance exercise.

Methods

Subjects

Eight resistance trained males (mean ± SD; age 26 ± 5 years, height 1.77 ± 0.07 m, weight 78.2 ± 8.7 kg) and eight resistance trained females (mean ± SD; age 25 ± 3 years, height 1.62 ± 0.06 m, weight 68.2 ± 3.0 kg) volunteered to participate in this study after providing informed written consent. All volunteers had at least 3-year resistance training experience (≥ 3 times per week for most training weeks of the year), with regular performance of both upper and lower body resistance exercises. All participants were familiar with the required exercise task (i.e. knee extension), and were right leg dominant, but none reported weekly performance of the movement. All procedures in this study were approved by the local institution human research ethics committee (H10839), and were conducted in accordance with the Declaration of Helsinki.

Experimental design

Participants made two preliminary visits to the laboratory separated by 24 to 48 h for familiarisation with the femoral

nerve stimulation protocol and isometric testing of the knee extensors (session 1), in addition to single-leg dynamic 1-repetition maximum (1-RM) knee extension testing (session 2; Hammer Strength Iso-lateral knee extension, Life Fitness, Sydney, AUS). The main experimental session took place 5–7 days after the second familiarization session. At the first familiarization session we ensured participants were not anticipating or reducing their torque output prior to stimulation by continuing to provide instruction and practise until there was no difference in maximal torque between trials with and without stimulation (Button and Behm 2008). We provide detailed instruction for how to perform the maximal contractions in the presence of the stimulation, which has been informed by our regular use of these techniques in our laboratories (Marshall et al. 2015, 2018). This instruction includes advice to "keep pushing through the stimulation", "don't try to guess when it will happen", in addition to the instruction for the maximal contraction to be "as fast and forceful as possible". Loud verbal encouragement was also provided throughout all maximal efforts. Participants were also familiarised with pre-test nutritional and exercise guidelines concerning restriction from alcohol (24 h) and caffeine (12 h) consumption, and resistance or strenuous aerobic exercise for the legs (48 h).

To standardize pre-workout nutrition, a beverage consisting of 0.5 g kg^{-1} BW of maltodextrin and 0.3 g kg^{-1} BW whey protein was consumed 1 h prior to testing. Maximal voluntary isometric contractions (MVC) of the knee extensors were performed before and after the experimental training session on a dynamometer (KinCom 125, Version 5.32, Chattanooga, USA). Participants were seated with their hip and knee joints flexed to 90° and 75°, respectively. The centre of rotation of the lever arm was aligned with the sagittal plane axis of the knee joint, and the lever arm of the dynamometer was firmly attached 2–3 cm superior to the lateral malleolus. The participant was firmly strapped into the chair with straps across the trunk during all MVCs. Torque output signals were continuously sampled from the dynamometer at 1000 Hz (Powerlab, ADI Instruments, Sydney, AUS), and low pass filtered at 10 Hz. Torque signals were calibrated in the resting test position for each participant's limb weight (after all straps were applied), and a predetermined calibration factor was applied to obtained signals for conversion of the recorded voltage to torque (N m).

Before pre-training MVCs, participants performed a series of sub-maximal isometric knee extension efforts (25, 50, 75% of perceived maximal effort). Two MVCs were then performed with 2 min rest between efforts. Each MVC was required to be as fast and forceful as possible, and maintained for 3–4 s. Surface electromyograms (sEMG) were continuously recorded from the vastus lateralis (VL) and vastus medialis (VM) during MVCs. Femoral nerve stimulation (see "Femoral nerve stimulation") was applied during and after each MVC. Strong verbal encouragement was provided during all MVCs. After the training session a post-training MVC was performed within 1–1.5 min after completion of the protocol.

Exercise session

Knee extension range of motion for each repetition was from the seated starting position on the knee extension machine with the participant reclined so the lower limb was vertical and the knee joint angle at 110° flexion, to the end range of motion with the lower limb approximately parallel to the floor (just before terminal knee extension). The session commenced with an un-weighted warm-up set of ten self-paced repetitions, followed by a self-paced warm-up set at 40% of 1-RM, from which range of motion was established (approximately 105°). Knee joint angular position was continuously monitored at 1000 Hz (10 Hz low pass filter) from a single axis electrogoniometer (ADI Instruments, Sydney, AUS). A coloured area, starting from 10° below maximal normal range of motion, was subsequently marked on the computer screen for a research assistant to objectively determine a successful knee extension repetition.

The resistance exercise session was prescribed to accrue volume across a range of high-intensity contractions based on the previously measured single leg 1-RM (male average 1-RM, 40.3 ± 8.3 kg; female average 1-RM, 21.3 ± 4.6 kg), similar to a strength-based session in clinical practice. The working sets included 10 repetitions (reps) × 60% 1-RM, 2 sets × 5 reps at 80% 1-RM, 1 set × 5 reps at 85% 1-RM, 1 set × 3 reps at 87.5% 1-RM, and 1 set × 2 reps at 90% 1-RM. Finally, participants were required to perform two sets to repetition failure (inability to reach minimum range of motion) at 80% 1-RM (1.5–2 min rest between sets). All repetitions were required to be performed as explosively as possible in the concentric phase, with a controlled lowering of 1.5–2 s.

Surface electromyography

sEMG was recorded from the VL and VM using pairs of Ag/AgCl surface electrodes (Maxsensor, Medimax Global, Australia). Electrodes (10 mm contact diameter, 10 mm inter-electrode distance) were placed in bipolar configuration parallel to the direction of the muscle fibres after careful skin preparation (shaving excess hair, careful abrasion with fine sandpaper and cleaning the skin with isopropyl alcohol swabs). The inferior VL electrode was placed 8–12 cm superior to the lateral aspect of the patella, and the inferior VM electrode 3–4 cm superior to the medial aspect of the patella. The reference electrode was placed on the right patella. sEMG signals were recorded using the ML138 Octal BioAmp (common mode rejection ratio > 85 dB at 50 Hz,

input impedance 200 MΩ) with 16-bit analog-to-digital conversion, sampled at 4000 Hz (ADI instruments, Sydney, AUS). Raw signals were filtered with a fourth-order Bessel filter between 20 and 500 Hz, and subsequently smoothed for analysis using a 50 ms root-mean-square calculation (RMS).

Femoral nerve stimulation

A 5 × 9 cm custom electrode of aluminium foil and conduction gel was taped to the lateral aspect of the hip, between the iliac crest and greater trochanter as the anode. To identify femoral nerve location for cathodal stimulation, a rubber insulated portable cathodal probe was used. The probe was moved around the femoral triangle using a single stimulus intensity of 30 mA until the largest muscle compound action potential (M-wave) was elicited from both the VL and VM recording sites. When optimal nerve location was identified, this was marked with a felt-tip pen and a 2 cm diameter Ag/AgCl surface electrode was applied.

The quadriceps were stimulated during all MVCs by supramaximal doublets applied to the femoral nerve (200-μs square pulses) at 100 Hz and 10 Hz by a high voltage (400 V) constant current stimulator (Digitimer DS7AH; Digitimer, Hertfordshire, UK). The two different stimulation frequencies were used to provide a profile of low-frequency fatigue (by comparison of the 100–10 Hz responses), and to provide two different methods for calculation of voluntary activation (VA) to ensure an accurate representation of maximal central motor output. Stimulation intensity to be used during testing was determined by progressively increasing the current in 10 mA increments until plateaus occurred in twitch amplitude and M-waves in response to 10 Hz doublet stimulation. Supramaximal stimulation was ensured by increasing the final intensity from the plateau by 30% (intensity range for testing 80–190 mA).

During each MVC two superimposed doublets (100 Hz and 10 Hz) were applied to the femoral nerve when torque had reached a visible plateau (Behm et al. 1996). A 1.5 s time period was used between applied doublets. Quadriceps resting potentiated twitches were evoked by delivering two doublets (10 Hz and 100 Hz) to the resting muscle, with the first stimulation in the doublet sequence delivered 2–3 s post contraction. Doublets were applied in a random order between all measurements. Similar to our previous report (Marshall et al. 2015a), dependent variables were not influenced by the order of doublet stimulation.

MVC data processing

Contraction onset for voluntary torque and resting evoked twitches were identified with an automated algorithm in the software as the point after which torque exceeded the baseline by 2.5 N m and 1 N m, respectively. VL and VM muscle onsets were visually determined (Hodges and Bui 1996). Torque recordings were used to analyse (1) the maximal voluntary torque recorded during the contraction up to the first point of stimulation (MVT, N m), (2) rate of voluntary torque development (vRTD) calculated as the average slope of the torque–time curve (Δtorque/Δtime) during the time periods 0–25 ms ($vRTD_{25}$), 0–50 ms ($vRTD_{50}$) and 0–75 ms ($vRTD_{100}$) post contraction onset, and (3) maximum voluntary RTD ($vRTD_{MAX}$) was calculated as the greatest average 10 ms slope throughout the first 200 ms of the contraction. All vRTD measures were normalised to the corresponding MVT to control for between-sex differences in strength.

Voluntary activation (VA) was estimated from the 10 Hz (VA_{10}) and 100 Hz (VA_{100}) stimulations using the superimposed twitch technique (Merton 1954) according to the following formula (Strojnik and Komi 1998): $VA\,(\%) = 100 - (D \times (T_{sup}/MVT)/PT) \times 100$, where D is the difference between the torque level just before the superimposed twitch (T_{sup}) and the maximum torque recorded during the twitch, MVT is maximal voluntary torque during the entire contraction (not including the twitch response), and PT is the maximal amplitude of the resting potentiated twitch for either the 10 Hz or 100 Hz doublet. In addition to the maximal amplitude of the resting potentiated twitch (PT_{10} and PT_{100}), the following variables were calculated: (1) the time-to-peak twitch (TPT_{10} and TPT_{100}) and (2) the half relaxation time (½ RT_{10} and ½ RT_{100}), calculated as the time from the peak amplitude until 50% of the maximal amplitude had been reached on the descending slope of the twitch torque curve.

All sEMG variables during maximal contractions were normalised to the first respective M-waves elicited during 10 Hz stimulation applied to each contraction for data analysis (EMG/M, %). sEMG recordings were used to analyse the following variables from each MVT measurement: (1) the electrically evoked M-wave from the first response to the 10 Hz doublet, calculated from the peak-to-peak amplitude of the VL and VM sEMG raw signal elicited during contraction, (2) the maximal amplitude of the VL (VL_{MAX}) and VM (VM_{MAX}) sEMG signal during MVTs based on processing the greatest average 250 ms RMS value, (3) the rate of sEMG rise for VL and VM (VL_{RER} and VM_{RER}) were calculated from the average slope of the RMS sEMG-time curve during the time periods 0–25, 0–50, and 0–75 ms post contraction onset, and (4) the maximal rate of sEMG rise for VL (VL_{RERmax}) and VM (VM_{RERmax}) calculated from the greatest 10 ms slope of the RMS EMG-time curve throughout the first 200 ms of the contraction.

Statistical analyses

Analysis of variance (ANOVA) procedures were used to examine the changes in the dependent variables over time,

and compare these changes between the sexes. When a significant main effect was observed, post-hoc tests with Bonferonni's correction were applied to identify differences. G-Power statistical software was used for d effect size and post-hoc power estimates (Erdfelder et al. 1996), where $d = 0.8$ is a large effect, $d = 0.5$ is moderate, and $d = 0.3$ a small effect. Unless otherwise stated data are mean ± SD. Statistical significance was defined as $p \leq 0.05$.

Results

Maximal torque and rate of torque development

Males and females experienced similar changes in maximal torque from baseline values of 254.5 ± 31.9 N m and 180.6 ± 32.0 N m, respectively, with an average reduction of − 26.3 ± 12.5% (main time effect $p < 0.001$: $d = 1.52$, $1 - \beta = 0.99$; males − 26.6 ± 16.9%, females − 25.9 ± 6.8%). Differences between the sexes were observed for reductions in vRTD in time intervals of 0–50, 0–75, and 0–100 ms after contraction onset in addition to vRTD max (Fig. 1; $p < 0.05$; effect size range for between-sex differences for vRTD measures, $d = 1.4$–2.2; lowest post-hoc power estimate $1 - \beta = 0.84$). Males experienced a mean reduction of between 446.5 and 806.3 N m s^{-1} ($p < 0.05$) after exercise in vRTD measures, while females did not decrease from pre-exercise values. An interaction between the sexes was observed for NvRTD in time intervals of 0–50, 0–75, and 0–100 ms post contraction onset ($p < 0.05$; effect size range for between-sex differences for vRTD measures, $d = 1.27$–1.6; lowest post-hoc power estimate $1 - \beta = 0.78$), and for NvRTDmax ($p = 0.014$). No reductions were observed for females (effect size range, $d = 0.15$–0.21). For males, NvRTD was reduced between 26.3 and 36.4% in time intervals from 0–50 to 0–100 ms post contraction onset, and 25.4 ± 14.5% for NvRTD max. For NvRTD 0–25 ms, a trend for the between-sex difference observed at all other time points was observed ($p = 0.064$, $d = 1.01$, $1 - \beta = 0.61$).

Central motor output

No changes were observed for VA_{10} ($d = 0.09$, $1 - \beta = 0.06$), VA_{100} ($d = 0.50$, $1 - \beta = 0.60$) (Table 1), or VL and VM max% ($d = 0.09$ and $d = 0.19$ respectively). Males and females experienced similar reductions in VL_{RER} sEMG in time intervals of 0–25 ms ($p = 0.032$, $d = 0.62$, $1 - \beta = 0.76$) and 0–50 ms ($p = 0.002$, $d = 0.99$, $1 - \beta = 0.99$) of between 7.9 to 16.4%.s^{-1} (Fig. 2). Similar reductions for both sexes were observed for VM_{RER} sEMG in time intervals of 0–25 ms and 0–50 ms between 2.6 and 10.6% s^{-1} ($p < 0.05$, $d = 0.54$ and $d = 0.62$, respectively, $1 - \beta = 0.66$). Between-sex differences in VL_{RERmax} were detected ($p = 0.02$, $d = 1.19$, $1 - \beta = 0.99$), with females not displaying a change over time while males experienced an average decrease of 82.5 ± 72.1% s^{-1} (Fig. 2).

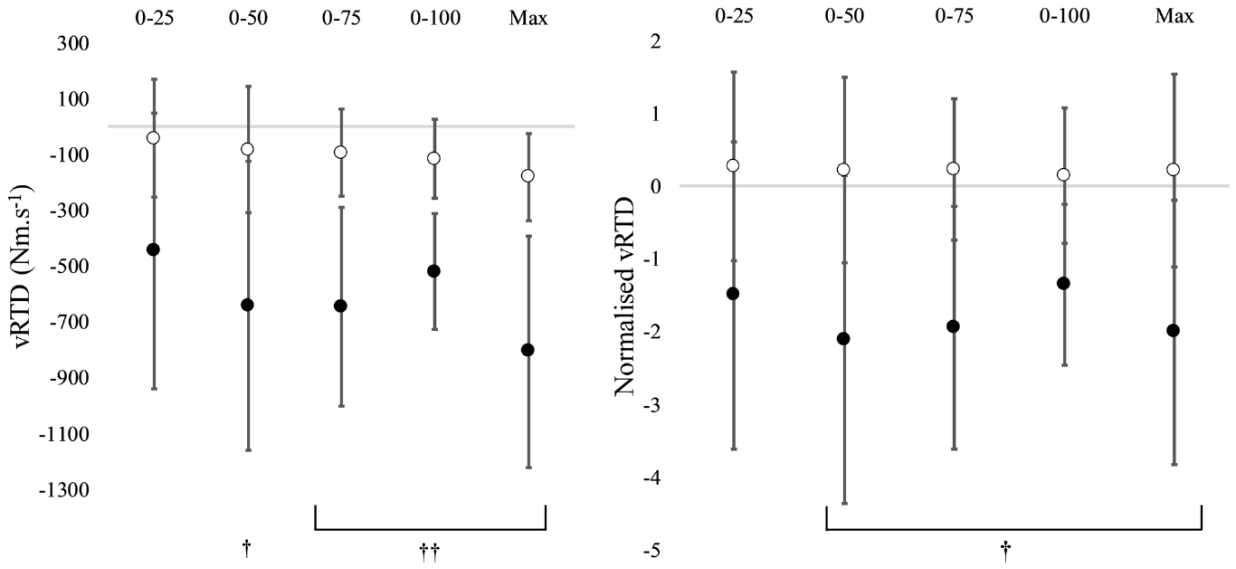

Fig. 1 Change from PRE exercise for voluntary (vRTD) and normalized rate of torque development (NvRTD) for males (filled circles) and females (open circles) after contraction onset. Values were only reduced from pre-exercise for males ($p < 0.05$). $^{\dagger}p < 0.05$ and $^{\dagger\dagger}p \leq 0.01$ for between-sex differences in the change score. Data are mean ± SD

Table 1 Change after the exercise session for measures of voluntary activation (VA, %), time-to-peak twitch (TPT, ms), ½ relaxation time (1/2 RT, ms), and peak amplitude of the resting twitches (PT, N m) measured with 10 Hz and 100 Hz stimulation frequencies

Doublet	Sex	VA (%)		TPT (ms)		½ RT (ms)		PT (N m)	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post
10 Hz	Male	88.2 ± 3.5	86.7 ± 5.1	158.6 ± 2.5	161.9 ± 16.3	76.3 ± 8.0	100.5 ± 23.7	92.5 ± 17.5	36.6 ± 13.8†
	Female	88.9 ± 5.1	89.6 ± 7.2	150.3 ± 5.3	148.1 ± 6.8	109.4 ± 43.1	94.3 ± 36.8	75.9 ± 5.7	40.8 ± 6.9***
100 Hz	Male	82.8 ± 84.6	84.6 ± 7.2	90.3 ± 4.5	88.2 ± 9.8	65.9 ± 7.7	89.8 ± 29.9	102.0 ± 11.0	55.2 ± 18.2†
	Female	76.0 ± 10.6	84.2 ± 8.1	90.9 ± 9.0	83.3 ± 10.9	82.2 ± 27.3	86.6 ± 20.7	68.4 ± 3.4	51.1 ± 6.2***

Data are mean ± SD

***$p < 0.001$ from pre exercise

$^{\dagger}p < 0.05$ for between-sex interaction

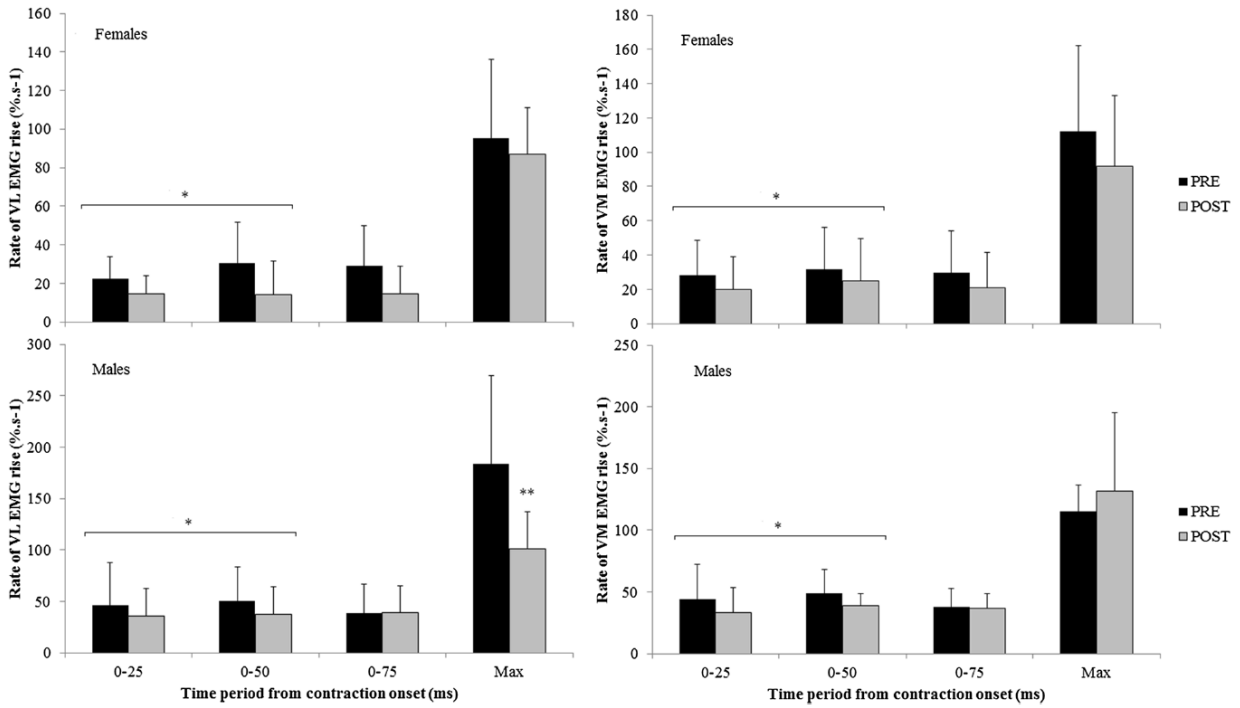

Fig. 2 VL and VM rate of EMG rise (RER, % s^{-1}) for female and male participants measured PRE and POST the resistance exercise session. Main time effects were observed for the 0–25 and 0–50 ms time periods for males and females. *$p < 0.05$ from PRE exercise values for the encompassed time intervals after contraction onset, and **$p < 0.01$ for the reduction from baseline for males. Data are mean and SD

Muscle contractility

Maximal twitch amplitudes measured at 10 Hz (males 92.5 ± 17.5 N m, females 75.9 ± 5.7 N m) and 100 Hz (males 102.0 ± 11.0 N m; females 68.4 ± 3.4 N m) were reduced for both sexes after exercise ($p < 0.001$, Table 1), although the reduction for males was greater than females for both stimulation intensities (Table 1, $p = 0.022$, between-sex differences for 10 Hz $d = 0.84$, 100 Hz $d = 1.24$, lowest $1 - \beta = 0.94$). No changes were observed for ½ RT and TPT (Table 1). Declines in rate of twitch development were observed for both sexes ($p < 0.01$, Fig. 3), with greater reductions observed for males (i.e. maximum rate of twitch development, − 49.9 ± 22.8% for males, − 31.5 ± 14.0% for females; $p = 0.01$, $d = 1.04$, $1 - \beta = 0.98$). VL and VM M-waves were 8.4 ± 2.5 mV and 16.4 ± 4.4 mV respectively at baseline, and remained unchanged after exercise.

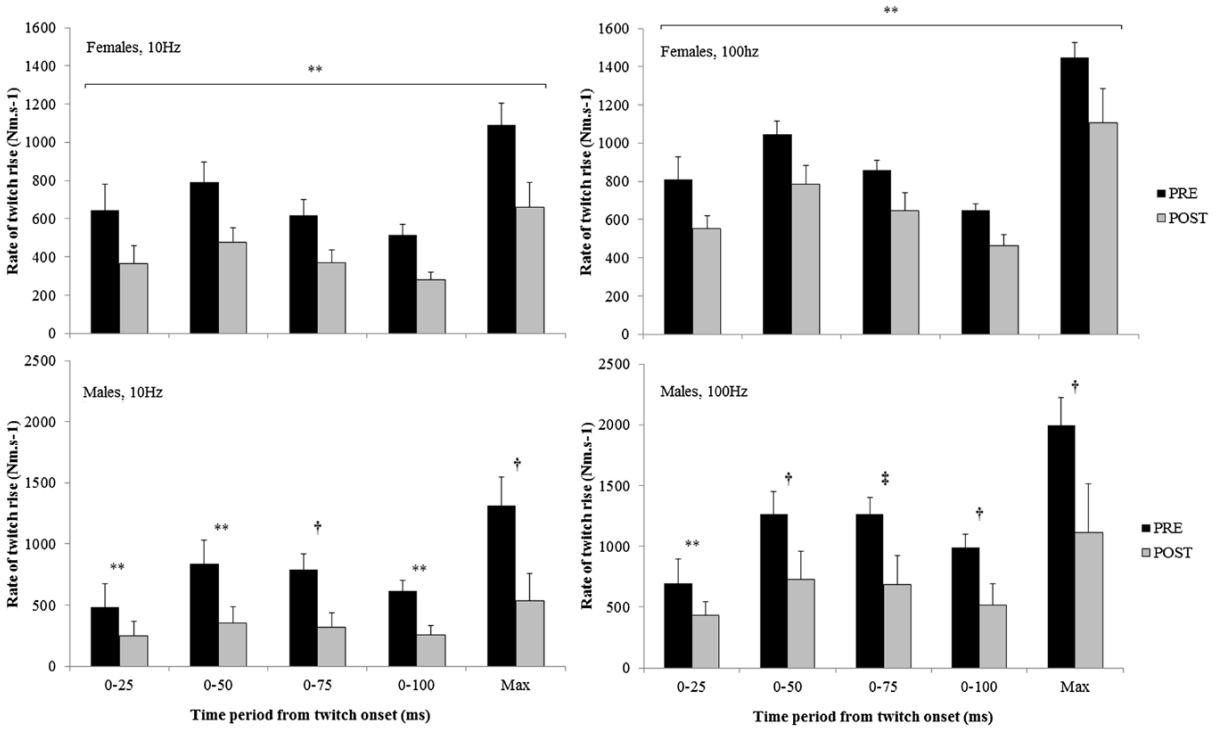

Fig. 3 Rate of twitch rise (N m s^{-1}) for female and male participants measured from the resting potentiated twitch PRE and POST the resistance exercise session. Twitch data is from the 10 Hz and 100 Hz doublets applied to the femoral nerve. $^{**}p < 0.01$ from PRE values for the encompassed time intervals after twitch onset, $^{\dagger}p < 0.05$ and $^{\ddagger}p < 0.01$ for greater reductions from PRE observed for males. Data are mean and SD

Discussion

To our knowledge, this is the first study that has assessed between-sex differences in the fatigability of trained individuals following a heavy resistance exercise session modeled off current industry best practice. The main finding of this study was that compared to trained females, trained males experienced larger absolute and relative reductions in voluntary rate of torque development while no between-sex differences were observed for declines in maximal torque. These between-sex differences appear to be explained by greater reductions in muscle contractility for trained males. A novel finding of this study was that resistance trained females maintained voluntary rate of torque development after the exercise session, despite reductions in maximal torque, early rates of muscle activation, and muscle contractility. These findings suggest females are less fatigable than males when exposed to the same exercise stimulus.

The between-sex difference for declines in both absolute and relative rate of torque development after the exercise session can be attributed to the greater loss in muscle contractility experienced by the males. While VL RERmax declined for males, all other measures for early rates of muscle activation declined similarly for both sexes. We believe the overall pattern of results suggest that early muscle activation declines similarly for both sexes, and therefore does not explain the greater declines in rate of torque development for males. Of interest, the greater decline for males in relative rate of torque development were present even when controlled for the between-sex differences in absolute muscle strength, which is often thought to be (combined with muscle mass) a primary reason for the greater fatigability of males (Hunter et al. 2004a, 2006b; Hunter and Enoka 2001). The between-sex differences in contractility observed in this study support similar findings in untrained males and females (Lee et al. 2017; Russ and Kent-Braun 2003), and extends these findings to trained individuals. Two factors that may contribute to the between-sex difference in muscle contractility loss after the resistance exercise session are the greater muscle perfusion (Hunter 2014; Tarnopolsky et al. 1990), and proportion of type I muscle fibers in females (Hunter 2014; Roepstorff et al. 2006; Staron et al. 2000).

Greater capillarization in the vastus lateralis of females (Roepstorff et al. 2006) combined with hormonally mediated vasodilation (Parker et al. 2007) allows increased perfusion and thus delivery of oxygen to the working muscle

in addition to increased clearance of metabolites (e.g. H^+) which may otherwise impede muscular contraction (Hunter 2014). Between-sex differences in fatigability have been eliminated through occlusion of blood flow to the muscle (Russ and Kent-Braun 2003), illustrating the relationship between muscle perfusion and fatigability. In addition to greater perfusion females also have a higher proportion of type I fibers relative to the area of muscle compared to males (Hunter 2014; Roepstorff et al. 2006; Staron et al. 2000). Type I fibers and muscles that are predominantly type I (e.g. triceps surae) exhibit slower electrically evoked contractile properties (e.g. time to peak twitch, rate of twitch development, relaxation time), and lower voluntary rate of torque development (Harridge et al. 1996; Siegler et al. 2016), but are more fatigue resistant than type II fibers and muscles that are predominantly type II (e.g. triceps brachii) (Fitts 2003; Schiaffino and Reggiani 2011). Therefore the greater contractility loss of males in this study may, in part, be explained by the greater area of muscle contributed to by type II fibers. A limitation to this study was that neither muscle perfusion or muscle fiber type and area were measured to provide insight into the between-sex contractility differences observed here.

In contrast to previous research, no between-sex differences were observed for declines in maximal central motor output, measured from voluntary activation and normalized quadriceps surface electromyograms. Indeed, we observed no reductions for either sex in measures of central motor output that are associated with production of maximal torque, and no difference between sexes for declines in early rates of muscle activation. Therefore, the overall pattern of results suggests that declines in both maximal torque and rate of torque development are likely explained by the reductions in muscle contractility observed in this study. The difference in findings between this study and previous reports suggesting greater voluntary activation reductions in males (Lee et al. 2017; Martin and Rattey 2007) is probably explained by our use of trained as opposed to untrained or novice individuals. Our findings support and extend recent observations from trained males to resistance trained females (Marshall et al. 2015), with these resistance trained participants exhibiting no reductions in maximal central output despite large reductions in muscle contractility. This resilience of the nervous system in trained participants to high levels of muscle fatigability may be influenced by both the duration and single type of resistance exercise used in the session. Similar to the previous observation for no declines in voluntary activation for trained males, we used a knee extension exercise model to provide a controlled exercise stimulus with a rapid post-exercise testing position (i.e. same movement for exercise and test). In contrast we recently observed declines in voluntary activation after a 1 h full-body resistance exercise session in trained males which included multiple lower body movements and incurred ~ 50% reduction in quadriceps twitch amplitude (Marshall et al. 2018). It may be likely that a different between-sex response in measures of central motor output could be observed after a longer duration full-body session. A longer session of resistance exercise may allow between-sex differences in both muscle perfusion and metabolism to manifest in different central motor output and contractility responses. It is a limitation of this study that we did not examine a longer full-body training session.

At present, the role of muscular fatigability as a necessary stimulus for positive training outcomes (e.g. strength, hypertrophy, and power) in combination with the manipulation of volume and load is still debated (Morton et al. 2016; Schoenfeld et al. 2015; Yoon et al. 2007). In this study, the reduced fatigability of female participants highlights multiple areas in which sex-specific exercise prescription should be further examined. In the present study, due to the acute nature of the study design, we were not able to assess inter-session recovery. As we demonstrated an acute reduced fatigability in females, it is logical to hypothesize that a shortened recovery time between sessions when compared to males may be warranted. Extrapolating further, this may have implications with regards to training frequency and the flow on effect of accumulation of volume, which is a known variable positively associated with muscular adaptation (Marshall et al. 2011; Morton et al. 2016). These questions need to be examined in a well-designed training study surrounding these particular sex-specific outcomes.

Conclusion

The results of this study show for the first time that trained females exhibit less fatigability of muscle contractile function, maximal rate of muscle activation, and rate of torque development compared to males after a resistance exercise session. These findings have implications for coaches and trainers in regards to the level of fatigue expected from a given training stimulus, which may have flow on ramifications regarding other prescriptive variables including frequency and volume.

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Author contributions PM conceived and designed the research. PM conducted the experiments. EM and AH processed and analysed the data. EM wrote the first draft of the manuscript. All authors contributed to the final editing and revision of the manuscript. All authors have read and approved the final manuscript.

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Appendix 2: Study Advertisement Flyer

WESTERN SYDNEY UNIVERSITY

Do resistance trained men and women fatigue and recover differently?

There is an absence of accurate resistance training guidelines for well-trained women, as women are significantly underrepresented in sport and exercise science research. This study aims to assess whether men and women respond differently to exercise by assessing muscle function before and up to 48 hours following a full-body training session.

If you would like to participate in this study, you will need to:

- Have performed resistance training regularly (3 or more times per week for the majority of the year) for 2 years or more.
- Be capable of a 1.5x bodyweight back squat and 1x bodyweight bench press (men), or a 1.2x bodyweight back squat and 0.8x bodyweight bench press (women).

If you qualify for this study and would like more information, please contact:

- Miss Emily Metcalf

  17716563@student.westernsydney.edu.au

  0418 688 626

- Assoc Prof Paul Marshall
  p.marshall@westernsydney.edu.au
  4620 3915

Western Sydney Human Research Ethics Committee Approval Number H12614

Appendix 3: Participant Information Sheet

WESTERN SYDNEY
UNIVERSITY

Participant Information Sheet

Project Title

Sex-based differences in the fatigue response of well-trained athletes

Project Summary

You are invited to participate in a research study being conducted by Emily Metcalf, a Master of Research Student at Western Sydney University in the school of Science and Health. The project will be supervised by Dr Paul Marshall, Associate Professor in Sport and Exercise Science at Western Sydney University in the school of Science and Health.

This study aims to identify any differences in the way men and women fatigue following a full-body resistance training session. Previous research has been performed on novice athletes, and found differences in the way the sexes fatigue. This project aims to determine whether this is the case in well-trained athletes. This study will assess the responses of the muscle and nervous system to a full-body resistance training session, and assess your recovery over a 48 hour period.

How is the study being paid for?

This study will be paid for via a grant from Western Sydney University as part of the Master of Research degree.

What will I be asked to do?

You will be asked to attend the laboratory once for approximately one hour, a week prior to the actual testing to familiarise you with the laboratory set up and testing procedures, as well as to fill out a health screening form.

You will then attend the lab on testing day and complete a full-body resistance training session with assessment of your blood flow during the session. Before, immediately after, and one hour after the resistance training session your muscle function will be assessed.

You will then be asked to come in for two more muscle function testing sessions, one at 24 and one at 48 hours following the resistance training session.

What benefits will I, and/or the broader community, receive for participating?

Currently, female athletes are significantly underrepresented in sport science research. This research will directly benefit female athletes, as it will build the knowledge base around their responses to exercise. In addition, it will offer high quality research on the fatigue response and recovery of male athletes, building upon the currently available knowledge base.

You will also be provided with your results from the study. These results will show you how much and where you fatigue after resistance exercise, and how long it takes you to recover from a resistance training session.

Will the study involve any risk or discomfort for me? If so, what will be done to rectify it?

Any potential risks have been reduced as much as possible, including using equipment designed with safety limits for human use, and an exercise session designed to reduce potential injury risk.

Your skin will need to be prepared prior to testing, including the removal of excess hair or dead skin through shaving, lightly abrading the skin, and cleansing with an isopropyl alcohol swab. Any skin irritation following this process can be remedied with moisturising cream.

The femoral nerve stimulation used in this study can be slightly uncomfortable, however extremely tolerable. The sensation is similar to that of a static shock, however is slightly stronger and coupled with an involuntary muscle contraction. Additionally, it will require an electrode to be placed in your hip crease at the top of your thigh, and an electrode to be placed on the side of your hip. The researchers will always act in a professional manner, and where possible ask for you to place electrodes in these areas. If you are uncomfortable with this or have further questions, please contact the Chief Investigator, Emily Metcalf (17716563@student.westernsydney.edu.au).

You may experience some muscle soreness for up to 48 hours following the full-body resistance training session. This is normal delayed onset muscle soreness (DOMS) that can occur with exercise, and the condition will rectify itself.

How do you intend to publish or disseminate the results?

It is anticipated that the results of this research project will be published and/or presented in a variety of forums such as a Master's thesis. In any publication and/or presentation, information will be provided in such a way that the participant cannot be identified, except with your permission.

Will the data and information that I have provided be disposed of?

Please be assured that only the researchers will have access to the raw data you provide. The data will not be linked to any of your personal identifying information.

Can I withdraw from the study?

Participation is entirely voluntary and you are not obliged to be involved. If you do participate you can withdraw at any time without giving reason without affecting any relationships with the researchers organisations involved, now or in the future.

If you do choose to withdraw, any information that you have supplied will be used in the study unless you express interest for its removal.

If you do wish do withdraw from the study, please contact Emily Metcalf (email: 17716563@student.westernsydney.edu.au).

Can I tell other people about the study?

Yes, you can tell other people about the study by providing them with the Chief Investigator's (Emily Metcalf) contact details to obtain a copy of the information sheet and discuss their potential participation in the research project.

What if I require further information?

Please contact any of the individuals below should you wish to discuss the research further before deciding whether or not to participate:

Emily Metcalf – Chief Investigator and Master of Research student

Email: 17716563@student.westernsydney.edu.au

Phone: 0418 688 626

Dr Paul Marshall – Supervisor

Email: p.marshall@westernsydney.edu.au

Phone: (02) 4620 3915

What if I have a complaint?

If you have any complaints or reservations about the ethical conduct of this research, you may contact the Ethics Committee through Research Engagement, Development and Innovation (REDI) on Tel +61 2 4736 0229 or email humanethics@westernsydney.edu.au.

Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.

If you agree to participate in this study, you may be asked to sign the Participant Consent Form. The information sheet is for you to keep and the consent form is retained by the researcher/s.

This study has been approved by the Western Sydney University Human Research Ethics Committee. The Approval number is H12614.

Appendix 4: Participant Consent Form

WESTERN SYDNEY
UNIVERSITY

Consent Form

Project Title: Sex-based differences in the fatigue response of well-trained athletes

I hereby consent to participate in the above named research project.

I acknowledge that:

- I have read the participant information sheet (or where appropriate, have had it read to me) and have been given the opportunity to discuss the information and my involvement in the project with the researcher/s
- The procedures required for the project and the time involved have been explained to me, and any questions I have about the project have been answered to my satisfaction.

I consent to:

☐ Participating in a full-body resistance training session

☐ Having nerve stimulation

☐ Having my physiological response to nerve stimulation non-invasively measured and recorded

☐ Having my muscle blood flow non-invasively measured and recorded

I consent for my data and information provided to be used in this project only.

I understand that my involvement is confidential and that the information gained during the study may be published but no information about me will be used in any way that reveals my identity.

I understand that I can withdraw from the study at any time without affecting my relationship with the researcher/s, and any organisations involved, now or in the future.

Signed:

Name:

Date:

This study has been approved by the Human Research Ethics Committee at Western Sydney University.

What if I have a complaint?

If you have any complaints or reservations about the ethical conduct of this research, you may contact the Ethics Committee through Research Engagement, Development and Innovation (REDI) on Tel +61 2 4736 0229 or email humanethics@westernsydney.edu.au.

Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.

Appendix 5: Perceptual Fatigue Assessment Form

Name:

Date:

Time point: Pre / IP / 1 Hr / 24 Hr / 48 Hr

PROFILE OF MOODS STATE

	Not at all	A little	Moderately	Quite a bit	Extremely
Worn out	0	1	2	3	4
Fatigued	0	1	2	3	4
Exhausted	0	1	2	3	4
Sluggish	0	1	2	3	4
Weary	0	1	2	3	4

Name:

Date:

Time point: Pre / IP / 1 Hr / 24 Hr / 48 Hr

QUADRICEPS SORENESS

Passive (seated):

0 No Soreness	**1**	**2**	**3**	**4**	**5** Moderate Soreness	**6**	**7**	**8**	**9**	**10** Worst Soreness

Active (following leg extension):

0 No Soreness	**1**	**2**	**3**	**4**	**5** Moderate Soreness	**6**	**7**	**8**	**9**	**10** Worst Soreness

Appendix 6: Exercise Session Record Sheet

Exercise Session

Name:

Exercise	Set 1	Set 2	Set 3	Set 4
Rack Pull				
Barbell Row				
Bench Off Pins				
Hang Power Clean (1/2 BW)				
DB Snatch (1/4 BW M, 1/5 BW F)				

Appendix 7: Session RPE Form

Name:

Date:

RATE OF PERCEIVED EXERTION (RPE)

SCALE 1: RPE
HOW WAS YOUR WORKOUT DURING THE SESSION?

Rating	Descriptor
0	**NOTHING AT ALL**
1	**VERY, VERY EASY**
2	**EASY**
3	**MODERATE**
4	**SOMEWHAT HARD**
5	**HARD**
6	
7	**VERY HARD**
8	
9	
10	**MAXIMAL**

BORG RATING OF PERCEIVED EXERTION SCALE MODIFIED BY FOSTER et *al.*, 1996

Session RPE: