Effect of Changes in the Force-generating Capacity of the Knee Extensors on Lower-limb Power Production during Cycling Exercises

A thesis submitted in fulfilment of the requirements of the degree of

DOCTOR OF PHILOSOPHY

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Abstract

Overview

Neuromuscular fatigue is defined as a reversible exercise-induced reduction in the ability to produce maximal voluntary force or power, originating from central (upper and lower motoneurons) and peripheral (skeletal muscle) sources. It is a symptom that can reduce exercise performance, diminish quality of life, and impair activities of daily living across a wide range of populations. In the lower-limb, the knee extensor muscles are of particular importance as they largely contribute to the execution of functional motor tasks (e.g. locomotion, sit to stand, climbing stairs). Therefore, fatigue of this muscle group is likely to have a large negative impact on the ability of the lower-limbs to generate power.

General methodology

Within this thesis, a series of three experiments were conducted to investigate the effect of neuromuscular fatigue in the knee extensor muscles on lower-limb power production. Neuromuscular fatigue of the knee extensor muscles was assessed via changes in isometric maximal voluntary force (IMVF), voluntary activation (VA), maximal evoked resting twitch forces (RT), maximal muscle compound action potentials (M-wave) and voluntary surface electromyography (EMG) amplitude normalized to M-wave (EMG.M-wave^{-1}). Lower-limb power production was measured on a stationary cycle ergometer. Motor command was investigated during cycling exercises via changes in: EMG activity of individual lower-limb muscles [*vastus lateralis* and *vastus medialis* (VAS), *rectus femoris* (RF), *gluteus maximus* (GMAX), *biceps femoris* and *semitendinosus* (hamstrings: HAM), medial and lateral *gastrocnemius* (GAS) and *soleus* (SOL) (ankle plantar flexors: APF) and *tibialis anterior* (TA)]; co-activation indices (CAI) of various muscle pairs [VAS/APF, VAS/HAM, GMAX,RF, GMAX/APF]; and muscle activation variability via the variance ratio (VR).

Chapter 3 - study one

Introduction: Neuromuscular fatigue of the knee extensors develops during prolonged high-intensity submaximal exercise and is thought to limit lower-limb power production during subsequent maximal exercise. ***Aims:*** The first aim was to investigate the association between changes in EMG activity of VAS muscles during prolonged high

intensity cycling exercise and the development of knee extensor fatigue. The second aim was to investigate the effect of knee extensor fatigue developed during prolonged high intensity cycling exercise on lower-limb power production and movement control during a subsequent maximal 30-s cycling exercise. ***Method:*** Seven physically active participants volunteered for the study. On one day, a maximal 30-s cycling exercise was completed. On the second day, a maximal 30-s cycling exercise was completed after 10-min of high-intensity cycling. ***Results:*** Over the course of high-intensity cycling, VAS EMG and GMAX/RF co-activation increased ($P \leq 0.05$). The increase in VAS EMG (range from 6% to 14%) was negatively correlated with the reduction in IMVF following high-intensity exercise (from -2% to -36%; $r = 0.791$, $P \leq 0.05$). During the 30-s maximal effort completed following high-intensity cycling, a positive correlation ($r = 0.757$, $P \leq 0.05$) was seen between changes in IMVF and the changes in maximal lower-limb power production (from 0% to -27%). EMG reduced for all muscles, especially GMAX (-21 ± 8%) and VAS (-16 ± 13%) ($P \leq 0.05$). Co-activation reduced for GMAX/RF and VAS/HAM (both $P \leq 0.05$), but did not change for VAS/GAS ($P > 0.05$). ***Discussion:*** Larger increases in VAS EMG during prolonged high-intensity cycling exercise were associated with greater levels of knee extensor fatigue, which subsequently decreased maximal power generated by the lower-limbs. The increase in co-activation for GMAX/RF during high intensity exercise and maintained co-activation for VAS/GAS during maximal exercise, suggests that movement control was adjusted to limit fatigue occurrence in the knee extensor muscles and to maximise lower-limb power production. ***Conclusion:*** Knee extensor fatigue developed during prolonged high-intensity exercise decreases maximal lower-limb power production during subsequent maximal exercise.

Chapter 4 - study two

Introduction: Fatigue is likely to accumulate in the lower-limb muscles during cycling exercises, making it difficult to isolate the effect of knee extensor fatigue on power production. Knee extensor fatigue may also induce movement variability and effect maximal activation of other lower-limb muscles. ***Aims:*** The first aim was to investigate if the level of fatigue induced by a pre-fatiguing knee extension exercise determines the level of reduction in power output during the extension and flexion phases of maximal cycling exercise. The second aim was to investigate how motor command during maximal cycling is affected by pre-fatigue of the knee extensors. ***Method:*** Ten physically active participants volunteered for this study. On one day, participants completed a 30-s maximal cycling exercise. On the second day, the same participants completed a 30-s maximal cycling exercise following a pre-fatiguing bilateral knee extension exercise.

Results: Pre-fatiguing knee extension exercise decreased IMVF by -52 ± 23% ($P \leq 0.05$). No association was reported between reductions in knee extensor IMVF following pre-fatiguing exercise (range = -18% to -82%, $P \leq 0.05$) and reductions in leg extension power during maximal cycling (range = -8% to -31%, $P \leq 0.05$) ($r = 0.19$). Large reductions were observed for VAS EMG (-15%) GMAX EMG (-12%) and VAS/APF co-activation (-15%) (all $P \leq 0.05$). For the primary flexion phase muscles, large reductions were observed for HAM EMG (-15%), TA EMG (-15%) and RF EMG (-11%) (all $P \leq 0.05$). Inter-individual variability increased for all crank forces and EMG activity for VAS, RF, HAM and TA (all $P \leq 0.05$). ***Discussion:*** Overall, the results indicate that knee extensor fatigue developed during pre-fatiguing exercise does not determine reductions in power output during maximal cycling exercise. Alterations in motor command likely explain this result, evidenced via large reductions in EMG of local and non-local muscles, and increased inter-individual variability in crank forces and muscle activation patterns. ***Conclusion:*** The level of isolated fatigue observed in the knee extensors does not determine the level of reduction in leg extension power during maximal cycling exercises, presumably due to increased movement variability.

Chapter 5 - study three

Introduction: Reducing the complexity of the cycling movement to a unilateral leg extension exercise would potentially reduce the degree of freedom and decrease variability in motor command. In this way, it is possible that knee extensor fatigue would determine the reduction in power output during the extension phase of maximal cycling. Knee extensor fatigue measurements are typically obtained post-exercise and within a time delay of 40-s to 5-min, although it remains unknown if such assessments provide an accurate measure of knee extensor fatigue developed during cycling exercise. ***Aims:*** The first aim was to compare the rate of fatigue occurrence in the knee extensors between an isolated knee extension exercise and a modified cycling exercise consisting of the leg extension phase only. The second aim was to investigate any differences in knee extensor fatigue measured post-exercise and the maximum time delays for which fatigue responses could be accurately assessed. ***Method:*** On separate days, 16 physically active participants completed 60 maximal knee extensions on an isokinetic dynamometer or 60 maximal leg extensions on an isokinetic cycle ergometer. A mechanical goniometer verified identical knee joint range of motion (~ 120° - 30° flexion, 0° = full extension) and angular velocity (~80°.s^{-1}). Electrical stimulation of the femoral nerve was automated during exercise at a consistent knee joint angle of 90°. Average measures of maximal torque, M-wave and VAS EMG.M-$wave^{-1}$ were calculated at the

start (contraction 2 - 4), middle (contraction 29 - 31) and end (contraction 58-60). IMVF, VA, $RT_{100\ HZ}$ and $RT_{10:100\ HZ}$ were measured pre-exercise, and again at 5-s, 20-s, 40-s, 1-min, 1.5-min, 2-min, 3-min, 4-min and 5-min post-exercise ***Results:*** Intra-individual reductions in maximal torque during knee extension were positively correlated to torque reduction during leg extension exercise at the middle (-45 ± 11% vs. -23 ± 12%, r = 0.79, P ≤ 0.05) and end (-59 ± 10% vs. -37 ± 13%, r = 0.86, P ≤ 0.05). Greater reductions during knee extension were shown for RF EMG (middle: -17 ± 15% vs -2 ± 20%; end: -34 ± 16% vs. -4 ± 22%) and VAS EMG.M-wave^{-1} (end: -21 ± 16% vs. -14 ± 17%) (all P ≤ 0.05). IMVF reduction measured 5-s post knee extension (-32 ± 12%) partially recovered within 2-min (P > 0.05), whereas the reduction in RT_{100} (-28 ± 18%) and $RT_{10:100}$ (-17 ± 15%) partially recovered within 20-s and 40-s, respectively (P > 0.05). ***Discussion:*** The level of fatigue developed in the knee extensors determines the reduction in maximal torque during leg extension exercise. This is likely due to the removal of the leg flexion phase and contribution of the contralateral leg during exercise. The longest time delay for accurate assessment of isometric maximal voluntary force of the knee extensors post-exercise was 1.5-min. To avoid underestimating high and low frequency peripheral fatigue, assessment must be conducted within less than 20-s and 40-s post-exercise, whereas reductions in central fatigue measurements were greatest between 20-s and 2-min post-exercise. ***Conclusion:*** Fatigue resistance in the knee extensors may predict the ability to maintain high levels of power during the extension phase of maximal cycling.

Summary:

Study one revealed that VAS EMG increase during high-intensity cycling exercise (6% to 14%) is associated to IMVF decrease (-2% to -36%), and that IMVF decrease is associated to reductions in maximal lower-limb power (0% to -27%) (r = 0.76). However, fatigue development was likely in other lower-limb muscles during high-intensity cycling, making it difficult to isolate the effects of knee extensor fatigue on lower-limb power production. Therefore, study two sought to isolate fatigue in the knee extensors prior to a maximal cycling effort, with the results from this study revealing no clear association between an isolated reduction in knee extensor IMVF (-18% to -82%) and reductions in maximal leg extension power (-8% to -31%) (r = 0.1), presumably due to alterations in movement control. Study three aimed compare the rate of fatigue occurrence in the knee extensors between an isolated knee extension exercise and a modified cycling exercise consisting of the leg extension phase only. The novel finding from this study was that torque reduction during knee extension was strongly associated to torque reduction

during leg extension from the start to middle (r = 0.79), middle to end (r = 0.67) and start to end periods of the exercise (r = 0.86). The results also highlighted the need to assess peripheral muscle fatigue within 20-s post-exercise, and isometric force within 1.5-min post-exercise, if accurate measures of the exercise-induced changes are to be obtained.

Practical implications and importance:

Collectively, the results from all studies suggest that individuals with a greater capacity to resist fatigue development in their knee extensors may have a greater capacity to maintain high levels of power during maximal cycling exercises. However, severe levels of knee extensor fatigue may lead some individuals to adopt a wider range of movement strategies to generate crank power. This information may be used by sport scientists and coaches to improve exercise prescription and performance outcomes.

Declaration

"I, Steven Jeffery O'Bryan declare that the PhD thesis entitled 'Effect of Changes in the Force-generating Capacity of the Knee Extensors on Lower-limb Power Production during Cycling Exercises' is no more than 100,000 words in length including quotes and exclusive of tables, figures, appendices, bibliography, references and footnotes. This thesis contains no material that has been submitted previously, in whole or in part, for the award of any other academic degree or diploma. Except where otherwise indicated, this thesis is my own work".

Signature  Date 05/10/2017

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List of Abbreviations

[ ]	Concentration
°	Degrees
°.s^{-1}	Degree per second
µm	Micrometre
ADP	Adenosine 5'-diphosphate
Ag-AgCl	Silver-silver chloride
APF	Ankle plantar flexors
ATP	Adenosine 5'-triphosphate
BDC	Bottom dead centre
BF	*Biceps femoris*
C_0	Estimated maximal cadence
Ca^{2+}	Calcium ion
CAI	Co-activation index
CI	Confidence interval
Cl^+	Chloride ion
cm^2	Square centimetre
C_{opt}	Estimated optimal cadence
EMG	Surface electromyography
EMG.M-wave^{-1}	Surface electromyography amplitude normalised to the maximal muscle compound action potential amplitude
F_{RAD}	Radial crank force
F_{TAN}	Tangential crank force
F_{TOT}	Total crank force
F-V	Force-velocity
GAS	*Gastrocnemius medialis* and *lateralis*
GMAX	*Gluteus maximus*
H^+	Hydrogen ion
HAM	Hamstrings

Hz	Hertz
ICC	Intra-class correlation coefficient
IMVF	Isometric maximal voluntary force
K^+	Potassium ion
kg	Kilogram
$m.s^{-1}$	Metre per second
Mg^{2+}	Magnesium ion
min	Minute
M-wave	Maximal muscle compound action potential
ms	Millisecond
mV	Millivolts
MΩ	Megaohm
N	Newton
N·m	Newton-metre
Na^+	Sodium ion
P-C	Power-cadence
PCr	Phosphocreatine
PCSA	Physiological cross-sectional area
Pi	Inorganic phosphate
P_{MAX}	Estimated maximal power
RF	*Rectus femoris*
RMS	Root mean square
ROM	Range of motion
rpm	Revolutions per minute
RT	Resting twitch
s	Seconds
SE	Standard error
SEE	Standard error of the estimate
SIT	Superimposed twitch
SOL	*Soleus*

ST	*Semitendinosus*
T_0	Estimated maximal torque
TA	*Tibialis anterior*
TDC	Top dead centre
TE	Typical error
VA	Voluntary activation
VAS	*Vastus lateralis* and *medialis*
VI	*Vastus intermedius*
VL	*Vastus lateralis*
VM	*Vastus medialis*
$\dot{V}_{O2}$	Rate of oxygen consumption
VR	Variance ratio
W	Watts
$W.kg^{-1}$	Watts per kilogram
π	pi

List of Publications

Study one (Chapter 3)

- **O'bryan, S. J**., Billaut, F., Taylor, J. L., & Rouffet, D. M. (2017). Knee extensor fatigue developed during high-intensity exercise limits lower-limb power production. *Journal of Sports Sciences*, 1-8

List of Conference Proceedings

Study two (Chapter 4)

- **O'Bryan, S.J**., Rouffet, D.M. Magnitude and Origin of Fatigue Changes during Repeated Maximal Knee Extensions. *European College of Sport Science Conference* (2015), Malmo, Sweden.
- **O'Bryan, S.J**., Bourke, R., Rouffet, D.M. Effect of Isolated Fatigue in the Knee Extensors on Muscle Activation and Crank Power during Maximal Cycling. *Exercise Sport Science Australia Conference* (2016), Melbourne, Australia.
- **O'Bryan, S.J**., Taylor, J.T., Rouffet, D.M. Effect of Bilateral Fatigue in the Knee Extensors on Crank Power during Sprint Cycling. *International Society of Electrophysiology and Kinesiology Conference* (2016), Chicago, United States of America.

List of Awards

- Australian Postgraduate Award - 2014 to 2016

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Chapter 1 INTRODUCTION

A reduction in the force-generating capacity of the knee extensor muscles can have a large negative impact on the execution of many lower-limb tasks such as walking, rising from a chair, and climbing stairs. It has been linked to reduced physical and social participation and quality of life in populations such as the elderly (Toebes et al. 2015; Callahan et al. 2015), obese (Tsiros et al. 2016; Batsis et al. 2015) and injured athletes (McCamey and Hartz 2014). A reduction in the force-generating capacity of the knee extensors is also becoming more recognized to contribute to morbidity in patients with chronic obstructive pulmonary disease (Hamnegård et al. 2004; Jakobsson et al. 1995), and can also be an effective predictor for knee osteoarthritis (Culvenor et al. 2016a) and knee replacement surgery (Skou et al. 2016; Culvenor et al. 2016b). Accordingly, knee extensor function is directly queried on functional status and disability surveys in the hospital and rehabilitation settings (Glenn and Samojla 2002). In addition to the importance of the knee extensors for the performance of functional tasks, individuals capable of generating high knee extensor forces have also been shown to generate greater amounts of lower-limb power during more complex ballistic movements such as cycling (Driss et al. 2002; Kordi et al. 2017) and jumping (Willigenburg et al. 2014; Tsiokanos et al. 2002; Malliou et al. 2003). Therefore, investigation into the factors which influence the force-generating capacity of the knee extensors is important within the clinical and sport science context and applicable to a wide range of populations.

A debilitating symptom contributing to a reduction in the force-generating capacity of the knee extensors is neuromuscular fatigue, most-widely defined by physiologists as “an exercise-induced reduction in the ability to generate force or power, regardless of whether or not the task can be sustained” (Bigland-Ritchie and Woods 1984; Gandevia 2001). The mechanisms which contribute to fatigue development originate within the central nervous system (Gandevia 2001; Meeusen et al. 2006; Taylor et al. 2016) and the skeletal muscle (Allen et al. 2008; Green 1997; Fitts 1994; Debold 2012), and are effected by complex feedback systems (Amann et al. 2014; Taylor et al. 2016; Gandevia 2001). The magnitude, rate and aetiology of fatigue is dependent on the type of exercise task (Enoka and Stuart 1992; Bigland-Ritchie et al. 1995) and the physiological characteristics of the individual (Hamada et al. 2003; Enoka and Duchateau 2008).

Due to the large contribution of the knee extensor muscles to crank power production during high-intensity and maximal cycling exercises (Raasch and Zajac 1999; Zajac et al. 2002; Ericson et al. 1986), fatigue development in the knee extensors is

largely thought to determine overall performance (e.g. time trial, time to task-failure, maximal power) (Fernandez del Olmo et al. 2013; Hunter et al. 2003; Hureau et al. 2014; Amann and Dempsey 2008). However, during sustained high-intensity submaximal cycling and maximal cycling exercise (e.g. 30-s), fatigue is likely to develop in other lower-limb muscles and increase movement variability (Martin and Brown 2009; Singh et al. 2010; Brochner Nielsen et al. 2016; Elmer et al. 2012; O'Bryan et al. 2014), making it difficult to determine how variations in the force-generating capacity of the knee extensors influences performance. Moreover, some studies have indicated large intra-individual variability in the effects of knee extensor fatigue on power production during maximal cycling exercise (Hureau et al. 2014), meaning that knee extensor fatigue is likely to affect individuals differently.

Following a review of the relevant literature, this thesis is comprised of three main studies all with the primary aim to determine how fatigue-induced reductions in the maximal force-generating capacity of the knee extensors influences crank power production during maximal cycling exercise.

Study one (Chapter 3) – Knee Extensor Fatigue Developed during High-intensity Exercise Limits Lower-limb Power Production

> Aims: To investigate: i) the association between changes in EMG activity of the *vastii* muscles during prolonged high-intensity exercise and knee extensor fatigue following exercise, and ii) the effect of knee extensor fatigue on power production and inter-muscular coordination during a subsequent 30-s maximal cycling effort.
>
> Hypothesis*:* i) Individuals that display a larger increase in vastii EMG activity over the course of a high-intensity cycling exercise would experience larger reductions in the maximal voluntary force capacity of the knee extensors, and ii) knee extensor fatigue developed during high-intensity cycling would reduce lower-limb power production during a subsequent maximal cycling effort.

Study two (Chapter 4) – Effect of Pre-fatiguing Knee Extension Exercise on Power Production and Movement Control during Maximal Cycling

> *Aims:* To investigate: i) if the level of fatigue induced by a pre-fatiguing knee extension exercise determines the level of reduction in power output during the extension and flexion phases of maximal cycling exercise, and ii) how motor command during maximal cycling exercise is affected by pre-fatigue of the knee extensors.

Hypothesis: i) Knee extensor fatigue developed during pre-fatiguing exercise would be associated to the reduction in power output during the extension phase of maximal cycling but not during the flexion phase, and ii) knee extensor fatigue would limit the capacity to maximally activate the lower-limb muscles and increase inter-individual variability in crank force and muscle activation patterns.

Study three (Chapter 5) – Fatigue Development and Short-term Recovery during Maximal Knee Extension and Leg Extension Exercise

Aims: To: i) compare the rate of fatigue occurrence in the knee extensors between an isolated knee extension exercise and a modified cycling exercise consisting of the leg extension phase only, and ii) investigate differences in knee extensor fatigue between the exercises post-exercise, and to determine the maximum time delay post-exercise for which fatigue responses could be accurately assessed.

Hypothesis: i) individuals displaying larger reductions in torque during knee extension exercise would also display larger reductions in torque during leg extension exercise, and ii) isometric maximal voluntary force and peripheral fatigue responses need to be assessed within less than 1-minute post-exercise, whereas the reduction in central fatigue responses would take longer to develop.

In the final chapter, the main findings of the studies are summarized and discussed, along with practical implications, direction for future research and overall conclusions.

Chapter 2 LITERATURE REVIEW

The literature review begins with a description of the anatomical and physiological characteristics of the knee extensor muscles and the factors which influence their ability to generate force. The second section will detail the contribution of the knee extensors and other major lower-limb muscles to power production during cycling exercises. Movement control factors such as in inter-muscular coordination and variability will also be discussed. Lastly, the techniques used to elucidate neuromuscular fatigue will be presented, along with current knowledge of fatigue in the knee extensors during isolated and cycling exercise.

2.1 The Knee Extensors

2.1.1 Anatomical features

The knee extension musculature is comprised of four primary muscle bellies including the mono-articular *vastus lateralis*, *vastus medialis* and *vastus intermedius*, and the bi-articular *rectus femoris*, which all reside within the anterior compartment of the thigh and aptly referred to as the 'quadriceps'. These muscles are innervated by branches of the femoral nerve originating from lumbar-sacral nerve roots two through four, and receive their blood supply from branches of the femoral artery (Standring 2015) (**Figure 2.1**). Each muscle has distinct anatomical features which influence force-generating capacity. This includes pennation angle (fibre angle relative to the force-generating axis), fibre length (length of the muscle fibre from origin to insertion) and physiological cross sectional area (PCSA: sum of the cross-sectional areas of all the muscle fibres) (Lieber and Friden 2000). The properties of the connective tissues (namely the quadriceps tendon) also effect force production, which is largely determined by Young's modulus of elasticity (slope of the stress – strain curve and representative of tissue stiffness) (Wiesinger et al. 2015; Enoka 2015). Typically, the knee extensor muscles are characterised by relatively high pennation angles, short muscle fibre lengths and large physiological cross-sectional area (PCSA), which deems them highly suitable for generating large muscle forces (Lieber and Friden 2000; O'Brien et al. 2010). Moreover, the quadriceps tendon is thick (~6 mm) and short (~ 20 mm) (Kopydlowski et al. 2014) making the tendon stiff and permitting rapid force development (Maffiuletti et al. 2016). The force-generating capacity of the knee extensors has been positively related with sporting performance during ballistic lower-limb exercises (Willigenburg et al. 2014; Driss et al. 2002; Tsiokanos et al. 2002; Malliou et al. 2003; Kordi et al. 2017), and they are the preferred site for muscle biopsies and surface electromyography

recordings during exercises involving the knee extensors and the lower-limbs (Coyle et al. 1991; Allemeier et al. 1994; Proctor et al. 1995).

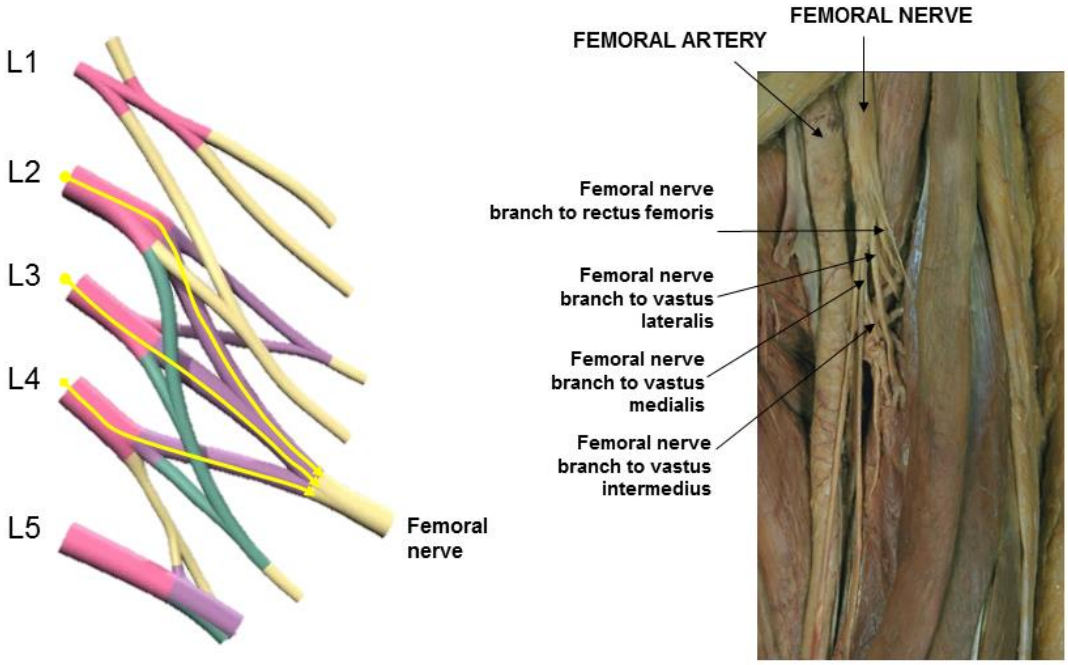

Figure 2.1 Anatomy and branches of the femoral nerve innervating the knee extensor muscles . (L1 – L5 represents the lumbar nerve roots). Adapted from Primal Pictures (2009a) and (2009b).

2.1.1.1 Vastus intermedius (VI)

VI is the deepest of the knee extensor muscles, and from a cross sectional point of view, wraps around the anterior, medial and lateral shaft of the femur in a 'C' shape fashion (Glenn and Samojla 2002; McCamey and Hartz 2014; Standring 2015) (**Figure 2.2 A**). The anterior portion is thick (~18 mm) with a low pennation angle (~6°), whereas the lateral portion is thin (~6 mm) and moderately pennated (16°) (Blazevich et al. 2006). Its specific origin is the anterior-lateral proximal two-thirds of the femur, lower half of the *linea aspera*, upper part of the lateral supracondylar line and the lateral intermuscular septum (Wheeless 1996; Glenn and Samojla 2002). The muscle blends into the *vastus lateralis* and *vastus medialis* muscles distally, with an insertion into the lateral border of the patella and lateral condyle of the femur via the quadriceps tendon (Glenn and Samojla 2002; Standring 2015). The aponeurosis from VI forms the deepest laminae of the quadriceps tendon (Pasta et al. 2010). VI is vascularized by a lateral branch of the lateral circumflex artery and a medial branch of the deep femoral artery, and innervated via lateral branches of the deep femoral nerve (Standring 2015; Grob et al. 2016). VI fascicle length is ~60 – 80 mm, and the PCSA is 10 – 40 cm² (Wickiewicz et al. 1983; Friederich and Brand 1990; Cutts 1988).

2.1.1.2 Vastus lateralis (VL)

VL is the largest of the knee extensor muscles and covers the lateral region of the femur (**Figure 2.2 B**), with its most lateral muscle fibres covered by the aponeurosis of *tensor fascia latae* and *gluteus maximus* (i.e. iliotibial band) (Standring 2015). In a proximal-distal direction, the muscle becomes thinner, with an average muscle thickness of ~20 mm (Blazevich et al. 2006). The proximal attachment site for VL is the upper part of the intertrochanteric line, the anterior inferior border of the greater trochanter, the lateral lip of the gluteal tuberosity and the adjacent proximal half of the lateral lip of the *linea aspera* of the femur (Becker et al. 2010; Becker et al. 2009; McCamey and Hartz 2014). VL inserts into the base and lateral border of the patella, blending into and partly forming the intermediate laminae of the quadriceps tendon (Standring 2015; McCamey and Hartz 2014; Pasta et al. 2010; Becker et al. 2009; Becker et al. 2010). Vascular supply for VL is provided by the three main branches of the deep femoral artery (also known as the *profunda femoris*); the lateral and medial circumflex arteries and the first of the perforating arteries (Standring 2015; Glenn and Samojla 2002). Innervation of VL is provided by two major proximal and distal branches of the femoral nerve, with the proximal nerve subdividing into a superficial and deep nerve branch, and the distal nerve subdividing into a mid-distal and distal nerve branch (Becker et al. 2010). The VL fasicles display a unipennate structure, however a clear trend towards a more obliquely directed fascicular orientation is seen in the distal part of the muscle giving rise to two distinct regions; the proximal VL *longus* and the more distal VL *obliquus* (Weinstabl et al. 1989; Becker et al. 2010). In the proximal VL *longus*, muscle fascicles generally display a pennation angle of ~10 - 13°, whereas the pennation angle is much greater in the distal oblique fascicles (35 - 50°) (Becker et al. 2009; Friederich and Brand 1990; Weinstabl et al. 1989; Blazevich et al. 2006). These oblique muscle fibres in the distal aspect of VL help to counteract the medial forces generated by the *vastus medialis* and stabilize the knee (McCamey and Hartz 2014). In healthy adults, average fascicular length for VL is ~66 – 80 mm and the PCSA ranges from 20 – 40 cm^2 (Becker et al. 2009; Fukunaga et al. 1997; Friederich and Brand 1990; Wickiewicz et al. 1983; Cutts 1988).

2.1.1.3 Vastus medialis (VM)

VM runs along the anterior-medial line of the femur, with the most proximal and medial fibres partly covered by the *rectus femoris* and *sartorious* muscles (**Figure 2.2 C**) (Kopydlowski et al. 2014; Standring 2015). The muscle becomes thinner moving in a proximal-distal direction, with an average muscle thickness of ~23 mm (Blazevich et al.

2006). This muscle has origins on the lower half of the intertrochanteric line, the medial lip of the *linea aspera*, upper part of the medial supracondylar line, the medial intermuscular septum and the tendons of the *adductor magnus* and *longus* muscles (McCamey and Hartz 2014; Standring 2015; Glenn and Samojla 2002). Point of insertion is the medial border of the patella and medial condyle of the femur, with the aponeurosis partly forming the intermediate laminae of the quadriceps tendon (Pasta et al. 2010; Standring 2015; Smith et al. 2009; Weinstabl et al. 1989). Three major branches of the superficial femoral artery vascularize the VM muscle; the superior, medial and inferior (Standring 2015; Glenn and Samojla 2002). Some variations in the current literature regarding muscle fibre alignment, the presence of a fascial plane and specific innervation to two separate regions of the VM muscle, has indicated this muscle may be comprised of two separate muscular entities with different functional roles; the proximal VM *longus* and the distal VM *obliquus* (Smith et al. 2009). For example, muscle fibres become increasingly oblique as the muscle moves distally, with fibres in the proximal region displaying a pennation angle of ~11 - 35°, with the fibres in the distal region ranging from ~40 - 80° (Smith et al. 2009; Weinstabl et al. 1989). Consequently, it has been suggested that the proximal *longus* muscle fibres have a greater contribution to knee extension, whereas the distal oblique fibres may act more as a stabilizer to lateral patella translation (Bennett et al. 1993). In a systematic review by Smith et al. (2009), VM was shown to be innervated by a single nerve trunk, whereas two nerve trunks (one short and deep branch to proximal fibres and one long superficial branch to distal fibres) was shown in the remaining 40%. Nonetheless, these nerve branches both stemmed from the femoral nerve. Only rarely is a fascial plane between the two regions of VM displayed (Smith et al. 2009; Peeler et al. 2005; Nozic et al. 1997). Therefore, despite distinct differences in muscle fibre orientation, clinical anatomic research and systematic reviews suggest that VM should be treated as one common muscular entity and not be dissociated as *obliquus* or *longus* (Smith et al. 2009; Peeler et al. 2005; Nozic et al. 1997; Hubbard et al. 1997). In healthy adults, VM fascicular length ranges from 65 – 79 mm and PCSA is 15 – 30 cm^2 (Wickiewicz et al. 1983; Friederich and Brand 1990; Cutts 1988).

2.1.1.4 Rectus femoris (RF)

RF is the most superficial of the knee extensors, and the only knee extensor muscle to cross multiple joints (**Figure 2.2 D**). The muscle becomes thinner moving in a proximal-distal direction, with an average muscle thickness of ~23 mm (Blazevich et al. 2006). RF is vascularized by branches of the femoral artery, with one or two small diameter pedicles supplying the superior third, and a single large diameter pedicle

supplying the distal two-thirds of the muscle (Yang and Morris 1999; Standring 2015). RF is innervated by a large nerve branch from the posterior division of the femoral nerve, which enters at the proximal posterior surface of the muscle and subdivides into two sub-branches (Yang and Morris 1999; Standring 2015). With multiple proximal attachments, RF has a direct superficial attachment to the anterior inferior iliac spine of the pelvis, and two deep indirect attachments to the superior-lateral rim of the acetabulum and the anterior joint capsule (Standring 2015; Kopydlowski et al. 2014; Pasta et al. 2010). The fibres in the proximal third of the muscle arise from the direct superficial tendon and run distally toward the patella to form a unipennate structure, whereas the fibres in the distal two-thirds of the muscle arise from the indirect tendon and run distally in a medial, lateral, or posterior direction toward the patella to create a bipennate muscle structure (Hasselman et al. 1995). RF forms the anterior laminae of the quadriceps tendon and inserts onto the anterior portion of the base of the patella and the superior third of the anterior surface the patella (Pasta et al. 2010; Hasselman et al. 1995). Pennation angle of the RF muscle fibres are between 5 - 18° and each fibre is ~55 – 68 mm long (Wickiewicz et al. 1983; Cutts 1988; Friederich and Brand 1990). In healthy adults, RF PCSA is reported to be 9 – 15 cm² (Wickiewicz et al. 1983).

2.1.1.5 A fifth knee extensor muscle? Tensor of vastus intermedius

On the basis of some researchers observing anatomical variation in VL muscle in particular (Becker et al. 2010; Willan et al. 2002), a recent study has suggested the existence of a fifth knee extensor muscle, which has been called the 'tensor of *vastus intermedius'* (Grob et al. 2016). A separate belly of this tensor-like muscle was observed in 85% of all investigated cases (22/26), sitting in between the fascia of VL and VI muscles (**Figure 2.2 E**). A common origin of this muscle with VL and VI was shown between the intertrochanteric line, greater trochanter of the femur and lateral lip of the *linea aspera*, with an insertion on the medial aspect of the patellar base. In just under 50% of cases, a tendon that was separable from VL and VI was shown, forming a deep portion of the medial laminae of the quadriceps tendon. In the remaining cases, the tendon blended into the aponeurosis of either VL, VI, or both. Specific branches of the lateral circumflex femoral artery (transverse and ascending branches) vascularize the muscle separately from VL and VI. The proximal portion of this muscle was independently innervated by branches of the deep femoral nerve, whereas the distal portion displayed a common innervation with the lateral region of VI. Functionally, the authors suggested that this muscle may be involved in controlling the motion of the patella, by counteracting medial forces imposed on the patella by VM (similar role to VL).

Alternatively, this muscle may exert tension on the VI aponeurosis and orientate the forces produced in this muscle in a more medial direction (hence the name, tensor of vastus intermedius). Currently, architectural information has not been presented for this muscle (i.e. fibre length, pennation angle and PCSA), and the contribution to the forces exerted during knee extension actions remain unknown.

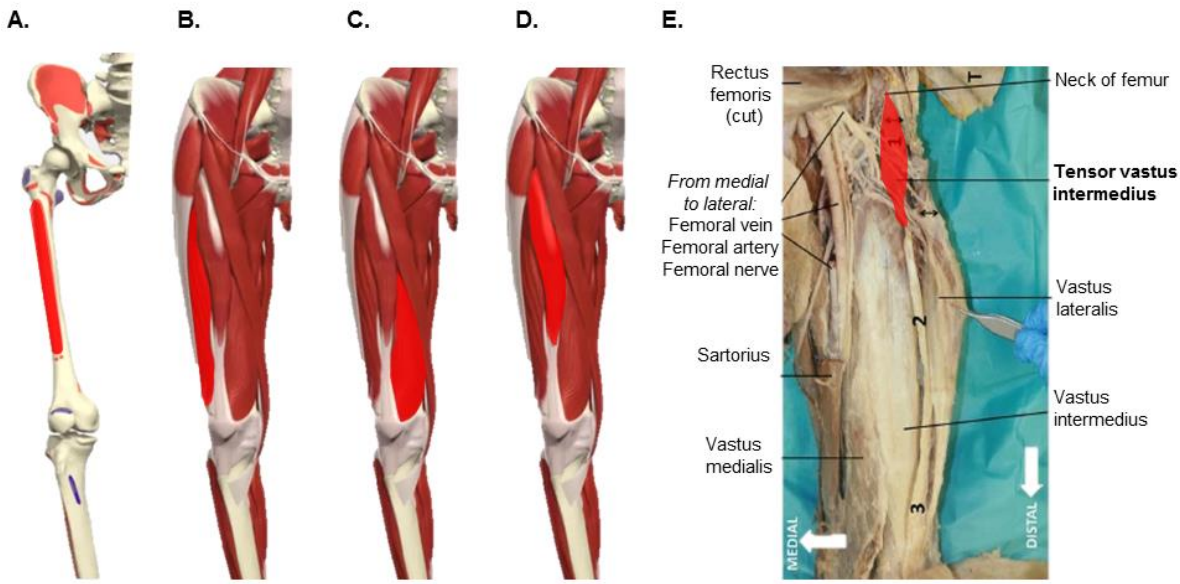

Figure 2.2 Anatomy of the knee extensor muscles: A - *vastus intermedius*, B - *vastus lateralis*, C - *vastus medialis*, D - *rectus femoris*, E - tensor of *vastus intermedius*. Adapted from Primal Pictures (2009c) and Grob et al. (2016).

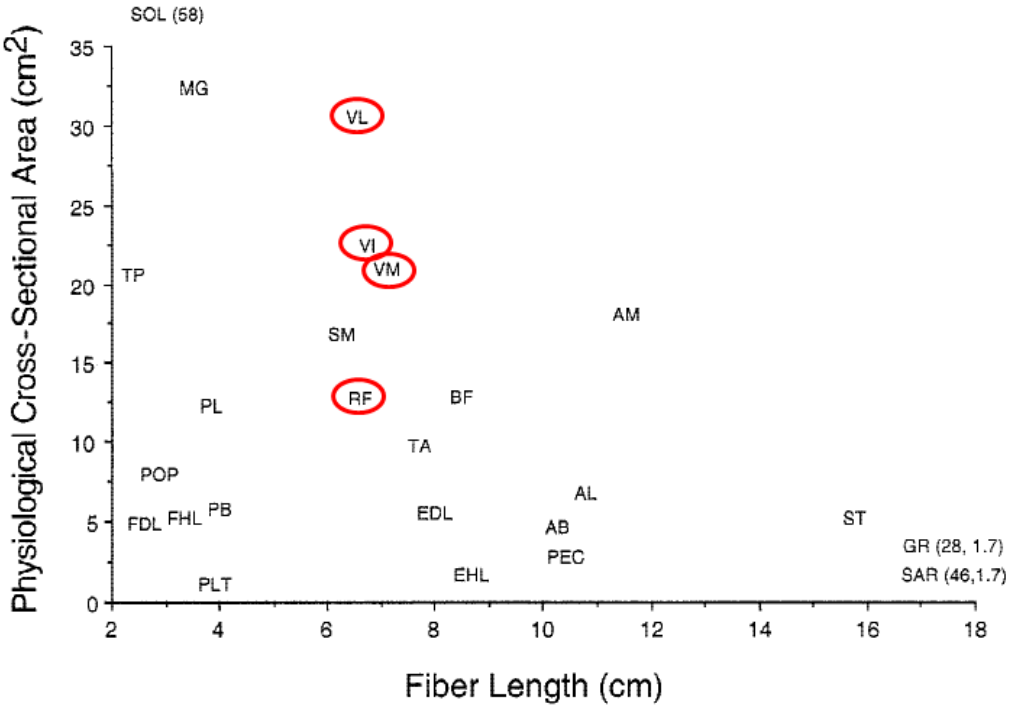

Figure 2.3 Scatter graph of the fibre length and physiological cross-sectional areas (PCSA) of muscles in the human lower limb. Note the relatively large PCSA and short muscle length of the primary knee extensor muscles, which makes them favourable for producing large muscle forces. (Abbreviations: AB = adductor brevis; Al = adductor longus; AM = adductor magnus; BF = biceps femoris; EDL = extensor digitorum longus; EHL = extensor halluces longus; FDL = Flexor digitorum longus; FHL = flexors hullucis longus; GR = gracilis; LG = lateral gastrocnemius; MG = medial gastrocnemius; PB = peroneus brevis; PEC = pectineus; PL = peroneus longus; PLT = plantaris; POP = popliteus; RF = rectus femoris; SAR = Sartorius; SM = semimembranosus; SOL = soleus; ST = semitendinosus; TA = tibialis anterior; TP = tibialis poster; VI = vastus intermedius; VL = vastus lateralis; VM = vastus medialis). Adapted from Lieber and Friden (2000). Data from Wickiewicz et al. (1983).

2.1.2 Physiological properties

2.1.2.1 Neural control

The alpha motoneuron and the muscle fibres they innervate form the motor unit, which is the true functional feature of the neuromuscular system (Liddell and Sherrington 1925). The motoneuron receives synaptic input from supraspinal sites and reflexive afferent nerve endings (Taylor et al. 2016). If the summation of all excitatory synaptic potentials is sufficient to drive the resting membrane potential of the motoneuron past threshold (from ~70 mV to ~50 mV) the motoneuron will discharge and engage the muscle fibres to generate force. Descending drive to the motoneurons results from depolarization of pyramidal cells within Brodmann's area 4 (primary motor cortex, M1) and 6 (supplementary and pre-motor areas) of the cerebral motor cortex (Riehle and Vaadia 2005; Porter and Lemon 1993; Schoenen and Grant 2004; Gilman and Newman 1996). Specifically, pyramidal cells descending to knee extensor motoneurons originate

near the vertex and lie deep to the muscles of the hip (Penfield and Boldrey 1937) (**Figure 2.4**). Descending from the cerebral cortex, the majority of pyramidal cell axons decussate at the level of the caudal medulla to form part of the lateral corticospinal tract to synapse directly or indirectly onto the motoneurons. The approximate location of knee extensor motoneurons is within lamina IX of the ventral horn spinal cord grey matter, spanning from lumbar nerve roots two through four (Gilman and Newman 1996; Brodal 2003; Standring 2015).

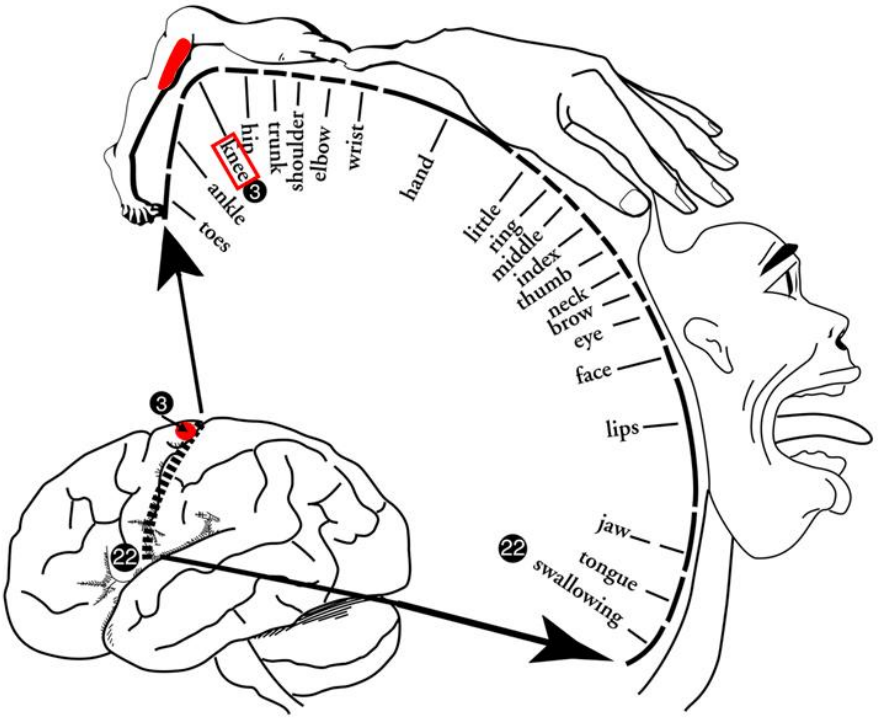

Figure 2.4 The motor homunculus. Note that knee extensor pyramidal cell neurons originate close to the vertex of the skull and deep to the muscles of the hip. In a medial-lateral direction, motor areas shift from the lower-limb, to the trunk, to the upper limb, to the neck, and to the face. Larger images represent muscles with smaller innervation ratios that are required for fine motor control. Adapted from Penfield and Boldrey (1937).

Reflexive afferent inputs to the motoneurons have generally been classified into five types based on their physiological and morphological properties in animals, and are proposed to by synonymous with humans (Matthews 1964; Edin and Vallbo 1990; Lloyd and Chang 1948; Gandevia 1998) (**Figure 2.5**). The receptors of group Ia afferents are the primary muscle spindles, located in parallel with skeletal muscle fibres and discharging in response to increases in dynamic and static muscle lengthening (i.e. stretch). The receptors of Ib afferents are the golgi tendon organs, which are located in series with the muscle tendons and discharge in response to changes in muscle tension (Garland and Kaufman 1995). Group II muscle spindle afferents respond to changes in

static muscle lengthening, whereas non-spindle group II afferents respond to muscle contraction and stretch. Group III muscle afferents discharge in response to chemical (e.g. the inflammatory mediators) and mechanical (e.g. pressure) stimuli (Kaufman et al. 2002), whereas group IV afferents discharge in response to noxious nocioceptive and metaboreceptive stimuli (e.g. K^+, H^+, free fatty acids) (Light et al. 2008; Kaufman et al. 2002; Rotto and Kaufman 1988; Sinoway et al. 1993). Thus, group III and IV afferents are primarily associated with a reduction in maximal force during fatiguing isolated contractions (Bigland-Ritchie et al. 1986b; Woods et al. 1987; Butler et al. 2003; Martin et al. 2006; Kennedy et al. 2015) and whole body cycling exercises (Amann et al. 2008; Amann et al. 2009; Hilty et al. 2011; Blain et al. 2016; Sidhu et al. 2017). In fact, inhibitory actions of group III and IV muscle afferents may also spread to and heteronymous muscles, such as synergist, antagonist or contralateral muscles of the upper and lower-limb (Kennedy et al. 2014; Martin et al. 2006; Kennedy et al. 2013; Ciubotariu et al. 2004; Kennedy et al. 2015; Halperin et al. 2015; Doix et al. 2013; Martin and Rattey 2007; Rattey et al. 2006).

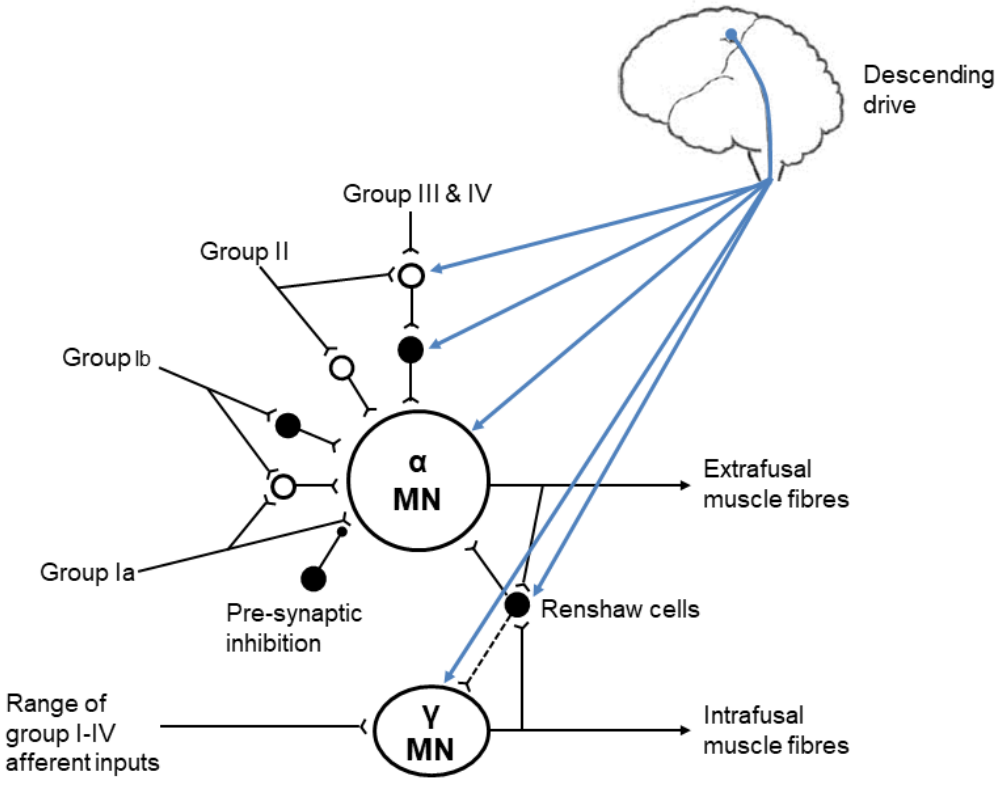

Figure 2.5 Summary of the inputs acting on the alpha (α) and gamma (γ) motoneuron of agonist muscles. Cells with solid circles are inhibitory. Adapted from Gandevia (2001).

Motor units are generally classified via their size, morphologic and physiological features (Enoka 1995; Burke 1981). The size of the motor unit is determined via its innervation ratio, which represents the ratio between the number of motoneurons to the

number of muscle fibres (Enoka 1995). For VL, the innervation ratio is ~1:1500, which makes this muscle favourable for generating large forces during gross motor tasks such as locomotion. The innervation ratio of small muscles of the hand such as the first dorsal interosseous is ~1:100, making these muscles favourable for fine motor control tasks (Burke 1981; De Luca and Contessa 2012; De Luca and Hostage 2010; Adam and De Luca 2005; Rich et al. 1998). Morphological and physiological properties include motoneuron soma and axon diameter, input resistance, conduction velocity, discharge pattern, and muscle fibre type (Enoka 1995; Burke 1981; Schiaffino and Reggiani 2011), which all influence the recruitment threshold and firing frequency of the motoneuron (Welsh et al. 2007; De Luca and Hostage 2010). Motor units with a small motoneuron soma diameter (≤ 60 μm) tend to have a high input resistance (≥ 0.9 MΩ), small motor axon diameter, tonic firing pattern, low conduction velocity (≤ 90 $m.s^{-1}$) and control type I skeletal muscle fibres (Burke 1981; Zengel et al. 1985; Kanning et al. 2010; Henneman and Mendell 1981; Schiaffino and Reggiani 2011). Motor units with a larger motoneuron soma diameter (≥ 60 μm) tend to have a low input resistance (≤ 0.9 MΩ), large motor axon diameter, phasic firing discharge pattern, fast conduction velocity (≥ 90 $m.s^{-1}$), and control type II skeletal muscle fibres (Burke 1981; Zengel et al. 1985; Kanning et al. 2010; Henneman and Mendell 1981; Schiaffino and Reggiani 2011). This means that higher synaptic inputs are required to depolarize larger motor units, and that for a given synaptic input, smaller motor units will depolarize before larger motor units. This is famously referred to as the size principle of orderly recruitment (Henneman 1957). This hierarchical control of motor units, leads to the progression in recruitment order from slow motor units to fast motor units with increases in strength during voluntary isometric and dynamic contractions (De Luca and Hostage 2010; De Luca and Contessa 2012; Duchateau et al. 2006).

At the beginning of a isometric ramp contraction of the knee extensors, VL and VM motor units begin regular discharge at ~4% maximal voluntary force, which is much lower than the 16% observed for RF (Welsh et al. 2007). This finding is consistent with Zhang et al. (2003), who showed that the relative contribution of each of the knee extensor muscles to force generation shifts from the deep VI, toward the superficial VL, VM and then RF with increases in maximal voluntary force. During a maximal voluntary contraction, VL motor units reach their maximal discharge rate of 25 - 30 pulses per second (pps) at ~75% maximal force (De Luca and Contessa 2012), whereas full recruitment is achieved at 90% (De Luca and Hostage 2010). Beyond this, increases in voluntary force may be achieved via modulating the discharge characteristics of other knee extensor muscles. However, despite maximal voluntary effort, the ability to achieve

full temporal and spatial recruitment of the knee extensor motor units as measured via the twitch interpolation technique is incomplete, with average values ranging between 90 – 95% (Place et al. 2007). Importantly, this is highly dependent on the angle of the knee joint, with maximal voluntary activation of knee extensor motor units decreasing when extending the knee from 90° to 30° (0° = straight leg) (Becker and Awiszus 2001) (**Figure 2.6**). This finding is likely attributed to decreased excitatory input to the motoneurons from type Ia muscle spindle afferents. Although this has large negative implications on force-generating capacity of the knee extensors, other factors such as changes in muscle length are also implicated.

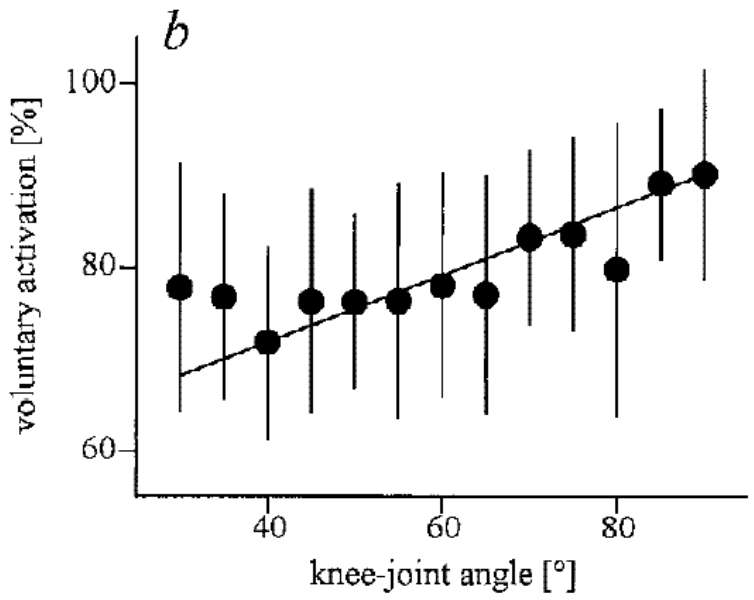

Figure 2.6 Effect of changes in knee joint angle on maximal voluntary activation of the knee extensor motor units.100% = full temporal and spatial summation. Retrieved from Becker and Awiszus (2001).

2.1.2.2 Skeletal muscle fibre types

For the muscle fibres controlled by the motor units to generate force, the axonal action potential generated by the motoneurons initiates opening of voltage gated calcium (Ca^{2+}) channels and influx Ca^{2+} into the terminal button, initiating exocytosis of acetylcholine (ACh) into the neuromuscular junction. This leads to opening of sodium (Na^{+}) channels and Na^{+} influx into the muscle cell, subsequently generating a sarcolemma action potential. The initiated sarcolemma action potential travels along the T-tubular system and activates dihydropyradine receptors (DHPR), located within the junctional region of the T-tubular membrane and sarcoplasmic reticulum terminal cisternae. DHPR receptors function as a voltage sensor and Ca^{2+} activating channel,

signalling ryanodine receptors (RyR) to open Ca^{2+} release channels from the sarcoplasmic reticulum and TO expel Ca^{2+} into the intracellular milieu. At rest, magnesium (Mg^{2+}) has a strong inhibitory action on the sarcoplasmic RyR Ca^{2+} release channels which prevents Ca^{2+} leakage. Activation of the DHPR receptors lowers the affinity of Mg^{2+} on the RyR Ca^{2+} release channels and therefore permits Ca^{2+} release from the sarcoplasmic reticulum. Following Ca^{2+} release into the intracellular milieu, free $[Ca^{2+}]_i$ increases only marginally, due primarily to the binding of Ca^{2+} to troponin C on the actin contractile protein. Once Ca^{2+} is bound to troponin C, the inhibiting action of tropomyosin is disengaged and the myosin-actin binding sites become exposed, permitting a transition of the sarcomere (i.e. the contractile actin and myosin component of the muscle fibre) from a weakly-bound cross-bridge state to a strongly-bound cross-bridge state. Driven by myosin ATPase, the myosin head then rotates to perform a 'power stroke' and produce skeletal muscle force, releasing inorganic phosphate (Pi) and adenosine-diphosphate (ADP) in the process. If adenosine-triphosphate (ATP) is present, this will be hydrolysed by myosin ATPase and 'reset' the cross bridge to a weakly-bound state, ready for a subsequent power stroke. For muscle relaxation to occur, two primary pre-requisites must be met including the removal of ACh from the neuromuscular junction via the enzyme acetylcholinesterase, and the re-sequestration of Ca^{2+} back into the sarcoplasmic reticulum via the ATP driven sarcoplasmic reticulum Ca^{2+} (SERCA) pumps (Stephenson et al. 1998; Westerblad et al. 2010; Allen et al. 2008; Debold 2012).

Skeletal muscle fibre types controlled by the motor units are generally classified on the basis of their myosin heavy chain isoform, which determines the magnitude of force generation and the speed of muscle fibre shortening (Allen et al. 2008; Harridge et al. 1996; Bottinelli et al. 1996). In human muscle, three major fibre types have been identified and classified as either slow oxidative (type I), fast oxidative glycolytic (type IIa) or fast glycolytic (type IIx) (Fitts 1994; Allen et al. 2008; Schiaffino and Reggiani 2011). Although a fourth fibre type has been identified in rodent muscle (type IIb), this isoform is not expressed in humans (Smerdu et al. 1994). Notable physiological properties which can differentiate the fibre types include sarcoplasmic reticulum Ca^{2+} pump content, myofibrillar ATPase content and mitochondrial density. When progressing from type I to IIa to IIx muscle fibres, sarcoplasmic reticulum Ca^{2+} pump and myofibrillar ATPase content increases, whereas mitochondrial density decreases (Fitts 1994; Buchthal and Schmalbruch 1980; Bottinelli and Reggiani 2000; Harridge et al. 1996; Larsson and Moss 1993; Schieppati 1987). The consequence of these physiological differences is a difference in force-generating capacity and fatigability. For example, fast

type IIx muscle fibres consume ATP via anaerobic glycolytic pathways much faster than it can be regenerated, leading to rapid accumulation of force inhibiting metabolic by-products (e.g. K+, Pi, Mg^{2+}) and rapid reductions in force capacity (Allen et al. 2008). Additionally, the higher density of Na^{+} channels and higher sarcoplasmic reticulum content in fast twitch muscle fibres compared to slow twitch fibres (Schiaffino and Reggiani 2011), deems them more likely to be affected by neuromuscular transmission failure and Pi induced faults in Ca^{2+} release (Stephenson et al. 1998). The speed of shortening decreases from type I to IIa to IIx, whereas no clear differences in the magnitude of the peak force normalized to cross sectional area has been reported (Bottinelli and Reggiani 2000). Thus, the amount of power generated by the muscles fibres increases when progressing from type I to IIa to IIx (Bottinelli et al. 1996) (**Figure 2.7**). Moreover, the resistance to fatigue decreases from type I to IIa to IIx muscle fibres, meaning that greater reductions in force and slowing in shortening velocity are reported for type IIx fibres for the same stimulation frequency (Allen et al. 2008). Of the four primary knee extensor muscles, a similar percentage of type I and II muscle fibres has been reported for VM (52/48%) and VI (53/47%), whereas more type II fibres have been shown for VL (46/54%) and RF (37/63%) (Travnik et al. 1995; Johnson et al. 1973; Edgerton et al. 1975; Pernuš and Eržen 1991; Lexell et al. 1992; Thorstensson et al. 1976; Bottinelli et al. 1996). However, considerable inter-individual variability exists and can be attributed to differences in training status (Gregor et al. 1979; Thorstensson et al. 1976), sex (Wüst et al. 2008) and age (Deschenes 2004).

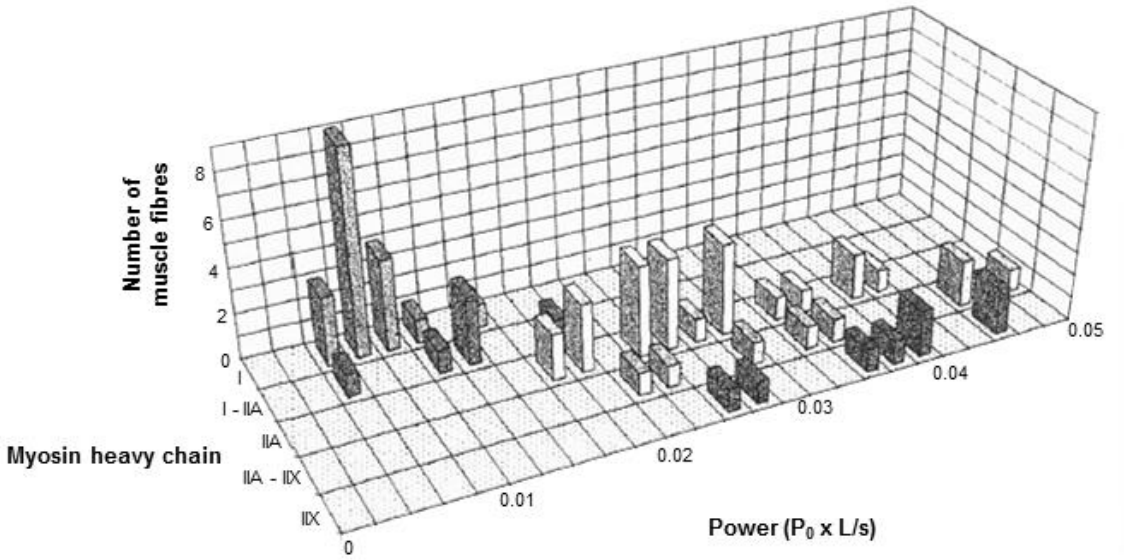

Figure 2.7 Peak power generated by different fibre types obtained from a muscle biopsy in vastus lateralis muscle of men (age = 30 ± 4 years). Power is calculated as the product of peak tetanic force (P_0) and muscle shortening velocity (change in fibre length per second, L/s). Retrieved from Harridge et al. (1996).

2.1.2.3 Length-tension relationship

A critical feature which influences the ability of skeletal muscle to generate force independent of neural control, is the parabolic relationship between muscle length and tension (Gordon et al. 1966; Cormie et al. 2011; Fitch and McComas 1985; Lindh 1978; Becker and Awiszus 2001; Lieber et al. 1994; Zajac 1989) and the hyperbolic relationship between muscle force and velocity (Cormie et al. 2011; Wilkie 1949; Seger and Thorstensson 2000; Wickiewicz et al. 1984; Thorstensson et al. 1976; Hill 1922; Zajac 1989; Hill 1938; Bobbert 2012). In single muscle fibre, the length-tension relationship describes that an optimal sarcomere length exists at which the actin and myosin filaments are able to reach their maximal potential for effective cross bridge formations, hence generating maximal levels of force. When muscle length is less than optimal, muscle force is inhibited due to an overlap between actin filaments and reduced myosin binding sites, as well as a compression of the myosin filaments during muscle contraction (Lieber and Friden 2000). When the muscle length exceeds its optimal value, the actin filaments become further apart, reducing the capacity for actin-myosin cross bridge formation (Gordon et al. 1966; Lieber et al. 1994). However, characterization of the length-tension relationship of single muscle fibres is not synonymous with that observed for whole muscle, because whole muscle is comprised of thousands of single muscle fibres and connective tissues with different architectural arrangements, forming the musculotendinous unit (MTU). The total force/tension generated by the MTU is influenced by the contractile element (synonymous with single muscle fibres and representative of the actin-myosin cross-bridge) as well as the passive structures, which includes series elastic (e.g. tendon) and parallel elastic (e.g. epimysium, perimysium, endomysium and structural proteins of the sarcomere) elements (Hill 1938) (**Figure 2.8**). The architectural properties of the muscle fibres such as fibre type distribution and pennation angle also influence the tension/force generated by the MTU (Lieber and Friden 2000).

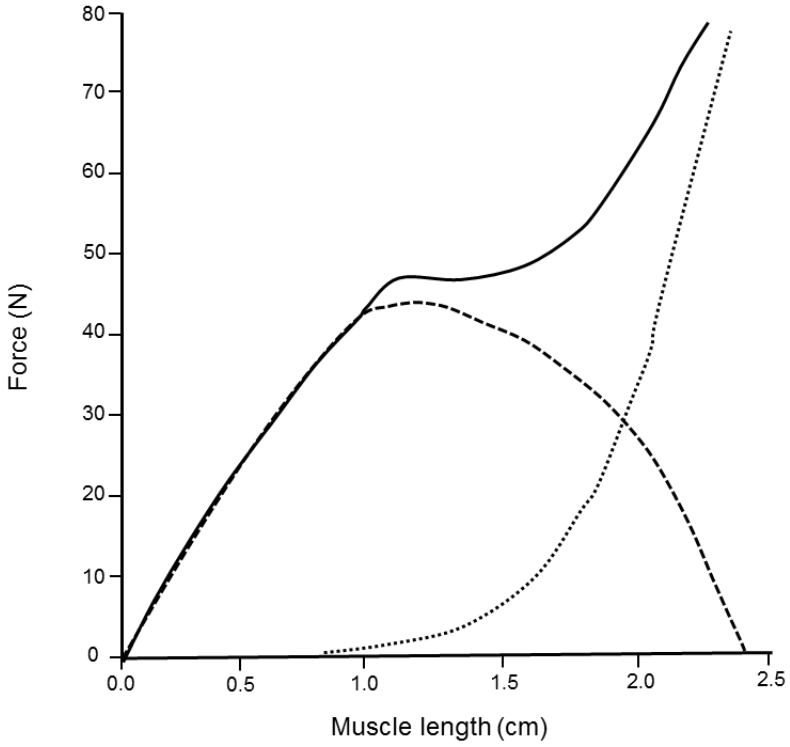

Figure 2.8 Contributions of the contractile (short dash) and series + parallel (dotted line) elements to the total force (solid line) generated by the MTU. Adapted from Enoka (2015).

For a surrogate of changes in the length of the MTU, numerous studies have re-constructed the length-tension relationship of the knee extensors by investigating the effect of changes in joint angle on maximal force capacity. Becker and Awiszus (2001) tested isometric knee extension force every 5° within knee angle ranges of 30 - 90° knee flexion (0° = full extension), and displayed a progressive increase in maximal force from 30 - 70°, after which minor, although non-significant, reductions were observed. Lindh (1978) reported similar changes in knee extensor force with changes in knee joint angle, illustrating a 3 to 4 fold increase in force between 15° and 60° knee flexion. Others have also supported these findings, suggesting that maximal knee extension force occurs at ~60 - 70° knee flexion (Thorstensson et al. 1976).

2.1.2.4 Force-velocity relationship

Fenn and Marsh (1935) and Hill (1938) first revealed in *in-vitro* that the maximal force-generating capacity of a single muscle fibre is greater during isometric contraction compared to when it is shortening (i.e. concentric contraction). During concentric muscle contractions, a reduction in force with increasing velocity has been attributed to decreased time for actin-myosin interaction and hence a reduction in the number of cross-bridges in a strongly-bound state (Huxley 1957). Another potential mechanism

associated with this relationship is decreased time for excitation-contraction coupling and Ca^{2+} activated force (Cormie et al. 2011; Neptune and Kautz 2001; Zajac 1989). As muscular power is a function of both force and shortening velocity, these relationships may also be used to construct power-velocity relationships, with maximal power occurring at ~one-third maximal velocity (Wilkie 1949; Hill 1938) (**Figure 2.9**).

Specific to the knee extensors, previous studies have indicated that the hyperbolic relationship that is commonly reported for single muscle may overestimate maximal force at low velocities (Perrine and Edgerton 1977; Wickiewicz et al. 1984) (**Figure 2.9**). These studies showed that when controlling for the duration of isometric and concentric contractions, and hence the time for muscle activation and cross bridge formation, peak knee extension force occurs at a velocity of ~60 - 90°.s^{-1} (Perrine and Edgerton 1977; Wickiewicz et al. 1984). It is important to note that considerable inter-individual variability in force-velocity relationships is common, likely due to variations in muscle fibre type composition (Gregor et al. 1979; Thorstensson et al. 1976). Indeed, differences in training status of subjects are evident between studies revealing conflicting results (Thorstensson et al. 1976; Perrine and Edgerton 1977; Wickiewicz et al. 1984).

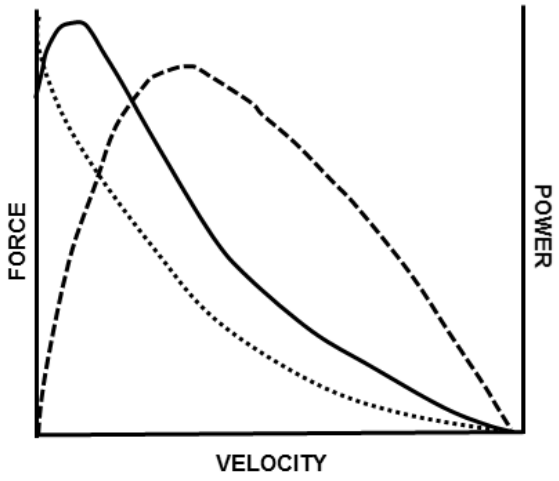

Figure 2.9 Typical force-velocity (dotted line) and power-velocity (short dash) relationship of muscle. Solid line represents the force-velocity relationship of the knee extensor muscles reported by Perrine and Edgerton (1977) and Wickiewicz et al. (1984).

2.1.3 Maximal knee extensor forces in different populations

The maximum force-generating capacity of the knee extensors is influenced by a number of factors including sex (Kanehisa et al. 1996; Clark et al. 2005; Wüst et al. 2008; Senefeld et al. 2013), training status (Narici et al. 1989; Aagaard et al. 2002; Pearson et al. 2002; Behrens et al. 2015) and age (Frontera et al. 1991; Welsh et al. 2007). Generally speaking, these studies show that men generate higher knee extensor

forces compared to women, strength training increases maximal force, and maximal force decreases with increases in age (**Table 2.1**). Individuals generating higher knee extensor forces during maximal isometric contractions generally possess a larger muscle mass (Hicks et al. 2001; Roth et al. 2002), greater knee extensor physiological cross sectional area (Kanehisa et al. 1996), higher percentage of type II muscle fibres (Wüst et al. 2008) and greater neural drive/decreased neural inhibition (Aagaard et al. 2002; Welsh et al. 2007).

Table 2.1 Normative data for maximal isometric force of the knee extensors in varying populations measured at a knee angle of 90° (0° = full extension). Data estimated from Pearson et al. (2002); Kanehisa et al. (1996); HortobÁgyi et al. (2001).

Population	Isometric Knee extensor Force (N)
Sedentary elderly women (66-85 years)	≤ 250
Sedentary men (18-30 years)	300 - 400
Physically active women (18-30 years)	300 - 400
Strength trained women (18-30 years)	450 - 550
Physically active men (18-30 years)	500 - 600
Strength trained elderly men (70-79 years)	500 - 600
Strength trained men (18-30 years)	600

2.2 Cycling Exercise

As described for the knee extensor muscles, the capacity to generate maximal force and power during multi-joint exercises such as jumping or cycling is influenced by the force-velocity and power-velocity relationships and the neural control of the lower-limb muscles (Samozino et al. 2012; Hill 1938; Hill 1950, 1922; Wilkie 1949; Van Soest and Casius 2000; Neptune and Kautz 2001). Previous simulation, biomechanical and surface electromyography (EMG) studies have provided extensive insight into how these factors influence power production and the individual contribution of the different lower-limb muscles to the total amount of work performed on the cranks (Dorel et al. 2012; Elmer et al. 2011; Zajac et al. 2002; Raasch et al. 1997; Hug and Dorel 2009; Hug et al. 2010; Van Ingen Schenau 1989). Moreover, power production during such complex tasks may be influenced by movement control factors, such as inter-muscular coordination and variability in crank force and EMG activation patterns (Latash 2012; Bernstein 1967).

2.2.1 Force-velocity and power-velocity relationships

Force-velocity and power-velocity relationships have been well established and consistently reproduced during cycling exercises, providing considerable insight into the mechanical properties of the lower-limb muscles and the capacity of individuals to generate lower-limb force and power (**Table 2.2**). These studies have suggested a linear inverse torque-velocity relationship, and a parabolic symmetrical power-velocity relationship. However, recent evidence suggests that the force-velocity relationship is quasi-linear, and that the ascending and descending limbs of the power-velocity relationship are not symmetrical (Bobbert 2012; Yeo et al. 2016). Therefore, the force-velocity relationship may be better defined via a 2^{nd} order polynomial, to account for force limiting factors such as neural inhibitions at low velocity (Westing et al. 1991; Babault et al. 2002; Perrine and Edgerton 1977), and activation-deactivation dynamics at high velocities (Van Soest and Casius 2000; Neptune and Kautz 2001). Modelling torque-cadence relationships in this way would permit a more accurate estimate of the maximal levels of torque and power that an individual can produce at a given cadence (between 0 and maximal cadence) (Yeo et al. 2016). In accordance with the relationship between power-velocity, every single cadence value has a corresponding maximal power value (Gardner et al. 2009; Dorel et al. 2010; Wilkie 1949; Sargeant et al. 1984). Therefore, to accurately assess changes in power output during cycling exercise, it is crucial that changes in cadence are accounted for. During maximal cycling exercise, the simplest

way this can be achieved is by employing an isokinetic protocol (Martin and Brown 2009; O'Bryan et al. 2014; Williams et al. 2006). Alternatively, isoinertial protocols may also be employed (Gardner et al. 2009; Yeo et al. 2016; Dorel et al. 2005). When the effect of changes in velocity are not accounted for during 30-s of prolonged maximal cycling exercise, lower-limb power reductions may be overestimated by ~15% (Gardner et al. 2009). Thus, quantification of fatigue during maximal cycling exercises not completed in isokinetic conditions require a reference to the power vs. cadence relationship.

Table 2.2 Mechanical properties of the lower-limbs measured during maximal cycling force-velocity tests for different populations. Note: tests were conducted on isoinertial cycle ergometers at different braking resistances.P_{MAX} = estimated maximal power output; T_0 = estimated maximal torque; C_0 = estimated maximal cadence; C_{opt} = estimated optimal cadence; N/A = not available.

Author (year)	Population	P_{MAX} (W)	T_0 (N·m)	C_0 (rpm)	C_{OPT} (rpm)
Seck et al. (1995)	Healthy - males	1003 ± 219	175 ± 42	*N/A*	*N/A*
Arsac et al. (1996)	Trained marathon/volleyball - males	868 ± 132	*N/A*	*N/A*	125 ± 9
Linossier et al. (1996)	Physically active – men and women	879 ± 103	*N/A*	*N/A*	126 ± 9
Martin et al. (1997)	Physically active - males	1317 ± 231	203 ± 32	237 ± 18	122 ± 7
Hintzy et al. (1999)	Physically active - males	826 ± 118	*N/A*	*N/A*	123 ± 11
(Martin et al. 2000)	Physically active - males (8 -12 yrs.)	417 ± 24	*N/A*	*N/A*	115 ± 12
	Physically active - males (12 -20 yrs.)	1060 ± 79	*N/A*	*N/A*	124 ± 8
	Physically active/competitive cyclists - males (20 -30 yrs.)	1322 ± 38	*N/A*	*N/A*	124 ± 8
	Competitive cyclists - males (30 -40 yrs.)	1335 ± 52	*N/A*	*N/A*	124 ± 8
Dore et al. (2003)	Physically active - males	1167 ± 162	*N/A*	*N/A*	*N/A*
	Physically active - females	790 ± 146	*N/A*	*N/A*	*N/A*

Dorel et al. (2005)	Competitive cyclists - males	1600 ± 166	236 ± 19	260 ± 8	130 ± 5
Gardner et al. (2007)	Competitive cyclists – males	1791 ± 169	266 ± 20	*N/A*	128 ± 7
Dorel et al. (2010)	Physically active - males	1132 ± 97	*N/A*	236 ± 11	117 ± 5
Yeo et al. (2016)	Competitive cyclists - males	1022 ± 180	157 ± 23	220 ± 22	118 ± 10

2.2.2 Neural control and contribution of the lower-limb muscles

The lower-limb muscles are active during regions of the crank cycle where they can most effectively contribute to the delivery of energy to the crank (Van Soest and Casius 2000; Neptune and Kautz 2001). Generally speaking, in depth analysis of EMG signals using recommendations from extensive reviews (Hug and Dorel 2009; Burden 2010) show that peak muscle activation is observed for VL, VM*, gluteus maximus* (GMAX), *soleus* (SOL), *gastrocnemius* (GAS), *biceps femoris* (BF) and *semitendinosus* (ST) during the extension phase (crank angle ~0 - 180°), whereas RF and *tibialis anterior* (TA) peak activity occurs during the flexion phase (crank angle ~180 - 360°) (Dorel et al. 2012; Hug and Dorel 2009; O'Bryan et al. 2014) (**Figure 2.10**). For the mono-articular knee extensor muscles (i.e. VL and VM), the period of the cycle for which peak muscle activation occurs corresponds to the portion of the crank cycle where the muscle can shorten (Van Soest and Casius 2000).

During high-intensity submaximal cycling exercise (200 – 250 W) close to 100% of crank power is generated during the extension phase, with very little or even negative work performed on the cranks during the flexion phase (Dorel et al. 2009; Sanderson and Black 2003; Coyle et al. 1991). The knee extensors are activated to a higher relative intensity (~40% peak EMG) then the hip extensors (~21%) and the knee flexors (~20%) (Dorel et al. 2012). Consequently, the knee extensors generate a higher percentage of their maximal joint power (~29%) (Elmer et al. 2011; Ericson 1988; Ericson et al. 1986). These findings have been shown to remain consistent across a wide range of crank velocities (Ericson 1988).

During maximal cycling exercise, most of the crank power (> 1000 W or 12 $W.kg^{-1}$) is generated during the extension phase (~75%), which is consistent across a wide range of crank velocities (80 - 170 rpm) (Dorel et al. 2005). The amount of power generated during the flexion phase is much less (~15 - 20%), although a higher

contribution of flexion power is observed when transitioning from low to high power outputs (Zameziati et al. 2006; Sanderson et al. 2000; Martin and Brown 2009; Dorel et al. 2005). The knee extensors and ankle plantar flexors are activated maximally (~100 - 120% of maximal isometric voluntary contraction), the knee flexors and ankle dorsi-flexors are activated submaximally, and a lack of agreement has been reported for the hip extensors (~70 – 130%) (Dorel et al. 2012; Rouffet and Hautier 2008). The major contributors to power production during maximal cycling are the monoarticular knee extensors, which generate ~35 - 40% of the total energy delivered to the crank (Raasch et al. 1997; Elmer et al. 2011). This is predominantly due to the favourable anatomical features of these muscles and their ability to directly generate tangential crank forces (Zajac et al. 2002; Raasch et al. 1997). In fact, the large contribution of the knee extensor muscles to crank power production during the extension phase, has been illustrated by strong correlations between both maximal isometric and isokinetic knee extensor force with maximal crank power (Driss et al. 2002; Kordi et al. 2017). Although a substantial amount of joint power is also generated during hip extension and ankle plantar flexion (Elmer et al. 2011), the direct contribution of GMAX and SOL/GAS to the total amount of work performed on the cranks is much lower (~21% and ~10%, respectively) (Raasch et al. 1997). BF generates work during the transition phase from extension to flexion (~10%), whereas RF generates energy when transitioning from the flexion to extension phases (~5%) (Raasch et al. 1997). TA also performs work on the cranks through the transition from flexion to extension (~5%) by transferring some of the energy generated by RF to the crank (Raasch et al. 1997).

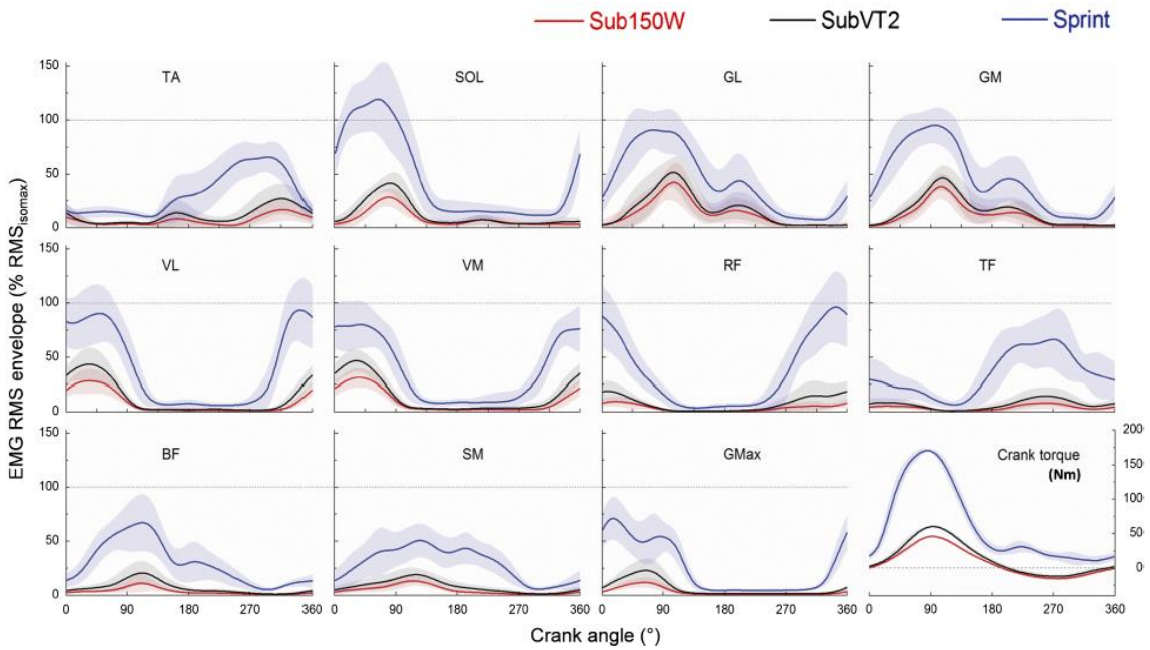

Figure 2.10 EMG and torque profiles during maximal and submaximal cycling. Blue line represents a maximal sprint, whereas red and black lines represent submaximal cycling at low and high intensities, respectively. TA = *tibialis anterior*; SOL = *soleus*; GL = *gastrocnemius lateralis*; GM = gastrocnemius medialis; VL = vastus lateralis; VM = vastus medialis; RF = *rectus femoris*; TF = *tensor fascia latae*; BF = *biceps femoris*; SM = semimembranos*us*; GMAX = *gluteus maximus*. Retrieved from Dorel et al. (2012).

2.2.2.1 Muscle synergies

To simplify the cycling movement, it has been suggested that CNS may employ a common drive to multiple muscles that are active at similar regions of the crank cycle. The overall goal of the muscle synergy is to reduce the degree of freedom and the complexity of the task (Cheung et al. 2005; Hug et al. 2011; Hug et al. 2010; Latash 2010; Raasch and Zajac 1999). During cycling exercises, as little as three muscle synergies have been proposed (Hug et al. 2010; Raasch and Zajac 1999) (**Figure 2.11**). Synergy number one includes the early to middle extension phase, and is comprised of GMAX, SOL and the three primary knee extensor muscles (VL, VM and RF). Peak activation of this synergy corresponds with the major power producing phase during extension. Synergy number two includes the second part of the extension phase and the early part of the flexion phase, and consists of the knee flexors (BF and ST) and the ankle plantar flexors (SOL and GAS). This synergy acts to propel the crank through the transition phase from extension to flexion. Synergy number three contains RF and TA, and includes the mid-flexion to early extension phase. This synergy acts to propel the crank through the transition from flexion to extension phases (Hug et al. 2010).

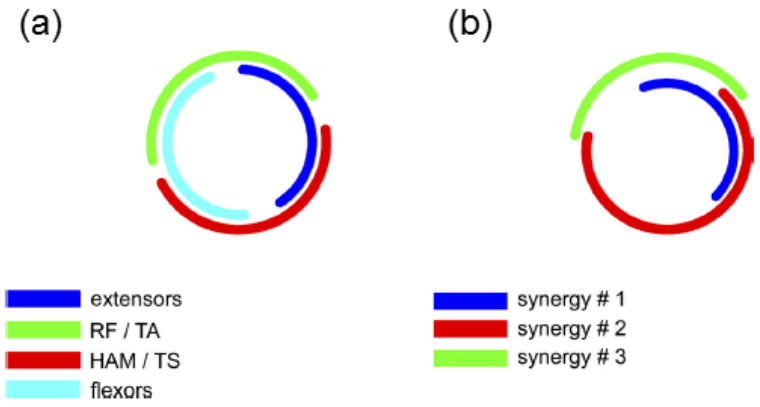

Figure 2.11 Schematic representation of the muscle synergies proposed during cycling exercise by (**a**) Raasch and Zajac (1999) and (**b**) Hug et al. (2010). RF = *rectus femoris*; TA = *tibialis anterior*; HAM = hamstrings; TS = *triceps surae*; Synergy #1 includes GMAX, SOL, VAS and RF; synergy #2 includes HAM, SOL and GAS; synergy #3 includes RF and TA.

2.2.2.2 Inter-muscular coordination

During multi-joint tasks, inter-muscular coordination represents how the CNS distributes and controls the distribution of muscular forces to optimise the application of the external forces (Prilutsky 2000). During cycling, the aim of the inter-muscular coordination strategy is to enhance the effective tangential component of the crank forces. Simulation studies have shown that this is largely achieved via the unique role of bi-articular lower-limb muscles (Van Ingen Schenau et al. 1992; Van Ingen Schenau 1989; Raasch et al. 1997; Zajac et al. 2002). For example, a biomechanical model proposed by Van Ingen Schenau (1989) describes that GMAX and *vastii* muscles generate power whilst the bi-articular antagonist RF and BF muscles orientate the power in reference to the rotation of the crank, which increases the effective tangential component of the crank forces. More specifically and in reference to **Figure 2.12 A**, activation of *vastii* muscles in isolation late during leg extension (e.g. 90-180°) would generate an ineffective/radial crank force orientated forwards. Co-activation with the antagonist BF, permits *vastii* forces to be orientated in a more backward direction, and thus, generating an effective/tangential crank force and accelerating the crank. Zajac et al. (2002) and Raasch et al. (1997) have proposed a biomechanical model of cycling which suggests that although the monoarticular GMAX and *vastii* muscles perform a large amount of work, they are limited by their ability to generate an effective/tangential crank force (**Figure 2.12B**). In fact, nearly 100% of the power generated by GMAX, and ~50% of the power generated by *vastii* muscles, is suggested to be transferred to the ankle plantar flexors (SOL and GAS), which are co-activated to stiffen the ankle joint and permit leg energy to be converted into an effective/tangential crank force. In reference to

these biomechanical models of cycling that have been derived from muscle-driven dynamics-based simulations, inter-muscular coordination has been quantified during cycling exercise by applying a co-activation index to EMG profiles of individual muscles (O'Bryan et al. 2014; Lewek et al. 2004). In this way, co-activation between agonist/antagonist pairs (e.g. *vastii*/BF and GMAX/RF) and proximal and distal muscles (e.g. *vastii* and GMAX with the ankle plantar flexors) has been shown to be greatest during the extension phase of the crank cycle, and is in accordance with synergy one and synergy two.

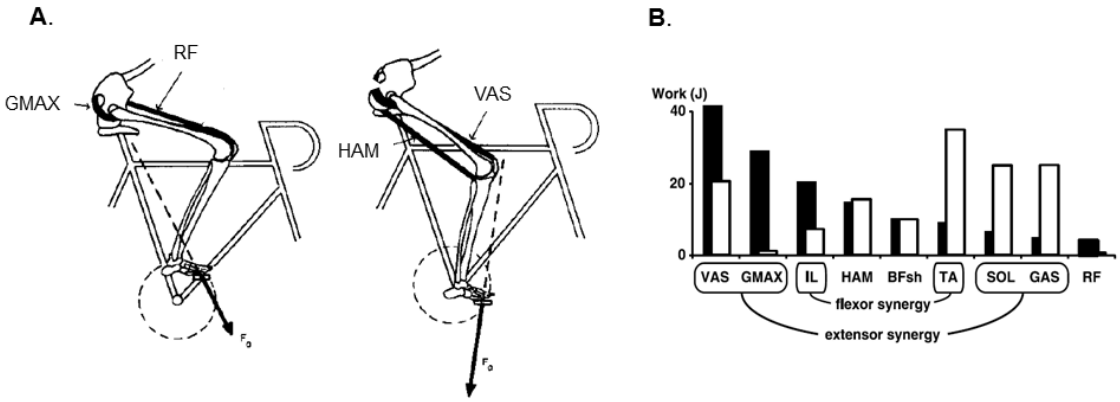

Figure 2.12 Inter-muscular coordination during cycling exercise. **A.** Model proposed by Van Ingen Schenau et al. (1992) to describe the unique role played by bi-articular muscles in effectively orientating forces generated by monoarticular muscles. **B.** Model proposed by Zajac et al. (2002) describing the work done by the lower-limb muscles (black bars) and energy delivered to the crank from the muscle's contribution to the effective tangential crank force (white bars). RF = *rectus femoris*; GMAX = *gluteus maximus*; HAM = hamstrings; VAS = *vastii*; IL = *illiacus*; BFsh = *biceps femoris* short head; TA = *tibialis anterior*; SOL = *soleus*; GAS = *gastrocnemius*.

2.2.2.3 Movement variability

Movement variability was most famously illustrated by the neurophysiologist Nikolai Bernstein (1896 – 1966), who in his landmark study in the early 20th century (Bernstein 1930), illustrated that the trajectory of a skilled blacksmiths' hammer was highly variable and never identically replicated, despite achieving a consistent outcome (i.e. hitting a chisel) (**Figure 2.13**). In reference to the concept of solution space, defined by Müller and Sternad (2009) as the total combination of execution variables available to achieve the same outcome, this describes vast variability in the execution variable (i.e. trajectory of the hammer) but maintenance of the outcome variable (i.e. effectively hitting the chisel). The extent of variability is determined by the degree of freedom, which can be characterized from something as large as the number of muscles or joints involved in the task, to something as little as the number of motor units and the frequency at which they fire (Latash 2012). Rather than considering the large number of muscles and joints

available for producing a task as a 'problem of motor redundancy', Latash (2012) viewed this situation as the 'bliss of motor abundance', which provides a near infinite number of solutions to achieve the same outcome and an extensive range of solutions for the CNS to overcome task constraints (e.g. fatigue, injury).

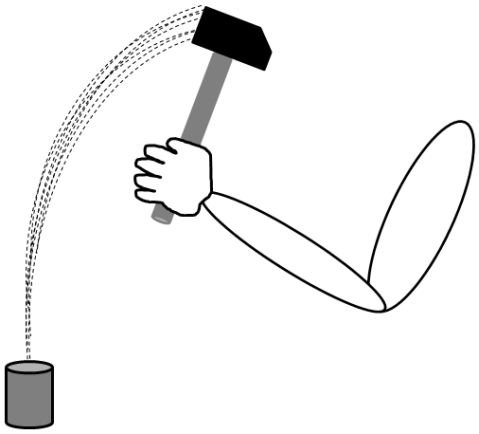

Figure 2.13 Variability in Bernsteins' hammering experiment. Adapted from Müller and Sternad (2009).

The cycling movement provides a valid model to study how the CNS can modify motor command to a large number of muscles while achieving the same task goal (i.e. maximising power output), due to the constrained nature of the interface between the shoe and the pedal. However, previous studies have shown that considerable variability in the application of crank forces and muscular activity still exists (Enders et al. 2013; Chapman et al. 2008; Rouffet and Hautier 2008; Ryan and Gregor 1992; Hug et al. 2010; Burden et al. 2003; Hug et al. 2008). This includes variability between individuals in the activation of the lower-limb muscles throughout the crank cycle (inter-individual variability), as well as variability between crank cycles within individuals (intra-individual variability). Several factors can influence inter-individual and intra-individual variability in EMG patterns, including muscle type (i.e. mono-articular versus bi-articular muscle) (Ryan and Gregor 1992; Hug et al. 2008), power output (Enders et al. 2014), cycling experience (Chapman et al. 2008), and EMG processing methods (Rouffet and Hautier 2008). Ryan and Gregor (1992) revealed that intra-individual variability appears to be highest for HAM, and lowest for GMAX, VL and VM when cycling at 250 W. Hug et al. (2008) displayed that inter-individual variability was larger for the EMG profiles of bi-articular lower-limb muscles and TA compared to the application of the crank forces when cycling at 150 W and 250 W. More recently and via the use of advanced EMG processing techniques (e.g. principle component analysis and sample entropy), Enders et al. (2014) showed that increasing the muscular demands to generate crank power

(from 150 W to 300 W) decreased intra-individual variability for the lower-limb muscles, and concluded that the solution space decreases when transitioning from 150 W to 300 W. During maximal cycling exercise, Rouffet and Hautier (2008) reported high intra-individual variability for GMAX, SOL and RF, and low intra-individual variability for GAS and VL. Overall, evidence for inter-individual and intra-individual variability in crank force and EMG profiles during cycling exercise illustrates that individuals adopt different movement strategies to generate power, and that between-cycle variations may be different between individuals and muscle groups.

The effects of fatigue on movement variability have been well studied during hopping (Bonnard et al. 1994), hammering (Côté et al. 2005), throwing (Huffenus et al. 2006; Forestier and Nougier 1998), push/pull tasks (Gates and Dingwell 2008), target tracking (Selen et al. 2007) and fine finger movements (Singh et al. 2010). Generally, these studies suggest that fatigue increases inter-individual and intra-individual variability, meaning that participants select different movement strategies with fatigue development, and that the effects of fatigue on performance outcomes are different between participants. Thus, increased variability with fatigue development is likely to provide the CNS with a range of solutions to adjust the movement control strategy.

2.3 Neuromuscular Fatigue during Knee Extension and Cycling Exercises

2.3.1 Techniques to assess neuromuscular fatigue

Assessment of neuromuscular fatigue requires a characterization of the activity of the motor units and the contractile properties of the muscle (Enoka and Duchateau 2015). This generally includes the use of multiple techniques such as EMG, maximal isometric voluntary contraction, electrical/magnetic peripheral nerve stimulation, and in some cases, transcranial magnetic stimulation (TMS). Although each one of these techniques possess their own limitations (Farina et al. 2004; Enoka and Duchateau 2015; Chipchase et al. 2012; Héroux et al. 2015; Millet et al. 2012), they can provide some good insight into the mechanisms of neuromuscular fatigue during and following exercise.

2.3.1.1 Surface electromyography

Surface electromyography (EMG) is a tool that has been used for decades to indirectly assess the integrity of the neuromuscular system. This experimental technique records the sum of the electrical contributions made by the active motor units located under the detection volume of electrodes placed over the skin. Therefore, the EMG signal is effected by physiological properties such as the neuromuscular transmission of the surface membrane action potential, and the number and/or discharge frequency of the motor unit (Farina et al. 2004; De Luca 1997). The two main parameters extracted from the EMG signal include both the amplitude and the spectral frequency, which are proposed to reflect the net activity of the motor unit and the discharge frequency, respectively (Farina et al. 2004). To estimate the amplitude of the EMG signal, the raw biphasic signal is rectified (signal is transformed from a biphasic signal into a positive and monophasic signal), filtered (filtering of 'noise' outside the physiological frequency range), smoothed (either via the root mean square algorithm (RMS) or a low pass filter) and generally normalized to a maximum reference value (achieved during a maximal voluntary contraction or a modality-specific maximal effort) (Hermens et al. 1999; Rouffet and Hautier 2008; Burden 2010). When the correct procedures are followed when preparing the skin and applying the surface electrodes (Hermens et al. 1999), an attractive feature of the amplitude of the EMG signal during non-fatiguing isometric contractions is that it can display a linear relationship with voluntary force (De Luca 1997; Farina et al. 2004; Bigland-Ritchie 1981).

In regard to fatigue, a reduction in the amplitude of the EMG signal during a maximal contraction may indicate a decrease in net motor unit activity and production of muscle force. In regards to a submaximal contraction to task failure, EMG amplitude commonly increases and is explained by an increase in motor recruitment and/or firing frequency in order to compensate for fatigue of the initially recruited motor units (Bigland-Ritchie 1981; Bigland-Ritchie et al. 1986c; Taylor and Gandevia 2008). However, due to factors such as amplitude cancellation (i.e. reduction in EMG amplitude due to cancellation of positive and negative phases of the signal), cross-talk from neighbouring muscles, and the wide range of non-physiological factors that can affect the EMG signal (e.g. thickness of subcutaneous tissue, size of the motor unit territories, shift in electrode in reference to underlying muscle), some caution is required when interpreting changes in the ratio between EMG amplitude and the force output of the muscle during fatiguing contractions (Farina et al. 2004).

The spectral characteristics of the EMG signal are proposed to reflect the conduction velocity of the muscle fibres during isometric contractions, which is commonly used to infer the changes in discharge frequency of the motor units and the type of motor unit recruited with fatigue (Farina 2008). This information is generally extracted from the raw EMG signal, via the application of the traditional Fast Fourier Transform algorithm to a specific time window, converting the time domain into a frequency domain (Reaz et al. 2006). This method is restricted to the assessment of isometric contractions, due to a number of limitations associated with dynamic contractions such as non-stationarity of the signal, relative shift of the electrodes in reference to the underlying muscle, and alterations in the conductivity properties of the tissues separating the muscle fibre and the electrodes (Farina 2006). In regards to fatigue, a reduction in the spectral frequency of the EMG signal during a fatiguing isometric contraction has been used to suggest a reduction in the conduction velocity of the fast twitch muscle fibres and/or a de-recruitment of their associated fast twitch motor units despite (Farina 2008; Farina et al. 2004; Dimitrova and Dimitrov 2003; Merletti et al. 1990).

2.3.1.2 Electrical and magnetic peripheral nerve stimulation

Supramaximal stimulation of the peripheral motor axon to assess neuromuscular function has been used by researchers for over sixty years (Merton 1954; Millet et al. 2011). Twitch interpolation is the most common technique utilised, which in conjunction with EMG permits considerable insight into the mechanisms contributing to reductions in maximal voluntary force and performance (Shield and Zhou 2004). This includes both

central fatigue, defined as a progressive exercise-induced reduction in voluntary activation of skeletal muscle (Gandevia et al. 1995), and peripheral fatigue, defined as a reduction in maximal contractile force capacity from mechanisms arising at or distal to the neuromuscular junction (Allen et al. 2008; Boyas and Guével 2011; Place et al. 2010) (**Figure 2.14**).

The twitch interpolation technique is to superimpose a supramaximal twitch (SIT) to the peripheral motor axon during a maximal isometric voluntary contraction, which is immediately followed by a supramaximal twitch applied to the potentiated muscle at rest (RT). Supramaximal stimulation (generally 120 - 150% of optimal stimulus intensity) ensures full spatial recruitment of the muscle fibres, albeit in a disorderly fashion (Millet et al. 2012; Rodriguez-Falces and Place 2013). The mode of supramaximal stimulus adopted for the twitch interpolation technique is traditionally a single (1 Hz) electrical pulse, which has been shown to provide reliable measures of the derived peripheral and central fatigue variables (Allen et al. 1995; Behm et al. 1996). However, an alternative method which essentially swaps electrical stimulation for magnetic stimulation has been proposed (Polkey et al. 1996), which can elicit similar force responses in the knee extensor muscles as electrical stimulation (Verges et al. 2009), and have the added benefit of reportedly being more tolerable (Taylor 2007). The major limitation of magnetic stimulation, however, is the uncertainty on whether supramaximal stimulus intensity can be reached (Millet et al. 2012). More recently, the use of high and/or low frequency paired pulses (100 Hz and 10 Hz) has been recommended as the preferred mode of stimulation (Place et al. 2007; Millet et al. 2011), as some researchers have shown that paired pulses induce a greater twitch force response than single pulses (Verges et al. 2009) and more information regarding peripheral fatigue mechanisms can be obtained.

The purpose of the SIT during maximal voluntary contraction, is to artificially generate additional action potentials to the peripheral motor axons. If the motor units are not recruited voluntarily or firing fast enough to drive the muscle fibres to generate maximal force during the voluntary contraction, the SIT will produce an increment in force (Taylor et al. 2006). The primary central fatigue variable extracted from twitch interpolation is voluntary activation (VA), which is calculated by applying the voluntary activation formula to the superimposed and resting twitch force responses (Taylor et al. 2009; Hales and Gandevia 1988) (***Eq. 2.1***). A decrease in motor unit recruitment/firing frequency will increase the size of the SIT and indicate central fatigue development (Taylor et al. 2009). A reduction in VA and the onset of central fatigue may arise from numerous mechanisms including a reduction in descending drive from supraspinal

regions (Gandevia et al. 1999; Porter and Lemon 1993), increased extracellular serotonin in supraspinal and spinal regions (Cotel et al. 2013; Meeusen et al. 2006; D'Amico et al. 2017), decreased facilitation/increased inhibition from peripheral sensory afferents (particularly group III and IV) (Taylor et al. 2000; Edin and Vallbo 1990; Lloyd and Chang 1948; Katz and Pierrot-Deseilligny 1999; Windhorst and Boorman 1995; Amann et al. 2009) and altered intrinsic properties of the motoneurons (Spielmann et al. 1993; Kernell and Monster 1982). If recording EMG during the maximal voluntary contraction, it is also possible to calculate the ratio between the processed EMG signal (e.g. RMS) prior to the SIT, with the peak-to-peak amplitude of the compound muscle action potential recorded in the raw EMG signal (M wave) following the SIT (EMG.M-wave^{-1}). This central fatigue measure accounts for any change in the voluntary EMG signal that may occur in response to fatigue-induced alterations in transmission of the action potential along the muscle fibre, and therefore may provide an indirect measure of the output from the motoneuron pool (Millet et al. 2003; Baudry et al. 2007).

$$VA = 1 - \left(\frac{SIT}{RT} \times 100\right)$$

Eq. 2.1

A confounding issue with the RT is that it can be affected by both fatigue and muscle potentiation (Millet et al. 2011). For example, muscle potentiation increases the sensitivity of the myofilaments to Ca^{2+} and hence can increase the RT, even in the presence of fatigue (Rassier and Macintosh 2000). Therefore, peripheral fatigue variables are generally obtained from the RT elicited immediately following maximal voluntary contraction, to induce muscle potentiation and provide a more sensitive measure of peripheral muscle fatigue (Kufel et al. 2002). As peripheral muscle fatigue manifests as a reduction in maximal force, reduced shortening velocity and slowed relaxation (Westerblad et al. 2010; Jones et al. 2006), this can be related to changes in peak twitch force, time to peak twitch force/maximal rate of force development, and time taken for the peak twitch to reduce by half/maximal relaxation rate, respectively. A fatigue-induced reduction in peak twitch force may occur as a result of impairments in excitation-contraction coupling (Place et al. 2007), whereas a reduction in time to peak twitch force and time for peak twitch force to reduce by half, may suggest faults in Ca^{2+} release and Ca^{2+} re-uptake, respectively (Buckthorpe et al. 2014). The twitch force response to high and low frequency paired pulses is suggested to be a more accurate measure of peripheral fatigue than the single twitch response, as the peak twitch force response can almost double the size of the single twitch (Place et al. 2007; Verges et al.

2009). Paired pulses also provide a measure of the possible high and low frequency fatigue mechanisms contributing to the reduction in muscle force. For example, a reduction in the peak twitch force elicited from a high frequency paired pulse (80-100 Hz) may indicate an impairment in excitation-contraction coupling, particularly arising from neuromuscular transmission failure (Cheng and Rice 2005; Bigland-Ritchie et al. 1979). Alternatively, a reduction in peak twitch force elicited from a low frequency doublet (10-20 Hz) or a reduction in the high to low frequency twitch force ratio (e.g. 10:100 Hz), may indicate fatigue induced damage to the sarcomere (particularly from repeated stretch shortening maximal contractions) or an impairment in Ca^{2+} release/re-uptake from the sarcoplasmic reticulum or Ca^{2+} sensitivity of the contractile apparatus (Jones et al. 1979; Jones 1996; Millet et al. 2011; Hill et al. 2001; Bigland-Ritchie et al. 1979; Place et al. 2010). Furthermore, neuromuscular transmission failure associated with high frequency fatigue may be observed via investigating changes in the temporal features of the M wave response elicited from a single or low frequency paired pulse (peak to peak amplitude) (Millet et al. 2012). However, limitations associated with this technique including the superficial nature of the recording (and therefore not reflecting T-tubule potentials) and possible synchronization of individual muscle fibre action potentials (Dimitrova and Dimitrov 2003), means that a reduction in high frequency twitch force may not always been associated with a lower M wave amplitude.

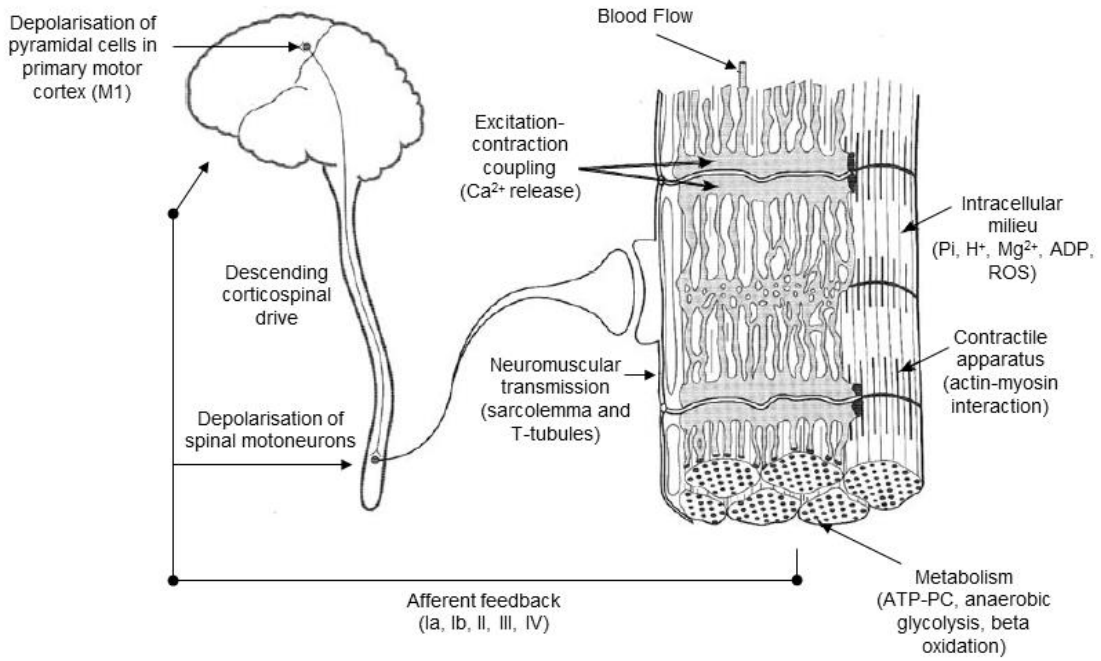

Figure 2.14 Processes involved in the development of neuromuscular fatigue. Adapted from Enoka (2015) and Bigland-Ritchie (1981).

2.3.1.3 Transcranial Magnetic Stimulation (TMS)

Originally adopted as a clinical tool in patients (Barker et al. 1985), TMS is now popular in the assessment of changes in the behaviour of the motor cortex during fatiguing exercise (Goodall et al. 2012; Taylor and Gandevia 2001). Thus, TMS has been used to investigate how alterations in descending drive from the pyramidal cells to the motoneurons contribute to central fatigue development. By placing a magnetic coil over the geographical location of the motor cortex that represents the muscle of interest (**Figure 2.4**), TMS generates a magnetic field and a perpendicular electrical current (i.e. eddy current), that penetrates the scalp and transynaptically activates pyramidal cell neurons (Terao and Ugawa 2002; Hallett 2000). During a voluntary contraction, it is possible to quantify the amplitude of the superimposed twitch force evoked via TMS, and the facilitative descending volley (motor evoked potential (MEP)) and the short latency silent period (SP) recorded in the EMG signal. If the superimposed twitch evoked via TMS during a maximal contraction increases, then the motor cortex is not able to drive the muscle fully, indicating suboptimal output from the motor cortex (Taylor et al. 2006). The latency of the MEP response provides a measure of the conduction time of the descending volley to the sarcolemma, and the peak-to-peak amplitude of the MEP response may provide a global measure of corticospinal excitability when normalized to the maximal M-wave response (i.e. the input-output properties of the pyramidal cells and motoneurons) (Goodall et al. 2012; Gandevia et al. 1996). A prolongation of the SP may indicate intracortical inhibition of the motor cortex (Taylor and Gandevia 2008; Gandevia 2001). Although TMS is an attractive tool to assess the excitability of the motor cortex, the reliability of the associated responses has been strongly challenged (Héroux et al. 2015).

2.3.1.4 Limitations associated with neuromuscular fatigue assessment

The classical method for neuromuscular fatigue assessment, is to transfer participants to a testing apparatus equipped to measure voluntary and evoked force and EMG responses within the shortest possible time delay following exercise. Following fatiguing exercises requiring a large active muscle mass such as cycling and running, the time delay varies between ~40-s to 5-min (Amann and Dempsey 2008; Fernandez del Olmo et al. 2013; Millet and Lepers 2004; Place et al. 2004; Hureau et al. 2014; Amann et al. 2013; Rossman et al. 2014). A major limitation with this approach is that substantial recovery of some central and peripheral fatigue variables is likely to occur rapidly (Jones 1996; Allen et al. 2008; Froyd et al. 2013; Cheng and Rice 2005; Senefeld

et al. 2013; Ciubotariu et al. 2007; Lindinger and Sjøgaard 1991). Adding to the limitation of a timely assessment of neuromuscular fatigue following exercises requiring a large active muscle mass, is that some studies interpret a change in voluntary EMG during exercise and a lack of change in M-wave amplitude post-exercise as a reduction in motor unit recruitment/discharge frequency and motoneuron excitability (Amann and Dempsey 2008; Amann et al. 2013; Pearcey et al. 2014; Hureau et al. 2014). However, these interpretations become troublesome when considering that postural changes and muscle activation level at the time of stimulation can influence M-wave responses (Frigon et al. 2007; Kim et al. 2005; Patikas et al. 2004), making it difficult to relate this to changes in EMG activity occurring during dynamic exercise where joint angles and activation levels are constantly changing. To overcome these limitations, it seems necessary to assess some aspects of neuromuscular fatigue during exercise and at comparable joint angles and activation levels, to permit a valid measure of the central and peripheral changes influencing exercise performance.

2.3.2 Isolated knee extension exercises

The severity and aetiology of neuromuscular fatigue developed in the knee extensors during isolated exercises varies depending on the number of repetitions (Babault et al. 2006), force level (maximal vs. submaximal) (Taylor and Gandevia 2008), contraction mode (sustained vs. intermittent) (Duchateau and Hainaut 1985), contraction type (isometric vs. concentric vs. eccentric) (Babault et al. 2006; Morel et al. 2014), work to rest ratio (Babault et al. 2006; Morel et al. 2014) and knee angle (Arendt-Nielsen et al. 1992). This section will focus on neuromuscular fatigue of the knee extensors developed during intermittent maximal concentric contractions.

Babault et al. (2006) investigated the progression of peripheral and central fatigue in the knee extensors following three sets of thirty maximal dynamic knee extensions completed at 60°.s^{-1} and work to rest ratio of 1:1. Knee extensor torque progressively declined from one series to the next, with an overall reduction of ~59% reported at the end of exercise. However, resting twitch force declined by ~33% after the first thirty contractions, after which no significant changes were observed. Conversely, voluntary activation progressively declined throughout each set, with a total reduction of ~27% observed at the end of the exercise. Thus, this study revealed that peripheral fatigue develops quickly during intermittent maximal knee extensions, with the severity of central fatigue progressively increasing with the number of repetitions. Morel et al. (2014) investigated the effects of changes in extension velocity on knee extensor fatigue

following twenty maximal concentric knee extensions at 0°.s^{-1}, 30°.s^{-1} and 240°.s^{-1}. This study revealed that reductions in knee extensor torque and high frequency twitch force were greater following concentric contractions performed at 240°.s^{-1} (~33% and ~24%) compared to 30°.s^{-1} (~16% and ~11%). However, greater reductions following 30°.s^{-1} were reported for voluntary activation (~8% vs. no change) and EMG.M-wave^{-1} (~18% vs. no change). Hence, this study revealed that increasing extension velocity exacerbates the severity of peripheral fatigue, but attenuates the development of central fatigue. Collectively, the findings from these studies indicate that the fatigue-induced reduction in maximal voluntary force of the knee extensors during isolated exercises is likely to be greatest following a high number of repetitions, and that the severity of central and peripheral fatigue is dependent on extension velocity.

Non-local and/or 'cross-over' fatigue denotes a temporary deficit in the performance of rested, contralateral, synergist or antagonist muscles following fatigue of a local muscle. Although evidenced in upper limb muscles (Kennedy et al. 2014; Martin et al. 2006), non-localized fatigue is commonly shown under conditions of knee extensor fatigue (Doix et al. 2013; Kennedy et al. 2015; Martin and Rattey 2007; Rattey et al. 2006). However, non-local fatigue arising from fatigue of the knee extensors during isolated contractions, may be dependent on intensity (submaximal vs. maximal), contraction type (isometric vs. concentric), and number of limbs (unilateral vs. bilateral) (Halperin et al. 2015). Kawamoto et al. (2014) showed a greater reduction in non-fatigued contralateral knee extensor force when the ipsilateral knee extensors held a sustained contraction to task failure at 70% MVC compared to 40% MVC (7% vs. 4%). In a series of studies (Halperin et al. 2014a; Halperin et al. 2015), dynamic and concentric bilateral knee extensor fatigue reduced elbow flexor voluntary force (5%), whereas isometric unilateral knee extensor fatigue did not affect elbow flexor force. Aboodarda et al. (2015) observed a reduction in knee extensor isometric force (8%) following isometric bilateral elbow flexor fatigue, but not following isometric unilateral elbow flexor fatigue. These studies indicate that more non-local fatigue may be observed when the fatiguing protocol is induced bilaterally via dynamic contractions at a high intensity. The mechanisms behind the observation of non-local fatigue are likely to directly or indirectly evolve from the catastrophic metabolic events arising from anaerobic metabolism (Halperin et al. 2015). Increased group III and IV afferent feedback associated with metabolic by-product accumulation can potentially decrease the output of the motoneuron pool in local and non-local muscles (Halperin et al. 2015; Sidhu et al. 2014; Takahashi et al. 2011).

Few authors have investigated the acute rate of recovery following maximal dynamic knee extensions (Cheng and Rice 2005; Senefeld et al. 2013; Michaut et al. 2003). Immediately following a series of maximal isotonic contractions to task failure (between 325°.s^{-1} and 222°.s^{-1} and defined as a reduction in extension velocity of 35%), Cheng and Rice (2005) observed that isometric maximal voluntary force of the knee extensors partially recovered within a 1.5-min post-exercise (~85% pre-exercise values). Voluntary activation was unchanged at task failure, although a delayed depressive response was observed between 1.5 and 10-min post-exercise (~8-10% reduction). The reduction in the ratio between low and high-frequency doublets was similar at 5 and 10-min post-exercise (~ 15%).

Following a high-intensity flexion and extension knee joint exercise that was claimed to mimic the high-intensity submaximal cycling, Froyd et al. (2013) revealed that knee extensor isometric maximal voluntary force and resting twitch force were lower than pre-exercise values up to 8-mins post-exercise (~65 - 70% pre-exercise values for both). However, both variables displayed a rapid rate of recovery over the first 2-min post-exercise. A limitation of this study was that central fatigue was not investigated, making it difficult to determine the rate of recovery in central fatigue variables following high-intensity exercise.

2.3.3 High-intensity submaximal cycling exercise

High-intensity cycling exercise may be classified as any power output that leads to neuromuscular fatigue development. In recreationally active males and females (age 18 – 30 years), Bergstrom et al. (2013) and Viitasalo et al. (1985) showed that the physical working capacity at fatigue threshold, defined as the power output which corresponds to the onset of neuromuscular fatigue in the VL muscle (Devries et al. 1987; Devries et al. 1990), occurs at ~190 - 225 W. Bergstrom et al. (2013) and Viitasalo et al. (1985) also showed that the anaerobic threshold, defined as the power output just below that which leads to an exponential increase in blood lactate concertation, occurs at ~212 - 225 W. Thus, when high-intensity cycling exercises are prolonged, fatigue develops and manifests as reductions in mean power during time trials or reduced time to task-failure during constant-power cycling (Amann and Dempsey 2008; Marcora et al. 2008; Decorte et al. 2012). When crank power is maintained at a constant level, EMG activity of VL and RF muscles generally increases over the course of the exercise (Amann and Dempsey 2008; Taylor et al. 1997; Decorte et al. 2012; Castronovo et al. 2012), whereas others have shown no change in joint power generated during knee extension

(Sanderson and Black 2003). Taken together, these findings indicate an increase in the EMG to force ratio, whereby EMG activity increases reflects a progressive increase unit recruitment/discharge frequency to compensate for a reduction in the force-generating capacity of the muscle fibres (Taylor and Gandevia 2008; Adam and De Luca 2005; Merletti et al. 1990; Bigland-Ritchie et al. 1986a). Following the exercises, fatigue of the knee extensors has been evidenced via reductions in maximal voluntary force of up to 20%. A considerable peripheral impairment has been shown via a reduction in potentiated resting twitch force of 20 - 40% between 2.5 min – 5 min post-exercise (Amann and Dempsey 2008; Decorte et al. 2012; Thomas et al. 2014; Marcora et al. 2008; Taylor et al. 1997). A central impairment has been shown at a similar time delay via a ~10% reduction in voluntary activation in some studies (Thomas et al. 2014; Decorte et al. 2012), but not all (Amann and Dempsey 2008). Knee extensor fatigue during high-intensity submaximal cycling exercise is generally characterized by peripheral impairment that develops early, with central contributions increasing as the duration of the exercise increases.

Numerous studies have investigated changes in inter-muscular coordination during high-intensity submaximal cycling exercises, via changes in lower-limb EMG (Dorel et al. 2009; Diefenthaeler et al. 2012) and joint power (e.g. inverse dynamics) (Sanderson and Black 2003; Bini and Diefenthaeler 2010; Bini et al. 2010). EMG studies have revealed an increase in EMG amplitude for GMAX and BF muscles toward the end of a constant-load cycling exercise to task failure (Dorel et al. 2009). Others have revealed no change in knee extension joint power but an increase in hip extension and knee flexion joint power (Sanderson and Black 2003). Together, these findings indicate that inter-muscular coordination may be altered during high-intensity submaximal cycling exercise to compensate for fatigue in the knee extensor muscles and to maintain the required power. Although this stagey may be beneficial for limiting excessive fatigue development in the knee extensor muscles, it can potentially be associated with a decrease in the index of mechanical effectiveness (Sanderson and Black 2003; Dorel et al. 2009) and muscle efficiency (Rouffet et al. 2009).

One study has previously shown that knee extensor fatigue developed during high-intensity cycling exercise can cause non-local fatigue development in rested upper limb muscles when group III and IV afferent feedback from the lower-limb muscles is facilitated (via lumbar intrathecal fentanyl) (Sidhu et al. 2014). In this study, non-local fatigue was characterized by a reduction in MEP amplitude (Sidhu et al. 2014). Thus, it is possible that high levels of knee extensor fatigue and associated group III and IV

afferent feedback developed during high-intensity cycling exercise, may decrease descending drive to non-fatigued muscles. Such an effect on non-fatigued lower-limb muscles is likely to contribute to a reduction in mean power output or reduced time to task failure. However, whether knee extensor fatigue induces non-local fatigue development in other muscles of the lower-limb remains unknown.

2.3.4 Maximal cycling exercise

During maximal cycling, fatigue manifests as a reduction in crank power. During prolonged maximal cycling for up to 30-s, reductions in maximal power of up to 50-60% have been reported (Martin and Brown 2009; O'Bryan et al. 2014). Some studies have showed that this occurs in conjunction with a decrease in *vastii* and/or RF EMG amplitude (Greer et al. 2006; O'Bryan et al. 2014), whereas others have shown no change (Stewart et al. 2011; Rana 2006; Hunter et al. 2003; Chtourou et al. 2011). Martin and Brown (2009) revealed that reductions in knee extension joint power somewhat parallel the reduction in maximal crank power. Following a maximal 30-s cycling sprint, only one study has quantified the degree of central and peripheral fatigue in the knee extensor muscles (Fernandez del Olmo et al. 2013). This study showed that at 5-min post-exercise, knee extensor maximal voluntary force decreased by 16% and was associated with a 34% reduction in potentiated twitch force. The authors also revealed an approximate 30% reduction in voluntary activation assessed via TMS, concluding that large levels of both peripheral and central fatigue develop in the knee extensor muscles during a 30-s maximal cycling sprint.

A small number of studies have investigated changes in inter-muscular coordination when maximal cycling efforts are repeated (Billaut et al. 2005; Hautier et al. 2000; Racinais et al. 2007). These studies have observed changes in the EMG amplitude and/or timing of BF muscles. Some authors have suggested that a reduction in BF EMG amplitude may occur as result of a reduction in the force-generating capacity of the knee extensors, thereby reducing the requirement of the bi-articular knee flexors to co-activate and transfer knee extension joint power to the crank (Hautier et al. 2000; Racinais et al. 2007). Although Martin and Brown (2009) evidenced large reductions in knee extension joint power (~60%) during a maximal 30-s cycling effort, they also revealed large reductions in ankle plantar flexion, hip extension (45%) and knee flexion joint power (53%). Similarly, although knee extensor EMG amplitude decreases during maximal cycling, reductions in EMG amplitude for GAS (20%), GMAX (16%) and *vastii* muscles (10%) also occurs (O'Bryan et al. 2014). The reductions in joint power and EMG reported

previously, may indicate fatigue development in the associated muscles and/or a change in inter-muscular coordination. To date, the reason for the change in EMG and joint powers for lower-limb muscles and joints other than the knee extensors is speculative, as it remains logistically difficult to quantify fatigue in multiple muscles using isometric maximal voluntary contractions and electrical stimulation techniques. In support of a change in inter-muscular coordination, a ~50% decrease in co-activation between hip and knee extensor muscles with the ankle plantar flexors, and a general observation of a shift in the timing of activation for the lower-limb muscles, has previously been reported (O'Bryan et al. 2014).

2.3.5 Effect of pre-fatiguing exercise on lower-limb power production

When prolonged submaximal cycling exercises are performed at ~200 - 300 W immediately prior to a maximal cycling effort, subsequent maximal crank cycling power can be reduced by up to ~30% (Elmer et al. 2012; Beelen and Sargeant 1991; Sargeant and Dolan 1987). These reductions in maximal crank power are commonly attributed to knee extensor fatigue. However, during maximal cycling performed following a high intensity submaximal cycling exercise, Elmer et al. (2012) observed large reductions in knee flexion (~52%), ankle plantar flexion (~43%), hip extension (~28%) and knee extension (~12%) joint power. From these findings, it seems difficult to ascertain how knee extensor fatigue effects maximal crank power, as the results suggest that fatigue may evolve in other lower-limb muscles during a pre-fatiguing cycling task. In support of this and following a similar high intensity submaximal cycling exercise, Racinais and Girard (2012) observed substantial reductions in ankle plantar flexor MVF (~8%), VA (~3%) and RT (15%), whereas minor, although non-significant reductions in knee flexor maximal voluntary force have been shown (Decorte et al. 2012). On the contrary, fatigue of the knee flexors and hip extensors following high-intensity submaximal cycling exercise has been questioned (Sanderson and Black 2003; Dorel et al. 2009; Decorte et al. 2012) and many fatigue-free mechanisms have been shown to affect ankle joint power and activation level (Sanderson et al. 2006; Martin and Brown 2009). Thus, the changes in joint power reported by Elmer et al. (2012), may be related to changes in inter-muscular coordination.

To permit an accurate insight into the effect of knee extensor fatigue on crank power and movement control during submaximal and maximal cycling, numerous studies have attempted to isolated fatigue to this muscle group via repeated voluntary contractions (Bieuzen et al. 2008) or myostimulation (Hureau et al. 2014; Brochner

Nielsen et al. 2016). Bieuzen et al. (2008) induced an 18% reduction in maximal voluntary force via repeated bilateral concentric knee extensions (110° - 0° knee flexion) prior to a constant load submaximal cycling task at 400 W. During the submaximal cycling task performed following pre-fatigue of the knee extensors, reductions in knee extensor force were associated with higher levels of activation for VL and RF knee extensor muscles (both ~ 80%) and BF knee flexor muscles (~120%). From this, it was suggested that motor unit recruitment/discharge frequency increased for the fatigued knee extensors, whereby EMG increased for the non-fatigued knee flexors, to generate the required power. A limitation of this study was that the activation level of other lower-limb muscles heavily involved in generating crank power were not considered (e.g. GMAX, SOL and GAS) (Zajac et al. 2002; Hug et al. 2010; Hug and Dorel 2009). Brochner Nielsen et al. (2016) recently provided an in-depth analysis of the effect of isolated unilateral knee extensor fatigue induced via myostimulation on inter-muscular coordination during submaximal cycling at 350 W. These authors revealed that a 28% reduction in unilateral knee extensor maximal voluntary force, led to an increase in hip flexion joint power and EMG activity of the contralateral leg to maintain the required power. In that study, the majority (but not all) of subjects increased the contribution of the contralateral leg to crank power during the flexion phase, suggesting that knee extensor fatigue may induce inter-individual variability in the movement strategy to satisfy the demands to produce crank power.

At the time of this thesis only one study has provided evidence as to the extent of which an isolated reduction in the force-generating capacity of the knee extensor muscles influences maximal lower-limb power production (Hureau et al. 2014). In this study, a reduction in knee extensor voluntary force of ~15% and evoked twitch force of ~29%, was induced prior to a 10 x 10-s repeated sprint protocol (30 s recovery) via myostimulation. Despite fatigue of the knee extensor muscles, maximal crank power and VL EMG during the initial sprints was only ~5% and ~8% lower than the control condition. Moreover, greater inter-individual variability in the reduction in isometric force of the knee extensors (range -5% to -25%) compared to the reduction in power output (range of -4% to -7%), indicated that fatigue of the knee extensors influenced the capacity for individuals to generate power differently. It seems that reductions in knee extensor force-generating capacity lead to relatively smaller reductions in crank power during maximal cycling, and that fatigue of the knee extensors influences individuals differently. However, ~10-min separated the knee extensor fatigue protocol and the beginning of the maximal sprints, during which significant recovery from peripheral mechanisms of fatigue may have occurred (Jones 1996; Allen et al. 2008; Froyd et al. 2013). Moreover, EMG

activity was recorded for the *vastii* knee extensor muscles only, making it difficult to determine if alterations in inter-muscular coordination and variability of the lower-limb muscles influenced power production. Based on these limitations, the extent of which reductions in the force-generating capacity of the knee extensor muscles influences maximal crank power remains unknown.

2.4 Summary

The anatomical and physiological profile of the knee extensor muscles deem them highly favourable for generating large forces, and as such, they are the major muscle group generating crank power during high-intensity and maximal cycling exercise. When these exercises are prolonged, neuromuscular fatigue develops in the knee extensor muscles and is thought to be largely responsible for decreasing performance. This suggests that individuals with a greater capacity to resist fatigue development in their knee extensors, may have a greater capacity to maintain high levels of power during cycling exercise. However, fatigue is also likely to develop in other lower-limb muscles and induce variability in the movement control strategy, which makes it difficult to determine how knee extensor fatigue influences cycling performance. Thus, the primary aims of the studies presented in this thesis were to determine how fatigue-induced reductions in the maximal force-generating capacity of the knee extensors influences crank power production during maximal cycling exercise.

References (Chapter 2)

Aagaard, P., Simonsen, E. B., Andersen, J. L., Magnusson, P., & Dyhre-Poulsen, P. (2002). Increased rate of force development and neural drive of human skeletal muscle following resistance training. *Journal of Applied Physiology, 93*(4), 1318-1326.

Aboodarda, S. J., Copithorne, D. B., Power, K. E., Drinkwater, E., & Behm, D. G. (2015). Elbow flexor fatigue modulates central excitability of the knee extensors. *Applied Physiology, Nutrition, and Metabolism, 40*(9), 924-930.

Adam, A., & De Luca, C. J. (2005). Firing rates of motor units in human vastus lateralis muscle during fatiguing isometric contractions. *Journal of Applied Physiology, 99*(1), 268-280.

Allemeier, C. A., Fry, A. C., Johnson, P., Hikida, R. S., Hagerman, F. C., & Staron, R. S. (1994). Effects of sprint cycle training on human skeletal muscle. *Journal of Applied Physiology, 77*(5), 2385-2390.

Allen, D. G., Lamb, G. D., & Westerblad, H. (2008). Skeletal muscle fatigue: cellular mechanisms. *Physiological Reviews, 88*(1), 287-332.

Allen, G. M., Gandevia, S. C., & Mckenzie, D. K. (1995). Reliability of measurements of muscle strength and voluntary activation using twitch interpolation. *Muscle & Nerve, 18*(6), 593-600.

Amann, M., & Dempsey, J. A. (2008). Locomotor muscle fatigue modifies central motor drive in healthy humans and imposes a limitation to exercise performance. *Journal of Physiology, 586*(1), 161-173.

Amann, M., Proctor, L. T., Sebranek, J. J., Eldridge, M. W., Pegelow, D. F., & Dempsey, J. A. (2008). Somatosensory feedback from the limbs exerts inhibitory influences on central neural drive during whole body endurance exercise. *Journal of Applied Physiology, 105*(6), 1714-1724.

Amann, M., Proctor, L. T., Sebranek, J. J., Pegelow, D. F., & Dempsey, J. A. (2009). Opioid-mediated muscle afferents inhibit central motor drive and limit peripheral muscle fatigue development in humans. *Journal of Physiology, 587*(Pt 1), 271-283.

Amann, M., Venturelli, M., Ives, S. J., McDaniel, J., Layec, G., Rossman, M. J., & Richardson, R. S. (2013). Peripheral fatigue limits endurance exercise via a sensory feedback-mediated reduction in spinal motoneuronal output. *Journal of Applied Physiology, 115*(3), 355-364.

Arendt-Nielsen, L., Gantchev, N., & Sinkjær, T. (1992). The influence of muscle length on muscle fibre conduction velocity and development of muscle fatigue. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 85*(3), 166-172.

Arsac, L. M., Belli, A., & Lacour, J. R. (1996). Muscle function during brief maximal exercise: Accurate measurements on a friction loaded cycle ergometer. *European Journal of Applied Physiology and Occupational Physiology, 74*(1-2), 100-106.

Babault, N., Desbrosses, K., Fabre, M.-S., Michaut, A., & Pousson, M. (2006). Neuromuscular fatigue development during maximal concentric and isometric knee extensions. *Journal of Applied Physiology, 100*(3), 780-785.

Babault, N., Pousson, M., Michaut, A., Ballay, Y., & Hoecke, J. (2002). EMG activity and voluntary activation during knee-extensor concentric torque generation. *European Journal of Applied Physiology, 86*(6), 541-547.

Barker, A. T., Jalinous, R., & Freeston, I. L. (1985). Non-invasive magnetic stimulation of human motor cortex. *Lancet, 1*(8437), 1106-1107.

Baudry, S., Klass, M., Pasquet, B., & Duchateau, J. (2007). Age-related fatigability of the ankle dorsiflexor muscles during concentric and eccentric contractions. *European Journal of Applied Physiology, 100*(5), 515-525.

Becker, I., Baxter, G., & Woodley, S. (2010). The vastus lateralis muscle: an anatomical investigation. *Clinical Anatomy, 23*(5), 575-585.

Becker, I., Woodley, S. J., & Baxter, G. D. (2009). Gross morphology of the vastus lateralis muscle: An anatomical review. *Clinical Anatomy, 22*(4), 436-450.

Becker, R., & Awiszus, F. (2001). Physiological alterations of maximal voluntary quadriceps activation by changes of knee joint angle. *Muscle & Nerve, 24*(5), 667-672.

Beelen, A., & Sargeant, A. (1991). Effect of fatigue on maximal power output at different contraction velocities in humans. *Journal of Applied Physiology, 71*(6), 2332-2337.

Behm, D., St-Pierre, D., & Perez, D. (1996). Muscle inactivation: assessment of interpolated twitch technique. *Journal of Applied Physiology, 81*(5), 2267-2273.

Behrens, M., Mau-Moeller, A., Mueller, K., Heise, S., Gube, M., Beuster, N., . . . Bruhn, S. (2015). Plyometric training improves voluntary activation and strength during isometric, concentric and eccentric contractions. *Journal of Science and Medicine in Sport*, *19*(2), 170-176

Bennett, W. F., Doherty, N., Hallisey, M. J., & Fulkerson, J. P. (1993). Insertion orientation of terminal vastus lateralis obliquus and vastus medialis obliquus muscle fibers in human knees. *Clinical Anatomy, 6*(3), 129-134.

Bergstrom, H. C., Housh, T. J., Cochrane, K. C., Jenkins, N. D., Lewis, R. W., Traylor, D. A., . . . Cramer, J. T. (2013). An examination of neuromuscular and metabolic fatigue thresholds. *Physiological Measurement, 34*(10), 1253-1267.

Bernstein, N. (1930). A new method of mirror cyclographie and its application towards the study of labor movements during work on a workbench. *Hygiene, Safety and Pathology of labor, 5*, 3-9.

Bernstein, N. A. (1967). The co-ordination and regulation of movements.

Bieuzen, F., Hausswirth, C., Couturier, A., & Brisswalter, J. (2008). Prior muscular exercise affects cycling pattern. *International Journal of Sports Medicine, 29*(5), 401-407.

Bigland-Ritchie, B. (1981). EMG/force relations and fatigue of human voluntary contractions. *Exercise and Sport Sciences Reviews, 9*(1), 75-118.

Bigland-Ritchie, B., Cafarelli, E., & Vollestad, N. K. (1986). Fatigue of submaximal static contractions. *Acta Physiolica Scandanvia Suppl, 556*, 137-148.

Bigland-Ritchie, B., Dawson, N., Johansson, R., & Lippold, O. (1986). Reflex origin for the slowing of motoneurone firing rates in fatigue of human voluntary contractions. *The Journal of Physiology, 379*(1), 451-459.

Bigland-Ritchie, B., Furbush, F., & Woods, J. (1986). Fatigue of intermittent submaximal voluntary contractions: central and peripheral factors. *Journal of Applied Physiology, 61*(2), 421-429.

Bigland-Ritchie, B., Jones, D. A., & Woods, J. J. (1979). Excitation frequency and muscle fatigue: Electrical responses during human voluntary and stimulated contractions. *Experimental Neurology, 64*(2), 414-427.

Billaut, F., Basset, F. A., & Falgairette, G. (2005). Muscle coordination changes during intermittent cycling sprints. *Neuroscience Letters, 380*(3), 265-269.

Bini, R. R., & Diefenthaeler, F. (2010). Kinetics and kinematics analysis of incremental cycling to exhaustion. *Sports Biomechanics, 9*(4), 223-235.

Bini, R. R., Diefenthaeler, F., & Mota, C. B. (2010). Fatigue effects on the coordinative pattern during cycling: Kinetics and kinematics evaluation. *Journal of Electromyography and Kinesiology, 20*(1), 102-107.

Blain, G. M., Mangum, T. S., Sidhu, S. K., Weavil, J. C., Hureau, T. J., Jessop, J. E., . . . Amann, M. (2016). Group III/IV muscle afferents limit the intramuscular metabolic perturbation during whole body exercise in humans. *The Journal of Physiology*, 594(18), 5303-5315.

Blazevich, A. J., Gill, N. D., & Zhou, S. (2006). Intra-and intermuscular variation in human quadriceps femoris architecture assessed in vivo. *Journal of Anatomy, 209*(3), 289-310.

Bobbert, M. F. (2012). Why is the force-velocity relationship in leg press tasks quasi-linear rather than hyperbolic? *Journal of Applied Physiology, 112*(12), 1975-1983.

Bonnard, M., Sirin, A. V., Oddsson, L., & Thorstensson, A. (1994). Different strategies to compensate for the effects of fatigue revealed by neuromuscular adaptation processes in humans. *Neuroscience Letters, 166*(1), 101-105.

Bottinelli, R., Canepari, M., Pellegrino, M., & Reggiani, C. (1996). Force-velocity properties of human skeletal muscle fibres: myosin heavy chain isoform and temperature dependence. *The Journal of Physiology, 495*(2), 573-586.

Bottinelli, R., & Reggiani, C. (2000). Human skeletal muscle fibres: molecular and functional diversity. *Progress in Biophysics and Molecular Biology, 73*(2), 195-262.

Boyas, S., & Guével, A. (2011). Neuromuscular fatigue in healthy muscle: Underlying factors and adaptation mechanisms. *Annals of Physical and Rehabilitation Medicine, 54*(2), 88-108.

Brochner Nielsen, N. P., Hug, F., Guevel, A., Fohanno, V., Lardy, J., & Dorel, S. (2016). Motor adaptations to unilateral quadriceps fatigue during a bilateral pedaling task. *Scandanavian Journal of Medicine and Science in Sports*, *27*(12), 1724-1738.

Brodal, P. (2003). *The central nervous system : structure and function* (3rd ed.): New York : Oxford University Press.

Buchthal, F., & Schmalbruch, H. (1980). Motor unit of mammalian muscle. *Physiological Reviews, 60*(1), 90-142.

Buckthorpe, M., Pain, M. T., & Folland, J. P. (2014). Central fatigue contributes to the greater reductions in explosive than maximal strength with high-intensity fatigue. *Experimental Physiology, 99*(7), 964-973.

Burden, A. (2010). How should we normalize electromyograms obtained from healthy participants? What we have learned from over 25years of research. *Journal of Electromyography and Kinesiology, 20*(6), 1023-1035.

Burden, A., Trew, M., & Baltzopoulos, V. (2003). Normalisation of gait EMGs: a re-examination. *Journal of Electromyography and Kinesiology, 13*(6), 519-532.

Burke, R. (1981). Motor units: Anatomy, physiology, and functional organization. *Handbook of Physiology, Sec 1*(1), 345-422.

Butler, J. E., Taylor, J. L., & Gandevia, S. C. (2003). Responses of Human Motoneurons to Corticospinal Stimulation during Maximal Voluntary Contractions and Ischemia. *Journal of Neuroscience, 23*(32), 10224-10230.

Castronovo, A., De Marchis, C., Bibbo, D., Conforto, S., Schmid, M., & D'Alessio, T. (2012). Neuromuscular adaptations during submaximal prolonged cycling *Engineering in Medicine and Biology Society (EMBC), Annual international conference of the IEEE* (pp. 3612-3615).

Chapman, A. R., Vicenzino, B., Blanch, P., & Hodges, P. W. (2008). Patterns of leg muscle recruitment vary between novice and highly trained cyclists. *Journal of Electromyography and Kinesiology, 18*(3), 359-371.

Cheng, A. J., & Rice, C. L. (2005). Fatigue and recovery of power and isometric torque following isotonic knee extensions. *Journal of Applied Physiology, 99*(4), 1446-1452.

Cheung, V. C., d'Avella, A., Tresch, M. C., & Bizzi, E. (2005). Central and sensory contributions to the activation and organization of muscle synergies during natural motor behaviors. *The Journal of Neuroscience, 25*(27), 6419-6434.

Chipchase, L., Schabrun, S., Cohen, L., Hodges, P., Ridding, M., Rothwell, J., . . . Ziemann, U. (2012). A checklist for assessing the methodological quality of studies using transcranial magnetic stimulation to study the motor system: An international consensus study. *Clinical Neurophysiology, 123*(9), 1698-1704.

Chtourou, H., Zarrouk, N., Chaouachi, A., Dogui, M., Behm, D. G., Chamari, K., . . . Souissi, N. (2011). Diurnal variation in Wingate-test performance and associated electromyographic parameters. *Chronobiology International, 28*(8), 706-713.

Ciubotariu, A., Arendt-Nielsen, L., & Graven-Nielsen, T. (2004). The influence of muscle pain and fatigue on the activity of synergistic muscles of the leg. *European Journal of Applied Physiology, 91*(5-6), 604-614.

Ciubotariu, A., Arendt-Nielsen, L., & Graven-Nielsen, T. (2007). Localized muscle pain causes prolonged recovery after fatiguing isometric contractions. *Experimental Brain Research, 181*(1), 147-158.

Clark, B. C., Collier, S. R., Manini, T. M., & Ploutz-Snyder, L. L. (2005). Sex differences in muscle fatigability and activation patterns of the human quadriceps femoris. *European Journal of Applied Physiology, 94*(1-2), 196-206.

Cormie, P., McGuigan, M. R., & Newton, R. U. (2011). Developing maximal neuromuscular power: Part 1-biological basis of maximal power production. *Sports Medicine, 41*(1), 17-38.

Côté, J. N., Raymond, D., Mathieu, P. A., Feldman, A. G., & Levin, M. F. (2005). Differences in multi-joint kinematic patterns of repetitive hammering in healthy, fatigued and shoulder-injured individuals. *Clinical Biomechanics, 20*(6), 581-590.

Cotel, F., Exley, R., Cragg, S. J., & Perrier, J. F. (2013). Serotonin spillover onto the axon initial segment of motoneurons induces central fatigue by inhibiting action potential initiation. *Proceedings of the National Academy of Sciences of the United States of America, 110*(12), 4774-4779.

Coyle, E., Feltner, M., Kautz, S., Hamilton, M., Montain, S., Baylor, A., . . . Petrek, G. (1991). Physiological and biomechanical factors associated with elite endurance cycling performance. *Medicine & Science in Sports & Exercise, 23*(1), 93-107.

Cutts, A. (1988). The range of sarcomere lengths in the muscles of the human lower limb. *Journal of Anatomy, 160*, 79.

D'Amico, J. M., Butler, A. A., Héroux, M. E., Cotel, F., Perrier, J. F. M., Butler, J. E., . . . Taylor, J. L. (2017). Human motoneurone excitability is depressed by activation of serotonin 1A receptors with buspirone. *The Journal of Physiology, 595*(5), 1763-1773.

De Luca, C. J. (1997). The use of surface electromyography in biomechanics. *Journal of Applied Biomechanics, 13*, 135-163.

De Luca, C. J., & Contessa, P. (2012). Hierarchical control of motor units in voluntary contractions. *Journal of Neurophysiology, 107*(1), 178-195.

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

Debold, E. P. (2012). Recent insights into muscle fatigue at the cross-bridge level. *Frontiers in Physiology, 3*.

Decorte, N., Lafaix, P. A., Millet, G. Y., Wuyam, B., & Verges, S. (2012). Central and peripheral fatigue kinetics during exhaustive constant-load cycling. *Scandinavian Journal of Medicine & Science in Sports, 22*(3), 381-391.

Deschenes, M. R. (2004). Effects of aging on muscle fibre type and size. *Sports Medicine, 34*(12), 809-824.

Devries, H. A., Housh, T. J., Johnson, G. O., Evans, S. A., Tharp, G. D., Housh, D. J., & Hughes, R. A. (1990). Factors affecting the estimation of physical working capacity at the fatigue threshold. *Ergonomics, 33*(1), 25-33.

Devries, H. A., Tichy, M. W., Housh, T. J., Smyth, K. D., Tichy, A. M., & Housh, D. J. (1987). A method for estimating physical working capacity at the fatigue threshold (PWCFT). *Ergonomics, 30*(8), 1195-1204.

Diefenthaeler, F., Coyle, E. F., Bini, R. R., Carpes, F. P., & Vaz, M. A. (2012). Muscle activity and pedal force profile of triathletes during cycling to exhaustion. *Sports Biomechanics, 11*(1), 10-19.

Dimitrova, N. A., & Dimitrov, G. V. (2003). Interpretation of EMG changes with fatigue: facts, pitfalls, and fallacies. *Journal of Electromyography and Kinesiology, 13*(1), 13-36.

Doix, A.-C. M., Lefèvre, F., & Colson, S. S. (2013). Time course of the cross-over effect of fatigue on the contralateral muscle after unilateral exercise, *8*(5), e64910

Dore, E., Duche, P., Rouffet, D., Ratel, S., Bedu, M., & Van Praagh, E. (2003). Measurement error in short-term power testing in young people. *Journal of Sports Sciences, 21*(2), 135-142.

Dorel, S., Couturier, A., Lacour, J.-R., Vandewalle, H., Hautier, C., & Hug, F. (2010). Force-velocity relationship in cycling revisited: benefit of two-dimensional pedal forces analysis. *Medicine & Science in Sports & Exercise, 42*(6), 1174-1183.

Dorel, S., Drouet, J. M., Couturier, A., Champoux, Y., & Hug, F. (2009). Changes of pedaling technique and muscle coordination during an exhaustive exercise. *Medicine and Science in Sports and Exercise, 41*(6), 1277.

Dorel, S., Guilhem, G., Couturier, A., & Hug, F. (2012). Adjustment of muscle coordination during an all-out sprint cycling task. *Medicine & Science in Sports & Exercise, 44*(11), 2154-2164.

Dorel, S., Hautier, C. A., Rambaud, O., Rouffet, D., Van Praagh, E., Lacour, J. R., & Bourdin, M. (2005). Torque and power-velocity relationships in cycling: relevance to track sprint performance in world-class cyclists. *International Journal of Sports Medicine, 26*(9), 739-746.

Driss, T., Vandewalle, H., Chevalier, J.-M. L., & Monod, H. (2002). Force-velocity relationship on a cycle ergometer and knee-extensor strength indices. *Canadian journal of applied physiology, 27*(3), 250-262.

Duchateau, J., & Hainaut, K. (1985). Electrical and mechanical failures during sustained and intermittent contractions in humans. *Journal of Applied Physiology, 58*(3), 942-947.

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

Edgerton, V. R., Smith, J., & Simpson, D. (1975). Muscle fibre type populations of human leg muscles. *The Histochemical Journal, 7*(3), 259-266.

Edin, B. B., & Vallbo, A. (1990). Muscle afferent responses to isometric contractions and relaxations in humans. *Journal of Neurophysiology, 63*(6), 1307-1313.

Elmer, S. J., Barratt, P. R., Korff, T., & Martin, J. C. (2011). Joint-specific power production during submaximal and maximal cycling. *Medicine & Science in Sports & Exercise, 43*(10), 1940-1947.

Elmer, S. J., Marshall, C. S., Wehmanen, K., Amann, M., McDaniel, J., Martin, J., & Martin, J. C. (2012). Effects of locomotor muscle fatigue on joint-specific power production during cycling. *Medicine & Science in Sports & Exercise, 44*, 1504-1511.

Enders, H., Maurer, C., Baltich, J., & Nigg, B. M. (2013). Task-oriented control of muscle coordination during cycling. *Medicine & Science in Sports & Exercise, 45*(12), 2298-2305.

Enders, H., von Tscharner, V., & Nigg, B. M. (2014). Neuromuscular Strategies during Cycling at Different Muscular Demands. *Medicine & Science in Sports & Exercise, 47*(7), 1450-1459.

Enoka, R. M. (1995). Morphological features and activation patterns of motor units. *Journal of Clinical Neurophysiology, 12*(6), 538-559.

Enoka, R. M. (2015). *Neuromechanics of human movement*: Champaign, IL : Human Kinetics, Fifth edition.

Enoka, R. M., & Duchateau, J. (2015). Inappropriate interpretation of surface EMG signals and muscle fiber characteristics impedes progress on understanding the control of neuromuscular function. *Journal of Applied Physiology*, *119*(12), 1516-1518.

Ericson, M. O. (1988). Mechanical muscular power output and work during ergometer cycling at different work loads and speeds. *European Journal of Applied Physiology and Occupational Physiology, 57*(4), 382-387.

Ericson, M. O., Nisell, R., Arborelius, U. P., & Ekholm, J. (1986). Power output and work in different muscle groups during ergometer cycling. *European Journal of Applied Physiology and Occupational Physiology, 55*(3), 229-235.

Farina, D. (2006). Interpretation of the surface electromyogram in dynamic contractions. *Exercise and Sport Sciences Reviews, 34*(3), 121-127.

Farina, D. (2008). Counterpoint: spectral properties of the surface EMG do not provide information about motor unit recruitment and muscle fiber type. *Journal of Applied Physiology, 105*(5), 1673-1674.

Farina, D., Merletti, R., & Enoka, R. M. (2004). The extraction of neural strategies from the surface EMG. *Journal of Applied Physiology, 96*(4), 1486-1495.

Fenn, W., & Marsh, B. (1935). Muscular force at different speeds of shortening. *The Journal of Physiology, 85*(3), 277.

Fernandez del Olmo, M., Rodriguez, F., Marquez, G., Iglesias, X., Marina, M., Benitez, A., . . . Acero, R. (2013). Isometric knee extensor fatigue following a Wingate test: peripheral and central mechanisms. *Scandinavian Journal of Medicine & Science in Sports, 23*(1), 57-65.

Fitch, S., & McComas, A. (1985). Influence of human muscle length on fatigue. *The Journal of Physiology, 362*(1), 205-213.

Fitts, R. H. (1994). Cellular mechanisms of muscle fatigue. *Physiological Reviews, 74*(1), 49-94.

Forestier, N., & Nougier, V. (1998). The effects of muscular fatigue on the coordination of a multijoint movement in human. *Neuroscience Letters, 252*(3), 187-190.

Friederich, J. A., & Brand, R. A. (1990). Muscle fiber architecture in the human lower limb. *Journal of Biomechanics, 23*(1), 91-95.

Frigon, A., Carroll, T. J., Jones, K. E., Zehr, E. P., & Collins, D. F. (2007). Ankle position and voluntary contraction alter maximal M waves in soleus and tibialis anterior. *Muscle & Nerve, 35*(6), 756-766.

Frontera, W. R., Hughes, V. A., Lutz, K. J., & Evans, W. J. (1991). A cross-sectional study of muscle strength and mass in 45-to 78-yr-old men and women. *Journal of Applied Physiology, 71*(2), 644-650.

Froyd, C., Millet, G. Y., & Noakes, T. D. (2013). The development of peripheral fatigue and short-term recovery during self-paced high-intensity exercise. *The Journal of Physiology, 591*(5), 1339-1346.

Fukunaga, T., Kawakami, Y., Kuno, S., Funato, K., & Fukashiro, S. (1997). Muscle architecture and function in humans. *Journal of biomechanics, 30*(5), 457-463.

Gandevia, S. (1998). Neural control in human muscle fatigue: changes in muscle afferents, moto neurones and moto cortical drive. *Acta Physiologica Scandinavica, 162*(3), 275-283.

Gandevia, S. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiological Reviews, 81*(4), 1725-1789.

Gandevia, S., Petersen, N., Butler, J., & Taylor, J. (1999). Impaired response of human motoneurones to corticospinal stimulation after voluntary exercise. *The Journal of Physiology, 521*(3), 749-759.

Gandevia, S. C., Allen, G. M., Butler, J. E., & Taylor, J. L. (1996). Supraspinal factors in human muscle fatigue: Evidence for suboptimal output from the motor cortex. *Journal of Physiology, 490*(2), 529-536.

Gandevia, S. C., Allen, G. M., & McKenzie, D. K. (1995). Central Fatigue. In S. C. Gandevia, R. M. Enoka, A. J. McComas, D. G. Stuart, C. K. Thomas & P. A. Pierce (Eds.), *Fatigue: Neural and Muscular Mechanisms* (pp. 281-294). Boston, MA: Springer US.

Gardner, A. S., Martin, D., Jenkins, D., Dyer, I., Van Eiden, J., Barras, M., & Martin, J. (2009). Velocity-specific fatigue: Quantifying fatigue during variable velocity cycling. *Medicine and Science in Sports and Exercise, 41*(4), 904.

Gardner, A. S., Martin, J. C., Martin, D. T., Barras, M., & Jenkins, D. G. (2007). Maximal torque- and power-pedaling rate relationships for elite sprint cyclists in laboratory and field tests. *European Journal of Applied Physiology, 101*(3), 287-292.

Garland, S., & Kaufman, M. (1995). Role of muscle afferents in the inhibition of motoneurons during fatigue. *Advances in Experimental Medicine and Biology, 384*, 271-278.

Gates, D. H., & Dingwell, J. B. (2008). The effects of neuromuscular fatigue on task performance during repetitive goal-directed movements. *Experimental Brain Research, 187*(4), 573-585.

Gilman, S., & Newman, S. W. (1996). *Manter and Gatz's essentials of clinical neuroanatomy and neurophysiology*: FA Davis Company.

Glenn, L. L., & Samojla, B. G. (2002). A critical reexamination of the morphology, neurovasculature, and fiber architecture of knee extensor muscles in animal models and humans. *Biological Research for Nursing, 4*(2), 128-143.

Goodall, S., Howatson, G., Romer, L., & Ross, E. (2012). Transcranial magnetic stimulation in sport science: A commentary. *European Journal of Sport Science, 14*(sup1), S332-S340.

Gordon, A., Huxley, A. F., & Julian, F. (1966). The variation in isometric tension with sarcomere length in vertebrate muscle fibres. *The Journal of Physiology, 184*(1), 170-192.

Greer, F., Morales, J., & Coles, M. (2006). Wingate performance and surface EMG frequency variables are not affected by caffeine ingestion. *Journal of Applied Physiology Nutrition and Metabolism, 31*(5), 597-603.

Gregor, R. J., Edgerton, V. R., Perrine, J. J., Campion, D. S., & DeBus, C. (1979). Torque-velocity relationships and muscle fiber composition in elite female athletes. *Journal of Applied Physiology, 47*(2), 388-392.

Grob, K., Ackland, T., Kuster, M., Manestar, M., & Filgueira, L. (2016). A newly discovered muscle: The tensor of the vastus intermedius. *Clinical Anatomy, 29*(2), 256-263.

Hales, J., & Gandevia, S. (1988). Assessment of maximal voluntary contraction with twitch interpolation: an instrument to measure twitch responses. *Journal of Neuroscience Methods, 25*(2), 97-102.

Hallett, M. (2000). Transcranial magnetic stimulation and the human brain. *Nature, 406*(6792), 147-150.

Halperin, I., Aboodarda, S. J., & Behm, D. G. (2014). Knee extension fatigue attenuates repeated force production of the elbow flexors. *European Journal of Sport Science, 14*(8), 823-829.

Halperin, I., Chapman, D. W., & Behm, D. G. (2015). Non-local muscle fatigue: effects and possible mechanisms. *European Journal of Applied Physiology, 115*(10), 2031-2048.

Harridge, S., Bottinelli, R., Canepari, M., Pellegrino, M., Reggiani, C., Esbjörnsson, M., & Saltin, B. (1996). Whole-muscle and single-fibre contractile properties and myosin heavy chain isoforms in humans. *Pflügers Archiv, 432*(5), 913-920.

Hasselman, C. T., Best, T. M., Hughes, C., Martinez, S., & Garrett, W. E. (1995). An explanation for various rectus femoris strain injuries using previously undescribed muscle architecture. *The American Journal of Sports Medicine, 23*(4), 493-499.

Hautier, C. A., Arsac, L. M., Deghdegh, K., Souquet, J., Belli, A., & Lacour, J. R. (2000). Influence of fatigue on EMG/force ratio and cocontraction in cycling. *Medicine & Science in Sports & Exercise, 32*(4), 839-843.

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

Henneman, E., & Mendell, L. M. (1981). Functional organization of motoneuron pool and its inputs. *Comprehensive Physiology*.

Hermens, H. J., Freriks, B., Merletti, R., Stegeman, D., Blok, J., Rau, G., . . . Hägg, G. (1999). *European Recommendations for Surface Electromyography* (Vol. 8): Roessingh Research and Development.

Héroux, M. E., Taylor, J. L., & Gandevia, S. C. (2015). The use and abuse of transcranial magnetic stimulation to modulate corticospinal excitability in humans. *PloS One, 10*(12), e0144151.

Hicks, A. L., Kent-Braun, J., & Ditor, D. S. (2001). Sex differences in human skeletal muscle fatigue. *Exercise and Sport Sciences Reviews, 29*(3), 109-112.

Hill, A. (1938). The heat of shortening and the dynamic constants of muscle. *Proceedings of the Royal Society of London B: Biological Sciences, 126*(843), 136-195.

Hill, A. V. (1922). The maximum work and mechanical efficiency of human muscles, and their most economical speed. *The Journal of Physiology, 56*(1-2), 19-41.

Hill, A. V. (1950). The dimensions of animals and their muscular dynamics. *Science Progress, 38*(150), 209-230.

Hill, C. A., Thompson, M. W., Ruell, P. A., Thom, J. M., & White, M. J. (2001). Sarcoplasmic reticulum function and muscle contractile character following fatiguing exercise in humans. *The Journal of Physiology, 531*(Pt 3), 871-878.

Hilty, L., Lutz, K., Maurer, K., Rodenkirch, T., Spengler, C. M., Boutellier, U., . . . Amann, M. (2011). Spinal opioid receptor-sensitive muscle afferents contribute to the fatigue-induced increase in intracortical inhibition in healthy humans. *Experimental Physiology, 96*(5), 505-517.

Hintzy, F., Belli, A., Grappe, F., & Rouillon, J. D. (1999). Optimal pedalling velocity characteristics during maximal and submaximal cycling in humans. *European Journal of Applied Physiology and Occupational Physiology, 79*(5), 426-432.

HortobÁgyi, T., Devita, P., Money, J., & Barrier, J. (2001). Effects of standard and eccentric overload strength training in young women. *Medicine & Science in Sports & Exercise, 33*(7), 1206-1212.

Hubbard, J. K., Sampson, H. W., & Elledge, J. R. (1997). Prevalence and morphology of the vastus medialis oblique muscle in human cadavers. *The Anatomical Record, 249*(1), 135-142.

Huffenus, A. F., Amarantini, D., & Forestier, N. (2006). Effects of distal and proximal arm muscles fatigue on multi-joint movement organization. *Experimental Brain Research, 170*(4), 438-447.

Hug, F., & Dorel, S. (2009). Electromyographic analysis of pedaling: a review. *Journal of Electromyography and Kinesiology, 19*(2), 182-198.

Hug, F., Drouet, J. M., Champoux, Y., Couturier, A., & Dorel, S. (2008). Interindividual variability of electromyographic patterns and pedal force profiles in trained cyclists. *European Journal of Applied Physiology, 104*(4), 667-678.

Hug, F., Turpin, N. A., Couturier, A., & Dorel, S. (2011). Consistency of muscle synergies during pedaling across different mechanical constraints. *Journal of Neurophysiology, 106*(1), 91-103.

Hug, F., Turpin, N. A., Guével, A., & Dorel, S. (2010). Is interindividual variability of EMG patterns in trained cyclists related to different muscle synergies? *Journal of Applied Physiology, 108*(6), 1727-1736.

Hunter, A. M., St Clair Gibson, A., Lambert, M. I., Nobbs, L., & Noakes, T. D. (2003). Effects of supramaximal exercise on the electromyographic signal. *British Journal of Sports Medicine, 37*(4), 296-299.

Hureau, T. J., Olivier, N., Millet, G. Y., Meste, O., & Blain, G. M. (2014). Exercise performance is regulated during repeated sprints to limit the development of peripheral fatigue beyond a critical threshold. *Experimental Physiology, 99*(7), 951-963.

Huxley, A. F. (1957). Muscle structure and theories of contraction. *Progress in Biophysics and Biophysical Chemistry, 7*, 255-318.

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

Jones, D. (1996). High-and low-frequency fatigue revisited. *Acta Physiologica Scandinavica, 156*(3), 265-270.

Jones, D., Bigland-Ritchie, B., & Edwards, R. (1979). Excitation frequency and muscle fatigue: mechanical responses during voluntary and stimulated contractions. *Experimental Neurology, 64*(2), 401-413.

Jones, D. A., De Ruiter, C., & De Haan, A. (2006). Change in contractile properties of human muscle in relationship to the loss of power and slowing of relaxation seen with fatigue. *The Journal of Physiology, 576*(3), 913-922.

Kanehisa, H., Okuyama, H., Ikegawa, S., & Fukunaga, T. (1996). Sex difference in force generation capacity during repeated maximal knee extensions. *European Journal of Applied Physiology and Occupational Physiology, 73*(6), 557-562.

Kanning, K. C., Kaplan, A., & Henderson, C. E. (2010). Motor neuron diversity in development and disease. *Annual Review of Neuroscience, 33*, 409-440.

Katz, R., & Pierrot-Deseilligny, E. (1999). Recurrent inhibition in humans. *Progress in Neurobiology, 57*(3), 325-355.

Kaufman, M. P., Hayes, S. G., Adreani, C. M., & Pickar, J. G. (2002). Discharge properties of group III and IV muscle afferents. *Sensorimotor Control of Movement and Posture* (pp. 25-32): Springer. Boston, MA

Kawamoto, J.-E., Aboodarda, S. J., & Behm, D. G. (2014). Effect of differing intensities of fatiguing dynamic contractions on contralateral homologous muscle performance. *Journal of Sports Science & Medicine, 13*(4), 836.

Kennedy, D. S., Fitzpatrick, S. C., Gandevia, S. C., & Taylor, J. L. (2015). Fatigue-related firing of muscle nociceptors reduces voluntary activation of ipsilateral but not contralateral lower limb muscles. *Journal of Applied Physiology, 118*(4), 408-418.

Kennedy, D. S., McNeil, C. J., Gandevia, S. C., & Taylor, J. L. (2013). Firing of antagonist small-diameter muscle afferents reduces voluntary activation and torque of elbow flexors. *The Journal of Physiology, 591*(14), 3591-3604.

Kennedy, D. S., McNeil, C. J., Gandevia, S. C., & Taylor, J. L. (2014). Fatigue-related firing of distal muscle nociceptors reduces voluntary activation of proximal muscles of the same limb. *Journal of Applied Physiology, 116*(4), 385-394.

Kernell, D., & Monster, A. (1982). Motoneurone properties and motor fatigue. *Experimental Brain Research, 46*(2), 197-204.

Kim, B.-J., Date, E. S., Park, B. K., Choi, B. Y., & Lee, S.-H. (2005). Physiologic changes of compound muscle action potentials related to voluntary contraction and muscle length in carpal tunnel syndrome. *Journal of Electromyography and Kinesiology, 15*(3), 275-281.

Kopydlowski, N. J., Weber, A. E., & Sekiya, J. K. (2014). Functional Anatomy of the Hamstrings and Quadriceps *Hamstring and Quadriceps Injuries in Athletes* (pp. 1-14): Springer.

Kordi, M., Goodall, S., Barratt, P., Leeder, J., Rowley, N., & Howatson, G. (2017). Maximum Voluntary Isometric Torque Production for Task specific and Single-joint Muscle groups and their Relation to Peak Power Output in Sprint Cycling. *Journal of Electromyography and Kinesiology*.

Kufel, T. J., Pineda, L. A., & Mador, M. J. (2002). Comparison of potentiated and unpotentiated twitches as an index of muscle fatigue. *Muscle & Nerve, 25*(3), 438-444.

Larsson, L., & Moss, R. (1993). Maximum velocity of shortening in relation to myosin isoform composition in single fibres from human skeletal muscles. *The Journal of Physiology, 472*, 595.

Latash, M. L. (2010). Motor synergies and the equilibrium-point hypothesis. *Motor Control, 14*(3), 294.

Latash, M. L. (2012). The bliss (not the problem) of motor abundance (not redundancy). *Experimental Brain Research, 217*(1), 1-5.

Lewek, M. D., Rudolph, K. S., & Snyder-Mackler, L. (2004). Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis. *Osteoarthritis Cartilage, 12*(9), 745-751.

Lexell, J., Sjöström, M., Nordlund, A. S., & Taylor, C. C. (1992). Growth and development of human muscle: a quantitative morphological study of whole vastus lateralis from childhood to adult age. *Muscle & Nerve, 15*(3), 404-409.

Liddell, E. G. T., & Sherrington, C. S. (1925). Recruitment and some other features of reflex inhibition. *Proceedings of the Royal Society of London. Series B, Containing Papers of a Biological Character, 97*(686), 488-518.

Lieber, R. L., & Friden, J. (2000). Functional and clinical significance of skeletal muscle architecture. *Muscle & Nerve, 23*, 1647-1666.

Lieber, R. L., Loren, G. J., & Friden, J. (1994). In vivo measurement of human wrist extensor muscle sarcomere length changes. *Journal of Neurophysiology, 71*(3), 874-881.

Light, A. R., Hughen, R. W., Zhang, J., Rainier, J., Liu, Z., & Lee, J. (2008). Dorsal root ganglion neurons innervating skeletal muscle respond to physiological combinations of protons, ATP, and lactate mediated by ASIC, P2X, and TRPV1. *Journal of Neurophysiology, 100*(3), 1184-1201.

Lindh, M. (1978). Increase of muscle strength from isometric quadriceps exercises at different knee angles. *Scandinavian Journal of Rehabilitation Medicine, 11*(1), 33-36.

Lindinger, M. I., & Sjøgaard, G. (1991). Potassium regulation during exercise and recovery. *Sports Medicine, 11*(6), 382-401.

Linossier, M.-T., Dormois, D., Fouquet, R., Geyssant, A., & Denis, C. (1996). Use of the force-velocity test to determine the optimal braking force for a sprint exercise on a friction-loaded cycle ergometer. *European Journal of Applied Physiology and Occupational Physiology, 74*(5), 420-427.

Lloyd, D. P., & Chang, H. T. (1948). Afferent fibers in muscle nerves. *Journal of Neurophysiology, 11*(3), 199-207.

Maffiuletti, N. A., Aagaard, P., Blazevich, A. J., Folland, J., Tillin, N., & Duchateau, J. (2016). Rate of force development: physiological and methodological considerations. *European Journal of Applied Physiology, 116*, 1091.

Malliou, P., Ispirlidis, I., Beneka, A., Taxildaris, K., & Godolias, G. (2003). Vertical jump and knee extensors isokinetic performance in professional soccer players related to the phase of the training period. *Isokinetics & Exercise Science, 11*(3), 165-169.

Marcora, S. M., Bosio, A., & de Morree, H. M. (2008). Locomotor muscle fatigue increases cardiorespiratory responses and reduces performance during intense cycling exercise independently from metabolic stress. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 294*(3), R874-R883.

Martin, J., Farrar, R., Wagner, B., & Spirduso, W. (2000). Maximal power across the lifespan. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 55*(6), M311-M316.

Martin, J. C., & Brown, N. A. (2009). Joint-specific power production and fatigue during maximal cycling. *Journal of Biomechanics, 42*(4), 474-479.

Martin, J. C., Wagner, B. M., & Coyle, E. F. (1997). Inertial-load method determines maximal cycling power in a single exercise bout. *Medicine & Science in Sports & Exercise, 29*(11), 1505-1512.

Martin, P., & Rattey, J. (2007). Central fatigue explains sex differences in muscle fatigue and contralateral cross-over effects of maximal contractions. *Pflügers Archiv - European Journal of Physiology, 454*(6), 957-969.

Martin, P. G., Smith, J. L., Butler, J. E., Gandevia, S. C., & Taylor, J. L. (2006). Fatigue-sensitive afferents inhibit extensor but not flexor motoneurons in humans. *The Journal of Neuroscience, 26*(18), 4796-4802.

Matthews, P. (1964). Muscle spindles and their motor control. *Physiological Reviews, 44*(2), 219-288.

McCamey, K., & Hartz, C. (2014). Proximal Quadriceps Injuries in Athletes *Hamstring and Quadriceps Injuries in Athletes* (pp. 87-94): Springer. Boston, MA

Meeusen, R., Watson, P., Hasegawa, H., Roelands, B., & Piacentini, M. F. (2006). Central fatigue: The serotonin hypothesis and beyond. *Sports Medicine, 36*(10), 881-909.

Merletti, R., Knaflitz, M., & De Luca, C. J. (1990). Myoelectric manifestations of fatigue in voluntary and electrically elicited contractions. *Journal of Applied Physiology*(5), 1810-1820.

Merton, P. (1954). Voluntary strength and fatigue. *The Journal of Physiology, 123*(3), 553-564.

Michaut, A., Pousson, M., Millet, G., Belleville, J., & Van Hoecke, J. (2003). Maximal voluntary eccentric, isometric and concentric torque recovery following a concentric isokinetic exercise. *International Journal of Sports Medicine, 24*(01), 51-56.

Millet, G. Y., Bachasson, D., Temesi, J., Wuyam, B., Féasson, L., Vergès, S., & Lévy, P. (2012). Potential interests and limits of magnetic and electrical stimulation techniques to assess neuromuscular fatigue. *Neuromuscular Disorders, 22, Supplement 3*(0), S181-S186.

Millet, G. Y., & Lepers, R. (2004). Alterations of Neuromuscular Function after Prolonged Running, Cycling and Skiing Exercises. *Sports Medicine, 34*(2), 105-116.

Millet, G. Y., Martin, V., Lattier, G., & Ballay, Y. (2003). Mechanisms contributing to knee extensor strength loss after prolonged running exercise. *Journal of Applied Physiology, 94*(1), 193-198.

Millet, G. Y., Martin, V., Martin, A., & Vergès, S. (2011). Electrical stimulation for testing neuromuscular function: from sport to pathology. *European Journal of Applied Physiology, 111*(10), 2489-2500.

Morel, B., Clemencon, M., Rota, S., Millet, G. Y., Bishop, D. J., Brosseau, O., . . . Hautier, C. A. (2014). Contraction velocity influence the magnitude and etiology of neuromuscular fatigue during repeated maximal contractions. *Scandinavian Journal of Medicine & Science in Sports, 25*(5).

Müller, H., & Sternad, D. (2009). Motor learning: changes in the structure of variability in a redundant task *Progress in Motor Control* (pp. 439-456): Springer. Boston, MA.

Narici, M. V., Roi, G., Landoni, L., Minetti, A., & Cerretelli, P. (1989). Changes in force, cross-sectional area and neural activation during strength training and detraining of the human

quadriceps. *European Journal of Applied Physiology and Occupational Physiology, 59*(4), 310-319.

Neptune, R. R., & Kautz, S. A. (2001). Muscle activation and deactivation dynamics: the governing properties in fast cyclical human movement performance? *Exercise Sport Science Reviews, 29*(2), 76-80.

Nozic, M., Mitchell, J., & de Klerk, D. (1997). A comparison of the proximal and distal parts of the vastus medialis muscle. *Australian Journal of Physiotherapy, 43*(4), 277-281.

O'Brien, T. D., Reeves, N. D., Baltzopoulos, V., Jones, D. A., & Maganaris, C. N. (2010). In vivo measurements of muscle specific tension in adults and children. *Experimental Physiology, 95*(1), 202-210.

O'Bryan, S. J., Brown, N. A., Billaut, F., & Rouffet, D. M. (2014). Changes in muscle coordination and power output during sprint cycling. *Neuroscience Letters, 576*, 11-16.

Pasta, G., Nanni, G., Molini, L., & Bianchi, S. (2010). Sonography of the quadriceps muscle: Examination technique, normal anatomy, and traumatic lesions. *Journal of Ultrasound, 13*(2), 76-84.

Patikas, D. A., Kotzamanidis, C., Robertson, C., & Koceja, D. (2004). The effect of the ankle joint angle in the level of soleus Ia afferent presynaptic inhibition. *Electromyography and Clinical Neurophysiology, 44*, 503-511.

Pearcey, G. E. P., Murphy, J. R., Behm, D. G., Hay, D. C., Power, K. E., & Button, D. C. (2014). Neuromuscular fatigue of the knee extensors during repeated maximal intensity intermittent-sprints on a cycle ergometer. *Muscle & Nerve, 51*(4), 569-579.

Pearson, S. J., Young, A., Macaluso, A., Devito, G., Nimmo, M. A., Cobbold, M., & Harridge, S. D. (2002). Muscle function in elite master weightlifters. *Medicine & Science in Sports & Exercise, 34*(7), 1199-1206.

Peeler, J., Cooper, J., Porter, M., Thliveris, J., & Anderson, J. (2005). Structural parameters of the vastus medialis muscle. *Clinical Anatomy, 18*(4), 281-289.

Penfield, W., & Boldrey, E. (1937). Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain: A Journal of Neurology*.

Pernuš, F., & Eržen, I. (1991). Arrangement of fiber types within fascicles of human vastus lateralis muscle. *Muscle & Nerve, 14*(4), 304-309.

Perrine, J. J., & Edgerton, V. R. (1977). Muscle force-velocity and power-velocity relationships under isokinetic loading. *Medicine and Science in Sports, 10*(3), 159-166.

Place, N., Lepers, R., Deley, G., & Millet, G. Y. (2004). Time course of neuromuscular alterations during a prolonged running exercise. *Medicine & Science in Sports & Exercise, 36*, 1347-1356.

Place, N., Maffiuletti, N. A., Martin, A., & Lepers, R. (2007). Assessment of the reliability of central and peripheral fatigue after sustained maximal voluntary contraction of the quadriceps muscle. *Muscle & Nerve, 35*(4), 486-495.

Place, N., Yamada, T., Bruton, J. D., & Westerblad, H. (2010). Muscle fatigue: from observations in humans to underlying mechanisms studied in intact single muscle fibres. *European Journal of Applied Physiology, 110*(1), 1-15.

Polkey, M. I., Kyroussis, D., Hamnegard, C. H., Mills, G. H., Green, M., & Moxham, J. (1996). Quadriceps strength and fatigue assessed by magnetic stimulation of the femoral nerve in man. *Muscle & Nerve, 19*(5), 549-555.

Porter, R., & Lemon, R. (1993). *Corticospinal function and voluntary movement*: Clarendon Press Oxford.

Prilutsky, B. (2000). Coordination of two-and one-joint muscles: functional consequences and implications for motor control. *Motor Control, 4*(1), 1.

Primal Pictures. (2009a). from 3D Atlas: Nervous System: Lumbar Plexus (layer 3) [image]

Primal Pictures. (2009b). from 3D Atlas: Nervous System: Lumbar Plexus: Anterior compartment of the thigh [image]

Primal Pictures. (2009c) from Anatomy and Physiology: Lower Limb (layer 1 and 12) [image]

Proctor, D. N., Sinning, W. E., Walro, J., Sieck, G. C., & Lemon, P. (1995). Oxidative capacity of human muscle fiber types: effects of age and training status. *Journal of Applied Physiology, 78*(6), 2033-2038.

Raasch, C. C., & Zajac, F. E. (1999). Locomotor strategy for pedaling: muscle groups and biomechanical functions. *Journal of Neurophysiology, 82*(2), 515-525.

Raasch, C. C., Zajac, F. E., Ma, B., & Levine, W. S. (1997). Muscle coordination of maximum-speed pedaling. *Journal of Biomechanics, 30*(6), 595-602.

Racinais, S., Bishop, D., Denis, R., Lattier, G., Mendez-Villaneuva, A., & Perrey, S. (2007). Muscle deoxygenation and neural drive to the muscle during repeated sprint cycling. *Medicine & Science in Sports & Exercise, 39*(2), 268.

Racinais, S., & Girard, O. (2012). Neuromuscular failure is unlikely to explain the early exercise cessation in hot ambient conditions. *Psychophysiology, 49*(6), 853-865.

Rana, S. R. (2006). Effect of the Wingate test on mechanomyography and electromyography. *Journal of Strength and Conditioning Research, 20*(2), 292-297.

Rassier, D., & Macintosh, B. (2000). Coexistence of potentiation and fatigue in skeletal muscle. *Brazilian Journal of Medical and Biological Research, 33*(5), 499-508.

Rattey, J., Martin, P. G., Kay, D., Cannon, J., & Marino, F. E. (2006). Contralateral muscle fatigue in human quadriceps muscle: evidence for a centrally mediated fatigue response and cross-over effect. *Pflügers Archiv, 452*(2), 199-207.

Reaz, M. B. I., Hussain, M., & Mohd-Yasin, F. (2006). Techniques of EMG signal analysis: detection, processing, classification and applications. *Biological Procedures Online, 8*(1), 11-35.

Rich, C., O'Brien, G. L., & Cafarelli, E. (1998). Probabilities associated with counting average motor unit firing rates in active human muscle. *Canadian Journal of Applied Physiology, 23*(1), 87-94.

Riehle, A., & Vaadia, E. (2005). *Motor cortex in voluntary movements : a distributed system for distributed functions*: Boca Raton. CRC Press.

Rodriguez-Falces, J., & Place, N. (2013). Recruitment order of quadriceps motor units: femoral nerve vs. direct quadriceps stimulation. *European Journal of Applied Physiology, 113*(12), 3069-3077.

Rossman, M. J., Garten, R. S., Venturelli, M., Amann, M., & Richardson, R. S. (2014). The role of active muscle mass in determining the magnitude of peripheral fatigue during dynamic exercise. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology, 306*(12), R934-R940.

Roth, S. M., Ferrell, R. E., Peters, D. G., Metter, E. J., Hurley, B. F., & Rogers, M. A. (2002). Influence of age, sex, and strength training on human muscle gene expression determined by microarray. *Physiological Genomics, 10*(3), 181-190.

Rotto, D. M., & Kaufman, M. P. (1988). Effect of metabolic products of muscular contraction on discharge of group III and IV afferents. *Journal of Applied Physiology, 64*(6), 2306-2313.

Rouffet, D. M., & Hautier, C. A. (2008). EMG normalization to study muscle activation in cycling. *Journal of Electromyography and Kinesiology, 18*(5), 866-878.

Rouffet, D. M., Mornieux, G., Zameziati, K., Belli, A., & Hautier, C. A. (2009). Timing of muscle activation of the lower limbs can be modulated to maintain a constant pedaling cadence. *Journal of Electromyography and Kinesiology, 19*(6), 1100-1107.

Ryan, M. M., & Gregor, R. J. (1992). EMG profiles of lower extremity muscles during cycling at constant workload and cadence. *Journal of Electromyography and Kinesiology, 2*(2), 69-80.

Samozino, P., Rejc, E., Di Prampero, P. E., Belli, A., & Morin, J.-B. (2012). Optimal Force–Velocity Profile in Ballistic. *Medicine & Science in Sports & Exercise, 44*(2), 313-322.

Sanderson, D. J., & Black, A. (2003). The effect of prolonged cycling on pedal forces. *Journal of Sports Sciences, 21*(3), 191-199.

Sanderson, D. J., Hennig, E. M., & Black, A. H. (2000). The influence of cadence and power output on force application and in-shoe pressure distribution during cycling by competitive and recreational cyclists. *Journal of Sports Sciences, 18*(3), 173-181.

Sanderson, D. J., Martin, P. E., Honeyman, G., & Keefer, J. (2006). Gastrocnemius and soleus muscle length, velocity, and EMG responses to changes in pedalling cadence. *Journal of Electromyography and Kinesiology, 16*(6), 642-649.

Sargeant, A., & Dolan, P. (1987). Effect of prior exercise on maximal short-term power output in humans. *Journal of Applied Physiology, 63*(4), 1475-1480.

Sargeant, A. J., Dolan, P., & Young*, A. (1984). Optimal Velocity for Maximal Short-term (Anaerobic) Power Output in Cycling. *International Journal of Sports Medicine, 5*, S124.

Schiaffino, S., & Reggiani, C. (2011). Fiber types in mammalian skeletal muscles. *Physiological Reviews, 91*(4), 1447-1531.

Schieppati, M. (1987). The Hoffmann reflex: a means of assessing spinal reflex excitability and its descending control in man. *Progress in Neurobiology, 28*(4), 345-376.

Schoenen, J., & Grant, G. (2004). Spinal cord: connections. *The human nervous system, 2nd edn.* Elsevier Academic Press, Amsterdam, 233-249.

Seck, D., Vandewalle, H., Decrops, N., & Monod, H. (1995). Maximal power and torque-velocity relationship on a cycle ergometer during the acceleration phase of a single all-out exercise. *European Journal of Applied Physiology and Occupational Physiology, 70*(2), 161-168.

Seger, J., & Thorstensson, A. (2000). Electrically evoked eccentric and concentric torque-velocity relationships in human knee extensor muscles. *Acta Physiologica Scandinavica, 169*(1), 63-69.

Selen, L., Beek, P., & Van Dieën, J. (2007). Fatigue-induced changes of impedance and performance in target tracking. *Experimental Brain Research, 181*(1), 99-108.

Senefeld, J., Yoon, T., Bement, M. H., & Hunter, S. K. (2013). Fatigue and recovery from dynamic contractions in men and women differ for arm and leg muscles. *Muscle & Nerve, 48*(3), 436-439.

Shield, A., & Zhou, S. (2004). Assessing voluntary muscle activation with the twitch interpolation technique. *Sports Medicine, 34*(4), 253-267.

Sidhu, S. K., Weavil, J. C., Mangum, T. S., Jessop, J. E., Richardson, R. S., Morgan, D. E., & Amann, M. (2017). Group III/IV locomotor muscle afferents alter motor cortical and corticospinal excitability and promote central fatigue during cycling exercise. *Clinical Neurophysiology, 128*(1), 44-55.

Sidhu, S. K., Weavil, J. C., Venturelli, M., Garten, R. S., Rossman, M. J., Richardson, R. S., . . . Amann, M. (2014). Spinal μ-opioid receptor-sensitive lower limb muscle afferents determine corticospinal responsiveness and promote central fatigue in upper limb muscle. *The Journal of Physiology, 592*(22), 5011-5024.

Singh, T., Varadhan, Zatsiorsky, V. M., & Latash, M. L. (2010). Fatigue and Motor Redundancy: Adaptive Increase in Finger Force Variance in Multi-Finger Tasks. *Journal of Neurophysiology, 103*(6), 2990-3000.

Sinoway, L. I., Hill, J. M., Pickar, J. G., & Kaufman, M. P. (1993). Effects of contraction and lactic acid on the discharge of group III muscle afferents in cats. *Journal of Neurophysiology, 69*(4), 1053-1059.

Smerdu, V., Karsch-Mizrachi, I., Campione, M., Leinwand, L., & Schiaffino, S. (1994). Type IIx myosin heavy chain transcripts are expressed in type IIb fibers of human skeletal muscle. *American Journal of Physiology-Cell Physiology, 267*(6), C1723-C1728.

Smith, T., Nichols, R., Harle, D., & Donell, S. (2009). Do the vastus medialis obliquus and vastus medialis longus really exist? A systematic review. *Clinical Anatomy, 22*(2), 183-199.

Spielmann, J., Laouris, Y., Nordstrom, M., Robinson, G., Reinking, R., & Stuart, D. (1993). Adaptation of cat motoneurons to sustained and intermittent extracellular activation. *The Journal of Physiology, 464*, 75.

Standring, S. (2015). *Gray's anatomy: the anatomical basis of clinical practice*: Elsevier Health Sciences.

Stephenson, D., Lamb, G., & Stephenson, G. (1998). Events of the excitation–contraction–relaxation (E–C–R) cycle in fast-and slow-twitch mammalian muscle fibres relevant to muscle fatigue. *Acta physiologica Scandinavica, 162*(3), 229-245.

Stewart, D., Farina, D., Shen, C., & Macaluso, A. (2011). Muscle fibre conduction velocity during a 30-s Wingate anaerobic test. *Journal of Electromyography and Kinesiology, 21*(3), 418-422.

Takahashi, K., Maruyama, A., Hirakoba, K., Maeda, M., Etoh, S., Kawahira, K., & Rothwell, J. C. (2011). Fatiguing intermittent lower limb exercise influences corticospinal and corticocortical excitability in the nonexercised upper limb. *Brain Stimulation, 4*(2), 90-96.

Taylor, A., Bronks, R., Smith, P., & Humphries, B. (1997). Myoelectric evidence of peripheral muscle fatigue during exercise in severe hypoxia: some references to m. vastus lateralis myosin heavy chain composition. *European Journal of Applied Physiology and Occupational Physiology, 75*(2), 151-159.

Taylor, J., Amann, M., Duchateau, J., Meeusen, R., & Rice, C. (2016). Neural Contributions to Muscle Fatigue: From the Brain to the Muscle and Back Again. *Medicine & Science in Sports & Exercise, 48*(11), 2294-2306.

Taylor, J. L. (2007). Magnetic muscle stimulation produces fatigue without effort. *Journal of Applied Physiology, 103*(3), 733-734.

Taylor, J. L., Butler, J. E., & Gandevia, S. (2000). Changes in muscle afferents, motoneurons and motor drive during muscle fatigue. *European Journal of Applied Physiology, 83*(2-3), 106-115.

Taylor, J. L., De Haan, A., Gerrits, K. H. L., & De Ruiter, C. J. (2009). Point:Counterpoint: The interpolated twitch does/does not provide a valid measure of the voluntary activation of muscle. *Journal of Applied Physiology, 107*(1), 354-357.

Taylor, J. L., & Gandevia, S. C. (2001). Transcranial magnetic stimulation and human muscle fatigue. *Muscle & Nerve, 24*(1), 18-29.

Taylor, J. L., & Gandevia, S. C. (2008). A comparison of central aspects of fatigue in submaximal and maximal voluntary contractions. *Journal of Applied Physiology, 104*(2), 542-550.

Taylor, J. L., Todd, G., & Gandevia, S. C. (2006). Evidence for a supraspinal contribution to human muscle fatigue. *Clinical and Experimental Pharmacology and Physiology, 33*(4), 400-405.

Terao, Y., & Ugawa, Y. (2002). Basic mechanisms of TMS. *Journal of Clinical Neurophysiology, 19*(4), 322-343.

Thomas, K., Goodall, S., Stone, M., Howatson, G., Gibson, A. S., & Ansley, L. (2014). Central and Peripheral Fatigue in Male Cyclists after 4-, 20-, and 40-km Time Trials. *Medicine & Science in Sports & Exercise*.

Thorstensson, A., Grimby, G., & Karlsson, J. (1976). Force-velocity relations and fiber composition in human knee extensor muscles. *Journal of Applied Physiology, 40*(1), 12-16.

Travnik, L., Pernus, F., & Erzen, I. (1995). Histochemical and morphometric characteristics of the normal human vastus medialis longus and vastus medialis obliquus muscles. *Journal of Anatomy, 187*(Pt 2), 403.

Tsiokanos, A., Kellis, E., Jamurtas, A., & Kellis, S. (2002). The relationship between jumping performance and isokinetic strength of hip and knee extensors and ankle plantar flexors. *Isokinetics and Exercise Science, 10*(2), 107-115.

Van Ingen Schenau, G., Boots, P., De Groot, G., Snackers, R., & Van Woensel, W. (1992). The constrained control of force and position in multi-joint movements. *Neuroscience, 46*(1), 197-207.

Van Ingen Schenau, G. J. (1989). From rotation to translation: constraints on multi-joint movements and the unique action of bi-articular muscles. *Human Movement Science, 8*(4), 301-337.

Van Soest, O., & Casius, L. (2000). Which factors determine the optimal pedaling rate in sprint cycling? *Medicine & Science in Sports & Exercise, 32*(11), 1927-1934.

Verges, S., Maffiuletti, N. A., Kerherve, H., Decorte, N., Wuyam, B., & Millet, G. Y. (2009). Comparison of electrical and magnetic stimulations to assess quadriceps muscle function. *Journal of Applied Physiology, 106*(2), 701-710.

Viitasalo, J. T., Luhtanen, P., Rahkila, P., & Rusko, H. (1985). Electromyographic activity related to aerobic and anaerobic threshold in ergometer bicycling. *Acta Physiologica Scandinavica, 124*(2), 287-293.

Weinstabl, R., Scharf, W., & Firbas, W. (1989). The extensor apparatus of the knee joint and its peripheral vasti: anatomic investigation and clinical relevance. *Surgical and Radiologic Anatomy, 11*(1), 17-22.

Welsh, S. J., Dinenno, D. V., & Tracy, B. L. (2007). Variability of quadriceps femoris motor neuron discharge and muscle force in human aging. *Experimental Brain Research, 179*(2), 219-233.

Westerblad, H., Bruton, J. D., & Katz, A. (2010). Skeletal muscle: energy metabolism, fiber types, fatigue and adaptability. *Experimental Cell Research, 316*(18), 3093-3099.

Westing, S., Cresswell, A., & Thorstensson, A. (1991). Muscle activation during maximal voluntary eccentric and concentric knee extension. *European Journal of Applied Physiology and Occupational Physiology, 62*(2), 104-108.

Wheeless, C. R. (1996). *Wheeless' textbook of orthopaedics*: CR Wheeless, MD.

Wickiewicz, T. L., Roy, R. R., Powell, P. L., & Edgerton, V. R. (1983). Muscle architecture of the human lower limb. *Clinical Orthopaedics and Related Research, 179*(179), 275-283.

Wickiewicz, T. L., Roy, R. R., Powell, P. L., Perrine, J. J., & Edgerton, V. R. (1984). Muscle architecture and force-velocity relationships in humans. *Journal of Applied Physiology, 57*(2), 435-443.

Wiesinger, H.-P., Kösters, A., Müller, E., & Seynnes, O. R. (2015). Effects of increased loading on in vivo tendon properties: a systematic review. *Medicine & Science in Sports & Exercise, 47*(9), 1885.

Wilkie, D. (1949). The relation between force and velocity in human muscle. *The Journal of Physiology, 110*(3-4), 249-280.

Willan, P., Ransome, J., & Mahon, M. (2002). Variability in human quadriceps muscles: quantitative study and review of clinical literature. *Clinical Anatomy, 15*(2), 116-128.

Williams, C., Doust, J., & Hammond, A. (2006). Power output and VO 2 responses during 30 s maximal isokinetic cycle sprints at different cadences in comparison to the Wingate test. *Isokinetics and Exercise Science, 14*(4), 327-333.

Willigenburg, N. W., McNally, M. P., & Hewett, T. E. (2014). Quadriceps and hamstrings strength in athletes, (pp. 15-28): Springer. Boston, MA

Windhorst, U., & Boorman, G. (1995). Overview: potential role of segmental motor circuitry in muscle fatigue. *Advances in Experimental Medicine and Biology, 384*, 241.

Woods, J., Furbush, F., & Bigland-Ritchie, B. (1987). Evidence for a fatigue-induced reflex inhibition of motoneuron firing rates. *Journal of Neurophysiology, 58*(1), 125-137.

Wüst, R. C. I., Morse, C. I., De Haan, A., Jones, D. A., & Degens, H. (2008). Sex differences in contractile properties and fatigue resistance of human skeletal muscle. *Experimental Physiology, 93*(7), 843-850.

Yang, D., & Morris, S. F. (1999). Neurovascular anatomy of the rectus femoris muscle related to functioning muscle transfer. *Plastic Reconstruction Surgery, 104*(1), 102-106.

Yeo, B. K., Rouffet, D. M., & Bonanno, D. R. (2016). Foot orthoses do not affect crank power output during maximal exercise on a cycle-ergometer. *Journal of Science and Medicine in Sport, 19*(5), 368-372.

Zajac, F. E. (1989). Muscle and tendon Properties: models scaling and application to biomechanics and motor. *Critical Reviews in Biomedical Engineering, 17*(4), 359-411.

Zajac, F. E., Neptune, R. R., & Kautz, S. A. (2002). Biomechanics and muscle coordination of human walking. Part I: introduction to concepts, power transfer, dynamics and simulations. *Gait Posture, 16*(3), 215-232.

Zameziati, K., Mornieux, G., Rouffet, D., & Belli, A. (2006). Relationship between the increase of effectiveness indexes and the increase of muscular efficiency with cycling power. *European Journal of Applied Physiology, 96*(3), 274-281.

Zengel, J. E., Reid, S. A., Sypert, G. W., & Munson, J. B. (1985). Membrane electrical properties and prediction of motor-unit type of medial gastrocnemius motoneurons in the cat. *Journal of Neurophysiology, 53*(5), 1323-1344.

Zhang, L. Q., Wang, G., Nuber, G. W., Press, J. M., & Koh, J. L. (2003). In vivo load sharing among the quadriceps components. *Journal of Orthopaedic Research, 21*(3), 565-571.

Chapter 3 KNEE EXTENSOR FATIGUE DEVELOPED DURING HIGH-INTENSITY EXERCISE LIMITS LOWER-LIMB POWER PRODUCTION DURING MAXIMAL CYCLING

3.1 Introduction

Locomotor fatigue, defined as an exercise-induced reduction in maximal voluntary force or power of the locomotor muscles (Gandevia 2001; Marcora et al. 2008), has been shown to limit performance during cycling exercise completed at submaximal (Amann and Dempsey 2008; Marcora et al. 2008; Decorte et al. 2012) and maximal intensities (Fernandez del Olmo et al. 2013; Billaut et al. 2013). Specifically, decreased performance has been accompanied by high levels of locomotor fatigue of both central (e.g. supraspinal and spinal regions) (Taylor et al. 2016) and peripheral origins (e.g. distal to the neuromuscular junction) (Allen et al. 2008). During road cycling events, it is common that high-intensity submaximal efforts are performed prior to a maximal effort to cross the finish line as quickly as possible (Ebert et al. 2006). Previous studies have shown that performance during these maximal efforts of short duration is dependent on both the power profile of the individual (Dorel et al. 2005), as well as locomotor fatigue accumulated during the maximal effort (Gardner et al. 2009). However, locomotor fatigue developed during the prolonged high-intensity period is also likely to limit the capacity to generate maximal power during the final all-out effort.

Prolonged high-intensity cycling exercise can cause locomotor fatigue, which manifests as reductions in mean power during time trials or reduced time to task-failure during constant-load cycling (Amann and Dempsey 2008; Marcora et al. 2008; Decorte et al. 2012). During these types of exercises (power output 200 – 250 W), the knee extensors generate ~60 – 70% of the total lower-limb power (Ericson 1988; Elmer et al. 2011). When these exercises are prolonged (> 10-min), *vastii* and *rectus femoris* EMG activity generally increases (Amann and Dempsey 2008; Taylor et al. 1997; Decorte et al. 2012; Castronovo et al. 2012; Diefenthaeler et al. 2012), whilst knee extension joint power remains unchanged (Sanderson and Black 2003). Post-exercise, large reductions in knee extensor isometric maximal voluntary force (~20%) and twitch force (~25 – 45%) have also been reported (Amann and Dempsey 2008; Decorte et al. 2012; Marcora et al. 2008; Taylor et al. 1997; Thomas et al. 2014). These findings indicate considerable peripheral fatigue development in the knee extensor muscles, which indicates that the number and/or firing frequency of the motor units may be increased during high-intensity cycling to compensate for a progressive reduction in the force-generating capacity of the

initially recruited motor units (Adam and De Luca 2005; Bigland-Ritchie et al. 1986a; Merletti et al. 1990; Taylor and Gandevia 2008). However, as the lower-limb muscles are not activated maximally during high-intensity cycling (Dorel et al. 2012; Rouffet and Hautier 2008), alterations in inter-muscular coordination may increase the activation level of other muscles groups without affecting power production (Latash 2012). For example, some individuals may increase the activation level of *gluteus maximus* and *biceps femoris* muscles and the power generated during hip extension and knee flexion (Dorel et al. 2009; Sanderson and Black 2003; Diefenthaeler et al. 2012; Decorte et al. 2012) to potentially compensate for peripheral fatigue development in the knee extensors. However, alterations in inter-muscular coordination may be better observed via changes in co-activation between monoarticular and bi-articular muscles. Co-activation between these muscle pairs has been suggested to optimize the transfer of power amongst the segments and orientation of the crank forces (Van Ingen Schenau 1989; Zajac et al. 2002).

When maximal cycling is performed immediately after high-intensity submaximal cycling, maximal lower-limb power decreases by ~25% (Beelen and Sargeant 1991; Elmer et al. 2012; Sargeant and Dolan 1987). As the majority of the lower-limb muscles are activated maximally during sprint cycling (Dorel et al. 2012; Rouffet and Hautier 2008), any reductions in the force-generating capacity and/or activation level of the lower-limb muscles is likely to contribute to reductions in maximal power. As the monoarticular knee extensor muscles (e.g. *vastus lateralis* and *vastus medialis*) generate considerable power during maximal cycling exercise (Elmer et al. 2011; Zajac et al. 2002; Raasch et al. 1997), fatigue in the knee extensors is likely to impair performance during maximal cycling. As such, previous studies have reported severe reductions in knee extensor twitch force (~30%) and moderate reductions in knee extensor maximal voluntary force (~15%) following 30-s of maximal cycling exercise (Fernandez del Olmo et al. 2013). Similarly, severe reductions in knee extension joint power (~60%) (Martin and Brown 2009), and moderate reductions in *vastii* muscle EMG (~10%) (O'Bryan et al. 2014) have been shown to occur in parallel with large reductions in crank power (~60%) (O'Bryan et al. 2014; Martin and Brown 2009). However, no study has specifically determined if knee extensor fatigue resulting from high-intensity submaximal cycling exercise is associated with reductions in power output during a subsequent maximal effort.

The aims of this study were to investigate: i) the association between changes in EMG activity of the *vastii* muscles during prolonged high-intensity exercise and knee

extensor fatigue following exercise, and ii) the effect of knee extensor fatigue on power production and inter-muscular coordination during a subsequent 30-s maximal cycling effort. First, it was hypothesised that participants displaying larger increases in *vastii* EMG activity over the course of the high-intensity cycling exercise would experience larger reductions in maximal voluntary force of the knee extensors. Second, we hypothesized that knee extensor fatigue developed during prolonged high-intensity cycling would reduce lower-limb power production during the initial part of a maximal cycling effort.

3.2 Methods

3.2.1 Participants

Sample size calculations were performed using G*Power version 3.0.10 software (Faul et al. 2007) using an alpha level set at 0.05 and a probability of avoiding a type II error set at 0.8. It was assumed that completion of the high-intensity cycling exercise would lead to large changes in the measured variables (F > 0.7, % reduction in knee extensor isometric maximal voluntary force ~10 ± 12%) (Decorte et al. 2012). It was calculated that a sample of n = 7 was required, and seven male adults were recruited (age 22.4 ± 2.6 years; body mass 88.2 ± 8.4 kg; height 181.3 ± 4.1 cm). Written informed consent was provided to participate in the study. All participants were physically active, with four participants playing amateur team sports (Australian football, basketball) and three undertaking regular resistance training. The average hours spent participating in these activities was 5.6 ± 1.5 hours/week. Participants with different training backgrounds were recruited assuming that it would lead to large inter-individual variations in muscle coordination and fatigue development during high-intensity cycling exercise (Chapman et al. 2005; Smirmaul et al. 2009). Testing protocols were conducted in accordance with the standards set by the Declaration of Helsinki and were approved by Victoria University's Human Research Ethics Committee.

3.2.2 Design

Participants were tested during two main sessions and instructed to avoid any strenuous physical activity during the 24 hours preceding each test. A preliminary visit was organized to familiarize participants with the different aspects of the protocol: i) high-intensity and maximal cycling exercises, ii) knee extension maximal isometric voluntary contractions, iii) magnetic stimulation of the femoral nerve, and iv) surface EMG recordings of the lower-limb muscles. We also assessed the fatigue-free maximal power

of all participants, which was subsequently used to define their power output during high-intensity cycling. Following a standardized warm-up, the participants completed six 4-s maximal cycling efforts in isokinetic mode at 75, 80 and 85 rpm (two at each cadence), with 5-min of rest between each effort. Each participant performed their 10-min high-intensity cycling exercise at 20% of maximal power (1088 ± 224 W) measured at 80 ± 5 rpm, which corresponded to 207.2 ± 31.6 W. This level of power was selected in reference to previous studies which reported an onset of neuromuscular fatigue in the *vastus lateralis* muscle when cycling at similar power outputs (Devries et al. 1987; Devries et al. 1990).

The order of the two main testing sessions was randomized. Each session started with a standardized warm-up on the cycle ergometer, with participants producing 1 W/kg at 80 rpm for 2-min, 1.5 W/kg at 80 rpm for 2-min, one 4-s maximal effort at 120 rpm, 2 W/kg at 80 rpm for 2-min, one 4-s maximal effort at 120 rpm, and 1 W/kg at 80 rpm for 1-min. Next, participants performed two isometric maximal voluntary contractions with their knee extensors before potentiated resting twitches (RT) were elicited using magnetic stimulation of the femoral nerve at increasing intensities, to identify the stimulation intensity required to elicit a maximal twitch. Two separate baseline measurements of knee extensor isometric maximal voluntary force (IMVF) and RT were then obtained (2-min rest). Participants then either sat passively on the ergometer for 2-min (control condition) or completed a 10-min high-intensity cycling exercise (207.2 ± 31.6 W at 80 rpm). IMVF and RT were measured ~1-min after the end of the 10-min high-intensity cycling exercise. Next, participants completed a 30-s maximal cycling effort. Finally, knee extensor IMVF and RT were measured ~1-min after the end of the 30-s maximal cycling effort (**Figure 3.1**).

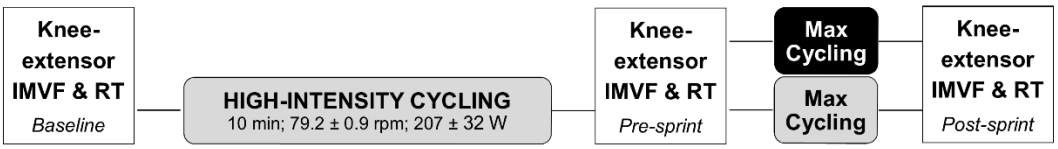

Figure 3.1 Testing protocol for the control cycling exercise (black fill) and experimental cycling exercise performed following high-intensity cycling (grey fill). IMVF = isometric maximal voluntary force; RT = resting twitch.

3.2.3 High-intensity and maximal cycling

Both cycling exercises were performed on a Lode® cycle ergometer (Excalibur Sport, The Netherlands; sampling frequency = 5 Hz). Vertical and horizontal positions of the seat and handlebar were replicated during both visits. For all cycling exercises, participants were instructed to remain seated with their hands in the lower portion of the

handlebars (i.e. ‘drops’) while their feet were firmly fastened to the pedals via a toe cage and non-compliant strap. The 30-s maximal cycling efforts were performed in isokinetic mode at 120 rpm, with maximal lower-limb power calculated as an average over the first and last 12 cycles/6-s of the 30-s maximal cycling exercises.

3.2.4 Surface electromyography

Surface EMG signals of eight muscles [*gluteus maximus* (GMAX), *rectus femoris* (RF), *vastus lateralis* (VL), *vastus medialis* (VM), *semitendinosus/semimembranosus* (ST/SM), *biceps femoris* long head (BF), *gastrocnemius medialis* (GM*)* and *gastrocnemius lateralis* (GL)] were continuously recorded from the left lower-limb using a Telemyo 2400 GT system (Noraxon Inc., USA). Bipolar surface electrodes of 10 mm diameter and inter-electrode distance of 20 mm (Noraxon dual electrodes, Noraxon USA Inc., Scottsdale, AZ) were positioned on the muscle bellies in accordance with the recommendations of the SENIAM project (Hermens et al. 2000). A ground electrode was placed over the superior aspect of the medial sacral crest. Prior to electrode application, the skin was shaved, lightly abraded and cleaned with an alcohol swab to reduce skin impedance. Location of the EMG electrodes was marked with an indelible marker during the first visit, and maintained for the remainder of the experiment to ensure consistent placement between visits. All EMG signals were pre-amplified at the level of the electrodes (gain of 500) before sampling at 1500 Hz. A +3 V electrical pulse generated by a reed switch attached to the ergometer frame was also transmitted. A pulse was generated when the left crank reached an upward and vertical position (corresponding to the start and end of a crank cycle). All signals were transmitted to a computer using a wireless receiver that was attached to the participants’ waists and were recorded using MyoResearch XP software (version 1.07.41, Noraxon USA Inc., Scottsdale, AZ).

All signals were processed in Visual3D, version 5.02.27 (C-Motion Inc., Germantown, MD, USA). Specifically, all EMG signals were band pass filtered (10-500 Hz) and root-mean-squared (100-ms moving rectangular window). The signal recorded using the reed switch was used to create time normalized (% crank cycle) EMG profiles for all the muscles. Average EMG profiles were calculated for three muscle groups: VL and VM (VAS), ST/SM and BF (hamstrings: HAM) and GM and GL (GAS). EMG profiles of GMAX and RF were not averaged with any other muscles, because of their distinctive functional roles. The average amplitude of all the EMG profiles (i.e. GMAX, VAS, RF, HAM and GAS) were normalized to the corresponding highest average EMG value obtained during the two 4-s maximal cycling efforts performed during the warm-up of the

corresponding session (Rouffet and Hautier 2008). The time normalized EMG signals were also used to calculate a co-activation index for the following muscle pairs: VAS/HAM, GMAX/RF and VAS/GAS (Lewek et al. 2004) as previously proposed (O'Bryan et al. 2014) (***Eq. 3.1***). Average EMG and co-activation indices were then calculated over the first and last 40 cycles/30-s of the 10-min high-intensity cycling exercise, and over the first and last 12 cycles/6-s of the 30-s maximal cycling exercises.

$$\mathrm{CAI} = \frac{1}{100}\sum_{i=1}^{100}\left[\left(\frac{\text{lower EMGi}}{\text{higher EMGi}}\right) \times (\text{lower EMGi} + \text{higher EMGi})\right]$$

Eq. 3.1

3.2.5 Knee extensor fatigue

Knee extensor fatigue was assessed by measuring changes in isometric maximal voluntary force (IMVF) and resting potentiated twitch force (RT) before and after the 10-min high-intensity cycling exercise and 30-s maximal cycling efforts. Measurements were obtained with participants in a supine position (hip angle = 0°) on a custom-made padded table with the right knee flexed at 90° and a non-compliant strap connecting their lower leg to a load cell (S1W, Xtran, Australia). Force signals were sampled at 100 Hz. IMVF was calculated as the maximum value over 100-ms, while RT was calculated as the maximum instantaneous value. Participants performed a 4-s isometric maximal voluntary contraction before relaxing their knee extensors while the experimenter stimulated the right femoral nerve three times (3-s between each stimulation) using a magnetic stimulator (Magstim RAPID^2; The Magstim Company, Wales, UK). A 70-mm figure of eight coil was used for the stimulation and the coil was repositioned at the same location for all assessments (site was marked with a permanent marker). The average peak force from the three RT was calculated (Verges et al. 2009; Billaut et al. 2013).

3.2.6 Ratings of perceived exertion

Ratings of perceived exertion (RPE) were obtained using the original 6-20 point Borg scale (Borg 1970). RPE values were collected at the start (first 30-s) and end (last 30-s) of the 10-min high-intensity cycling exercise, and immediately after the end of the maximal cycling efforts.

3.2.7 Statistics

Two-way ANOVAs (time x muscle or time x muscle pair) with repeated measures were used to investigate changes in EMG and co-activation during the 10-min high-intensity cycling exercise. Two-way ANOVAs (time x condition) with repeated measures were used to investigate changes in EMG, co-activation and lower-limb power during the 30-s maximal cycling exercises. Two-way ANOVAs (condition x time) with repeated measures were used to investigate changes in knee extensor IMVF and RT. Following a significant *F* statistic Bonferroni adjusted post-hoc tests were performed. The lower and upper limits of the 95% confidence interval for mean differences (CI) and Cohens *d* effect sizes (ES; trivial: 0 - 0.19, small: 0.2 - 0.49, moderate: 0.5 – 0.79, large: > 0.8) were then reported (Cohen 1992). Pearson product-moment correlations were also used to investigate if: i) changes in the EMG activity of VAS muscles measured during the 10-min high-intensity cycling exercise were associated with changes in IMVF and RT of the knee extensors obtained after the same exercise, and ii) if between-session differences in IMVF and RT of the knee extensors measured before the 30-s maximal cycling efforts were associated with between-session differences in lower-limb power measured during the initial (0-6 s) part of the maximal cycling exercise. Statistics were performed using SPSS software (version 21.0, Chicago, IL, USA). The significance level for all tests was set at $P \leq 0.05$. Mean ± standard deviation values are reported in text.

3.3 Results

3.3.1 High-intensity cycling

Results from the ANOVA examining changes in EMG during the high-intensity submaximal cycling exercise showed significant main effects of time ($F_{1,6} = 36.6$, $P = 0.001$), muscle ($F_{4,24} = 9.4$, $P \leq 0.001$) and a time x muscle interaction ($F_{4,24} = 7.7$, $P \leq 0.001$). Post-hoc analysis revealed an increase in EMG from the start to the end of the exercise for VAS (10 ± 3%, $P \leq 0.001$, CI [7.5%, 12.1%], ES = 0.96) and RF (9 ± 4%, $P \leq 0.001$, CI [5.5%, 12.8%], ES = 1.1), and that VAS was activated higher than all muscles other than GAS (**Figure 3.2**). For co-activation, the ANOVA displayed a significant time x co-activation interaction ($F_{3,18} = 9.7$, $P = 0.001$), with an increase reported for GMAX/RF ($P \leq 0.05$, ES = 0.55) and a decrease reported for VAS/GAS ($P \leq 0.01$, ES = 0.55) (**Figure 3.2**). RPE increased from 12.6 ± 1.3 to 18.1 ± 1.9 between the start and the end of the exercise ($P \leq 0.001$, CI [4.0, 7.1], ES = 1.7).

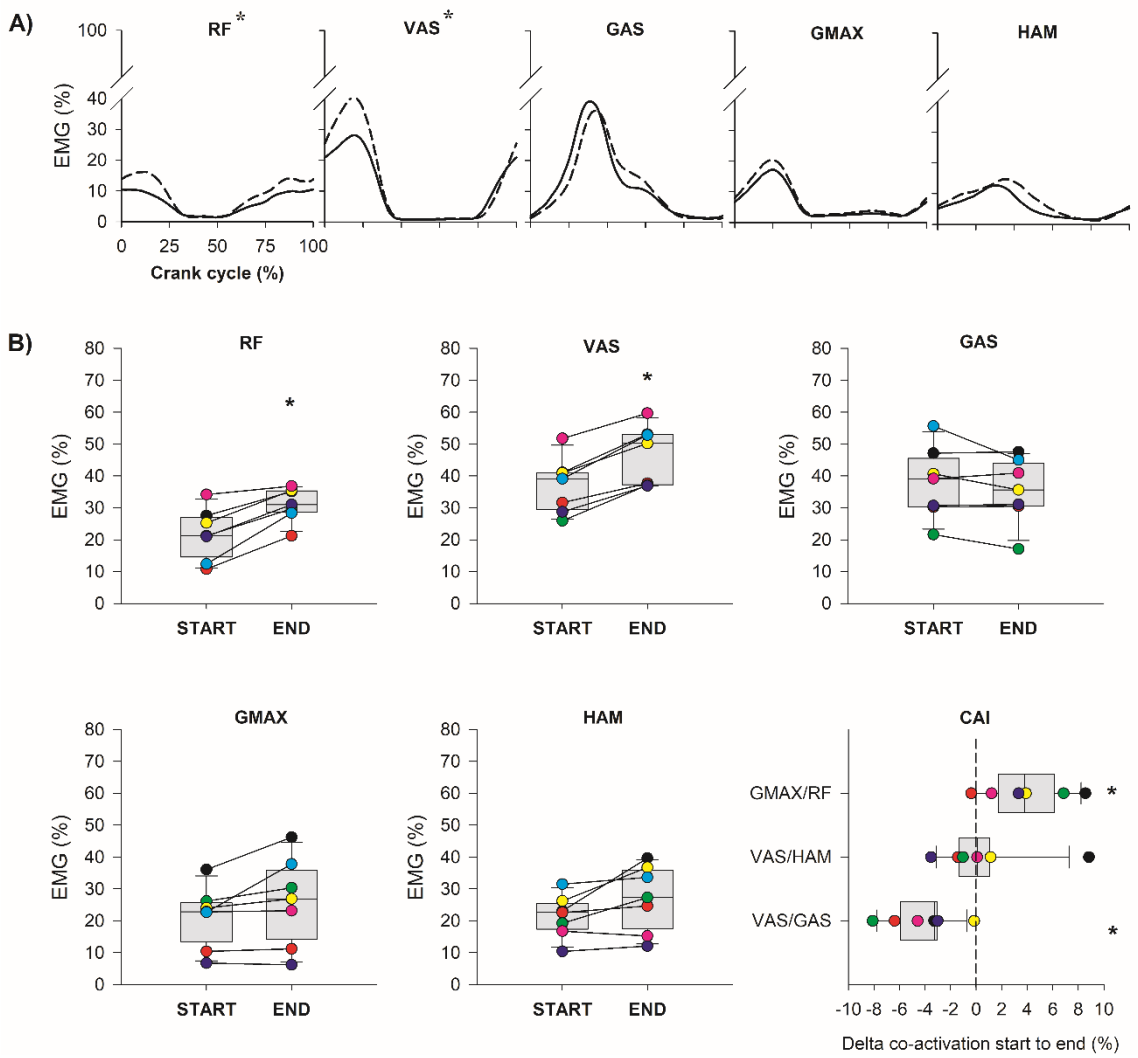

Figure 3.2 A) EMG profiles of the lower-limb muscles during the start (solid) and end (dash) of high-intensity cycling exercise. **B**) Mean (box plot) and individual (line and scatter plot) changes in EMG and co-activation for the lower-limb muscles from the start to end of high-intensity exercise. RF = *rectus femoris*; VAS = *vastii*; GAS = *gastrocnemius*; GMAX = *gluteus maximus*; HAM = *hamstrings*; CAI = co-activation index.
* significantly different from the start period (P ≤ 0.05).

3.3.2 Knee extensor fatigue following high-intensity cycling

Following the 10-min high-intensity cycling exercise, knee extensor IMVF was reduced from 587 ± 70 N to 490 ± 100 N (P ≤ 0.01, CI [-26.2 N, -168.1 N], ES = 1.0). This represented a relative reduction of -17 ± 12%, with all individual changes in IMVF ranging from -2% to -36%. As shown in **Figure 3.3 A**, a negative correlation was observed between the changes in VAS EMG over the course of the 10-min high-intensity cycling exercise (from 6% to 14%) with the changes in knee extensor IMVF (r = -0.791, P ≤ 0.05). Following 10-min high-intensity cycling, RT reduced from 171 ± 24 N to 98 ± 31 N (P ≤ 0.001, CI [-44.7 N, -100.2 N], ES = 1.6), representing a relative reduction of -

42 ± 16%. The reductions in knee extensor RT tended to be negatively associated with the increases in VAS EMG activity (r = -0.749, P = 0.053; **Figure 3.3 B**).

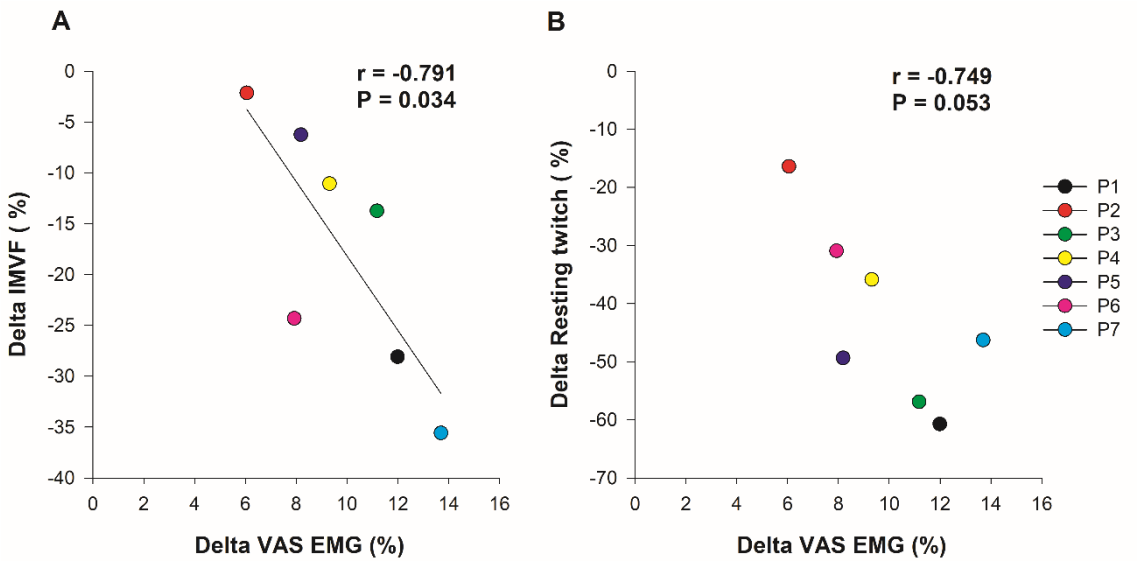

Figure 3.3 Correlation of the changes in VAS EMG (measured between the start and end of the high-intensity cycling exercise) and knee extensor isometric maximal voluntary force (IMVF) (A), and resting twitch force (B) (calculated between measurements obtained before and ~1-min after the high-intensity cycling exercise). Pearson correlation coefficients (r) and significance levels (P) are reported.

3.3.3 Maximal cycling and knee extensor fatigue

Maximal power generated at the start of the control cycling exercise was positively correlated to pre-exercise IMVF (r = 0.78, P = 0.038). A time effect was shown for lower-limb power (**Figure 3.4**), EMG for all muscles (**Figure 3.5**) and co-activation for all pairs (**Figure 3.6**) ($P \leq 0.05$), with all reducing at the end of the 30-s maximal cycling effort. A condition effect for lower-limb power ($F_{1,6} = 10.6$, $P \leq 0.05$), EMG activity of GMAX ($F_{1,6} = 22.5$, $P \leq 0.05$), VAS ($F_{1,6} = 13.8$, $P \leq 0.05$), RF ($F_{1,6} = 10.5$, $P \leq 0.05$), HAM ($F_{1,6} = 10.6$, $P \leq 0.05$) and GAS ($F_{1,6} = 17.1$, $P \leq 0.05$), and co-activation indices for GMAX/RF ($F_{1,6} = 11.1$, $P \leq 0.05$), VAS/HAM ($F_{1,6} = 8.9$, $P \leq 0.05$) and VAS/GAS ($F_{1,6} = 11.4$, $P \leq 0.05$), revealed overall lower values for the maximal effort completed following high-intensity cycling exercise.

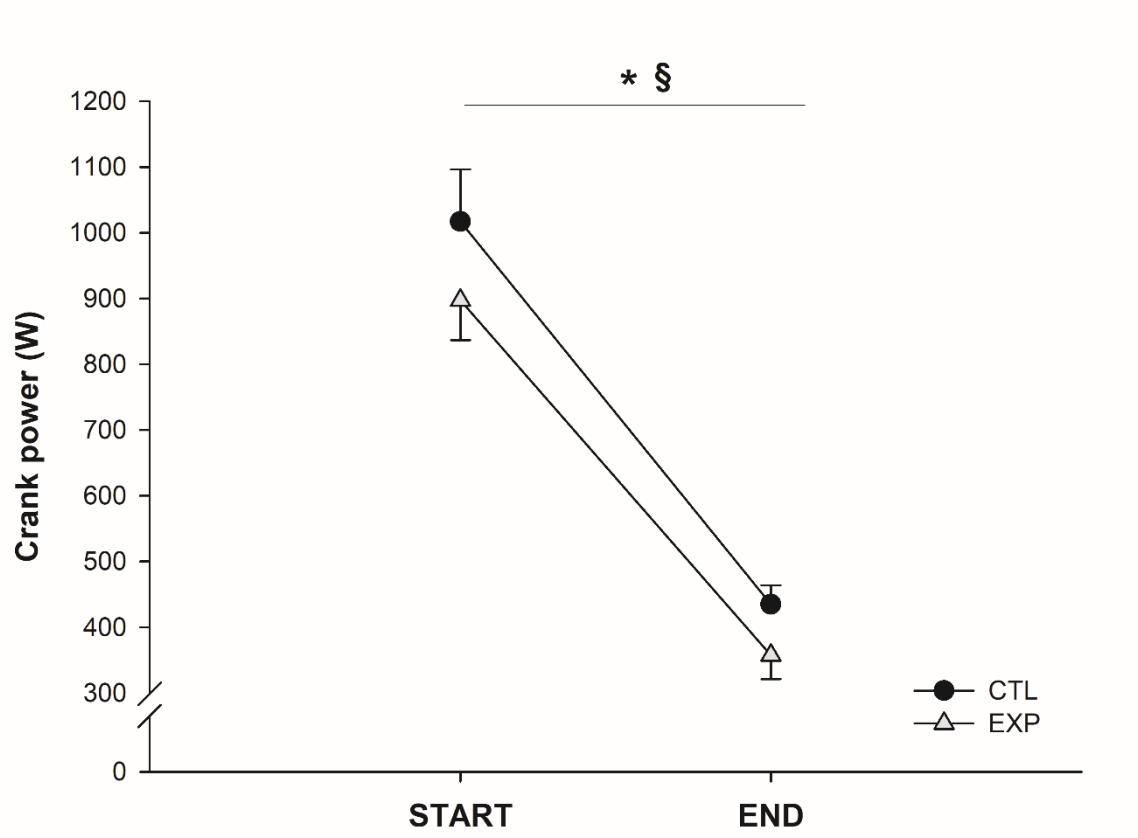

Figure 3.4 Maximal lower-limb power measured at the start (first 6-s) and end (last 6-s) of the 30-s all-out cycling effort performed in the control condition (CTL) and after 10-min of cycling at high-intensity (EXP).
* indicates a difference between values measured in the CTL and EXP condition ($P \leq 0.05$).
§ indicates a difference between the start and end in the two conditions ($P \leq 0.05$).

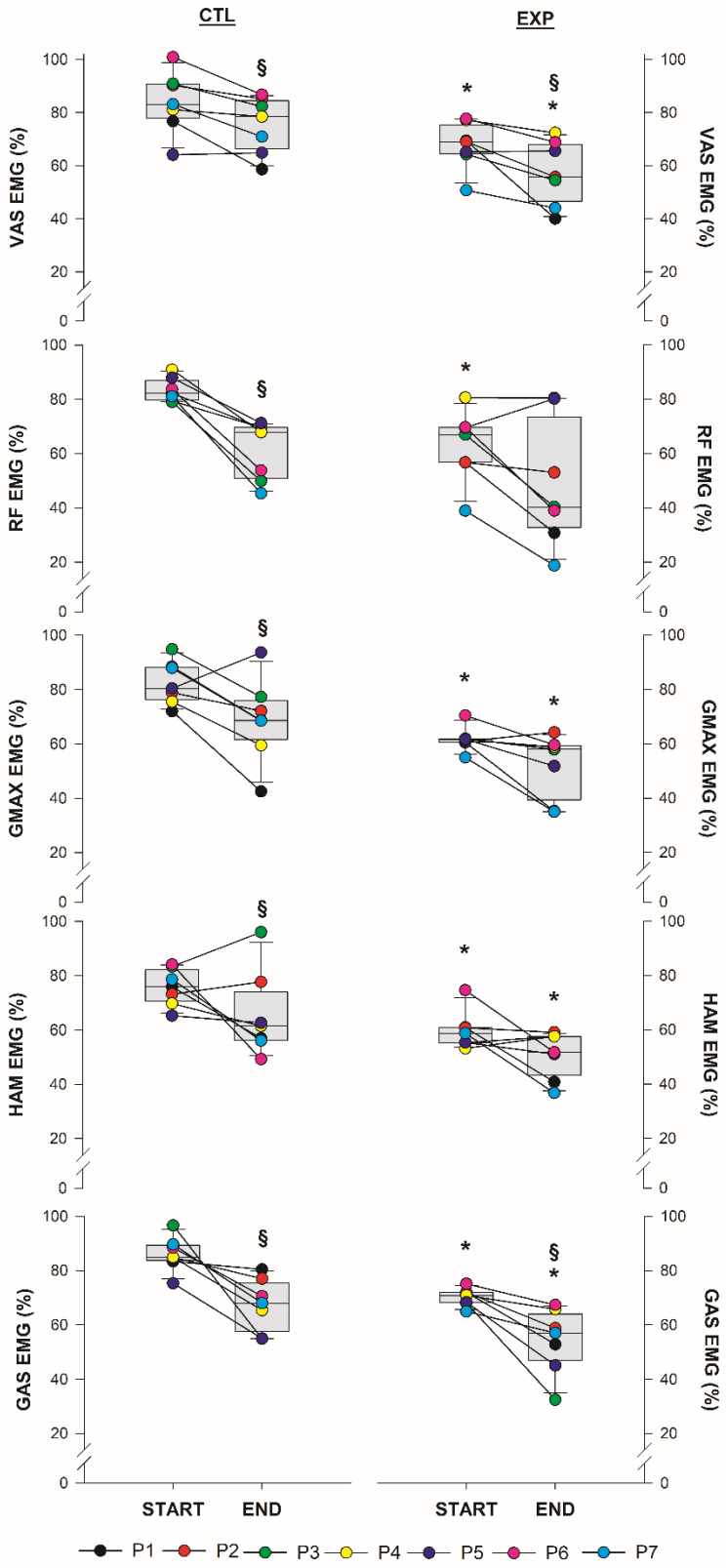

Figure 3.5 Normalized EMG activity for all lower-limb muscles measured at the start (first 6-s) and end (last 6-s) of the 30-s all-out cycling effort performed in the control condition (CTL) and after 10-min of cycling at high-intensity (EXP).
VAS = *vastii*; RF = *rectus femoris*; GMAX = *gluteus maximus*; HAM = hamstrings; GAS = *gastrocnemius*.* indicates a difference between values measured in the CTL and EXP condition ($P \leq 0.05$).

§ indicates a difference between values measured the start and end for the same exercise (P ≤ 0.05).

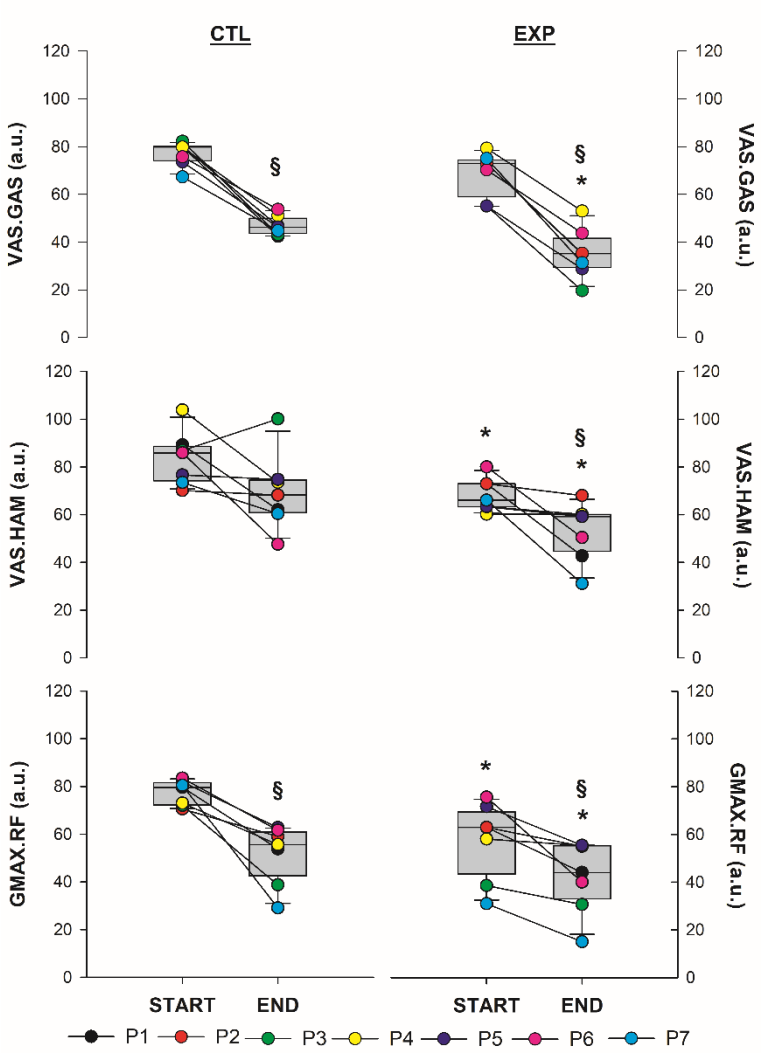

Figure 3.6 Co-activation index for all lower-limb muscles measured at the start (first 6-s) and end (last 6-s) of the 30-s all-out cycling effort performed in the control condition (CTL) and after 10-min of cycling at high-intensity (EXP). VAS = *vastii*; RF = *rectus femoris*; GMAX = *gluteus maximus*; HAM = hamstrings; GAS = *gastrocnemius*.
* indicates a difference between values measured in the CTL and EXP condition (P ≤ 0.05).
§ indicates a difference between values measured the start and end for the same exercise (P ≤ 0.05).

Specific to the initial part of the maximal effort, post-hoc tests revealed an overall reduction of lower-limb power following high-intensity cycling (1017 ± 211 W vs. 898 ± 160 W; P ≤ 0.05, CI [-14.6 W, -224.8 W], ES = 0.6), with relative differences from control ranging from 0% to -27%. A positive correlation was observed between the reduction in lower-limb power at the start of the maximal cycling effort and the decrease in knee extensor IMVF that resulted from high-intensity cycling (r = 0.757, P ≤ 0.05; **Figure 3.7 A**), however, this was not shown for RT (r = 0.457, P = 0.3; **Figure 3.7 B**). Post-hoc tests

also revealed that EMG activity of all muscles and all co-activation indices (except VAS/GAS) were reduced at the start of the maximal cycling effort (**Figure 3.5** and **Figure 3.6**).

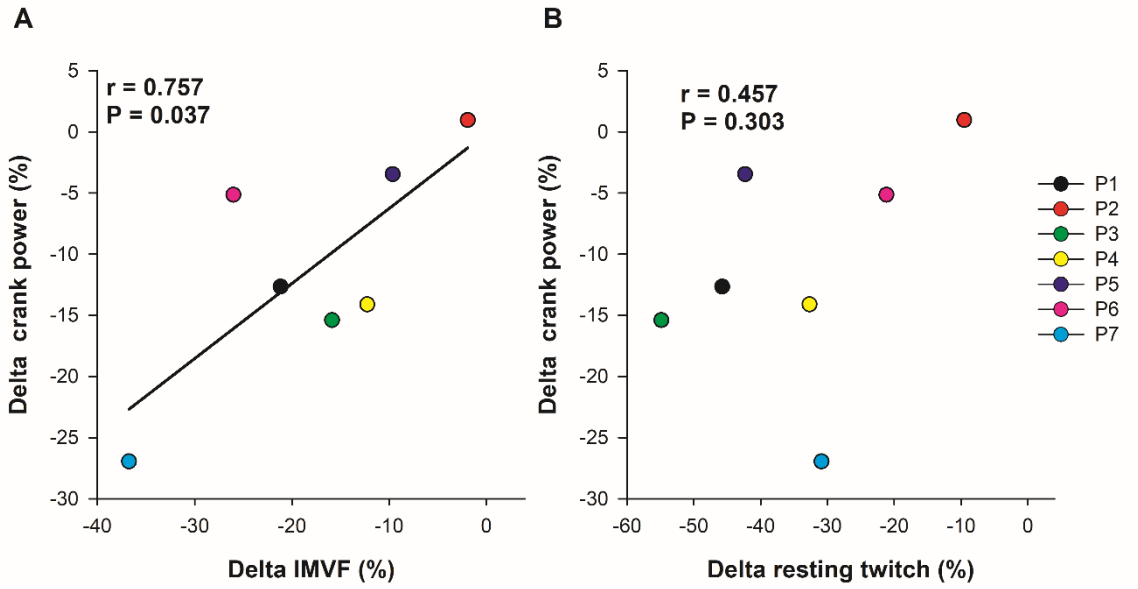

Figure 3.7 Correlation of the difference between the conditions in lower-limb power (measured at the start of the all-out cycling effort) and knee extensor isometric maximal voluntary force (IMVF) (A), and resting twitch force (B) (measured ~1-min prior to all-out effort). Pearson correlation coefficients (r) and significance levels (P) are reported.

3.4 Discussion

3.4.1 Summary of main findings

The aims of the study were to investigate: i) the association between changes in *vastii* EMG during a high-intensity cycling exercise and the development of muscle fatigue in the knee extensors, and ii) the effect of knee extensor fatigue on maximal lower-limb power and changes in inter-muscular coordination during a subsequent 30-s maximal cycling effort. The results revealed an association between increases in *vastii* EMG during high intensity cycling and the development of muscle fatigue in the knee extensors, which subsequently determined the reduction in power output during the maximal cycling effort. Co-activation was also altered during high-intensity cycling exercise, indicating that inter-muscular coordination may have been adjusted to limit the occurrence of knee extensor fatigue and to maximise lower-limb power production during the subsequent maximal effort.

3.4.2 Knee extensor fatigue developed during high-intensity exercise

Vastii muscles displayed a higher EMG relative to their maximal value compared to all muscles except GAS, illustrating the heavy reliance placed on these muscles to generate power during high-intensity cycling exercise (Ericson et al. 1986; Zajac et al. 2002; Rouffet et al. 2008; Dorel et al. 2012). The increase in knee extensor EMG for VAS and RF muscles (~10%) from the start to end of high-intensity submaximal cycling (**Figure 3.2**) is in accordance with previous studies with comparable cycling protocols (Amann and Dempsey 2008; Decorte et al. 2012; Taylor et al. 1997; Thomas et al. 2014). The magnitude of the reduction in knee extensor IMVF (-17 ± 12%) and RT (-42 ± 16%) following high-intensity submaximal cycling provided clear evidence that the exercise induced a substantial level of fatigue in the knee extensors. The negative correlation observed between the increase in *vastii* EMG during high-intensity exercise and the reduction in isometric maximal voluntary force of the knee extensors following the exercise (**Figure 3.3**), suggests that an increased firing frequency and/or the number of motor units recruited within the *vastii* muscles was associated with larger levels of knee extensor fatigue (Adam and De Luca 2005; Bigland-Ritchie et al. 1986a; Merletti et al. 1990; Taylor and Gandevia 2008). The increase in EMG during the high-intensity exercise performed at a constant power, can be interpreted as evidence of peripheral muscle fatigue, which could be due to impairments in neuromuscular transmission or excitation-contraction coupling (Bigland-Ritchie 1981; Decorte et al. 2012; Amann and Dempsey 2008). This interpretation is partly supported by the trend for a correlation (P = 0.053) between the increase in *vastii* EMG during high-intensity cycling and the reduction in resting twitch following the exercise (**Figure 3.3**). It is speculated that participants who displayed larger increases in VAS EMG activity over the course of the high-intensity cycling exercise, and ultimately experienced larger levels of peripheral fatigue, possessed higher percentages of type II fibres in their *vastii* muscles (Hamada et al. 2003). Finally, it is likely that peripheral fatigue developed over the course of the prolonged high-intensity cycling exercise also caused an increased firing of the group III and IV sensory afferent receptors, which ultimately resulted in the development of central fatigue that reduced the force-generating capacity of the knee extensor muscles (Taylor et al. 2000).

3.4.3 Inter-muscular coordination during high-intensity exercise

As expected, co-activation between *vastii* and GAS muscles was relatively high at the start of the high-intensity cycling exercise, suggesting that participants initially

selected an inter-muscular coordination strategy aimed at optimizing the transfer of energy from the *vastii* muscles to the crank via the ankle plantar flexors (Zajac et al. 2002). At the end of the high-intensity cycling exercise and in parallel to the changes in individual EMG activities, we observed an increase in GMAX/RF co-activation that was accompanied by a decrease in VAS/GAS co-activation (**Figure 3.2**), suggesting that the movement control strategy was modified. These changes in co-activation suggest that participants attempted to increase the transfer of energy from the hip extensors to the crank via *rectus femoris,* while reducing the transfer of energy from the knee extensors to the crank via the ankle plantar flexors (Dorel et al. 2009). Such changes in the movement control strategy may have increased the effective crank forces generated during the early extension phase while decreasing the effective crank forces generated during the late extension phase (Van Ingen Schenau et al. 1992; Zajac et al. 2002) in response to the occurrence of knee extensor fatigue towards the end of the high-intensity cycling exercise. This modification would have permitted the participants to maintain the required load despite a loss in the effective crank forces generated from the contribution of the knee extensors. Thus, the increase in GMAX/RF co-activation may indicate a shift in the movement control strategy toward increasing the hip extensor contribution to lower-limb power to limit fatigue development in the knee extensors (Dorel et al. 2009).

3.4.4 Effect of knee extensor fatigue developed during high-intensity exercise on lower-limb power during maximal cycling

A strong positive correlation was observed between the reduction in knee extensor IMVF following high-intensity exercise (range = -2% to -36%) and the reduction in maximal power during the subsequent maximal cycling exercise (range = 0 to -27%) (**Figure 3.7**). This finding clearly supported the hypothesis that the severity of knee extensor fatigue developed during high intensity submaximal cycling would lead to dose-dependent reductions in maximal lower-limb power. However, no significant association was observed between the reductions in power production during the maximal cycling effort and the decrease in resting twitch, indicating that peripheral fatigue developed over the course of the 10-min high-intensity cycling exercise was not strongly related to the reduction in maximal lower-limb power. That is, changes in maximal cycling performance were predicted better by changes in isometric maximal voluntary force, which is influenced by central as well as peripheral factors, than by the resting twitch, which reflects only peripheral fatigue. Hence, the results suggest that central fatigue plays a role in the reduction in maximal cycling performance following high-intensity cycling. The reductions in EMG of all the muscles (**Figure 3.5**) suggest that fatigue may have

developed in other locomotor muscles (e.g. GMAX, GAS and HAM) and contributed to the reductions in lower-limb power at the start of the maximal cycling effort. It is possible that an increased firing of the group III and IV sensory afferents from the knee extensor muscles (Gandevia 2001; Amann and Dempsey 2008) over the course of the high-intensity cycling exercise caused reductions in neural drive to synergist GMAX and GAS muscles (Ciubotariu et al. 2004; Hayward et al. 1988; Sacco et al. 1997) but also antagonist HAM muscle (Kennedy et al. 2015) during the maximal cycling effort. Finally, the lack of change in co-activation between VAS/GAS during the initial part of the maximal effort, despite a decrease in both VAS and GAS EMG activities (**Figure 3.6**), suggests that participants may have selected a movement strategy aimed at maximizing the transfer of energy from the knee extensors to the crank via the ankle plantar flexors (Zajac et al. 2002). It is possible that this strategy allowed participants to limit the impact of knee extensor fatigue on maximal power production following high-intensity cycling.

3.4.5 Limitations

A potential limitation of magnetic stimulation is that the stimulator intensity may be limited by stimulator output (Millet et al. 2012), meaning that the size of the resting twitch may have been underestimated. However, up to four isometric maximal voluntary knee extensions were performed prior to baseline twitch measurements, which is sufficient to fully potentiate the response (Kufel et al. 2002). Moreover, others have shown that 100% stimulator intensity can elicit a supramaximal twitch response (Polkey et al. 1996; Hamnegård et al. 2004).

3.5 Conclusion

The results show that monitoring increases in *vastii* EMG over the course of a high-intensity cycling exercise offers a non-invasive solution to detect muscle fatigue in the knee extensors, which ultimately reduces power production during a subsequent maximal cycling effort. The results also suggest that slight modifications in the movement control strategy may limit the development of fatigue during high-intensity cycling, and maximize lower-limb power production in the presence of knee extensor fatigue during maximal cycling. Because EMG of various lower-limb muscles (e.g. GMAX, HAM, GAS) was reduced during the maximal cycling effort, the high-intensity cycling exercise may have induced fatigue in these muscles, potentially affecting lower-limb power and inter-muscular coordination during the maximal effort. Therefore, further studies are required to investigate the effect of isolated fatigue of the knee extensors on lower-limb power production and inter-muscular coordination during maximal cycling exercises.

Author contributions

SJ O'bryan was responsible for data collection and analysis, preparation of figures, drafting the chapter and revising the chapter for important intellectual content. **F Billaut** was responsible for conception and design of experiments and revising the chapter for important intellectual content. **JL Taylor** was responsible for revising the chapter for important intellectual content. **DM Rouffet** was responsible for conception and design of experiments, data analysis, preparation of figures and revising the chapter for important intellectual content.

Chapter 4 EFFECT OF PRE-FATIGUING KNEE EXTENSION EXERCISE ON POWER PRODUCTION AND MOVEMENT CONTROL DURING MAXIMAL CYCLING

4.1 Introduction

The maximal force-generating capacity of the knee extensors is a good predictor of performance during lower-limb exercises such as jumping (Tsiokanos et al. 2002), hopping (Willigenburg et al. 2014) and maximal cycling (Driss et al. 2002; Kordi et al. 2017). Specifically, during cycling exercise, the maximal isometric force-generating capacity of the knee extensors is strongly correlated to the apex of the power-cadence relationship when calculated over a full cycle (i.e. P_{MAX}, r = 0.71 – 0.75) (Driss et al. 2002; Kordi et al. 2017). These findings illustrate that individuals with a greater capacity to generate high levels of knee extensor force have a greater capacity to generate high levels of crank power. During maximal cycling, this association presumably occurs as the *vastus lateralis* and *vastus medialis* muscles generate more work than any other lower-limb muscle group (Raasch et al. 1997). However, these muscles are activated maximally to generate large tangential crank forces during the extension phase of the crank cycle only (crank angle ~0 – 180°) (Martin and Brown 2009; Elmer et al. 2011; Rouffet and Hautier 2008; Dorel et al. 2010; Dorel et al. 2012; Raasch et al. 1997).

During repeated or sustained maximal cycling exercises, reductions in crank power are thought to evolve from fatigue development in the knee extensors (Fernandez del Olmo et al. 2013; Hunter et al. 2003; Hureau et al. 2014). However, reductions in power output during 30-s of maximal cycling (up to 60%) (O'Bryan et al. 2014; Martin and Brown 2009) far outweigh reductions in isometric force of the knee extensors (~16%) (Fernandez del Olmo et al. 2013). Fatigue development in other lower-limb muscles is therefore also likely, as evidenced via large reductions in hip extension, knee flexion and ankle plantar flexion joint power (Martin and Brown 2009) and EMG amplitude of *gluteus maximus* and *gastrocnemius* muscles (O'Bryan et al. 2014). This makes it difficult to isolate the effects of knee extensor fatigue to reductions in power output during maximal cycling. Hureau et al. (2014) applied myostimulation to the knee extensors prior to a maximal 10-s cycling sprint, and revealed that reductions in isometric maximal force (range = -5% to -25%) led to much smaller reductions in peak (range = -5% to -8%) and mean (range = -4% to -7%) power output. The greater variability in the reduction in isometric force of the knee extensors compared to the reduction in power output, indicates that fatigue of the knee extensors influences the capacity for individuals to

generate power differently. However, crank power calculations were not phase specific, and EMG activity of other lower-limb muscles involved in power production were not investigated. These limitations make it difficult to ascertain how fatigue of the knee extensors influences power production during maximal cycling. In conjunction with in-depth EMG analysis of multiple lower-limb muscles, it may be possible to elucidate some of the mechanisms influencing these relationships, such as variability in the movement control strategy and the potential for fatigue development in other lower-limb muscles.

The principle of motor redundancy is that the CNS can use multiple movement strategies to perform a given task (Latash 2012; Bernstein 1967). The effects of fatigue on variability in movement strategies has been well studied during hopping (Bonnard et al. 1994), hammering (Côté et al. 2005), throwing (Huffenus et al. 2006; Forestier and Nougier 1998), push/pull tasks (Gates and Dingwell 2008), target tracking (Selen et al. 2007) and fine finger movements (Singh et al. 2010). Generally, these studies suggest that fatigue increases inter-individual and intra-individual variability, meaning that participants select different movement strategies with fatigue development, and that the effects of fatigue on performance outcomes are different between participants. Previous findings during cycling exercise have revealed that intra-individual variability decreases with increases in the demand to generate crank power (Enders et al. 2014). Brochner Nielsen et al. (2016) revealed that a reduction in isometric force of the knee extensors induced by myostimulation (range ~ -21 to -35%) increased inter-individual variability in the movement strategy, with some participants increasing the relative amount of power generated during the flexion phase. However, no studies have explored fatigue-induced changes in inter-individual variability of movement strategies during maximal cycling. The effects of knee extensor fatigue on movement variability during maximal cycling exercises remains unknown.

Isolated ipsilateral knee extension exercise has previously been shown to reduce maximal voluntary force of the non-exercised contralateral knee extensor muscles (Prieske et al. 2017; Kawamoto et al. 2014; Halperin et al. 2014b). Others have shown that isolated fatigue of the ankle plantar flexors (Sacco et al. 1997; Ciubotariu et al. 2004) and the knee flexors (Kennedy et al. 2015), can induce a temporary deficit in non-exercised synergistic and antagonist muscles. Although the precise mechanisms for this phenomenon remain unclear, a fatigue-induced increase in group III and IV afferents is thought to play a role in inhibiting complex supraspinal and spinal circuits (Halperin et al. 2015), potentially reducing the ability to maximally activate local and non-local muscles. Thus, it is possible that isolated fatigue of the knee extensors could negatively influence

the ability to maximally activate antagonist and/or synergistic muscles of the lower-limb. Such inhibition of non-local muscles during maximal cycling could result from a pre-fatiguing exercise of the knee extensors and might exacerbate reductions in power output during different phases of the crank cycle (e.g. extension and flexion phases).

The first aim of this study was to investigate if the level of fatigue induced by a pre-fatiguing knee extension exercise determines the level of reduction in power output during the extension and flexion phases of maximal cycling exercise. The second aim was to investigate how motor command during maximal cycling is affected by pre-fatigue of the knee extensors. To address these aims, fatigue was induced in the knee extensors via an isolated pre-fatiguing exercise immediately prior to a maximal 30-s cycling effort, and power output during cycling was calculated during phase-specific regions of the crank cycle (e.g. leg extension and leg flexion). It was hypothesized that knee extensor fatigue developed during pre-fatiguing exercise would be associated to reductions in power output during the extension phase, but not during the flexion phase. It was also hypothesized that knee extensor fatigue would limit the capacity to maximally activate lower-limb muscles and increase inter-individual variability in crank force and muscle activation patterns.

4.2 Methods

4.2.1 Participants and ethics

Sample size calculations were performed using G*Power version 3.0.10 software (Faul et al. 2007) using an alpha level set at 0.05 and a probability of avoiding a type II error set at 0.8. It was assumed that completion of pre-fatiguing exercise would lead to large reductions in maximal knee extensor force-generating capacity ($F > 0.6$) (Cohen 1992; Babault et al. 2006). From the sample size calculations, six male and four female (n = 10) physically active participants accustomed to regular high-intensity exercise volunteered (age: 26 ± 4 years; height: 179 ± 6 cm; mass: 74 ± 11 kg). The range of exercises included regular resistance training, running, competitive sports (e.g. basketball, tennis) and recreational cycling. Individual participant characteristics are presented in **Table 4.1**. Prior to any testing, a risk assessment questionnaire was completed to deem participants free from any existing cardiovascular, musculoskeletal or neuromuscular disorders. Written informed consent was obtained from each participant, and the study was approved by Victoria University's Human Research Ethics Committee (application number HRE14-182) in accordance with the standards set by the Declaration of Helsinki.

Table 4.1 Physical characteristics of study two participants. Note: mechanical data was calculated during the extension phase of the crank cycle during the force-velocity test (i.e. 0 - 180°). P_{MAX} = estimated maximal power output; T_0 = estimated maximal torque; C_0 = estimated maximal cadence; C_{opt} = estimated optimal cadence.

Subject	Age	Sex	Body mass (kg)	P_{MAX} ($W.kg^{-1}$)	T_0 ($N{\cdot}m.kg^{-1}$)	C_{OPT} (rpm)	C_0 (rpm)
1	23	F	61	12.37	1.35	133	228
2	23	M	82	12.37	1.49	129	232
3	33	M	95	13.16	1.81	129	246
4	30	M	77	13.29	1.81	132	251
5	27	F	65	10.37	1.34	119	209
6	28	M	75	13.16	1.36	127	218
7	23	F	70	11.82	1.20	139	250
8	23	M	80	15.39	1.36	151	281
9	19	F	57	12.20	1.54	130	238
10	28	M	81	12.23	1.79	131	270
Mean	26	-	74	12.64	1.50	132	242
SE	4	-	11	0.41	0.07	2.63	7.03

4.2.2 Equipment and data acquisition

4.2.2.1 Pre-fatiguing knee extension exercise

An isokinetic dynamometer was used to perform pre-fatiguing bilateral knee extension exercise (Cybex Isokinetic Dynamometer; Humac NORM, Canada). The dynamometer calculated hip and knee joint angles in reference to each participants' anatomical 0° (i.e. full knee extension). Participants sat in the dynamometer with straps across the thorax and pelvis and hip angle maintained at 100° flexion. The axis of rotation of the knee joint was estimated from the lateral epicondyle of the femur and aligned with the axis of rotation of the dynamometer arm. A steel custom-built lever arm, which extended far enough to permit bilateral contractions, was attached to the dynamometer. The height of the lever arm was manipulated to provide contact with the distal aspect of the left and right tibia. Torque (N·m), joint angle (°) and angular velocity ($°.s^{-1}$) were continuously recorded by the dynamometer software at a sampling frequency of 100 Hz and stored for later analysis.

4.2.2.2 Fatigue testing of the knee extensors

Fatigue testing of the left knee extensors was performed on the dynamometer chair used for pre-fatiguing exercise, with hip and knee angle fixed at 100° and 90° flexion, respectively. The left ankle was securely attached to a force transducer (AMS-1 S Type, AWE, Ingleburn, Australia) fixed to the base of the dynamometer chair via a custom-built steel frame. A non-compliant connection between the force transducer and

the ankle was created via a steel threaded rod and a padded strap fixed superior to the malleoli. The frame was built with multiple fixation heights to accommodate for differences in leg length between participants and to maintain a horizontal displacement of knee extensor forces. The raw signal from the force transducer was amplified (gain = 500) and sampled at 3000 Hz using a wireless receiver (Telemyo DTS wireless Noraxon Inc., AZ, USA) connected to a PC running MyoResearch software (Noraxon Inc., AZ, USA). The raw signal (mV) was calibrated with known masses and transformed into a force signal (N) using linear regression.

Electrical stimulation (ES) of the femoral nerve was delivered via a constant-current electrical stimulator (model DS7AH, Digitimer, Welwyn Garden City, UK) set at 400 V and a pulse duration of 1 ms. Electrical stimulations were delivered via a hand-held dome-shaped cathode (diameter 20 mm) placed high in the femoral triangle and a self-adhesive rectangular anode placed laterally in the gluteal fold to avoid the sciatic nerve (90 mm x 50 mm). The area of the femoral triangle resembling the greatest twitch force response and *vastus lateralis* M-wave amplitude at a stimulation intensity of 50 mA was identified and marked with indelible ink to identify the optimal stimulation site. A stimulus-response curve was then constructed via delivering two stimulations at 10 mA increments, interspersed with a consistent rest period of 5 s, until a plateau was observed in the maximal resting twitch force response and M-wave amplitude. Supramaximal intensity was set at 150% of plateau intensity (Kennedy et al. 2015). Consistent pressure was maintained on the femoral nerve during stimulation and delivered by the same experimenter throughout and between all trials. Stimulations were delivered at 1 Hz.

4.2.2.3 Maximal cycling exercise

Cycling exercise was performed on a custom-built cycle ergometer fitted with 172.5 mm instrumented cranks (Axis Cranks Pty, Australia) and an 11-speed gearing system (Shimano Alfine 11, Osaka, Japan). Crank angle (°), tangential torque (N·m) and radial forces (N) applied to the left and right cranks were recorded separately at a frequency of 100 Hz and sent continuously to Axis bike crank software for later analysis (Swift Performance Equipment, Australia). A static calibration of the instrumented cranks was performed prior to recording any data. Participants wore cycling shoes with a cleat/pedal arrangement (Shimano SPD SL cleat with 4° float) and seat height was manipulated to allow a maximum knee flexion angle of ~25 - 35° (Peveler et al. 2007; Bini et al. 2012). Participants remained seated with their hands in the lower portion of the handlebars during all cycling exercise.

4.2.2.4 Surface electromyography (EMG)

EMG signals were continuously recorded and sent to a wireless receiver (Telemyo DTS wireless Noraxon Inc., AZ, USA) connected to a PC running MyoResearch software (Noraxon Inc., AZ, USA). During maximal cycling exercise, EMG signals were recorded at 1500 Hz for the left *gluteus maximus* (GMAX), *vastus lateralis* (VL), *vastus medialis* (VM), *rectus femoris* (RF), *biceps femoris* (HAM), *gastrocnemius medialis* (GAS), *soleus* (SOL) and *tibialis anterior* (TA). Closure of a reed switch generated a 3-volt pulse in an auxiliary analogue channel of the EMG system when the left crank passed top dead centre (0/360° - LTDC) (Hug and Dorel 2009; Burden 2010). During knee extensor fatigue testing, EMG signals were recorded at 3000 Hz for the left VL, VM and HAM and synchronized with the raw force signal. Prior to placement of EMG electrodes, the skin was prepared by shaving all hair, lightly abrading and cleaning with alcohol swab. Disposable pre-gelled Ag - AgCl surface electrodes (Blue sensor N, Ambu, Ballerup, Denmark) were attached to the skin with an inter-electrode distance of 20 mm, and aligned parallel to the muscle fibres in accordance with the recommendations of the SENIAM project (Hermens et al. 2000). Electrodes and wireless sensors were secured with adhesive tape to ensure good contact with the skin and to reduce movement artefact.

4.2.3 Experimental protocol

Participants visited the laboratory on four separate occasions, with a minimum of 72 hours separating each visit. The first session was a familiarization, where participants became accustomed to all aspects of the experiment, including pre-fatiguing bilateral knee extension exercise, fatigue testing of the knee extensors, maximal cycling exercise, and EMG procedures. During the second session, participants completed a force-velocity (F-V) test on a cycle ergometer to characterize individual force-velocity and power-velocity relationships (Arsac et al. 1996; Gardner et al. 2009). In a randomized cross-over fashion and for the subsequent two sessions (**Figure 4.1**) participants completed either a 30-s maximal cycling exercise (control), or a 30-s maximal cycling exercise following pre-fatiguing bilateral knee extension exercise (bilateral knee extensor fatigue). Knee extensor fatigue testing was completed before and after all exercise. Changes in isometric maximal voluntary force (IMVF), voluntary activation (VA), resting twitch force (RT) and muscle compound action potential (M-wave) amplitude and duration were quantified before and after knee extension and cycling exercises.

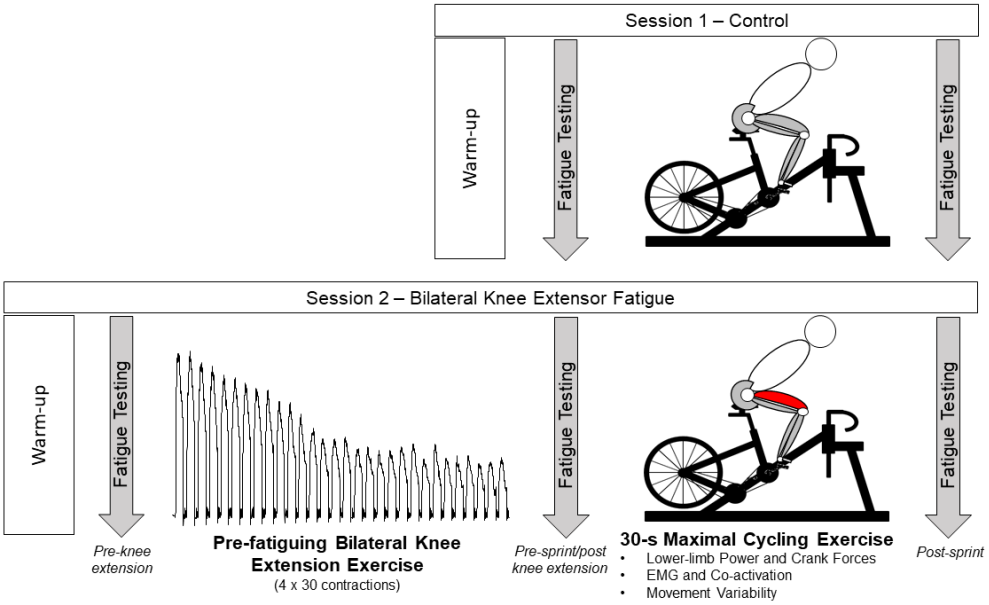

Figure 4.1 Outline of the randomized cross-over experimental protocol of study two. During session one, participants completed a 30-s maximal cycling exercise (control). During session two, participants completed a pre-fatiguing bilateral knee extension exercise (consisting of a total of 120 concentric knee extensions) prior to performing a 30-s maximal cycling exercise (bilateral knee extensor fatigue). A raw torque trace from the pre-fatiguing bilateral knee extension exercise is shown, which represents 1 x 30 maximal contractions. Fatigue testing of the knee extensors was quantified via pre-to-post exercise changes in isometric maximal voluntary force (IMVF), resting twitch force (RT), voluntary activation (VA), M-wave amplitude and duration. The time delay between the end of the pre-fatiguing exercise and beginning of the maximal cycling exercise was ~2-min, during which fatigue testing was performed and the participant transferred to the cycle ergometer. The time delay for the post-sprint fatigue testing was ~1-min.

4.2.3.1 Pre-fatiguing knee extension exercise

The pre-fatiguing bilateral knee extension exercise consisted of 120 concentric maximal contractions. Knee joint range of motion was maintained at 100 - 30° flexion (total ROM = 70°) and angular velocity was 15°.s^{-1}. Maximal contractions were repeated every 6 s, resulting in a work to rest ratio of 1:0.3 (contraction duration = 4.6 s). After 30 maximal contractions, 1.5-min of rest was given, during which fatigue testing of the knee extensors was assessed (presented at European College of Sport Science (ECSS), Malmo, Sweden, 2015, Appendix 4 - Conference abstracts). The protocol was designed to induce high levels of fatigue in the knee extensor muscles throughout the knee range of motion that is typically observed during cycling exercise (Elmer et al. 2011; McDaniel et al. 2014).

4.2.3.2 Fatigue testing of the knee extensors

To quantify the magnitude and aetiology of knee extensor fatigue, participants performed a unilateral 4-s isometric maximal voluntary contraction, with a supramaximal electrical stimulus delivered to the femoral nerve at the plateau in voluntary force (~2-s

into the contraction). Two resting potentiated twitches were elicited ~1.5-s and 3-s following the maximal voluntary contraction. For the control session, knee extensor fatigue measures were obtained before (pre-sprint) and ~1-min after maximal cycling exercise (post-sprint). For the bilateral knee extensor fatigue session, knee extensor fatigue measures were obtained before pre-fatiguing bilateral knee extension exercise (pre-knee extension), ~5-s after bilateral knee extension exercise (post-knee extension/pre-sprint) and ~1-min after 30-s maximal cycling exercise (post-sprint) (**Figure 4.2**).

4.2.3.3 Maximal cycling exercise

First, a standardized cycling warm-up was completed, consisting of 2-min of cycling at 1 $W.kg^{-1}$ and 80 rpm; 2-min at 2 $W.kg^{-1}$ and 80 rpm; 6-s maximal effort with high resistance from a stationary start; 1-min at ~2 $W.kg^{-1}$ and 80 rpm; 6-s maximal effort with low resistance from a rolling start, and 1-min at 1 $W.kg^{-1}$ and 80 rpm. For the F-V test completed during the second session, a total of five maximal 5-s efforts were completed at varied resistances and cadences, each interspersed with a 5-min rest period. Specifically, the following maximal efforts were performed in a randomized order: i) stationary start and high resistance; ii) rolling start with an initial cadence of ~50 rpm and moderate to high resistance; iii) rolling start with an initial cadence of ~70 rpm and moderate resistance; iv) rolling start with an initial cadence of ~90 rpm and low- moderate resistance; v) rolling start with an initial cadence of ~110 rpm and low resistance. Data processing was completed after each individual sprint so the resistance and initial cadence could be adjusted if required. Participants were vigorously encouraged to go ‘as hard as possible’ during each effort.

For the 30-s maximal cycling efforts, participants were required to accelerate the flywheel from a stationary start and with the left crank placed immediately prior to LTDC (i.e. ~350°). During the effort, the experimenter held down the participant’s pelvis to ensure that they remained seated. Gear selection was determined from the familiarization session, and chosen as the gear at which cadence was restricted to ~100 rpm despite maximal effort. Strong verbal encouragement was provided to the participants to push and pull on the pedals as hard as they could for each crank cycle.

4.2.4 Data analysis

All data analysis was completed using Visual 3D software version 5 (C-Motion Inc., Germantown, USA).

4.2.4.1 Fatigue testing of the knee extensors

The calibrated force signal was low-pass filtered with a 30 Hz 1st order Butterworth filter (Wüst et al. 2008). Isometric maximal voluntary force of the knee extensors (IMVF) was calculated as an average over a 500-ms window immediately preceding superimposed stimulation (Babault et al. 2006) (**Figure 4.2**). Superimposed twitch force (SIT) was calculated by subtracting the voluntary force at the time of the stimulation from the peak force achieved within a 100-ms window following the stimulation. Peak potentiated resting twitch force (RT) was calculated as an average of the two responses elicited following isometric maximal voluntary contraction. Voluntary activation (VA) was calculated from the SIT and RT data (***Eq. 2.1***) (Taylor et al. 2009). From the raw EMG signals recorded from VL and VM during fatigue testing, M-wave peak-to-peak amplitude and duration were calculated. M-wave amplitude was equal to the change in mV from the most positive to negative peaks detected within a 30-ms window following stimulation, whereas M-wave duration was equal to the time (ms) between positive and negative peaks. Additionally, VL and VM EMG calculated during IMVF and from the processed EMG signal (over identical 500-ms window) was normalized to M-wave amplitude to obtain a EMG.M-wave^{-1} ratio (Millet et al. 2003). M-wave data for RF was not achievable in this study, due to severe artefact in the EMG signal during electrical stimulation.

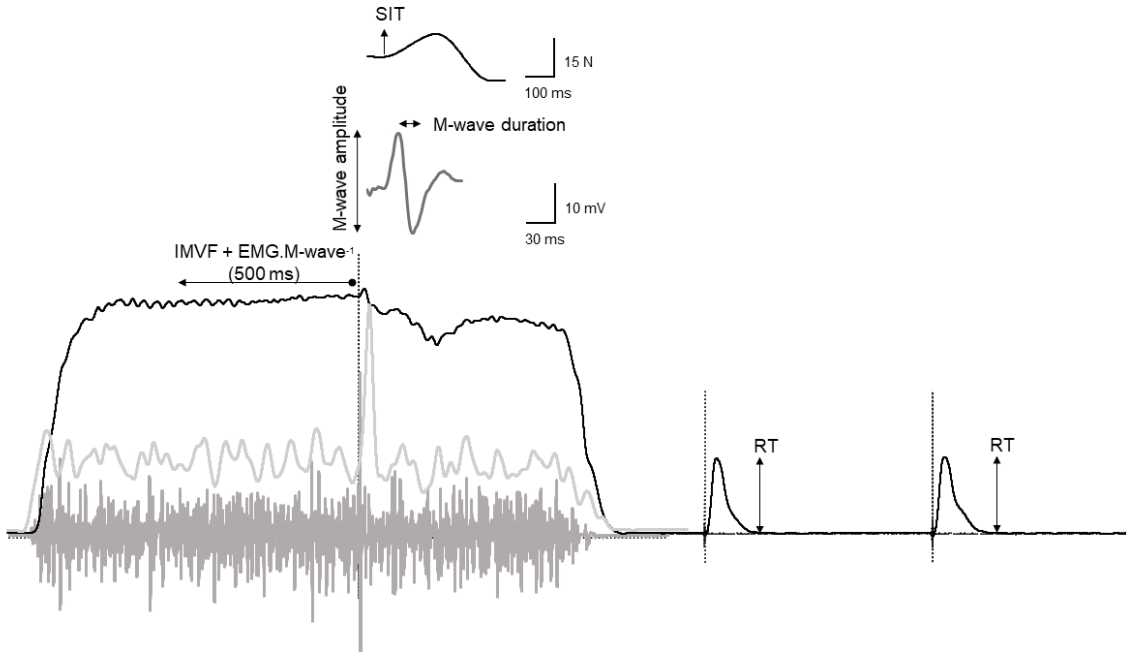

Figure 4.2 Quantification of knee extensor fatigue for one subject. Force signals (black), raw EMG signals (dark grey), processed EMG signal (light grey) and electrical stimulus artefact (dotted) were synchronized in the EMG system. Participants completed a 4-s isometric maximal voluntary contraction of the knee extensors (IMVF) with a superimposed interpolated twitch (SIT) generated

at the plateau in maximal voluntary force. Two potentiated resting twitches (RT) followed ~1.5-s and ~3-s after the maximal voluntary contraction.

4.2.4.2 Maximal cycling exercise

The first ten and final ten crank cycles completed during maximal cycling were chosen for analysis, forming the start and end periods, respectively.

Average cadence and power were calculated during the extension phase (crank angle 0 - 180°) and flexion phase (crank angle 180 - 360°) for the left and right cranks separately (Martin et al. 1997). Tangential crank forces (F_{TAN}) were calculated by dividing the tangential crank torque by the standardized crank length (0.1725 m). From F_{TAN} and the recorded radial crank forces (F_{RAD}), total crank forces (F_{TOT}) were calculated using the following formula;

$$F_{TOT} = \sqrt{F_{TAN}^2 + F_{RAD}^2}$$

Eq. 4.1

For the force-velocity test, the highest value of power and torque obtained from each maximum effort and for each cadence interval of 5 rpm (extension and flexion phases) were selected to create sets of maximal-points. These points were used to construct individual force-velocity and power-velocity relationships for the left and right cranks separately. Individual force-velocity relationships were fitted with a 2nd order polynomial regression, with the y and x-axis intercept forming the theoretical measure of maximal torque (T_0) and maximal cadence (C_0), respectively (Yeo et al. 2016; Arsac et al. 1996; Hautier et al. 1996). Individual power-velocity relationships were fitted with a 3rd order polynomial regression, with a fixed y-intercept set at zero (Yeo et al. 2016; Arsac et al. 1996; Hautier et al. 1996). Maximal power (P_{MAX}) and the corresponding optimal cadence (C_{opt}) were identified at the apex of the power-velocity relationship and calculated using Microsoft Excel Solver (version 2010). The goodness of fit of the polynomial regressions used to construct force-velocity and power-velocity relationships were determined by calculating r^2 values and standard error of the estimate (SEE) (Appendix B - Study two).

The forces applied to the left and right cranks were time normalized to LTDC to permit the construction of force profiles over a full crank cycle. Average measures of crank power (W) and crank forces (F_{TAN}, F_{RAD} and F_{TOT}) were calculated during the extension and flexion phases and from left and right cranks separately. The equation from the polynomial regression used to model individual power-velocity relationships was

used to calculate velocity-specific power (Gardner et al. 2009). This technique corrected for the effect of changes in crank velocity on maximal power production.

Raw EMG signals were band-pass filtered (20 Hz - 500 Hz) to remove noise outside the physiological range (De Luca 1997), full wave rectified, and smoothed with a 7 Hz low-pass filter to create a linear envelope (Merletti and Torino 1999). Average EMG profiles were calculated for three muscle groups: *vastus lateralis* and *vastus medialis* (VAS), *semitendinosus* and *biceps femoris* (hamstrings: HAM) and medial *gastrocnemius and soleus* (ankle plantar flexors: APF), while EMG profiles of GMAX and RF were not averaged with any other muscles because of their distinctive functional roles. EMG signals were time normalized in reference to LTDC to construct EMG activity profiles over the crank cycle (Hug and Dorel 2009; Burden 2010). The peak EMG amplitude from each profile was calculated and normalized in reference to the peak value achieved during the maximal fatigue-free efforts performed during the standardized cycling warm-up protocol (O'Bryan et al. 2014). This task specific normalization procedure has previously been shown to be reliable during maximal cycling exercise (Rouffet and Hautier 2008) permitting between-session comparison of EMG results. Time normalized EMG profiles were also used to calculate a co-activation index (CAI) for the following muscle pairs (O'Bryan et al. 2014): VAS/HAM, VAS/APF, GMAX/RF and GMAX/APF (Lewek et al. 2004) ***(Eq. 3.1)***. Peak values were extracted from each CAI profile and for each muscle pair. In line with the mechanical cycling data, peak EMG and CAI values obtained from the profiles were averaged over the first ten and final ten crank cycles, forming the start and end periods of the maximal cycling effort, respectively.

Inter-individual variability in the application of the crank forces and lower-limb EMG profiles were assessed by calculating variance ratios (VR) (Rouffet and Hautier 2008; Hershler and Milner 1978):

$$VR = \frac{\sum_{i=1}^{k}\sum_{j=1}^{n}\left(X_{ij} - \overline{X}_i\right)^2 / k(n-1)}{\sum_{i=1}^{k}\sum_{j=1}^{n}\left(X_{ij} - \overline{X}\right)^2 / (kn-1)}$$

$$\text{Where; } \overline{X} = \frac{1}{k}\sum_{i=1}^{k}\overline{\mathrm{X}}_i$$

Eq. 4.2

In this equation, k is equal to the number of intervals considered over the crank cycle (i.e. 101 for time normalized profiles); n is equal to the total number of subjects; $\mathrm{X_{ij}}$

corresponds to the value at the ith interval for the jth subject; and $\overline{X}_i$ is the average value for the ith interval calculated over the n subjects.

4.2.5 Statistics

The sample size was reduced to n = 9 for GMAX EMG, RF EMG and all associated CAIs', due to artefact in the EMG signal for one participant. The VA sample size was also reduced to n = 9 due to an artefact in the SIT response during the bilateral knee extensor fatigue session. All statistical analysis was completed using SPSS software (version 22). Normal distribution of the data was examined via a Shapiro-Wilk test, with a transformation applied to data violating this assumption (e.g. logarithmic or square root). Sphericity of the data was assessed with Mauchleys test, with a Greenhouse Geisser correction applied when the assumption of sphericity was violated. For the pre-exercise knee extensor fatigue variables, inter-day reliability was assessed via the following: i) intra-class correlation coefficients (ICC: 95% confidence intervals) with a two-way random effects model for single measure reliability (Todd et al. 2004; Place et al. 2007), ii) typical error (TE: original unit of measurement), iii) coefficients of variation (CV: %), and iv) paired samples *t*-test. Knee extensor fatigue and maximal cycling data was analysed via a two-way repeated measures ANOVA for condition and time. Bonferonni post-hoc and paired samples *t*-tests were then performed where appropriate. The mean ± standard deviation, lower and upper limits of the 95% confidence interval for mean differences (CI), and effect sizes (ES) are reported in text (Cohens *d* - small: 0 – 0.49; moderate: 0.5 - 0.79; large: > 0.8) (Cohen 1992). Pearson product-moment correlations (r) assessed the relationship between IMVF and power production (low: 0.3 – 0.5, moderate: 0.5 – 0.7, strong: > 0.7) (Mukaka 2012). Inter-individual variance ratio data violated the assumption of normality required for parametric tests (despite attempts to transform the data). Therefore, a non-parametric equivalent in the Wilcoxon signed-rank test (*T*) was used. Effect sizes were also reported for this test statistic (Cohens *r* - small: 0 – 0.3; moderate: 0.3 - 0.5; large: > 0.5) (Cohen 1992). Significance level for all parametric and non-parametric tests was set at $P \leq 0.05$.

4.3 Results

4.3.1 Reliability of knee extensor fatigue variables

Inter-day reliability of pre-exercise knee extensor fatigue measurements are reported in **Table 4.2**. No inter-day differences were observed between the two sessions for any variable (P > 0.05).

Table 4.2 Inter-day reliability of the pre-exercise knee extensor fatigue variables. Mean ± SE reported. TE = Typical error; ICC = Intra-class correlation co-efficient with lower and upper limits of the 95% confidence interval; CV = co-efficient of variation; IMVF = isometric maximal voluntary contraction; RT = resting twitch; VA = voluntary activation.

	Day 1	Day 2	TE	ICC	CV (%)	P
IMVF (N)	491 ± 57	488 ± 49	30 (20, 54)	0.98 (0.91, 0.99)	5 ± 1	0.8
RT (N)	136 ± 13	142 ± 13	13 (9, 23)	0.93 (0.75, 0.98)	8 ± 1	0.3
VA (%)	90 ± 2	91 ± 1	3 (2, 5)	0.69 (0.1, 0.92)	3 ± 1	0.4
EMG.M-wave^{-1}	0.056 ± 0.004	0.053 ± 0.004	0.008 (0.006, 0.012)	0.57 (0.15, 0.91)	12 ± 3	0.7
M-wave amplitude (mV)	9.5 ± 1.1	9.5 ± 1.0	2.0 (1.5, 3.0)	0.67 (0.31, 0.86)	10 ± 3	0.6
M-wave duration (ms)	4.9 ± 0.2	5.1 ± 0.3	0.4 (0.3, 0.6)	0.68 (0.34, 0.86)	8 ± 2	0.2

4.3.2 Pre-fatiguing bilateral knee extension exercise

After pre-fatiguing exercise, large reductions in IMVF were reported (488 ± 156 N to 221 ± 97 N, P ≤ 0.001, CI [-142 N, -398 N], ES = 1.4), ranging from -18% to -82%. Large reductions were reported for RT (142 ± 41 N to 77 ± 26 N, P ≤ 0.01, CI [-28 N, -90 N], ES = 1.3), VA (91 ± 4% to 67 ± 14%, P ≤ 0.01, CI [-10%, -36%], ES = 1.5) and EMG.M-wave^{-1} (0.053 ± 0.012 to 0.035 ± 0.016, P ≤ 0.01, CI [-0.008, -0.031], ES = 1.2), whereas a moderate increase was reported for M-wave duration (5.1 ± 0.8 ms to 5.6 ± 0.1 ms, P ≤ 0.01, CI [0.3 ms, 1.0 ms], ES = 0.7). No changes were reported for M-wave amplitude (P = 0.2). The reduction in IMVF, VA and EMG.M-wave^{-1} were greater than reported following the control 30-s cycling exercise (P ≤ 0.05), whereas no differences were seen for the reduction in RT (P = 0.1).

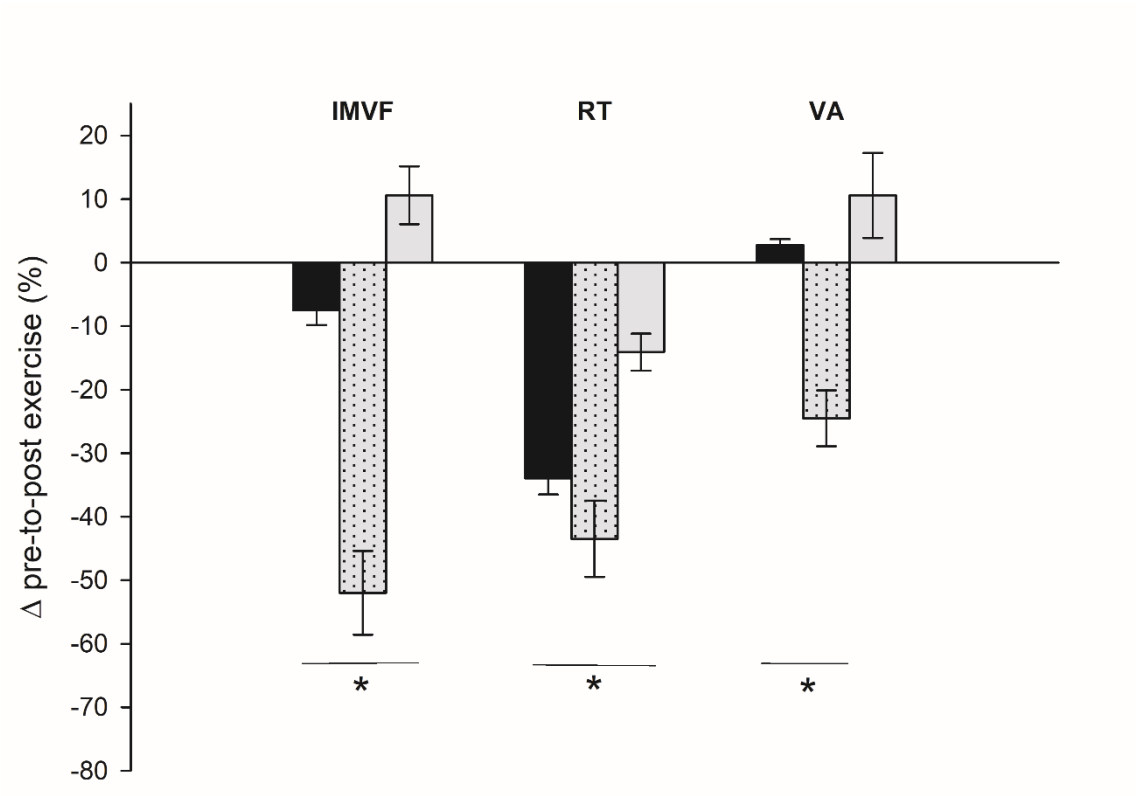

Figure 4.3 Pre-to-post exercise changes in knee extensor fatigue variables for the control cycling exercise (black), pre-fatiguing bilateral knee extension exercise (grey with dots) and cycling exercise performed following pre-fatiguing bilateral knee extension exercise (grey). Mean ± SE reported. IMVF = isometric maximal voluntary force; RT = resting twitch; VA = voluntary activation. * different than pre-exercise values (P ≤ 0.05).

4.3.3 Maximal cycling following pre-fatiguing bilateral knee extension exercise

4.3.3.1 Power production during the extension and flexion phases

During the extension phase, power production was lower following the pre-fatiguing knee extension exercise ($F_{1,19}$ = 57.6, P ≤ 0.001). The spread of the reductions ranged from -8% to -31% at the start (P ≤ 0.001, CI [-63 W, -127 W], ES = 0.6), and from -8% to -25% at the end (P ≤ 0.001, CI [-55 W, -98 W], ES = 0.8). A main interaction effect for cadence-specific power ($F_{1,19}$ = 7.1, P ≤ 0.05) revealed that the magnitude of the reduction was greatest at the start (**Figure 4.4 A**)

During the flexion phase, absolute power was lower following pre-fatiguing knee extension exercise ($F_{1,19}$ = 34.2, P ≤ 0.001) at both the start (P ≤ 0.001, CI [-21 W, -45 W], ES = 0.8) and end (P ≤ 0.01, CI [-3 W, -17 W], ES = 0.5). A main interaction effect for absolute power ($F_{1,19}$ = 14.0, P ≤ 0.001) and cadence-specific power ($F_{1,19}$ = 34.6, P ≤ 0.001) revealed that the magnitude of the reduction was greatest at the start (**Figure 4.4 B**).

Table 4.3 Power output and cadence during the extension and flexion phases of maximal cycling exercise. Mean ± SE reported.
* significantly different to control (P ≤ 0.05).
# significantly different to the start (P ≤ 0.05).

	Control		Bilateral Knee Extensor Fatigue	
Extension	*Start*	*End*	*Start*	*End*
Power (W)	619 ± 49	490 ± 38 #	524 ± 40 *	413 ± 30 *#
Power (%)	94 ± 2.3	56 ± 2.1 #	84 ± 2.2 *	48 ± 1.7 *#
Cadence (rpm)	68 ± 1	102 ± 2 #	64 ± 1 *	96 ± 2 *#
Flexion				
Power (W)	117 ± 15	5 ± 5 #	84 ± 9 *	-5 ± 7 *#
Power (%)	88 ± 2.7	8.3 ± 6.5 #	68 ± 6.6 *	1 ± 5.8 *#
Cadence (rpm)	68 ± 1	102 ± 2 #	64 ± 1 *	96 ± 2 *#

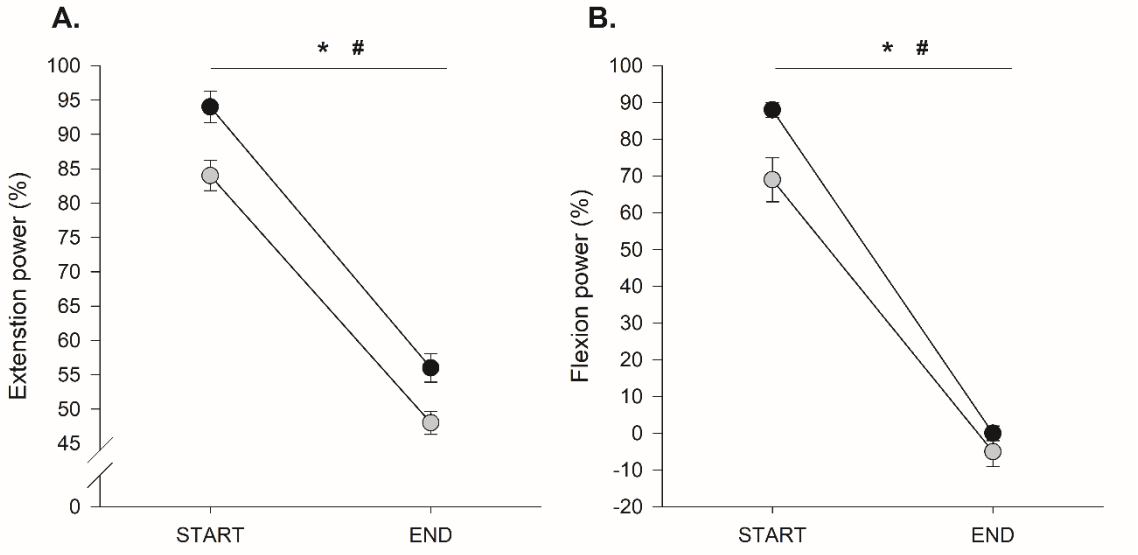

Figure 4.4 Cadence-specific extension power (A) and flexion power (B) during the control cycling exercise (black) and the cycling exercise performed following pre-fatiguing bilateral knee extension exercise (grey). Mean ± SE reported.
* Lower than the control (P ≤ 0.05).
# Lower than the start (P ≤ 0.05).

4.3.3.2 Association between extension power and knee extensor IMVF

Pre-exercise knee extensor IMVF was positively correlated to power production during the extension phase at the start of the control cycling exercise (r = 0.86, P ≤ 0.01), but not at the start of the cycling exercise performed following pre-fatiguing knee extension exercise (r = 0.01, P = 0.9) (**Figure 4.5**). Post-exercise knee extensor IMVF was positively correlated to power production during the extension phase at the end of

both the control cycling exercise (r = 0.82, P ≤ 0.01) and cycling exercise performed following pre-fatiguing knee extension exercise (r = 0.82, P ≤ 0.01).

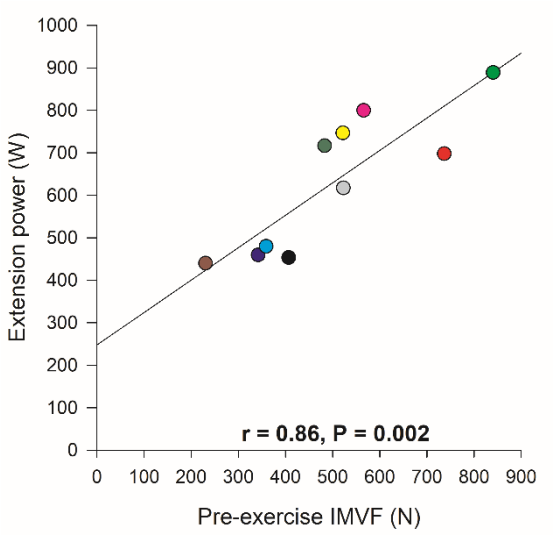

Figure 4.5 Inter-individual comparisons between pre-exercise knee extensor isometric maximal voluntary force (IMVF) and extension power measured at the start of the control cycling exercise.

No correlation was reported between the reduction in knee extensor IMVF following pre-fatiguing exercise (-52 ± 21%) and the reduction in power during the extension phase at the start of maximal cycling (-15 ± 8%) (r = 0.19, P = 0.6) (**Figure 4.6 A**). Similarly, no correlation was reported between the reduction in knee extensor IMVF after maximal cycling (-37 ± 10%) and the decrease in extension power at the end (-18 ± 5%) (r = -0.1, P = 0.77) (**Figure 4.6 B**).

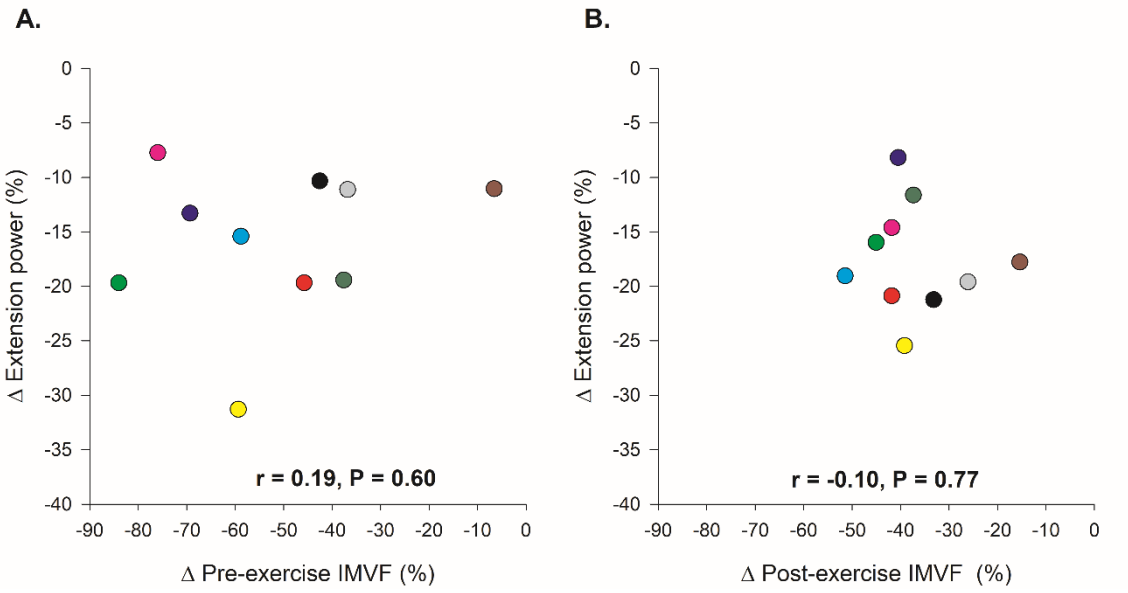

Figure 4.6 Intra-individual comparisons between the relative reduction in pre-exercise isometric maximal voluntary force (IMVF) and extension power at the start (A) and post-exercise IMVF and extension power at the end (B). Delta calculated between the two conditions.

4.3.3.3 Association between flexion power and knee extensor IMVF

Pre-exercise knee extensor IMVF was positively correlated to power production during the flexion phase at the start of the control cycling exercise (r = 0.77, P ≤ 0.01) (**Figure 4.7**), but not at the start of the cycling exercise performed following pre-fatiguing knee extension exercise (r = -0.03, P = 0.9). Post-exercise IMVF was not correlated to flexion power measured at the end of the control cycling exercise (r = 0.42, P = 0.23) or the cycling exercise performed following pre-fatiguing knee extension exercise (r = 0.44, P = 0.2).

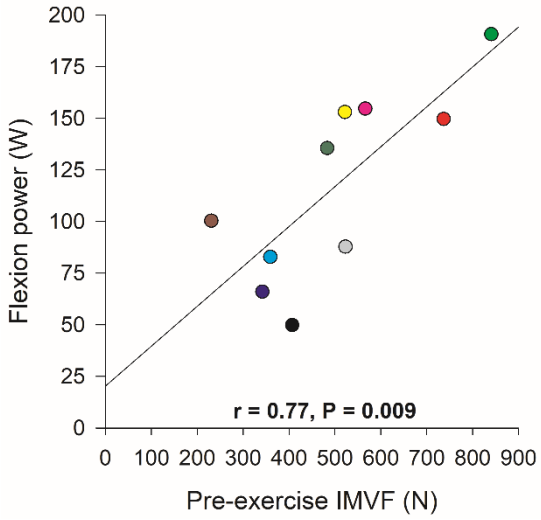

Figure 4.7 Inter-individual comparisons between pre-exercise knee extensor isometric maximal voluntary force (IMVF) and flexion power measured at the start of the control cycling exercise.

No correlation was reported between the reduction in knee extensor IMVF following pre-fatiguing exercise and the reduction in flexion power measured at the start of maximal cycling exercise (-25 ± 18%) (r = 0.16, P = 0.65). Likewise, no correlation was reported between the reduction in knee extensor IMVF after maximal cycling and the decrease in flexion power at the end (-6 ± 8%) (r = -0.46, P = 0.17).

4.3.3.4 Crank forces, EMG and co-activation

During the extension phase, all crank forces were reduced during maximal cycling performed following pre-fatiguing knee extension exercise (all P ≤ 0.01) (**Table 4.4** and **Figure 4.8**). Likewise, VAS EMG ($F_{1,19}$ = 45.5, P ≤ 0.001), GMAX EMG ($F_{1,8}$ = 15.5, P ≤ 0.01) and co-activation for all pairs was reduced (all P ≤ 0.01) (**Figure 4.9**). No difference between the exercises was reported for APF EMG ($F_{1,18}$ = 4.2, P = 0.054). A

main interaction effect for F_{TAN} ($F_{1,19}$ = 18.1, P ≤ 0.001), F_{RAD} ($F_{1,19}$ = 4.7, P ≤ 0.05), F_{TOT} ($F_{1,19}$ = 15.4, P ≤ 0.001) and VAS/APF ($F_{1,37}$ = 6.4, P ≤ 0.05) revealed that the magnitude of the reduction was greatest at the start of the cycling exercise.

During the flexion phase, all crank forces were reduced during maximal cycling performed following pre-fatiguing knee extension exercise (all P ≤ 0.01) (**Table 4.4** and **Figure 4.8**). Similarly, RF EMG ($F_{1,9}$ = 17.3, P ≤ 0.01), HAM EMG ($F_{1,9}$ = 37.9, P ≤ 0.001) and TA EMG ($F_{1,9}$ = 15.2, P ≤ 0.01) were all reduced (**Figure 4.10**). A main interaction effect for F_{TAN} ($F_{1,19}$ = 9.1, P ≤ 0.01) and F_{RAD} ($F_{1,19}$ = 8.7, P ≤ 0.01) revealed that the magnitude of the reduction was greatest at the start of the cycling exercise.

Table 4.4 Crank and EMG data during the extension and flexion phases of maximal cycling exercise. Mean ± SE reported. F_{TAN} = tangential crank force; F_{RAD} = radial crank force; F_{TOT} = total crank forces; VAS = *vastii* EMG amplitude; GMAX = *gluteus maximus* EMG amplitude; APF = ankle plantar flexor EMG amplitude; RF = *rectus femoris* EMG amplitude; HAM = hamstring EMG amplitude; TA = *tibialis anterior* EMG amplitude; VAS/HAM = *vastii* and hamstring co-activation index; VAS/APF = *vastii* and ankle plantar flexor co-activation index; GMAX/RF = *gluteus maximus* and *rectus femoris* co-activation index; GMAX/APF = *gluteus maximus* and ankle plantar flexor co-activation index.
* significantly different to control (P ≤ 0.05).
# significantly different to the start (P ≤ 0.05).

	Control		**Bilateral Knee Extensor Fatigue**	
Extension	*Start*	*End*	*Start*	*End*
F_{TAN} (N)	880 ± 42	483 ± 28 #	796 ± 37 *	455 ± 24 *#
F_{RAD} (N)	533 ± 43	158 ± 26 #	459 ± 35 *	142 ± 21 *#
F_{TOT} (N)	936 ± 40	522 ± 30 #	831 ± 36 *	481 ± 25 *#
VAS (%)	90 ± 2	83 ± 3	75 ± 2 *	68 ± 4 *
GMAX (%)	89 ± 2	76 ± 6	77 ± 6 *	60 ± 5 *#
APF (%)	89 ± 2	57 ± 4 #	84 ± 3	51 ± 4 #
VAS/HAM (a.u.)	99 ± 3	82 ± 6 #	81 ± 4 *	65 ± 4 *#
VAS/APF (a.u.)	125 ± 3	73 ± 5 #	106 ± 4 *	62 ± 4 *#
GMAX/RF (a.u.)	115 ± 4	84 ± 10 #	93 ± 4 *	69 ± 10 *#
GMAX/APF (a.u.)	134 ± 4	74 ± 6 #	119 ± 5 *	62 ± 5 *#
Flexion				
F_{TAN} (N)	210 ± 15	74 ± 5 #	164 ± 10 *	56 ± 5 *#
F_{RAD} (N)	284 ± 30	64 ± 16 #	224 ± 19 *	39 ± 10 *#
F_{TOT} (N)	379 ± 26	321 ± 20 #	334 ± 18 *	265 ± 16 *#
RF (%)	93 ± 1	71 ± 7 #	82 ± 5 *	58 ± 7 *#
HAM (%)	83 ± 3	62 ± 8 #	68 ± 4 *	48 ± 5 *#
TA (%)	87 ± 3	73 ± 4 *	58 ± 5 #	47 ± 6 *#

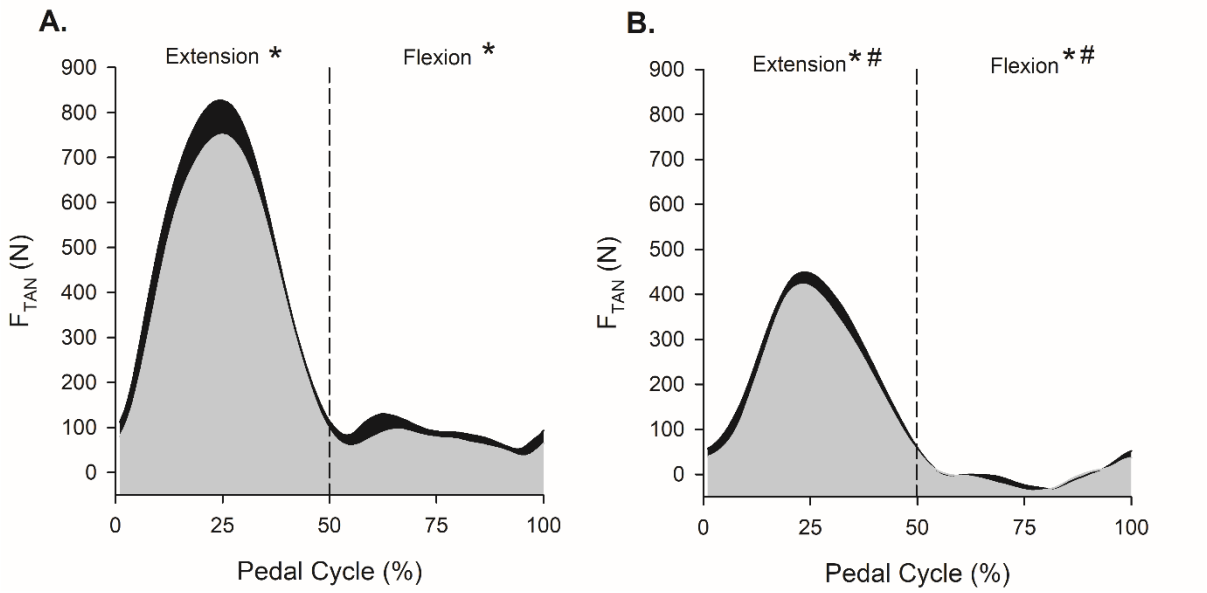

Figure 4.8 Tangential crank force (F_{TAN}) profiles of the left crank for the start (A) and end (B) periods of maximal cycling exercise. The control cycling exercise is in black and the cycling exercise performed following pre-fatiguing bilateral knee extension exercise is in grey.
* significantly different than control ($P \leq 0.05$).
# significantly different than the start ($P \leq 0.05$).

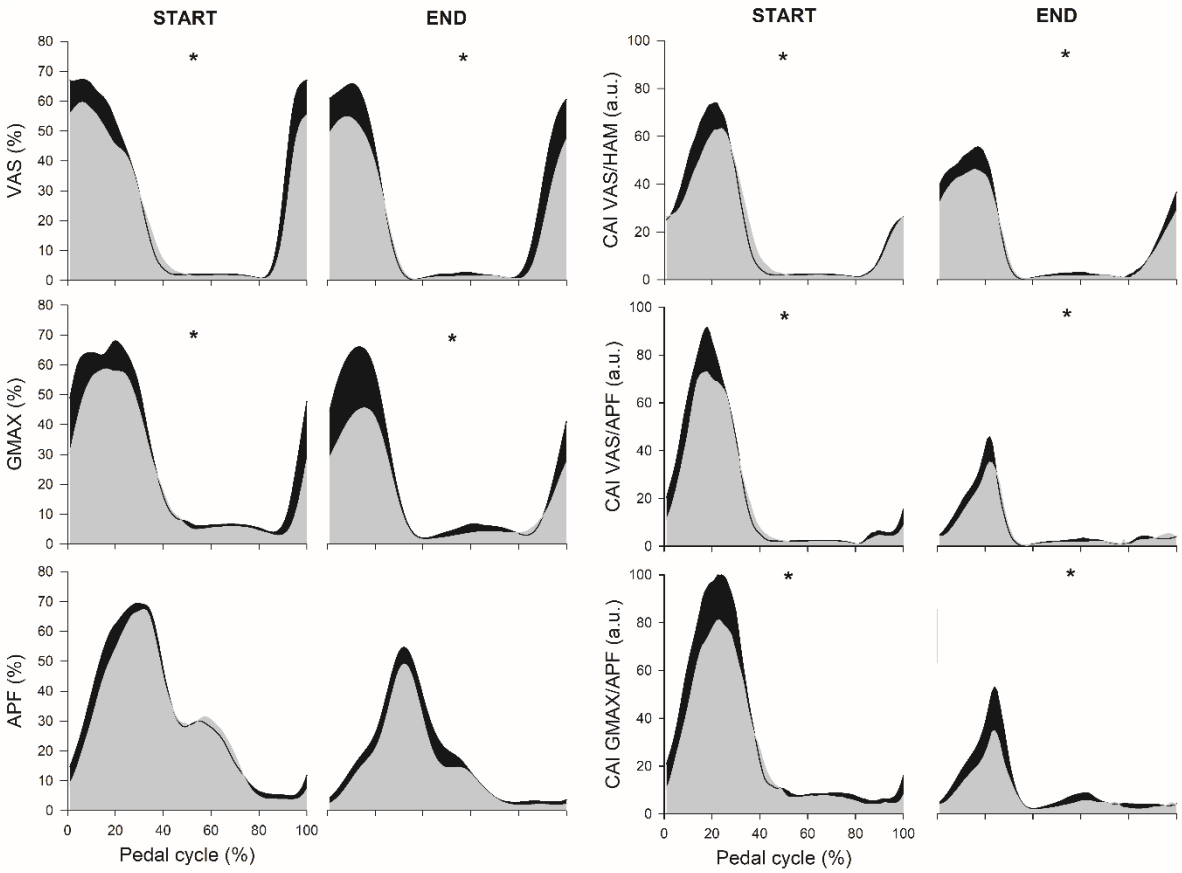

Figure 4.9 Average EMG (left) and co-activation (right) profiles for muscles/pairs primarily involved in power production during the extension phase. The control cycling exercise is in black and the cycling exercise performed following pre-fatiguing bilateral knee extension exercise is in grey. VAS = *vastii*; GMAX = *gluteus maximus*; APF = ankle plantar flexors; HAM = hamstrings.
* significantly different than control ($P \leq 0.05$).

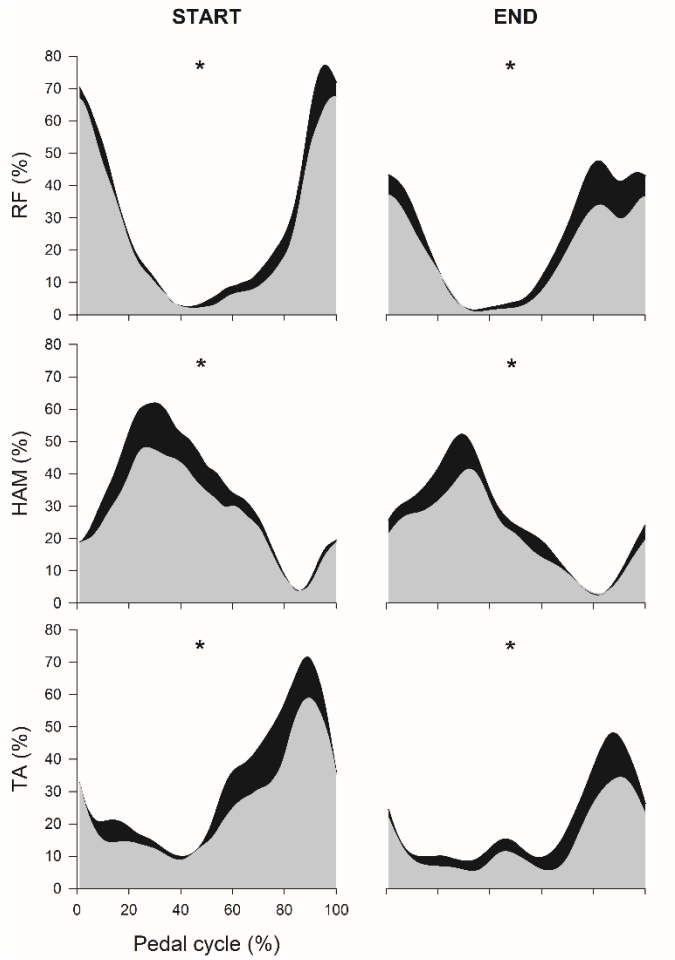

Figure 4.10 Average EMG profiles for muscles primarily involved in power production during the flexion phase. The control cycling exercise is in black and the cycling exercise performed following pre-fatiguing bilateral knee extension exercise is in grey. RF = *rectus femoris*; HAM = hamstrings; TA = *tibialis anterior*.
* significantly different than control (P ≤ 0.05).

4.3.3.5 Inter-individual variability in crank force and EMG profiles

During maximal cycling performed following pre-fatiguing knee extension exercise, inter-individual variability increased at the start for F_{TAN} (*T* = 26, P ≤ 0.01, ES = 0.6), F_{RAD} (*T* = 28, P ≤ 0.01, ES = 0.7), F_{TOT} (*T* = 32, P ≤ 0.01, ES = 0.6), VAS EMG (*T* = 26, P ≤ 0.01, ES = 0.7), HAM EMG (*T* = 0, P ≤ 0.01, ES = 0.9) and TA EMG (*T* = 8, P ≤ 0.05, ES = 0.6) (**Figure 4.11 A**). At the end of maximal cycling performed following pre-fatiguing knee extension exercise, inter-individual variability increased for HAM EMG (*T* = 0, P ≤ 0.01, ES = 0.9), RF EMG (*T* = 5, P ≤ 0.05, ES = 0.7) and TA EMG (*T* = 8, P ≤ 0.05, ES = 0.6) (**Figure 4.11 B**).

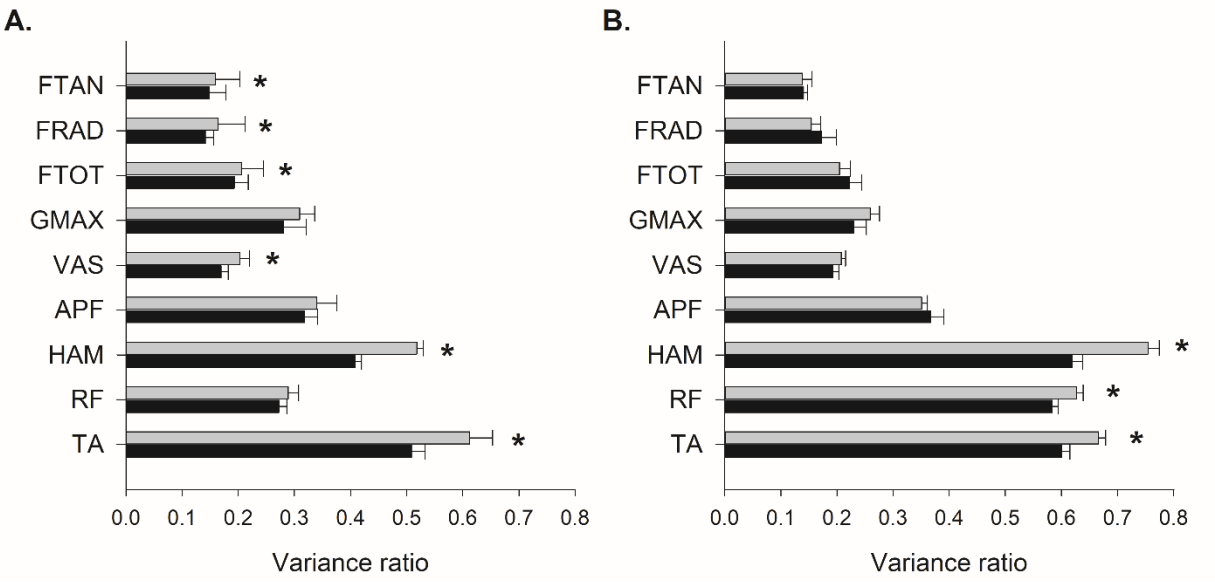

Figure 4.11 Inter-individual variance ratios for crank forces and lower-limb muscles during maximal cycling exercise at the start (A) and end (B). The control cycling exercise is in black and the cycling exercise performed following pre-fatiguing bilateral knee extension exercise is in grey. Mean ± SE reported. FTAN = tangential crank force; FRAD = tangential radial force; FTOT = total crank force; GMAX = *gluteus maximus*; VAS = *vastii*; APF = ankle plantar flexors; HAM = hamstrings; RF = *rectus femoris*; TA = *tibialis anterior*.
* significantly different than control (P ≤ 0.05).

4.4 Discussion

4.4.1 Summary of main findings

The first aim of this study was to investigate if the level of fatigue induced by a pre-fatiguing knee extension exercise determines the level of reduction in power output during the extension and flexion phases of maximal cycling exercise. No association was reported between reductions in knee extensor IMVF following pre-fatiguing exercise (range = -18% to -82%) and reductions in extension power at the start of maximal cycling (range = -8% to -31%) (r = 0.19). Similarly, no correlation was reported between IMVF reduction following pre-fatiguing exercise and the reduction in power production during the flexion phase at the start (range = +11% to -39%, r = 0.16). The second aim was to investigate how motor command during maximal cycling is affected by pre-fatigue of the knee extensors. Following pre-fatiguing exercise, VA decreased by -25 ± 14%. During maximal cycling and for the primary extension phase muscles, large reductions were observed for VAS EMG (-15%) GMAX EMG (-12%) and VAS/APF co-activation (-15%). For the primary flexion phase muscles, large reductions were observed for HAM EMG (-15%), TA EMG (-15%) and RF EMG (-11%). Inter-individual variability increased for all crank forces and EMG activity for VAS, RF, HAM and TA. Overall, the results indicate that knee extensor fatigue developed during pre-fatiguing exercise does not determine

reductions in power output during maximal cycling exercise. Alterations in motor command likely explain this result, evidenced via large reductions in EMG of local and non-local muscles, and increased inter-individual variability in crank force and muscle activation patterns.

4.4.2 Association between knee extensor fatigue and power production during maximal cycling exercise

4.4.2.1 Extension phase

The strength of the positive correlation between knee extensor IMVF and extension power calculated at the start of the control cycling exercise (r = 0.86) (**Figure 4.5**), was stronger than previously reported for fatigue-free power calculated over a full crank cycle (r = 0.71 – 0.75) (Driss et al. 2002; Kordi et al. 2017). It was also shown that knee extensor IMVF was strongly correlated to extension power production at the end of both cycling exercises (r = 0.82). Thus, these results indicate that participants adopted similar movement strategies to generate extension power during fatigue-free maximal cycling and when fatigue was likely to develop in the locomotor muscles. This strategy was likely associated to the maximal force-generating capacity of the knee extensors, as the knee extensors are shortening and activated maximally during the extension phase to generate large tangential crank forces (Van Ingen Schenau et al. 1992; Raasch et al. 1997). Indeed, on observation of the crank force and VAS EMG profiles (**Figure 4.8** and **Figure 4.9**), peak F_{TAN} occurred at a similar period of the extension phase as peak activation of *vastii* muscles when accounting for a standardized electromechanical delay of 100 ms (i.e. ~11% of crank cycle) (Samozino et al. 2007). Moreover, only minor pre-to-post sprint reductions in knee extensor IMVF were reported during the control cycling exercise (range = 0% to -16%), and a partial recovery in IMVF was reported during maximal cycling performed following pre-fatiguing exercise (range = -6% to +33%) (**Figure 4.3**). The partial recovery in knee extensor IMVF during maximal cycling performed after pre-fatiguing exercise, likely explains why reductions in power output and peak crank forces during the extension phase were greater at the start compared to the end.

No correlation was observed between inter-individual differences in knee extensor IMVF and power production during the extension phase at the start of maximal cycling exercise performed after pre-fatiguing knee extension exercise (r = 0.01) (**Figure 4.5**). This finding illustrates that individuals generating higher knee extensor forces following pre-fatiguing exercise did not generate higher power outputs during the

extension phase. Similarly, the intra-individual comparisons revealed no correlation between the reduction in knee extensor IMVF following pre-fatiguing knee extension exercise and the reduction in extension power at the start and end of maximal cycling exercise (r = 0.19 and -0.10, respectively) (**Figure 4.6**). This finding illustrates that participants who experienced the greatest reduction in knee extensor force following pre-fatiguing exercise did not lose the most amount of power during the extension phase. Thus, it is likely that severe peripheral and central fatigue developed during pre-fatiguing knee extension exercise led participants to use different movement strategies to generate power during the extension phase. Peripheral fatigue was characterized by the large spread of the reduction in RT (-8% to -76%) and increased M-wave duration (-5% to + 37%), suggesting impairment in Ca^{2+} handling/sensitivity (Westerblad et al. 2002; Dahlstedt et al. 2001; Allen et al. 2008) and potential slowing of the sarcolemma action potential (Fuglevand et al. 1993). Central fatigue was characterized by the large spread of the reduction in VA (-6% to -49%), indicating an impairment in the recruitment/discharge frequency of the motor units, likely arising from supraspinal or spinal mechanisms (Gandevia 2001; Taylor and Gandevia 2001). This heterogeneity in the fatigue responses following pre-fatiguing exercise and the lack of correlation between knee extensor IMVF and power production during the extension phase, may have evolved from inter-individual differences in fibre type (Hamada et al. 2003) and exacerbated by sex differences (Wust et al. 2008). The large spread in P_{MAX} from 10.4 $W.kg^{-1}$ to 15.4 $W.kg^{-1}$ supports large inter-individual differences in fibre type (Cormie et al. 2011). Fatigue development and recovery time is largely influenced by fibre type composition, with force decreasing and recovering at a faster rate in fast type II muscle fibres, presumably due to a larger density of Na^+/K^+ channels, greater number of SERCA pumps and higher metabolic perturbation (Allen et al. 2008; Westerblad et al. 2010). Thus, potential differences in fibre type between the participants would have influenced the rate of which knee extensor fatigue recovered during the 1-min time delay between IMVF and power measurements, influencing the spread of the reductions in the fatigue variables and the correlations between knee extensor IMVF and power output. In particular, peripheral fatigue responses (e.g. RT and M-wave) have been shown to recover within ~1-min post high-intensity knee extension exercise (Froyd et al. 2013; Cheng and Rice 2005), presumably accelerating IMVF recovery.

At the end of maximal cycling exercise, the lack of association between reductions in knee extensor IMVF and extension power likely evolved from intra-individual differences in the level of fatigue developed in GMAX and the severity of reductions in co-activation between muscle pairs (**Table 4.4**). Indeed, 30-s of maximal

cycling exercise has been shown to result in large reductions in hip-extension joint power (Martin and Brown 2009) and large variability in the reductions in co-activation between mono-articular and bi-articular muscle pairs has also been shown (O'Bryan et al. 2014), presumably exacerbating reductions in power production during the extension phase.

4.4.2.2 Flexion phase

The strong positive correlation between inter-individual differences in knee extensor IMVF and power output during the flexion phase at the start of the control cycling exercise (r = 0.77) (**Figure 4.7**), revealed that the force-generating capacity of the knee extensors was a good predictor of maximal flexion power in fatigue-free conditions. This correlation may be explained by the contribution of RF to both knee extensor IMVF (Maffiuletti and Lepers 2003) and flexion power (Van Ingen Schenau 1989; Zajac et al. 2002). Alternatively, maximal knee extensor force may simply be a good indicator of overall lower-limb power, as previously reported during other exercises (Willigenburg et al. 2014; Tsiokanos et al. 2002). In particular, the force capacity of the knee extensors is likely to be associated to the force capacity of the knee flexors (Aagaard et al. 1998), as the knee flexors counteract knee extension forces and prevent knee hyperextension during common lower-limb exercises such as running, jumping and kicking (Willigenburg et al. 2014). Such a relationship may explain the correlation between knee extensor IMVF and flexion power, as the knee flexors generate most of the tangential crank forces during the flexion phase (Raasch et al. 1997; Zajac et al. 2002).

Contrary to what was reported during fatigue-free maximal cycling, knee extensor IMVF was not correlated to power production during the flexion phase at the end of the control cycling exercise (r = 0.42) or at the start or end of cycling exercise performed following pre-fatiguing exercise (r = -0.03 and 0.44) (**Figure 4.7**). Likewise, reductions in knee extensor IMVF following pre-fatiguing exercise were not correlated to the reduction in flexion power during the subsequent maximal cycling exercise (start: r = 0.16; end: r = -0.46) (**Error! Reference source not found.**). These results indicate large inter-individual and intra-individual variability in the effects of knee extensor and locomotor fatigue on power production during the flexion phase. This finding supports previous suggestions that the movement strategy for power production during the flexion phase is as individualized as fingerprints (Kautz et al. 1991; Hug et al. 2008). Alternatively, RF fatigue was likely following pre-fatiguing exercise (Perry-Rana et al. 2002) and inter-individual differences in RF fibre type and unequal rates of recovery may have

contributed to the lack of correlations reported, as previously discussed for VAS muscles during the extension phase.

4.4.3 Effect of knee extensor fatigue on motor command

Increased variability in the movement control strategy for power production at the start of maximal cycling performed following pre-fatiguing knee extension exercise, was supported by increased inter-individual variability in the application of the crank forces (**Figure 4.11**). During the extension phase, this likely evolved from increased inter-individual variability in VAS EMG. This result supports the suggestion that some participants altered the movement strategy for power production during the extension phase, thereby increasing inter-individual variability in the demands for the knee extensors to generate effective crank forces. Alternatively, increased inter-individual variability in VAS EMG may have evolved from the large spread of the reduction in VA following pre-fatiguing exercise, thereby leading to large differences in the capacity to maximise the discharge number and rate of *vastii* motor units (Gandevia 2001). It is also possible that the large spread in the change in GMAX EMG (range = -26% to +20%) and co-activation for all muscle pairs (especially VAS/APF, range = -20% to +20%) influenced the intra-individual correlations between knee extensor IMVF and extension power. Unequal reductions in GMAX EMG within the participants (n = 8), may have evolved from differences in the level of knee extensor fatigue and associated group III and IV afferent feedback to the GMAX motoneuron pool. Indeed, the inhibitory influence of group III and IV afferent feedback is not specific to the fatigued muscles involved in a locomotor task such as cycling (Sidhu et al. 2014), and inhibition of GMAX is likely as it is part of the same muscle synergy as VAS muscles (Sacco et al. 1997; Ciubotariu et al. 2004; Hug et al. 2010; Raasch and Zajac 1999). The reduction in GMAX EMG may indicate non-local fatigue development in this muscle due to high levels of central fatigue in the knee extensors (Halperin et al. 2015). Unequal reductions in VAS/APF co-activation (n = 8) revealed that the overlap of individual EMG bursts was reduced for some participants more than others. This change in co-activation likely influenced the ability of the ankle plantar flexors to effectively transfer knee extension power to the crank during the first part of the extension phase (crank angle ~0-90°) (Zajac et al. 2002), thereby leading to suboptimal inter-muscular coordination and increasing inter-individual variability in the effective crank forces.

Evidence for an alteration in the movement strategy during the flexion phase was supported by increased inter-individual variability in HAM, TA and RF EMG (**Figure**

4.11). These muscles have previously been shown to exhibit large inter-individual variability due to their role in transferring power amongst the segments and orientating crank forces (Hug et al. 2004; Hug et al. 2008; Hug et al. 2010; Ryan and Gregor 1992). Indeed, the knee extensors generate the most amount of work during maximal cycling (Raasch et al. 1997), and therefore inter-individual differences in knee extensor fatigue are likely to lead to unequal requirements to distribute and transfer leg energy to the crank. It is also possible that increased inter-individual variability in activation patterns of flexion muscles occurred due to some participants focusing on pulling up on the pedals during the flexion phase. HAM muscles have the capacity to generate large tangential crank forces during the early flexion phase (Zajac et al. 2002; Elmer et al. 2011), and a similar strategy has previously been reported during submaximal cycling and in the presence of unilateral knee extensor fatigue (Brochner Nielsen et al. 2016). Due to the bilateral nature of the cycling exercise and the mechanical coupling of the cranks, this strategy would also assist in accelerating the contralateral crank during the extension phase. Hence, evidence for large inter-individual variability and a change to the movement strategy during the flexion phase, may have influenced the correlations between knee extensor IMVF and power production during the flexion and extension phases. Intra-individual correlations between knee extensor IMVF and flexion power were also likely influenced by the large spread in the reduction in HAM EMG (range = -0.5% to -34%), TA EMG (range = +1% to -49%) and RF EMG (range = -2% to -29%). As the contractile properties of HAM and TA muscles were presumably unchanged following pre-fatiguing exercise, it is possible that intra-individual differences in knee extensor fatigue and group III and IV afferent feedback led to variable degrees of non-local fatigue in these muscles (Sidhu et al. 2014; Halperin et al. 2015). At the end of the maximal cycling exercise, large inter-individual variability in the activation patterns of HAM, RF and TA muscles occurred without increased variability in the application of the crank forces. This finding supports previous results reported during submaximal cycling exercise (Hug et al. 2008) and illustrates the redundancy of the motor system during fatiguing maximal cycling exercise.

4.4.4 Limitations

The associations between knee extensor IMVF and power production during maximal cycling may have been blurred by inter-individual differences in the rate of fatigue recovery during the 1-min time delay between fatigue assessment and the start of maximal cycling (Froyd et al. 2013; Hamada et al. 2003; Cheng and Rice 2005). This time delay was unavoidable due to the requirement to transfer participants from the pre-

fatiguing exercise equipment to the cycle ergometer. From an anatomical perspective, it is also possible that the stimulating electrode configuration (i.e. anode in the gluteal fold) may have evoked some co-activation in the antagonist hamstring muscles and influenced the knee extensor twitch force response.

4.5 Conclusion

The amount of knee extensor fatigue developed during isolated pre-fatiguing exercise does not determine the reduction in power output during the extension or flexion phases of maximal cycling exercise. This is likely due to changes in motor command, including increased variability in the movement control strategy and non-local fatigue development in lower-limb muscle groups. More research is required to elucidate the movement strategies that influence the relationship between knee extensor fatigue and crank power during maximal cycling, and to determine the rate of recovery between fatigue and crank power measurements.

Author contributions

SJ O'bryan was responsible for conception and design of experiments, data collection and analysis, preparation of figures, drafting the chapter and revising the chapter for important intellectual content. **JL Taylor** was responsible for reviewing the chapter and providing feedback. **DM Rouffet** was responsible for conception and design of experiments, data collection and analysis, preparation of figures and reviewing the chapter and providing feedback. **R Bourke** assisted with data collection.

Chapter 5 FATIGUE DEVELOPMENT AND SHORT-TERM RECOVERY DURING MAXIMAL KNEE EXTENSION AND LEG EXTENSION EXERCISE

5.1 Introduction

As shown in study two, variability in motor command is increased following pre-fatiguing exercises targeting the knee extensors. In line with previous findings (Brochner Nielsen et al. 2016), this was primarily evident during the flexion phase and suggests an alteration to the movement strategy to attenuate reductions in maximal power output. Therefore, reducing the complexity of the cycling movement to a unilateral leg extension exercise would potentially reduce the degree of freedom and decrease variability in motor command. In this way, it is likely that knee extensor fatigue would determine the reduction in power output during the extension phase, as any alteration to the movement control strategy would be limited.

Vastii and *rectus femoris* knee extensor muscles are activated similarly during maximal isolated and cycling exercises (Dorel et al. 2012; Rouffet and Hautier 2008), however the severity and aetiology of fatigue developed in the knee extensors when these exercises are prolonged is vastly different (Hureau et al. 2016; Babault et al. 2006; Fernandez del Olmo et al. 2013; Tomazin et al. 2016; Morel et al. 2014). This is likely due to numerous task-specific differences between the exercises such as the number of completed contractions (Babault et al. 2006; Tomas et al. 2010), contraction mode (e.g. isometric vs. concentric) (Babault et al. 2006; Morel et al. 2014), muscle shortening velocity (Babault et al. 2006; Morel et al. 2014; Gardner et al. 2009; Mathiassen 1989), muscle length/range of motion (Fitch and McComas 1985; Arendt-Nielsen et al. 1992) and size of the active muscle mass (Matkowski et al. 2011; Rossman et al. 2014). Babault et al. (2006) revealed that increasing the number of maximal concentric knee extensions from 30 to 60 to 90, exacerbated reductions in maximal torque and voluntary activation, but did not alter the reduction in resting twitch. Furthermore, Morel et al. (2014) illustrated that increasing joint angular velocity from 30°.s^{-1} - 240°.s^{-1} exacerbated reductions in isometric knee extensor force and resting twitch, but attenuated reductions in voluntary activation. Compared to the results from study one and two, obtained following 30-s maximal cycling exercise and for a similar number of contractions (~60) (Babault et al. 2006) and knee angular velocity (~300°.s^{-1}) (Froyd et al. 2013; McDaniel et al. 2014), isolated exercises seem to induce a similar reduction in resting twitch (-40% vs. -35%) but a greater reduction in voluntary activation (-15% vs. +3%). Thus, the greater reduction in knee extensor IMVF reported by Babault et al. (2006) following

isolated knee extension exercise (-52%) compared to maximal cycling in study one and two (-8 to -13%), could be due to task-specific differences in central fatigue development. Higher central fatigue during isolated exercise may occur due to the smaller active muscle mass, which may increase the local metabolic perturbation and exacerbate group III and IV inhibitory feedback (Rossman et al. 2014), decreasing the capacity to maximise the discharge of knee extensor motor units (Matkowski et al. 2011).

The typical time delay for fatigue assessment following maximal cycling exercise ranges between 40-s to 5-min (Billaut et al. 2013; Fernandez del Olmo et al. 2013; Girard et al. 2013; Hureau et al. 2014; Pearcey et al. 2014; Tomazin et al. 2016). During this time, considerable short-term recovery in the force-generating capacity of the knee extensors is likely due to rapid restoration of harmful metabolites known to impede maximal force production (e.g. K+, Pi) (Allen et al. 2008; Jones 1996; Cairns and Dulhunty 1995; Harris et al. 1976; Sahlin and Ren 1989). Accordingly, results obtained from isolated exercises where the time delay can be avoided, are commonly used to estimate the short-term recovery following cycling exercise. Froyd et al. (2013) revealed that knee extensor IMVF and resting twitch force (high and low frequency) partially recover within ~1 to 2-min following ~6-min of high-intensity knee extension/flexion exercise ($300°.s^{-1}$). Cheng and Rice (2005) showed a similar time-course of recovery for knee extensor IMVF following maximal isotonic knee extensions (~40 s between $320°.s^{-1}$ and $200°.s^{-1}$) and a delayed depression in VA from 1.5-min to 10-min post-exercise. Thus, measurements of knee extensor isometric force and peripheral fatigue following cycling exercise may be inaccurate if the time delay exceeds 1-min, whereas reductions in central fatigue are greatest between 1.5-min and 10-min post-exercise. However, these results may not accurately reflect the rate of recovery that can be expected following cycling exercise, due to the task-specific differences previously described (Carroll et al. 2017). Therefore, it currently remains unknown what will be the longest possible time delay post-exercise that enables an accurate description of the mechanisms that characterize fatigue in the knee extensors during maximal cycling.

Electrical stimulation of the femoral nerve during exercise has been employed to assess continuous changes in central and peripheral fatigue responses during isometric (Rodriguez-Falces et al. 2013; Kennedy et al. 2015; Gruet et al. 2014; Kennedy et al. 2016) and concentric knee extensions (Babault et al. 2006). Although harder to employ, a small number of studies have utilised this technique during cycling exercise to assess continuous changes in knee extensor H-reflex (Larsen and Voigt 2006) and M-wave characteristics (Sidhu et al. 2012; Stewart et al. 2007). Stewart et al. (2007) revealed

that M-wave amplitude decreased after 60-min of submaximal cycling at 60% $\dot{V}_{O2Peak}$, whereas M-wave duration remained unchanged. This may be interpreted as a reduction in membrane excitability but maintenance of muscle fibre conduction velocity (Millet et al. 2011; Karelis et al. 2004; Lepers et al. 2002; Rodriguez-Falces et al. 2015). This method can also be used to indirectly investigate changes in the output from knee extensor motoneurons, which may be achieved by normalising the voluntary EMG_{RMS} to maximal M-wave amplitude (EMG.M-wave^{-1}) (Millet et al. 2011; Baudry et al. 2007). Currently, electrical stimulation of the femoral nerve during maximal cycling exercise has not been used to assess continuous changes in M-wave and EMG.M-wave^{-1} responses. This method is likely to provide a more accurate description of the potential central and peripheral mechanisms that influence the ability to generate power during maximal cycling, as it is not affected by time delay in measurement.

The first aim of this study was to compare the rate of fatigue occurrence in the knee extensors between an isolated knee extension exercise and a modified cycling exercise consisting of the leg extension phase only. The second aim was to investigate any differences in knee extensor fatigue measured post-exercise and the maximum time delays for which fatigue responses could be accurately assessed. It was hypothesized that individuals displaying larger torque reductions during knee extension exercise would also display larger torque reductions during leg extension exercise. It was also hypothesized that force and peripheral fatigue responses would need to be assessed within less than 1-min post-exercise, whereas the reduction in central fatigue responses would take longer to develop.

5.2 Methods

5.2.1 Participants and ethics

Sample size calculations were performed using G*Power version 3.0.10 software (Faul et al. 2007) using an alpha level set at 0.05 and a probability of avoiding a type II error set at 0.8. Using a repeated-measures statistical test and a large effect size of 0.65 (based off the change in knee extensor isometric force following sixty maximal knee extensions in Chapter 4) it was calculated that fourteen participants were required for the study. However, sixteen (11 male and 5 female) physically active volunteers accustomed to regular maximal exercise completed the study (age: 27 ± 1 years; height: 178 ± 3 cm; mass: 75 ± 3 kg). Prior to any testing, each participant completed a risk assessment questionnaire to deem them free from any existing cardiovascular, musculoskeletal or neuromuscular disorders. Written informed consent was obtained

from each participant, and the study was approved by Victoria University's Human Research Ethics Committee (HRE-15224) in accordance with the standards set by the Declaration of Helsinki.

5.2.2 Data acquisition

5.2.2.1 Knee extension exercise

Knee extension exercise was performed on a Cybex isokinetic dynamometer (Humac NORM, Canada). The dynamometer calculated hip and knee joint angles in reference to each participants' anatomical 0° (i.e. full extension). Participants sat in the dynamometer chair with straps across the thorax and pelvis, with hip angle maintained at 100° flexion. The axis of rotation of the knee joint was estimated from the lateral epicondyle of the femur and aligned with the axis of rotation of the dynamometer arm. A standardized lever arm was attached to the dynamometer, which provided contact with the distal aspect of the left tibia. Torque (N·m), joint angle (°) and angular velocity (°.s^{-1}) were continuously recorded by the dynamometer software at a sampling frequency of 100 Hz and stored for later analysis.

5.2.2.2 Leg extension exercise

Leg extension exercise was performed on a Lode® cycle ergometer fitted with a pedal force measurement system (Excalibur Sport, The Netherlands) and calibrated per manufacturer's guidelines prior to each session. Tangential crank torque applied to the left crank was continuously recorded at a sampling frequency of 5 Hz. The left leg was fixed to the left pedal via a cleat/pedal arrangement (Shimano SPD SL cleat with no float), whilst the right foot rested passively on the right pedal. This eliminated the capacity for participants to 'pull up' on the right pedal during the upstroke phase. Seat height was manipulated to permit a minimum knee angle of ~25-35° (0° = full extension) (Peveler et al. 2007; Bini et al. 2012). The ergometer was set in isokinetic mode with cadence fixed at 30 rpm.

5.2.2.3 Fatigue testing and electrical stimulation

For fatigue testing, participants were seated in the isokinetic dynamometer used for knee extension exercise, with hip and knee angle set at 100° and 90° flexion. The left ankle was securely attached to a force transducer (AMS-1 S Type, AWE, Ingleburn, Australia) that was fixed to the base of the dynamometer via a custom-built steel frame. A padded strap fixed immediately superior to the malleoli, clipped onto a steel rod that

threaded into the force transducer. This created a non-compliant connection between the left ankle and force transducer. The frame was built with multiple fixation heights to accommodate for differences in leg length between participants and to maintain a horizontal displacement of knee extensor forces. Participants were instructed to remain as still as possible with their arms placed across their thorax to prevent postural effects on force and M-wave responses (Rochette et al. 2003; Zehr 2002). The raw signal from the force transducer was amplified (gain = 500) and sampled at 3000 Hz within a channel of the EMG system (see section 5.2.2.4), to permit synchronization with EMG signals and the electrical stimulation artefact. The raw signal (mV) was calibrated with known masses and transformed into a force signal (N) via linear regression.

Electrical stimulation (ES) of the left femoral nerve was delivered via a constant-current electrical stimulator (model DS7AH, Digitimer, Welwyn Garden City, UK) and a custom-built pulse frequency generator. Voltage was set to maximum (400 V) and pulse duration to 1-ms. The electrical stimulation artefact was recorded as an 8-mV pulse in a channel of the EMG system (see section 5.2.2.4). A 20-mm diameter hand held cathode and a 90-mm x 50-mm self-adhesive rectangular anode (placed midway between the superior aspect of iliac crest and the greater trochanter of the femur) was used to probe the femoral triangle until the greatest twitch and M-wave response was elicited at 40 mA. This area was then marked with indelible ink. The hand-held cathode was then replaced with a 20-mm diameter custom made steel dome cathode. This was fixed over the optimal stimulation site with a large Velcro strap that wrapped around the upper thigh and waist. A stimulus-response curve was then constructed via delivering 1 Hz stimulations at 10 mA increments from 50 mA, until a plateau was observed in the twitch and M-wave response. Supramaximal current intensity was set at 150% of plateau intensity (Kennedy et al. 2015).

During knee extension and leg extension exercise, electrical stimulation of the femoral nerve was administered at the same knee joint angle (~90° flexion), which was verified by a mechanical goniometer (see section 5.2.2.4) This attempted to control for the number of active motor units recorded under the detection surface of the EMG electrodes, and to permit a valid comparison between the exercises (Frigon et al. 2007; Garland et al. 1994). During knee extension, electrical stimulation was achieved via an optical distance sensor (GP2Y0D05, Sharp Microelectrics of the Americas, Oregan, United States) attached to the dynamometer in parallel with the lever arm. A 1 Hz stimulation was delivered when the lever arm passed within a 50-mm detection range of the optical distance sensor. For leg extension exercise, a custom-made low power red

laser assembly was fixed to the axis of the left pedal. The laser projected onto a flat metal surface that was aligned immediately parallel to the pedal. A freely moveable photoelectric sensor (WE170-P132, Sick Pty Ltd, Heidelberg West, Australia) was mounted to the metal surface via a magnet and connected to the electrical stimulator unit (**Figure 5.1**). A single 1 Hz stimulation of the femoral nerve was generated when the laser crossed the photoelectric sensor during leg extension.

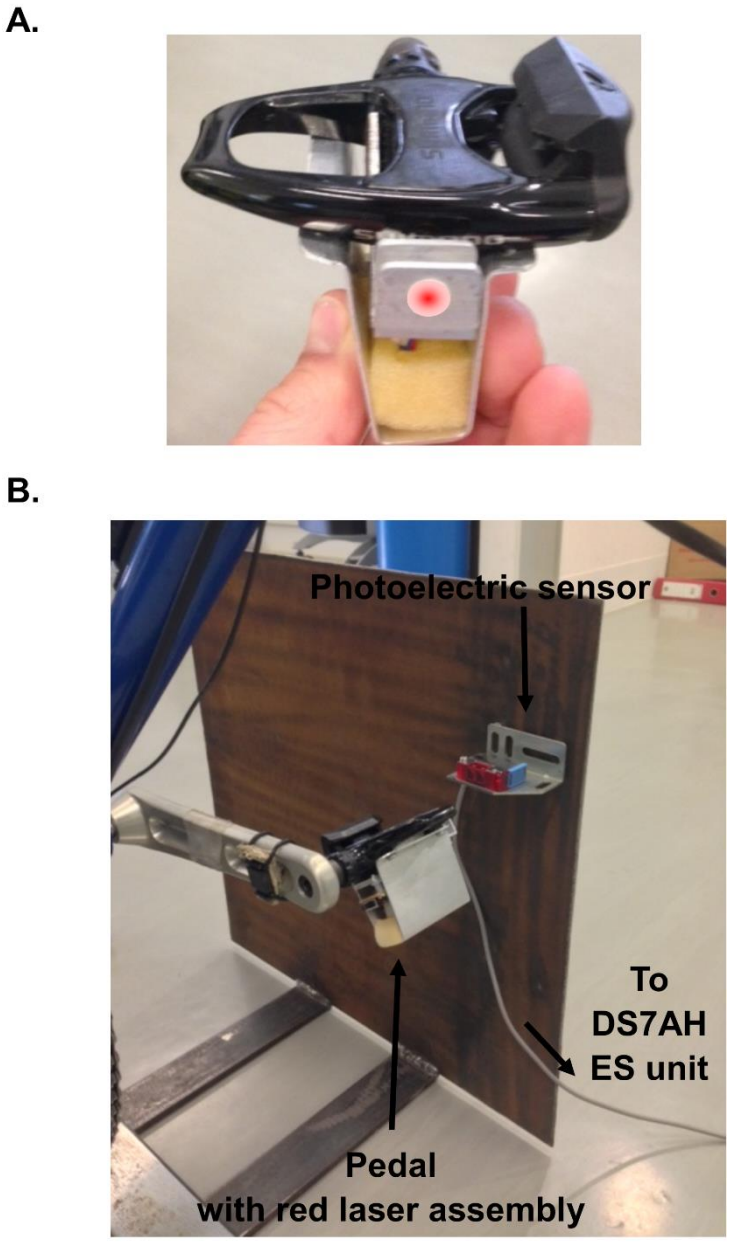

Figure 5.1 Equipment used to administer electrical stimulation during leg extension exercise. A modified pedal with a red laser assembly (**A**) was detected by a photoelectric sensor which triggered the electrical stimulator unit (**B**). (Note: for illustration purposes an alternate cycle ergometer than the one used in this study is pictured).

5.2.2.4 Surface Electromyography (EMG) and goniometry

EMG signals were recorded continuously by a wireless receiver (Telemyo DTS wireless Noraxon Inc., AZ, USA) connected to a PC running MyoResearch software (Noraxon Inc., AZ, USA). Disposable pre-gelled Ag-AgCl surface electrodes (Blue sensor N, Ambu, Ballerup, Denmark) and wireless EMG probes (DTS Model 542, Noraxon Inc., AZ, USA) were used to record EMG signals unilaterally for *vastus lateralis* (VL), *vastus medialis* (VM), *rectus femoris* (RF) *biceps femoris* (BF) and *semitendinosus* (ST) muscles at a sampling frequency of 3000 Hz. Surface electrodes were positioned at an inter-electrode distance of 20 mm apart and aligned parallel to the muscle fibres in accordance with the recommendations of the SENIAM project (Hermens et al. 2000). Prior to placement of EMG electrodes, the skin was prepared by shaving, lightly abrading and cleaning with an alcohol swab. EMG electrodes and wireless sensors were secured with adhesive tape to ensure good contact with the skin and reduce movement artefact.

During the first session, knee kinematics were sampled from the left knee using a wireless electrical goniometer (DTS Model 504, Noraxon Inc., AZ, USA) recorded in an analogue channel of the EMG system. The axis of rotation for the goniometer was aligned with the axis of rotation of the knee, with both arms aligned parallel to the femur and fibula as per the manufacturer's guidelines. Calibration of the goniometer was performed on the isokinetic dynamometer using several known knee angles (total of 7 angles). The equation from the linear regression was then used to transform the raw goniometer signal to degrees ($r^2 > 0.9$). The goniometer was fixed to the surface of the skin via strong double-sided tape and secured with adhesive tape.

5.2.3 Experimental protocol

Participants visited the lab on three occasions and were asked to refrain from strenuous activity in the preceding 72 hrs and caffeine on the day of each session. During the first visit, participants were familiarized with all aspects of the study, including knee extension exercise, leg extension exercise, fatigue testing and electrical stimulation. The goniometer was used to ensure that knee range of motion and angular velocity was identical between the exercises. We also compared the level of activation for the *vastii* muscles and the amplitude and duration of the M-wave response during maximal isometric contractions, knee extension and leg extension exercises (section 5.2.3.1). In a randomized cross-over experimental design and for the next two sessions, participants completed a knee extension exercise consisting of sixty maximal isokinetic knee extensions, or a modified cycling exercise consisting of sixty maximal isokinetic leg

extensions (i.e. extension or downstroke phase only of the crank cycle). Maximal torque, EMG and M-wave were continuously recorded during exercise. Fatigue in the knee extensors was assessed between 5-s and 5-mins post-exercise.

5.2.3.1 Comparison of kinematics, EMG and M-wave during isometric contractions, knee extension and leg extension exercise

To match the kinematics of the knee during knee extension and leg extension exercises, participants were required to complete ten submaximal leg extensions on the cycle ergometer with cadence fixed at 30 rpm (isokinetic mode). The range of motion of the knee was recorded from the electrical goniometer, and average values for maximum and minimum knee angles and angular velocity were calculated. These values were subsequently used to set the limits for knee range of motion and angular velocity during knee extension exercise performed on the isokinetic dynamometer. Participants then completed a standardized cycling warm-up which consisted of 2-min at 1 $W.kg^{-1}$ and 80 rpm, 2-min at 2 $W.kg^{-1}$ and 80 rpm, 6-s maximal effort with high resistance from a stationary start, 1-min at ~2 $W.kg^{-1}$ and 80 rpm, 6-s maximal effort with low resistance from a rolling start, and 1-min at 1 $W.kg^{-1}$ and 80 rpm. Then in a randomized fashion, participants completed three maximal isometric contractions of their knee extensors, three maximal isokinetic knee extensions and three maximal isokinetic leg extensions, with 2-min of rest separating each single effort. Maximal M-waves were elicited at comparable knee joint angles (~90° flexion). If the participant deemed a single effort to be below maximal, this was dismissed and an additional effort was performed.

Table 5.1 Comparison of kinematics, M-wave and EMG responses between maximal isometric contractions, isokinetic knee extensions and isokinetic leg extensions. TE = typical error, ICC = intra-class correlation co-efficient (95% confidence interval), P = alpha level; ROM = range of motion; VAS = *vastii*

	Isometric contraction	Isokinetic knee extension	Isokinetic leg extension	TE	ICC	P
Kinematics						
Max angle (°)	90	120 ± 3	120 ± 2	7.3 (5.2, 12.0)	0.29 (-0.28, 0.71)	0.9
Min angle (°)	90	27 ± 2	27 ± 4	6.5 (4.7, 10.7)	0.70 (0.27, 0.90)	0.9
ROM (°)	0	93 ± 3	94 ± 5	11.0 (7.9, 18.2)	0.44 (-0.12, 0.79)	0.9
Angular velocity ($°.s^{-1}$)	0	80 ± 4	82 ± 3	11.0 (7.8, 18.1)	0.54 (0.02, 0.83)	0.6
EMG and M-wave						
VAS M-wave amplitude (mV)	15.6 ± 1.3	15.0 ± 1.3	14.9 ± 1.2	0.6 (0.5, 0.9)	0.98 (0.95, 0.99)	0.02
VAS M-wave duration (ms)	6.5 ± 0.2	6.6 ± 0.2	6.6 ± 0.3	0.4 (0.3, 0.6)	0.79 (0.53, 0.93)	0.4
VAS EMG (µV)	789 ± 89	875 ± 108	845 ± 109	68 (52, 102)	0.97 (0.93, 0.99)	0.02
VAS EMG (% M-wave amplitude)	5.2 ± 0.2	5.7 ± 0.3	5.5 ± 0.3	0.4 (0.3, 0.6)	0.86 (0.67, 0.95)	0.08

5.2.3.2 Knee extension and leg extension exercise

The standardized cycling warm-up was completed and followed by three maximal isometric knee flexions (separated by 2-min of rest) to permit normalization of hamstring EMG signals. Following baseline fatigue testing of the knee extensors, participants completed the knee extension or leg extension exercise protocol. For knee extension exercise, participants performed a total of sixty maximal knee extensions on the isokinetic dynamometer. Following each contraction, the participant was instructed to relax while the experimenter manually returned the lever arm of the dynamometer back to the starting position. Maximal knee extensions were initiated every 3-s with a work:rest ratio of 1:1. For leg extension, participants sat on the cycle ergometer with their hands in the lower portion of the handlebars (i.e. drops), and performed sixty maximal leg

extensions (i.e. extension or downstroke phase only of the crank cycle; crank angle 0-180°). At the end of the extension phase, the experimenter reset the left crank angle back to 0°, by manually rotating the right crank in a counter-clockwise direction. Maximal leg extensions were initiated every 3-s with a work:rest ratio of 1:1, in an identical fashion to knee extension exercise. For knee extension and leg extension exercises, electrical stimulation of the femoral nerve was generated at 90° flexion for contractions 2 - 4, 29 - 31 and 58 - 60. Participants were vigorously encouraged to produce a maximal contraction for each repeated effort. Fatigue testing of the knee extensor muscles assessed the short-term recovery for a period of up 5-min post-exercise.

5.2.3.3 Fatigue testing of the knee extensors

The fatigue testing procedure of the knee extensors consisted of a brief (~3-s) isometric maximal voluntary contraction superimposed with a 1 Hz electrical stimulus, followed by two potentiated resting doublets at 10 Hz and 100 Hz, each interspersed by 1.5 s. Up to five baseline measurements were obtained following the warm-up and prior to exercise (minimum of 2-min rest period between measurements) to ensure that voluntary and evoked forces were fully potentiated (Kufel et al. 2002). Following knee extension exercise, fatigue testing was repeated at 5-s, 20-s, 40-s, 1-min, 1.5-min, 2-min, 3-min, 4-min and 5-min. Following leg extension exercise, the transition time from the cycle ergometer to the fatigue testing equipment was ~30 s, meaning that measures at 5-s and 20-s were not attainable.

5.2.4 Data Analysis

All data analysis was completed using Spike2 software (version 7.13, Cambridge Electronic Design, Cambridge, UK).

5.2.4.1 Knee extension and leg extension exercise

For knee extension and leg extension exercise, contractions 2 - 4, 29 - 31 and 58 - 60 were chosen for analysis. The first effort was commonly shown to be lower than the second, and therefore was not included. Raw EMG signals were band-pass filtered (20 Hz - 500 Hz) and root mean squared (RMS) over a 25-ms window (Dorel et al. 2012). For each contraction, torque and RMS signals were averaged over a 200-ms window before the electrical stimulation artefact, which corresponded to a knee angle range of ~106 - 90° flexion (crank angle range ~24 - 60° during leg extension). RMS signals from RF and HAM muscles were normalized in reference to the maximum value achieved during baseline isometric maximal voluntary contraction (% MVC). VL and VM RMS

signals were normalized to M-wave peak-to-peak amplitude which was calculated from the raw EMG signal and for the same contraction (EMG.M-wave^{-1}) (Millet et al. 2003). Antagonist/agonist co-activation was calculated by dividing normalized BF and ST signals by VL and VM (Remaud et al. 2009).

5.2.4.2 Fatigue testing

The calibrated force signal was low-pass filtered with a 30 Hz 1st order Butterworth filter (Wüst et al. 2008). During isometric maximal voluntary contractions, force (IMVF) and RMS were averaged over a 500-ms window immediately preceding the electrical stimulation artefact (Babault et al. 2006) (**Figure 5.2**). Superimposed twitch force (SIT) was calculated by subtracting the voluntary force at the time of stimulation from the peak force achieved within a 100-ms window following stimulation. From the potentiated resting doublets, peak force was calculated from the 10 Hz (RT_{10}) and 100 Hz doublet (RT_{100}). A ratio between the peak force obtained from the 10 Hz and 100 Hz doublets ($RT_{10:100}$) was also calculated to assess the severity of low-frequency fatigue (Verges et al. 2009). The peak twitch force from the first of the resting 10 Hz doublets, was used to calculate voluntary activation (VA) (***Eq. 2.1***).

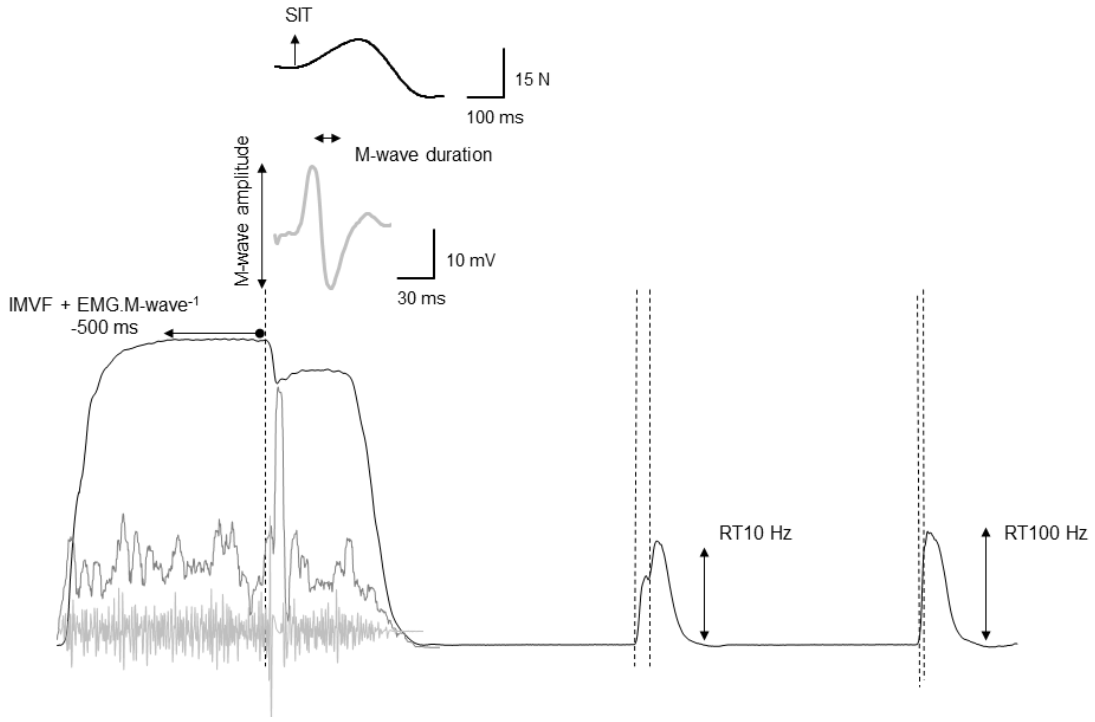

Figure 5.2 Quantification of fatigue in the knee extensors for one subject. Force signals (black), raw EMG signals (light grey), root mean square (RMS) EMG signal (dark grey) and electrical stimulus (dotted) were synchronized in the EMG system. Participants completed a ~3-s isometric maximal voluntary contraction of the knee extensors (IMVF) with a 1 Hz superimposed interpolated twitch (SIT) generated at the plateau in maximal voluntary force. Two potentiated resting twitches (RT) were then elicited ~1.5-s (RT at 10 Hz) and ~3-s (RT at 100 Hz) after the maximal voluntary contraction.

5.2.5 Statistics

For statistical analysis, data was pooled together for VL and VM muscles to form *vastii* (VAS) as no differentiation was made between the two muscles in this study. Similarly, this was done for BF and ST muscles to form hamstrings (HAM). Due to a technical error in the recording of the raw force trace during three testing sessions, the sample size was reduced to n = 13 for force measurements obtained during fatigue testing. The sample size was also reduced to n = 14 for M-wave variables, due to excessive artefact in the responses. All statistical analysis was completed using SPSS software (version 22). Normal distribution of the data was examined via a Shapiro-Wilk test, with a transformation applied to data violating this assumption (e.g. logarithmic or square root). Sphericity of the data was assessed with Mauchleys test, with a Huynh-Feldt correction applied when the assumption of sphericity was violated. For the baseline fatigue variables, inter-day reliability was assessed via the following: i) intra-class correlation coefficients (ICC: 95% confidence intervals) with a two-way random effects model for single measure reliability (Todd et al. 2004; Place et al. 2007), ii) typical error (TE: original unit of measurement), and iii) paired samples *t*-test. A two-way repeated measure ANOVA (exercise x time) investigated changes in torque, EMG and M-wave during knee extension and leg extension exercise. A one-way repeated measure ANOVA (time delay) investigated the short-term recovery of fatigue responses following knee extension exercise, and a paired *t*-test was used to compare the two exercises at comparable time points. LSD post-hoc tests were performed following a significant *F* statistic. Pearson product-moment correlations (r) assessed the relationship between variations in maximal torque during knee extension and leg extension exercises (low: 0.3 – 0.5, moderate: 0.5 – 0.7, strong: > 0.7) (Mukaka 2012). The mean ± standard deviation, lower and upper limits of the 95% confidence interval for mean differences (CI), and Cohens *d* effect sizes are reported in text (small: 0 – 0.49; moderate: 0.5 - 0.79; large: > 0.8) (Cohen 1992). Significance level for all tests was set at $P \leq 0.05$.

5.3 Results

5.3.1 Reliability of fatigue measurements

The inter-day reliability of baseline fatigue measurements are reported in **Table 5.2**. No differences were observed between knee extension and leg extension for any variable (P > 0.05).

Table 5.2 Baseline neuromuscular fatigue measurements obtained prior to knee extension and leg extension exercises. Mean ± SE reported. TE = typical error; ICC = intra-class correlation coefficient (95% confidence interval); P = alpha level; IMVF = isometric maximal voluntary force; VAS = vastii; RF = rectus femoris; HAM = hamstrings; HAM/VAS = hamstring and vastii co-activation index; VA = voluntary activation; RT100 = resting twitch 100 Hz; RT10:100 = resting twitch 10 Hz to resting twitch 100 Hz ratio.

	Knee extension	Leg extension	TE	ICC	P value
IMVF (N)	634 ± 46	633 ± 47	24 (17, 40)	0.98 (0.93, 0.99)	0.9
VAS EMG.M-wave^{-1} (%)	6.5 ± 0.6	6.5 ± 0.6	0.64 (0.5, 1.0)	0.90 (0.75, 0.97)	0.9
RF EMG (% MVC)	95 ± 1	94 ± 1	2 (1.5, 3)	0.42 (-0.8, 0.75)	0.2
HAM EMG (% MVC)	13 ± 2	12 ± 2	4 (3, 6)	0.55 (0.09, 0.81)	0.9
HAM/VAS co-activation (%)	13 ± 2	13 ± 2	4 (3, 6)	0.53 (0.06, 0.81)	0.9
M-wave amplitude (mV)	14.7 ± 1.3	14.1 ± 1.1	1.1 (0.8, 1.8)	0.93 (0.79, 0.98)	0.3
M-wave duration (ms)	6.5 ± 0.2	6.5 ± 0.3	0.4 (0.3, 0.7)	0.77 (0.40, 0.92)	0.9
VA (%)	93 ± 1	92 ± 1	1.6 (1, 3)	0.76 (0.43, 0.91)	0.2
RT_{100} (N)	250 ± 17	253 ± 16	13 (9, 21)	0.95 (0.86, 0.99)	0.6
$RT_{10:100}$	0.93 ± 0.03	0.90 ± 0.04	0.05 (0.04, 0.08)	0.81 (0.55, 0.93)	0.2

5.3.2 Variables measured before, during and after knee extension and leg extension exercise

5.3.2.1 Torque and IMVF

No differences between the exercises were revealed for IMVF at baseline (P = 0.9, CI [-20 N, 21 N], *d* = 0.005) or for torque at the start of exercise (P = 0.1, CI [-30 N·m, 3 N·m], *d* = 0.4). During knee extension exercise, torque decreased by -45 ± 11%

at the middle period and by -60 ± 10% at the end period, whereas smaller reductions of -23 ± 12% at the middle and -38 ± 14% at the end were reported during leg extension exercise (main interaction effect, $F_{2,24}$ = 29.5, P ≤ 0.001) (**Figure 5.3**). Maximal torque during knee extension was positively correlated to maximal torque during leg extension at the start (r = 0.72, P = 0.002), middle (r = 0.62, P = 0.011) and end (r = 0.64, P = 0.008) (**Figure 5.4**). Similarly, the reduction in torque during knee extension was positively correlated to the reduction in torque during leg extension from the start to middle (r = 0.79, P ≤ 0.001), middle to end (r = 0.67, P ≤ 0.01) and start to end (r = 0.86, P ≤ 0.001) periods of the exercise (**Figure 5.5**).

IMVF was lower than baseline post-knee extension and leg extension exercise at all time delays (all P ≤ 0.001). The reduction in IMVF following knee extension was not different than the reduction in IMVF following leg extension post-exercise (P > 0.05). A partial recovery in IMVF was reported from 2-min post-exercise (P ≤ 0.05) (**Figure 5.3**).

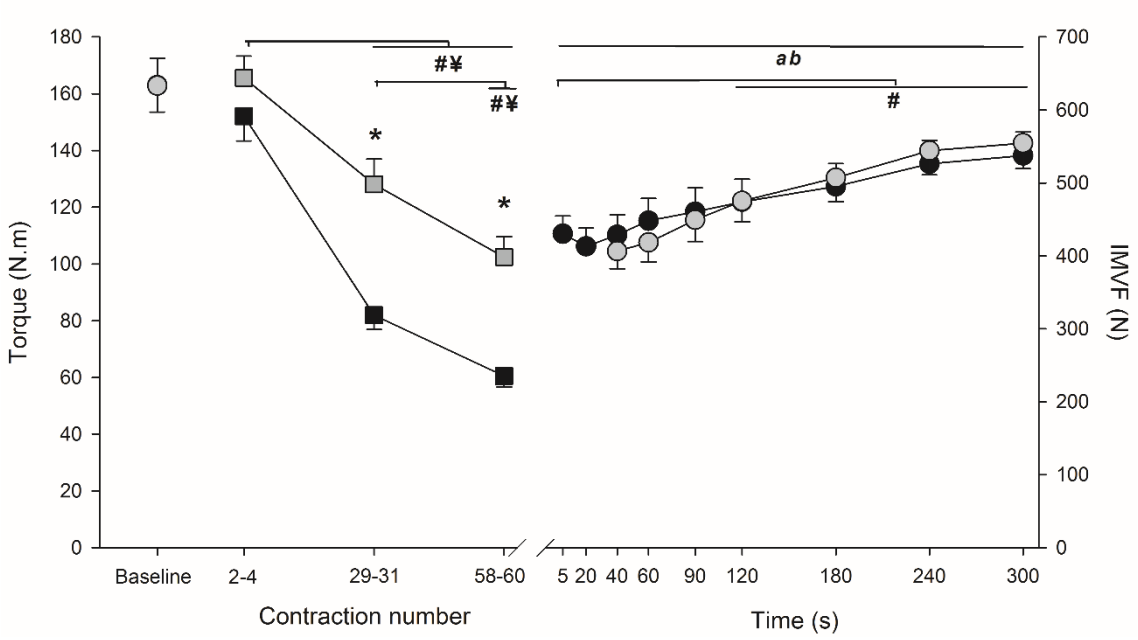

Figure 5.3 Torque (squares) and isometric maximal voluntary force of the knee extensors (IMVF) (circles) measured during knee extension (black) and leg extension (grey) exercise.
difference during knee extension (P ≤ 0.05).
¥ difference during leg extension (P ≤ 0.05).
* difference between the exercises (P ≤ 0.05).
a lower than baseline post knee extension (P ≤ 0.05).
b lower than baseline post leg extension (P ≤ 0.05).

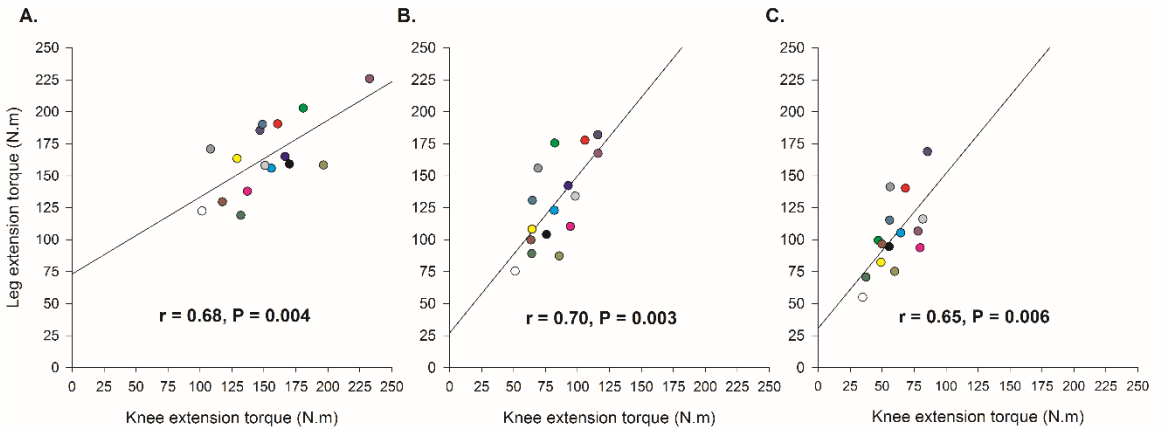

Figure 5.4 Pearson correlations for inter-individual differences in torque production during knee extension and leg extension exercise at the start (A), middle (B) and end (C) periods.

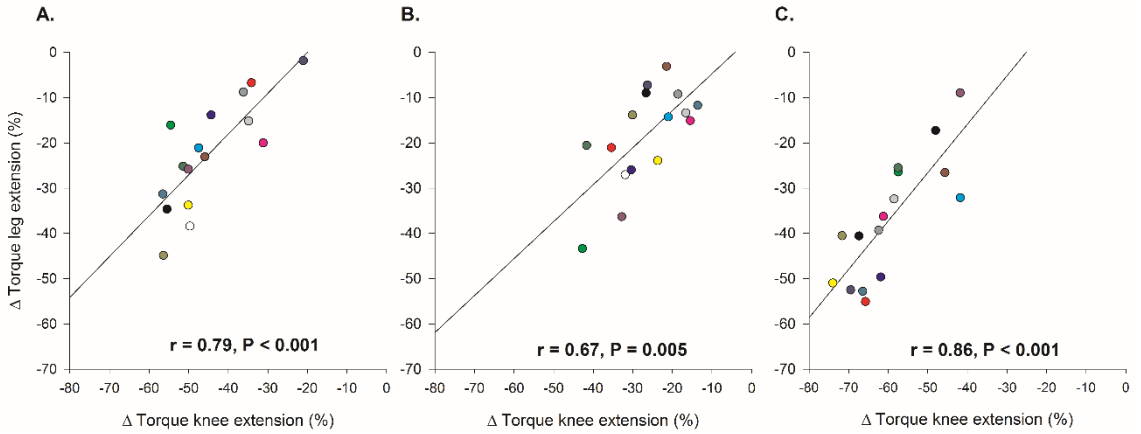

Figure 5.5 Pearson correlations for the intra-individual reductions in torque during knee extension and leg extension exercise. A - delta calculated between start and middle periods, B - delta calculated between middle and end periods, C - delta calculated between start and end periods.

5.3.2.1 EMG and HAM/VAS co-activation

Baseline EMG and HAM/VAS co-activation measurements were not different between knee extension and leg extension (all P > 0.05).

No difference between the exercises was reported for VAS EMG.M-wave^{-1} ($F_{1,31}$ = 2.9, P = 0.1), whereas RF EMG was higher during knee extension ($F_{1,12}$ = 26.3, P ≤ 0.001). During knee extension, VAS EMG.M-wave^{-1} decreased from the start to middle period (P ≤ 0.001, CI [-0.4, -1.2%], *d* = 0.44) and from the middle to end period (P ≤ 0.001, CI [-0.4%, -1%], *d* = 0.36), whereas a reduction from the start to middle period only was reported during leg extension (P ≤ 0.001, CI [-0.5%, -1.2%], *d* = 0.37) (main interaction effect, $F_{2,62}$ = 4.3, P ≤ 0.05) (**Figure 5.6 A**). RF EMG decreased during knee extension from the start to middle (P ≤ 0.001, CI [-12, -25%], *d* = 0.92) and middle to end (P ≤ 0.001, CI [-9, -20%], *d* = 0.77), whereas no changes were reported during leg extension (main interaction effect, $F_{2,30}$ = 12.4, P ≤ 0.001) (**Figure 5.6 B**).

HAM EMG ($F_{1,31}$ = 17.4, P ≤ 0.001) and HAM/VAS co-activation ($F_{1,15}$ = 13.4, P ≤0.01) were higher during leg extension exercise. HAM EMG decreased during leg extension from start to middle (P ≤ 0.001, CI [-4%, -13%], *d* = 0.67) and middle to end (P ≤ 0.001, CI [-2%, -9%], *d* = 0.49), whereas no changes were observed during knee extension (main interaction effect, $F_{2,62}$ = 21.7, P ≤ 0.001) (**Figure 5.6 C)**. HAM/VAS co-activation decreased during leg extension from the start to middle (P ≤ 0.05, CI [-0.2%, -12%], *d* = 0.47) and middle to end (P ≤ 0.05, CI [-0.7%, -10%], *d* = 0.49), whereas a minor increase at the end was reported for knee extension (P ≤ 0.05, CI [0.5%, 2%], *d* = 0.39) (main interaction effect, $F_{2,30}$ = 7.7, P ≤ 0.01) (**Figure 5.6 D**).

VAS EMG.M-wave^{-1} and RF EMG were both lower than baseline values at all time delays post-knee extension and leg extension exercise (all P ≤ 0.05), with greater reductions reported for knee extension (all P ≤ 0.05). The reduction in VAS EMG.M-wave^{-1} reported at 5-s post-knee extension was less than reported between 20-s and 5-min (all P ≤ 0.05), whereas the reduction in RF EMG at 5-s post-knee extension was less than reported between 20-s and 2-min (all P ≤ 0.05). HAM EMG and HAM/VAS co-activation did not change from baseline post-knee extension and leg extension (all P > 0.05), and no differences were reported between the exercises (all P > 0.05).

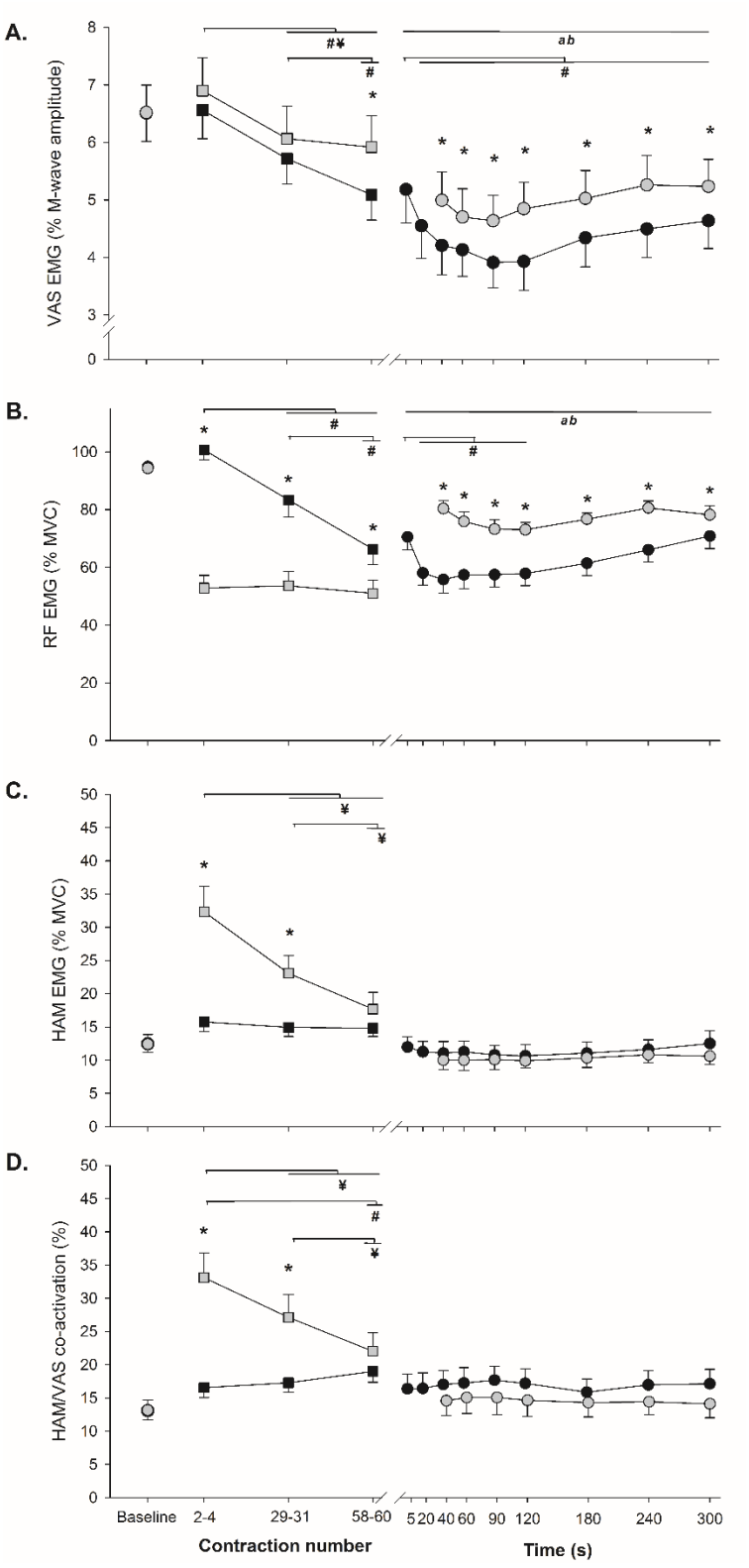

Figure 5.6 VAS EMG.M-wave^{-1} (A), RF EMG (B), HAM EMG (C) and HAM/VAS co-activation (D) measured during exercise (squares) and before/post-exercise (circles) for knee extension (black) and leg extension (grey). VAS = *vastii*; RF = *rectus femoris*; HAM = hamstrings.
difference during knee extension (P ≤ 0.05).
¥ difference during leg extension (P ≤ 0.05).
* difference between the exercises (P ≤ 0.05).
a lower than baseline post knee extension (P ≤ 0.05).
b lower than baseline post leg extension (P ≤ 0.05).

5.3.2.2 M-wave amplitude and duration

M-wave amplitude was not different between knee extension and leg extension at baseline (P = 0.75, CI [-1%, 1%], *d* = 0.02) or during the exercise ($F_{1,29}$ = 1.3, P = 0.3). M-wave amplitude increased from the middle to end periods during knee extension (P = 0.01, CI [1%, 6%], *d* = 0.4) and did not change during leg extension ($F_{2,58}$ = 2.4, P = 0.09) (**Figure 5.7 A**), however no main interaction effects were revealed ($F_{2,28}$ = 0.9, P = 0.4).

M-wave duration was not different between knee extension and leg extension at baseline (P = 0.69, CI [-1%, 2%], *d* = 0.15) or during the exercise ($F_{1,29}$ = 2.2, P = 0.15). M-wave duration increased from the start to middle period during knee extension (P ≤ 0.001, CI [9%, 17%], *d* = 1.0) and leg extension (P ≤ 0.001, CI [9%, 18%], *d* = 1.3) (**Figure 5.7 B**). The change in M-wave duration was not different between the exercises ($F_{2,62}$ = 0.8, P = 0.9).

M-wave amplitude and duration were both higher than baseline values at all time delays post-knee extension and leg extension exercise (all P ≤ 0.05), with no differences between the exercises reported (all P > 0.05). The increase in M-wave amplitude measured after knee extension exercise was similar between 5-s and 5-min (all P > 0.05), whereas the increase in M-wave duration was similar between 5-s and 3-min (all P > 0.05).

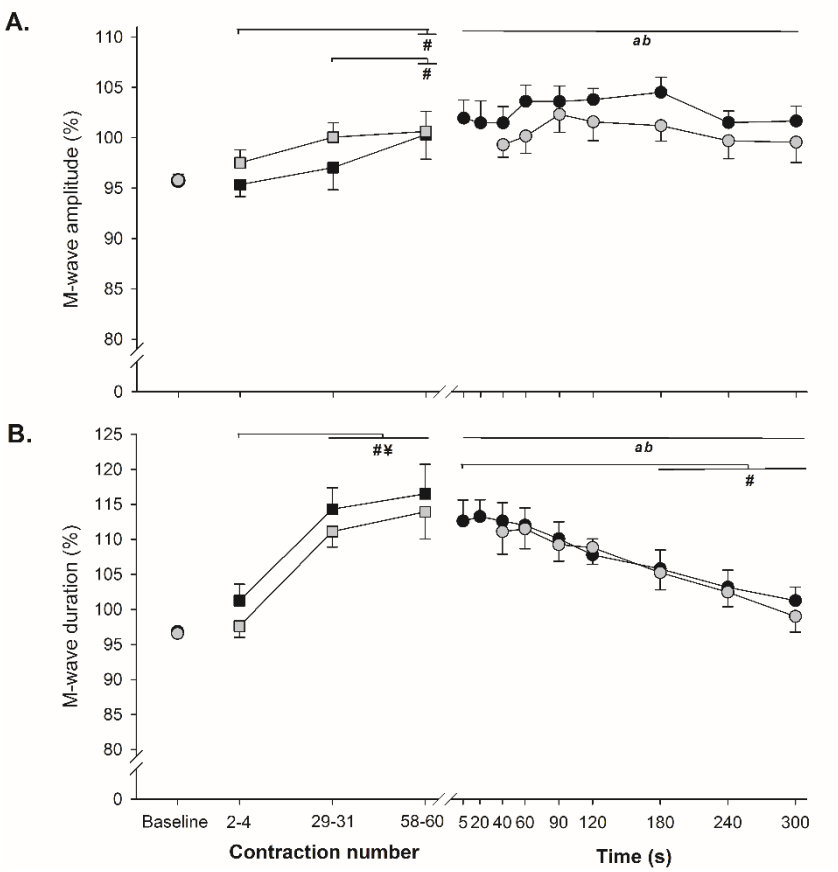

Figure 5.7 M-wave amplitude (A) and duration (B) measured during exercise (squares) and before/post-exercise (circles) for knee extension (black) and leg extension (grey).
difference during knee extension (P ≤ 0.05).
¥ difference during leg extension (P ≤ 0.05).
* difference between the exercises (P ≤ 0.05).
a lower than baseline post knee extension (P ≤ 0.05).
b lower than baseline post leg extension (P ≤ 0.05).

5.3.3 Variables measured before and after knee extension and leg extension exercise

5.3.3.1 Voluntary activation and resting twitch

No differences between the exercises were reported at baseline for VA (P = 0.3, CI [0.6%, 2%], *d* = 0.3), RT_{100} (P =0.6, CI [8 N, 14 N], *d* = 0.06) or $RT_{10:100}$ (P = 0.2, CI [0.01, 0.06], *d* = 0.2).

Voluntary activation was lower than baseline at all time delays post-knee extension and leg extension exercise (all P ≤ 0.05). Greater reductions in VA were reported for knee extension between 40-s and 4-min (all P ≤ 0.05). The reduction in VA measured after knee extension exercise was similar between 5-s and 5-min (all P > 0.05), although it tended to be greatest between 20-s and 2-min post-exercise (**Figure 5.8 A**).

RT_{100} was lower than baseline at all time delays post-knee extension and leg extension exercise (all P ≤ 0.05), with no differences reported between the exercises (all P > 0.05). The reduction in RT_{100} measured at 5-s post-knee extension recovered within ≤ 20-s (P ≤ 0.05) (**Figure 5.8 B**).

$RT_{10:100}$ was lower than baseline between 5-s and 1-min post-knee extension exercise (all P ≤ 0.05), and between 5-s and 5-min following leg extension exercise (all P ≤ 0.05). The reduction in $RT_{10:100}$ measured post-leg extension exercise was greater than knee extension exercise at all comparable periods (all P ≤0.05). $RT_{10:100}$ partially recovered within ≤ 40-s post-knee extension (P > 0.05) (**Figure 5.8 C**).

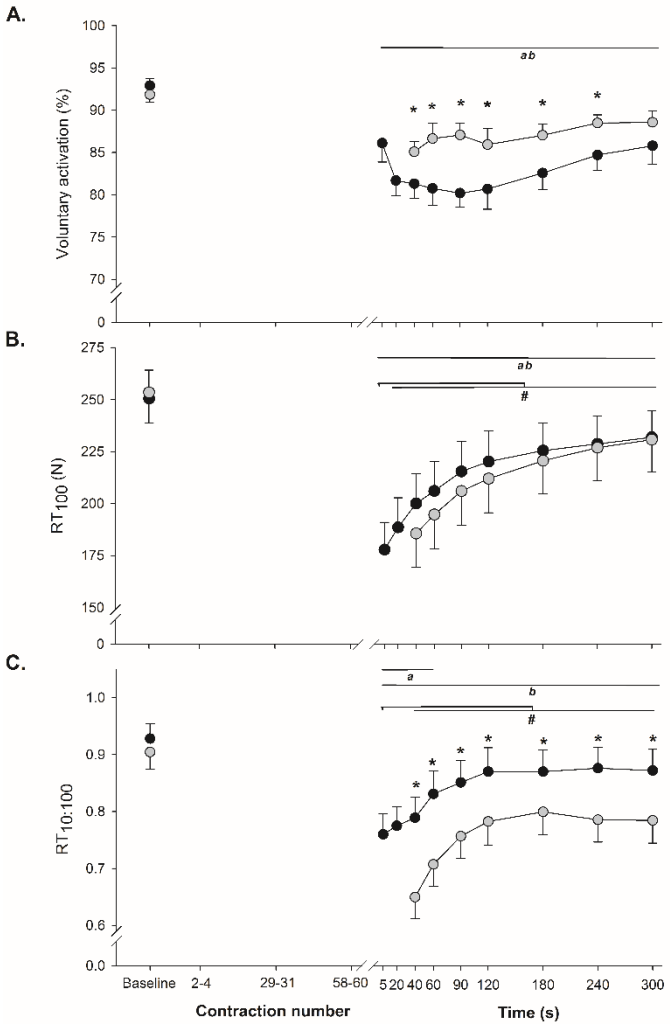

Figure 5.8 Voluntary activation (A), RT_{100} (B) and $RT_{10:100}$ (C) measured at baseline and following knee extension (black) and leg extension (grey) exercise. RT_{100} = resting twitch force elicited at 100 Hz; RT_{10}: resting twitch force elicited at 10 Hz.
difference during knee extension (P ≤ 0.05).
¥ difference during leg extension (P ≤ 0.05).
* difference between the exercises (P ≤ 0.05).
a lower than baseline post knee extension (P ≤ 0.05).
b lower than baseline post leg extension (P ≤ 0.05).

5.4 Discussion

5.4.1 Summary of main findings

The aims of this study were to compare the rate of fatigue occurrence in the knee extensors during knee extension and leg extension exercises, and to investigate any differences in knee extensor fatigue measured post-exercise and the maximum time delays for which fatigue measurements could be accurately assessed. The results revealed that the level of fatigue developed in the knee extensors during isolated exercise determines the reduction in torque during leg extension exercise. To avoid inaccurate measurements of fatigue, knee extensor IMVF must be measured within 1.5-min post-exercise, whereas high and low frequency peripheral fatigue must be measured within 20-s and 40-s, respectively. However, central fatigue changes are greatest within 20-s and 2-min post-exercise.

5.4.2 Fatigue occurrence during knee extension and leg extension exercise

The intra-individual correlations revealed that torque reduction during knee extension exercise was positively associated to torque reduction during leg extension exercise (**Figure 5.5**). This was evident in the torque reduction from start to middle ($r = 0.79$), middle to end ($r = 0.67$) and start to end periods ($r = 0.86$). This finding demonstrates that the level of fatigue developed in the knee extensors determines the reduction in maximal torque during leg extension exercise. This is different to what was reported in study two, which showed no association between an isolated reduction in knee extensor force and leg extension power. The positive association reported in this study is likely due to the removal of the leg flexion phase and contribution of the contralateral leg during exercise. In doing so, this would have reduced the degree of freedom and subsequent opportunities for participants to alter their movement control strategy (e.g. increased focus on the flexion phase of the crank cycle). This lack of alteration to the movement strategy with fatigue development is supported by the positive correlations observed between inter-individual differences in knee extension and leg extension torque at the middle and end periods ($r = 0.70$ and $r = 0.65$, respectively) (**Figure 5.4**). Thus, it is suggested that the maximal force-generating capacity of the knee extensors may better predict maximal leg extension torque during a fatiguing exercise of lower complexity. Maximal torque production during leg extension exercise is strongly influenced by the force-generating capacity of the knee extensors, which possess the

greatest capacity to directly generate effective crank forces (Driss et al. 2002; Kordi et al. 2017; Raasch et al. 1997).

At the start of both exercises, a similar level of VAS EMG.M-wave^{-1} that was comparable to that reported during maximal isometric contraction (**Figure 5.6 A**), indicated that *vastii* muscles were activated maximally to achieve the highest amount of torque possible (Dorel et al. 2012; Rouffet and Hautier 2008). However, RF EMG was submaximal during leg extension (53 ± 6%) and lower compared to knee extension (97 ± 2%) (**Figure 5.6 B**), indicating a lower requirement to generate torque. This likely occurred due to the removal of the transition phase from flexion to extension, during which RF is activated maximally (Rouffet and Hautier 2008; Dorel et al. 2012; Raasch et al. 1997). HAM EMG (33 ± 15% vs. 16 ± 6%) (**Figure 5.6 C**) and HAM/VAS co-activation (33 ± 16% vs. 17 ± 6%) were higher during leg extension (**Figure 5.6 D**), presumably due to the unique role of the bi-articular knee-flexors in optimising the orientation of knee extensor forces (Van Ingen Schenau et al. 1992; Van Ingen Schenau 1989). However, HAM EMG reported at the start of leg extension exercise was less than what has previously been reported during maximal cycling and for a full crank cycle (Rouffet and Hautier 2008; Dorel et al. 2012). This may suggest that the requirement of the knee flexors to orientate knee extension forces during the leg extension phase are presumably less than what is required during the transition phase from extension to flexion. It is important to note that other lower-limb muscles composing the extensor synergy (i.e. *gluteus maximus* and ankle-plantar flexors) would have contributed to the torque generated during leg extension, albeit it to a lesser extent (Van Ingen Schenau 1989; Zajac et al. 2002; Elmer et al. 2011; Martin and Brown 2009; Hug et al. 2010; Raasch and Zajac 1999). Thus, despite the results observed at the start of exercise indicating that the amount of torque generated during knee extension translates into an equal torque that can be generated during leg extension (r = 0.68), torque production during leg extension is the product of the entire leg extensor synergy and knee-flexor co-activation.

The absolute reduction in torque was greater during knee extension at both the middle (-45 ± 11% vs. -23 ± 12%) and end (-60 ± 10% vs. -38 ± 14%) periods (**Figure 5.3**). Distinct differences between the exercises may explain the unequal reduction in torque. At the middle period, large reductions in RF EMG were reported during knee extension only (-17 ± 15%), which presumably indicates that fatigue developed rapidly in RF due to its maximal level of activation (Richardson et al. 1998) and high percentage of type IIx muscle fibres (Johnson et al. 1973; Edgerton et al. 1975). At the end, a greater

reduction in RF EMG during knee extension was also accompanied by a greater reduction in VAS EMG.M-wave^{-1} (**Figure 5.6**) and an increase in HAM/VAS co-activation. The greater reduction in VAS EMG.M-wave^{-1} suggests a greater reduction in supraspinal and/or spinal drive to the knee extensors (via decreased excitability/increased inhibition of pyramidal cells or motoneurons) (Millet et al. 2011; Baudry et al. 2007). This would result in a greater reduction in the number and/or discharge frequency of knee extensor motor units and exacerbate reductions in maximal torque. The minor increase in HAM/VAS co-activation at the end of knee extension exercise may indicate that the total reduction in maximal knee extension torque was marginally overestimated. That is, a small portion of torque generated by the knee extensors may have been required to overcome a potential increase in opposing knee-flexion forces (Psek and Cafarelli 1993). Although HAM/VAS co-activation was similar between the exercises at the end, the large reduction reported during leg extension exercise was probably due to a reduction in knee extensor forces (O'Bryan et al. 2014; Hautier et al. 2000). It is not believed this was due to fatigue development in the knee flexors, as HAM EMG was very low throughout leg extension exercise (less than ~ 35% of MVC, **Figure 5.6 C**).

Comparisons of potential peripheral fatigue mechanisms detected during exercise revealed no differences in M-wave amplitude or duration, which both increased throughout the exercise (**Figure 5.7**). The potentiation in M-wave amplitude may suggest enhanced neuromuscular transmission (Rodriguez-Falces et al. 2013), whereas increased M-wave duration may demonstrate a decrease in propagation velocity and impaired neuromuscular transmission (Fuglevand et al. 1993). This somewhat conflicting result may be explained by a narrowing of the conduction velocity distribution of the sarcolemma action potentials and increased synchronization, which would increase M-wave amplitude without major changes in muscle potentiation (Rodriguez-Falces et al. 2013; Place et al. 2005). Therefore, analysis of M-wave duration seems necessary to detect potential changes in neuromuscular transmission during maximal exercise.

5.4.3 Comparison of fatigue post-exercise and time-delay for accurate assessment

Despite the unequal reduction in torque during knee extension and leg extension exercise, no differences in knee extensor IMVF were observed post-exercise (**Figure 5.3**). Thus, one can assume that knee extensor fatigue was similar between the two exercises, although the reduction in torque was greater during knee extension. Although the reduction in IMVF was comparable between the exercises, some important differences in the central and peripheral mechanisms contributing to IMVF reduction

were observed. First, greater reductions in VA, VAS EMG.M-wave^{-1} and RF EMG were reported following knee extension exercise. This supports the change in VAS EMG.M-wave^{-1} during exercise, and is evidence of a greater degree of central fatigue. Although central fatigue development is thought to be largely mediated by group III and IV afferent feedback associated with peripheral fatigue development (Blain et al. 2016; Rossman et al. 2014), we reported a higher degree of low-frequency peripheral fatigue following leg extension exercise. Thus, central fatigue developed during knee extension exercise may have also been influenced by other mechanisms, such as increased GABA mediated cortical inhibition (McDonnell et al. 2006; Gandevia 2001; Taylor et al. 2016), reduced Ia spindle facilitation (Hagbarth and Macefield 1995), serotonin spill-over (D'Amico et al. 2017) or alterations to the intrinsic properties of the motoneurons (Kernell and Monster 1982; Spielmann et al. 1993). The greater low-frequency peripheral fatigue developed during leg extension exercise was potentially due to greater Pi accumulation (Hogan et al. 1999) and subsequent impairment in Ca^{2+} handling/sensitivity (Allen et al. 2008; Westerblad et al. 2002). Indeed, the larger active muscle mass during leg extension presumably increased cardiovascular and ventilatory demands (Shephard et al. 1988; Kayser et al. 1994; Rasmussen et al. 1991) which has the potential to decrease arterial O_2 saturation and exacerbate Pi accumulation (Hogan et al. 1999).

The results obtained following knee extension were used to estimate the longest possible time delay post-exercise that enabled an accurate description of knee extensor fatigue developed during exercise, as measurements were obtained within 5-s post-exercise. The reduction in IMVF measured 5-s post-exercise (-33 ± 12%) was not different than measurements obtained at a time delay of up to 1.5-min (**Figure 5.3**). The partial recovery in knee extensor IMVF reported from 2-min post-exercise is in line with previous findings obtained following isometric (Gruet et al. 2014) and dynamic (Froyd et al. 2013; Cheng and Rice 2005) knee extension exercises. A delayed depression in VAS EMG.M-wave^{-1} from 20-s to 5-min and in RF EMG from 20-s to 2-min was also observed (**Figure 5.6**). Although similar changes could not be detected for VA, this parameter tended to decrease between 20-s and 2-min post-exercise (**Figure 5.8 A**), in line with previous findings (Cheng and Rice 2005). These changes in central fatigue variables occurred despite a rapid partial recovery in RT_{100} (≤ 20-s) and $RT_{10:100}$ (≤ 40-s) (**Figure 5.8**). This may support our earlier suggestion that a wider range of mechanisms other than just group III and IV afferent feedback contributed to central fatigue development during knee extension exercise. The mechanisms responsible for the delayed onset of central fatigue post-exercise remain unclear, however others have shown that the knee extensor TMS evoked silent period, motor evoked potential and thoracic motor evoked

potential all recover toward baseline values immediately following sustained isometric contraction of the knee extensors (Kennedy et al. 2016; Gruet et al. 2014). Thus, complex mechanisms acting 'upstream' to the motor cortex (e.g. motor association areas, basal ganglia) (Chaudhuri and Behan 2000; Rupp and Perrey 2008; Rasmussen et al. 2007) may explain this delayed onset of central fatigue. Recovery in knee extensor IMVF seemed mediated by low-frequency peripheral mechanisms, supported by the full recovery in $RT_{10:100}$ within 1.5-min. The partial recovery in IMVF and full recovery in $RT_{10:100}$ at 1.5-min post-exercise, supports the general time-course of evacuation of intramuscular metabolites known to impede Ca^{2+} activated force (e.g. Pi) and contribute to low-frequency fatigue (Westerblad et al. 2002; Allen et al. 2008; Sahlin and Ren 1989; Harris et al. 1976; Harris et al. 1981).

5.4.4 Limitations

It is possible that the use of the single pulse method to assess VA led to a reduction in the sensitivity of the responses to central fatigue development (Verges et al. 2009; Place et al. 2007). Voluntary activation was assessed in this way as we wanted to compare the M-wave response between isometric and dynamic contractions, which was not possible with the use of high frequency paired pulses. Although stimulation intensity was set at 150% of the maximum in an attempt to maintain supramaximal stimulation during isometric contractions and dynamic exercise (Babault et al. 2006; Kennedy 2015), the reproducibility results in table 5.1 indicated that VAS maximal M-wave amplitude was slightly lower during dynamic exercise compared to isometric contractions (mean difference = -3.6 ± 4.4%; effect size = 0.16). Thus, extra muscle movement and contractions during cycling exercise may have a small effect on the capacity to supramaximally stimulate the femoral nerve. Lastly, the lack of cardiovascular and respiratory measurements (e.g. heart rate, O_2 saturation and O_2 consumption) make it difficult to determine how these potential changes affected the aetiology and severity of fatigue during knee extension and leg extension exercise.

5.5 Conclusion

Fatigue developed in the knee extensors during maximal isolated exercise determines the reduction in torque during maximal leg extension exercise. Thus, these findings suggest that movement variability during the flexion phase may attenuate reductions in leg extension power during maximal cycling exercise. Distinct differences in the aetiology of fatigue between the exercises suggest that it may not be appropriate to relate findings from isolated knee extension exercises to that expected during maximal

cycling exercises. The longest possible time delay for accurate assessment of isometric maximal voluntary force of the knee extensors post-exercise was 1.5-min. To avoid underestimating high and low frequency peripheral fatigue, assessment must be conducted within less than 20-s and 40-s post-exercise, whereas reductions in central fatigue measurements are greatest between 20-s and 2-min post-exercise.

Author contributions

SJ O'bryan was responsible for conception and design of experiments, data collection and analysis, preparation of figures, drafting the chapter and revising the chapter for important intellectual content. **DM Rouffet** was responsible for conception and design of experiments, data collection and analysis, preparation of figures and reviewing the chapter and providing feedback. **R Bourke** assisted with data collection.

Chapter 6 GENERAL DISCUSSION AND CONCLUSIONS

6.1 Summary of main findings

Study one revealed that increases in VAS EMG during prolonged high-intensity cycling exercise (from 6% to 14%) were negatively correlated with the level of fatigue experienced in the knee extensor muscles (IMVF decrease -2% to -36%, r = -0.79). During the 30-s maximal cycling exercise performed subsequently, crank power and EMG for all muscles was reduced, while VAS/GAS co-activation did not change. Knee extensor fatigue developed following high-intensity cycling was positively correlated to the reductions in maximal crank power during maximal cycling (from 0% to -27%, r = 0.76). The results from this study showed that knee extensor fatigue developed during prolonged high-intensity exercise determines the magnitude of the reductions in power production during a subsequent maximal cycling exercise. The lack of changes in VAS/GAS co-activation may have maximised power production during the extension phase of the maximal cycling exercise.

In study two, fatigue developed in the knee extensor muscles following pre-fatiguing isolated exercise (IMVF decrease from -18% to -82%) was not associated to reductions in power output during the extension phase (from -8% to -31%, r = 0.1) or flexion phase (+11% to -39%, r = 0.16) during maximal cycling. Following the pre-fatiguing knee extension exercise, VAS EMG decreased (-15%) and inter-individual variability in VAS EMG profiles increased. A decrease was also reported for GMAX EMG (-12%) and co-activation for all muscle pairs, especially VAS/APF (-15%). HAM EMG (-15%), TA EMG (-15%) and RF EMG (-11%) decreased and inter-individual variability increased. Overall, the results indicated that a reduction in the force-generating capacity of the knee extensors does not explain reductions in lower-limb power during maximal cycling exercises. The increased variability in the movement control strategies selected by the participants following the pre-fatiguing exercise, is likely to explain why no association between knee extensor fatigue and reductions in power production during the extension phase of the maximal cycling exercise was observed.

Finally in study three, a positive correlation was observed between reductions in maximal torque during knee extension and leg extension exercise at the middle (-45 ± 11% vs. -23 ± 12%, r = 0.79) and end (-59 ± 10% vs. -37 ± 13%, r = 0.86). The torque reduction was larger for the knee extension exercise and was accompanied by a greater reduction in RF EMG (middle: -17 ± 15% vs -2 ± 20%; end: -34 ± 16% vs. -4 ± 22%) and VAS EMG.M-wave^{-1} (end: -21 ± 16% vs. -14 ± 17%). The maximum time delay for

accurate measures of knee extensor IMVF post-exercise was 1.5-min. RT_{100} and $RT_{10:100}$ partially recovered within less than 20-s and 40-s post-exercise, respectively. VAS EMG.M-wave^{-1} decreased after 20-s post-exercise, and reductions in VA were greatest between 20-s and 2-min post-exercise. It was concluded that knee extensor fatigue determines the level of fatigue developed during the extension phase of the crank cycle. To avoid inaccurate measurements of fatigue developed during exercise, knee extensor IMVF must be measured within 1.5-min post-exercise, whereas high and low frequency peripheral fatigue must be measured within 20-s and 40-s, respectively. However, central fatigue changes are greatest within 20-s and 2-min post-exercise.

6.2 General discussion

Across all studies, the maximal force-generating capacity of the knee extensors was a good predictor of maximal cycling power during fatigue-free exercise (r range = 0.58 – 0.86). These findings were in accordance with results previously reported for highly trained cyclists (r = 0.71 – 0.75) (Driss et al. 2002; Kordi et al. 2017), demonstrating that maximal knee extensor force is a good predictor of maximal cycling power irrespective of training status. The strongest positive correlation between knee extensor force and cycling power was reported in study two, presumably as power output was calculated during the extension phase and during peak EMG activity of *vastii* muscles (~25% of pedal cycle when accounting for an electromechanical delay of 100 ms) (Raasch et al. 1997; van Ingen Schenau et al. 1992; Samozino et al. 2007;Dorel et al. 2012). Thus, greater task-specific similarities between measures likely permitted a stronger correlation (Wilson et al. 1996). This assumption was tested in study three, with isokinetic knee extensor torque providing a stronger prediction of isokinetic leg extension torque (r = 0.72, P = 0.002) compared to maximal isometric force of the knee extensors (r = 0.58, P = 0.038). Larger inter-individual variability in measures of fatigue-free maximal torque compared to measures of maximal power, likely explain the lower correlations reported in study three (Driss et al. 2002). Indeed, the co-efficient of variation calculated for maximal torque in study three (35%) was higher than calculated for maximal power in studies one and two (21 - 25%).

The effect of fatigue development in the knee extensors on maximal cycling power revealed some interesting results across the studies. In study one, the reduction in knee extensor IMVF following high-intensity cycling exercise (range = -2% to -36%) accurately predicted the reduction in maximal power during the subsequent cycling exercise (range = 0% to -27%) (r = 0.75). The average ratio of the loss in knee extensor IMVF following high-intensity cycling exercise to the reduction in maximal power during

the cycling effort was 1:0.5. This ratio was higher than the comparison between crank power and knee extension joint power reported for trained cyclists (Elmer et al. 2012) (1:0.35), suggesting that non-trained cyclists may place a larger demand on the knee extensors to generate maximal power when fatigue is likely to develop in the locomotor muscles. This hypothesis may be supported by the positive correlations between knee extensor IMVF and power production at the end of the maximal cycling exercise in study two (r = 0.87), and the positive correlation between knee extensor torque and leg-extension torque at the middle and end periods of maximal exercise in study three (r = 0.62 and 0.64, respectively). However, in study two when fatigue was isolated to the knee extensor muscles and cycling power was calculated for the extension and flexion phases separately, no association was reported between the relative reduction in knee extensor IMVF (range = -18% to -82%) and the relative reduction in power output during the extension phase (range = -8% to -31%) (r = 0.19). Thus, participants who experienced the greatest reduction in knee extensor force following isolated pre-fatiguing exercise, did not lose the most amount of power during the extension phase of maximal cycling. It is possible isolated fatigue of the knee extensors may have led participants to use different movement strategies to generate power during the extension phase of maximal cycling. One possible strategy may be an increased emphasis on pulling up on the cranks during the flexion phase occurring simultaneously on the contralateral side. In doing so, this would accelerate the cranks and influence power output. This strategy may be supported by the large increase in inter-individual variability in EMG profiles of HAM, RF and TA muscles, which are heavily involved in generating crank power during the flexion phase (van Ingen Schenau et al. 1992; Zajac et al. 2002). This suggestion is in accordance with previous findings reported during submaximal cycling exercise (Brochner Nielsen et al. 2016).This alteration in the movement strategy may have influenced the correlation between the relative reductions in knee extensor IMVF and maximal power during the extension phase, due to the bilateral nature of the exercise and the mechanical coupling of the cranks.

The results from study three confirmed that the flexion phase limits the effects of knee extensor fatigue on crank power production. Restricting the cycling movement to the leg extension phase only led to strong positive correlations between the relative reduction in knee extensor torque and leg extension torque from the start to middle (r = 0.79), middle to end (r = 0.67) and start to end periods of the exercise (r = 0.86). Hence, by reducing the degree of freedom and number of movement control strategies, knee extensor fatigue was more clearly associated with reductions in leg extension torque. The average ratio between the reduction in knee extension torque and leg extension

torque at the end of the exercises was 1:0.7. This ratio was higher than reported in study one, probably due to the greater localisation of the exercise to the knee extensor muscles and reduced chance for alterations to the movement strategy during the flexion phase.

It was also hypothesized that the lack of association between knee extensor force measured after isolated pre-fatiguing exercise and power production during the extension phase of maximal cycling, resulted from inter-individual differences in the rate of recovery during the time delay between force and power measurements (1-min). However, the results from study three determined that the time delay between measurements of knee extensor force and crank power in study one and two (1-min) was not likely to influence the relationship between the two variables, as partial recovery in knee extensor IMVF was reported from 1.5-min post-exercise, similar to previous findings (Froyd et al. 2013; Cheng and Rice 2005). Thus, these results support that increased variability in the movement strategy for power production likely explain the lack of correlations between knee extensor IMVF and leg extension power reported in study two. This strategy likely limited fatigue development in the knee extensor muscles and attenuated reductions in maximal power output. When reducing the degree of freedom and complexity of the cycling movement to a unilateral leg extension exercise in study three, the reduction in knee extensor IMVF post exercise (-33 ± 11%) was greater than reported following normal maximal cycling exercise in study one and two (-13 ± 11% and -8 ± 6%, respectively). These differences are not likely to be explained by the difference in the number of cycles (60 for both study one and study three, 43 ± 2 for study two) (Tomas et al. 2010), extension velocity (decreasing extension velocity attenuates IMVF reduction but velocity was lowest in study three) (Prieske et al. 2017; Morel et al. 2014) or the size of the exercising muscle mass (no differences in knee extensor IMVF measured 40-s post isolated knee extension and leg extension exercise in study three).

6.3 Practical implications and considerations for future research

The results from this thesis provide an extensive analysis of how fatigue in the knee extensor muscles effects power production during maximal cycling exercises in a healthy and physically active population. The ability of the knee extensors to generate force and lower-limb power is critical for sporting performance and the execution of locomotor tasks (Kordi et al. 2017; Driss et al. 2002; Glenn and Samojla 2002; Hamnegård et al. 2004; Jakobsson et al. 1995). Therefore, the findings may also extend to athletes. Methodological considerations for fatigue assessment have also been

presented, extending the relevance of the findings to future research. As such, the following practical implications and future recommendations may apply:

- Sports scientists and coaches may prescribe exercises that promote fatigue resistance in the knee extensor muscles to improve the ability to generate power during cycling exercise. Study one showed that this may apply to cycling road races, where the ability to resist fatigue development in knee extensors prior to the final sprint is likely to enhance maximal power output at the finish line. In study three, this may apply to longer duration track events (e.g. 1000 m time trial, 4000 m pursuit), whereby the ability to resist fatigue development throughout the maximal event is likely to increase the duration of which high levels of power output can be maintained.
- The clearer association between knee extensor isometric force and power production during the extension phase in study two ($r = 0.86$) compared to the full crank cycle in study one ($r = 0.78$), highlights the need for future research to calculate crank power during phase specific regions of the crank cycle. This approach is likely to increase the validity of relating variations in knee extensor force to power production during maximal cycling exercise.
- Study one revealed that monitoring changes in VAS EMG over the course of a prolonged high-intensity cycling exercise at a constant power output may provide a non-invasive method of detecting fatigue development in the knee extensors. This may offer a solution to future research when neuromuscular fatigue assessment post-exercise is not possible.
- The results from study three revealed that supramaximal stimulation of the peripheral nerve during maximal exercise may be used as a reliable method to detect high-frequency peripheral fatigue mechanisms. This may offer a solution for future research when the time delay for peripheral fatigue assessment post-exercise cannot be restricted to ≤ 20-s. Ideally, there is a need for future research to develop methods which can potentially monitor changes in the force response to supramaximal stimulation during exercise, in order to quantify fatigue and avoid the limitation of time delay and associated recovery as highlighted in study three. Alternatively, it may be appropriate to adopt the classical method for neuromuscular fatigue assessment post-exercise, but only if the need to transfer participants between equipment can be avoided and if assessment can begin immediately following the cessation of exercise.
- The fatigue responses reported throughout this thesis illustrate the need for future research to report inter-individual variability (e.g. variance ratio, coefficient of

variation) and the range of the observed changes (e.g. confidence intervals) rather than just mean values. This information would provide a more holistic view of the effect of fatigue on force and power production and how this differs between individuals.

- Future research could include kinematic analysis of the lower-limbs to EMG and crank torque analysis during cycling to provide further evidence for alterations in the movement strategy with fatigue development of the knee extensors (Dingwell et al. 2008).

6.4 Conclusion

Collectively, the results from all studies suggest that individuals with a greater capacity to resist fatigue development in their knee extensors may have a greater capacity to maintain high levels of crank power during maximal cycling exercises. However, when severe levels of fatigue develop in the knee extensors, some individuals may be able to adopt a wider range of movement strategies to generate power.

References (Chapter 3 – 6)

Aagaard, P., Simonsen, E. B., Magnusson, S. P., Larsson, B., & Dyhre-Poulsen, P. (1998). A new concept for isokinetic hamstring:quadriceps muscle strength ratio. *The American Journal of Sports Medicine, 26*(2), 231-237.

Adam, A., & De Luca, C. J. (2005). Firing rates of motor units in human vastus lateralis muscle during fatiguing isometric contractions. *Journal of Applied Physiology, 99*(1), 268-280.

Allen, D. G., Lamb, G. D., & Westerblad, H. (2008). Skeletal muscle fatigue: cellular mechanisms. *Physiological Reviews, 88*(1), 287-332.

Amann, M., & Dempsey, J. A. (2008). Locomotor muscle fatigue modifies central motor drive in healthy humans and imposes a limitation to exercise performance. *Journal of Physiology, 586*(1), 161-173.

Arendt-Nielsen, L., Gantchev, N., & Sinkjær, T. (1992). The influence of muscle length on muscle fibre conduction velocity and development of muscle fatigue. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 85*(3), 166-172.

Arsac, L. M., Belli, A., & Lacour, J. R. (1996). Muscle function during brief maximal exercise: Accurate measurements on a friction loaded cycle ergometer. *European Journal of Applied Physiology and Occupational Physiology, 74*(1-2), 100-106.

Babault, N., Desbrosses, K., Fabre, M.-S., Michaut, A., & Pousson, M. (2006). Neuromuscular fatigue development during maximal concentric and isometric knee extensions. *Journal of Applied Physiology, 100*(3), 780-785.

Baudry, S., Klass, M., Pasquet, B., & Duchateau, J. (2007). Age-related fatigability of the ankle dorsiflexor muscles during concentric and eccentric contractions. *European Journal of Applied Physiology, 100*(5), 515-525.

Beelen, A., & Sargeant, A. (1991). Effect of fatigue on maximal power output at different contraction velocities in humans. *Journal of Applied Physiology, 71*(6), 2332-2337.

Bernstein, N. A. (1967). The co-ordination and regulation of movements.

Bigland-Ritchie, B. (1981). EMG/force relations and fatigue of human voluntary contractions. *Exercise and Sport Sciences Reviews, 9*(1), 75-118.

Bigland-Ritchie, B., Cafarelli, E., & Vollestad, N. K. (1986). Fatigue of submaximal static contractions. *Acta Physiolica Scandinavia Suppl, 556*, 137-148.

Billaut, F., Kerris, J. P., Rodriguez, R. F., Martin, D. T., Gore, C. J., & Bishop, D. J. (2013). Interaction of central and peripheral factors during repeated sprints at different levels of arterial O2 saturation. *PloS One, 8*(10), e77297.

Bini, R.R, Hume, P. A., & Croft, J. L. (2012). Effects of Bicycle Saddle Height on Knee Injury Risk and Cycling Performance. *Sports Medicine, 41*(6), 463-476.

Blain, G. M., Mangum, T. S., Sidhu, S. K., Weavil, J. C., Hureau, T. J., Jessop, J. E., . . . Amann, M. (2016). Group III/IV muscle afferents limit the intramuscular metabolic perturbation during whole body exercise in humans. *The Journal of Physiology*, 594(18), 5303-5315.

Bonnard, M., Sirin, A. V., Oddsson, L., & Thorstensson, A. (1994). Different strategies to compensate for the effects of fatigue revealed by neuromuscular adaptation processes in humans. *Neuroscience Letters, 166*(1), 101-105.

Borg, G. (1970). Perceived exertion as an indicator of somatic stress. *Scandinavian Journal of Rehabilitation Medicine, 2*(2), 92.

Brochner Nielsen, N. P., Hug, F., Guevel, A., Fohanno, V., Lardy, J., & Dorel, S. (2016). Motor adaptations to unilateral quadriceps fatigue during a bilateral pedaling task. *Scandanavian Journal of Medicine and Science in Sports*, *27*(12), 1724-1738.

Burden, A. (2010). How should we normalize electromyograms obtained from healthy participants? What we have learned from over 25years of research. *Journal of Electromyography and Kinesiology, 20*(6), 1023-1035.

Cairns, S. P., & Dulhunty, A. F. (1995). High-frequency fatigue in rat skeletal muscle: role of extracellular ion concentrations. *Muscle & Nerve, 18*(8), 890-898.

Carroll, T. J., Taylor, J. L., & Gandevia, S. C. (2017). Recovery of central and peripheral neuromuscular fatigue after exercise. *Journal of Applied Physiology, 122*(5), 1068-1076.

Castronovo, A., De Marchis, C., Bibbo, D., Conforto, S., Schmid, M., & D'Alessio, T. (2012). Neuromuscular adaptations during submaximal prolonged cycling *Engineering in Medicine and Biology Society (EMBC), Annual international conference of the IEEE* (pp. 3612-3615).

Chaudhuri, A., & Behan, P. O. (2000). Fatigue and basal ganglia. *Journal of the Neurological Sciences, 179*(1), 34-42.

Cheng, A. J., & Rice, C. L. (2005). Fatigue and recovery of power and isometric torque following isotonic knee extensions. *Journal of Applied Physiology, 99*(4), 1446-1452.

Ciubotariu, A., Arendt-Nielsen, L., & Graven-Nielsen, T. (2004). The influence of muscle pain and fatigue on the activity of synergistic muscles of the leg. *European Journal of Applied Physiology, 91*(5-6), 604-614.

Cohen, J. (1992). A power primer. *Psychological Bulletin, 112*(1), 155.

Cormie, P., McGuigan, M. R., & Newton, R. U. (2011). Developing maximal neuromuscular power: Part 1-biological basis of maximal power production. *Sports Medicine, 41*(1), 17-38.

Côté, J. N., Raymond, D., Mathieu, P. A., Feldman, A. G., & Levin, M. F. (2005). Differences in multi-joint kinematic patterns of repetitive hammering in healthy, fatigued and shoulder-injured individuals. *Clinical Biomechanics, 20*(6), 581-590.

D'Amico, J. M., Butler, A. A., Héroux, M. E., Cotel, F., Perrier, J. F. M., Butler, J. E., . . . Taylor, J. L. (2017). Human motoneurone excitability is depressed by activation of serotonin 1A receptors with buspirone. *The Journal of Physiology, 595*(5), 1763-1773.

Dahlstedt, A. J., Katz, A., & Westerblad, H. (2001). Role of myoplasmic phosphate in contractile function of skeletal muscle: studies on creatine kinase-deficient mice. *The Journal of Physiology, 533*(2), 379-388.

De Luca, C. J. (1997). The use of surface electromyography in biomechanics. *Journal of Applied Biomechanics, 13*, 135-163.

Decorte, N., Lafaix, P. A., Millet, G. Y., Wuyam, B., & Verges, S. (2012). Central and peripheral fatigue kinetics during exhaustive constant-load cycling. *Scandinavian Journal of Medicine & Science in Sports, 22*(3), 381-391.

Devries, H. A., Housh, T. J., Johnson, G. O., Evans, S. A., Tharp, G. D., Housh, D. J., & Hughes, R. A. (1990). Factors affecting the estimation of physical working capacity at the fatigue threshold. *Ergonomics, 33*(1), 25-33.

Devries, H. A., Tichy, M. W., Housh, T. J., Smyth, K. D., Tichy, A. M., & Housh, D. J. (1987). A method for estimating physical working capacity at the fatigue threshold (PWCFT). *Ergonomics, 30*(8), 1195-1204.

Diefenthaeler, F., Coyle, E. F., Bini, R. R., Carpes, F. P., & Vaz, M. A. (2012). Muscle activity and pedal force profile of triathletes during cycling to exhaustion. *Sports Biomechanics, 11*(1), 10-19.

Dorel, S., Couturier, A., Lacour, J.-R., Vandewalle, H., Hautier, C., & Hug, F. (2010). Force-velocity relationship in cycling revisited: benefit of two-dimensional pedal forces analysis. *Medicine & Science in Sports & Exercise, 42*(6), 1174-1183.

Dorel, S., Drouet, J. M., Couturier, A., Champoux, Y., & Hug, F. (2009). Changes of pedaling technique and muscle coordination during an exhaustive exercise. *Medicine and Science in Sports and Exercise, 41*(6), 1277.

Dorel, S., Guilhem, G., Couturier, A., & Hug, F. (2012). Adjustment of muscle coordination during an all-out sprint cycling task. *Medicine & Science in Sports & Exercise, 44*(11), 2154-2164.

Dorel, S., Hautier, C. A., Rambaud, O., Rouffet, D., Van Praagh, E., Lacour, J. R., & Bourdin, M. (2005). Torque and power-velocity relationships in cycling: relevance to track sprint performance in world-class cyclists. *International Journal of Sports Medicine, 26*(9), 739-746.

Driss, T., Vandewalle, H., Chevalier, J.-M. L., & Monod, H. (2002). Force-velocity relationship on a cycle ergometer and knee-extensor strength indices. *Canadian Journal of Applied Physiology, 27*(3), 250-262.

Ebert, T. R., Martin, D. T., Stephens, B., & Withers, R. T. (2006). Power output during a professional men's road-cycling tour. *International Journal of Sports Physiology and Performance, 1*(4), 324.

Edgerton, V. R., Smith, J., & Simpson, D. (1975). Muscle fibre type populations of human leg muscles. *The Histochemical Journal, 7*(3), 259-266.

Elmer, S. J., Barratt, P. R., Korff, T., & Martin, J. C. (2011). Joint-specific power production during submaximal and maximal cycling. *Medicine & Science in Sports & Exercise, 43*(10), 1940-1947.

Elmer, S. J., Marshall, C. S., Wehmanen, K., Amann, M., McDaniel, J., Martin, J., & Martin, J. C. (2012). Effects of locomotor muscle fatigue on joint-specific power production during cycling. *Medicine & Science in Sports & Exercise, 44*, 1504-1511.

Enders, H., von Tscharner, V., & Nigg, B. M. (2014). Neuromuscular Strategies during Cycling at Different Muscular Demands. *Medicine & Science in Sports & Exercise, 47*(7), 1450-1459.

Ericson, M. O. (1988). Mechanical muscular power output and work during ergometer cycling at different work loads and speeds. *European Journal of Applied Physiology and Occupational Physiology, 57*(4), 382-387.

Ericson, M. O., Nisell, R., Arborelius, U. P., & Ekholm, J. (1986). Power output and work in different muscle groups during ergometer cycling. *European Journal of Applied Physiology and Occupational Physiology, 55*(3), 229-235.

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39*(2), 175-191.

Fernandez del Olmo, M., Rodriguez, F., Marquez, G., Iglesias, X., Marina, M., Benitez, A., . . . Acero, R. (2013). Isometric knee extensor fatigue following a Wingate test: peripheral and central mechanisms. *Scandinavian Journal of Medicine & Science in Sports, 23*(1), 57-65.

Fitch, S., & McComas, A. (1985). Influence of human muscle length on fatigue. *The Journal of Physiology, 362*(1), 205-213.

Forestier, N., & Nougier, V. (1998). The effects of muscular fatigue on the coordination of a multijoint movement in human. *Neuroscience Letters, 252*(3), 187-190.

Frigon, A., Carroll, T. J., Jones, K. E., Zehr, E. P., & Collins, D. F. (2007). Ankle position and voluntary contraction alter maximal M waves in soleus and tibialis anterior. *Muscle & Nerve, 35*(6), 756-766.

Froyd, C., Millet, G. Y., & Noakes, T. D. (2013). The development of peripheral fatigue and short-term recovery during self-paced high-intensity exercise. *The Journal of Physiology, 591*(5), 1339-1346.

Fuglevand, A., Zackowski, K., Huey, K., & Enoka, R. (1993). Impairment of neuromuscular propagation during human fatiguing contractions at submaximal forces. *The Journal of Physiology, 460*(1), 549-572.

Gandevia, S. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiological Reviews, 81*(4), 1725-1789.

Gardner, A. S., Martin, D., Jenkins, D., Dyer, I., Van Eiden, J., Barras, M., & Martin, J. (2009). Velocity-specific fatigue: Quantifying fatigue during variable velocity cycling. *Medicine and Science in Sports and Exercise, 41*(4), 904.

Garland, S. J., Gerilovsky, L., & Enoka, R. M. (1994). Association between muscle architecture and quadriceps femoris H-reflex. *Muscle & Nerve, 17*(6), 581-592.

Gates, D. H., & Dingwell, J. B. (2008). The effects of neuromuscular fatigue on task performance during repetitive goal-directed movements. *Experimental Brain Research, 187*(4), 573-585.

Girard, O., Bishop, D. J., & Racinais, S. (2013). Neuromuscular Adjustments of the Quadriceps Muscle after Repeated Cycling Sprints. *PLoS One, 8*(5), e61793.

Glenn, L. L., & Samojla, B. G. (2002). A critical reexamination of the morphology, neurovasculature, and fiber architecture of knee extensor muscles in animal models and humans. *Biological Research for Nursing, 4*(2), 128-143.

Gruet, M., Temesi, J., Rupp, T., Levy, P., Verges, S., & Millet, G. Y. (2014). Dynamics of corticospinal changes during and after a high-intensity quadriceps exercise. *Experimental Physiology*, *99*(8), 1053-1064.

Hagbarth, K. E., & Macefield, V. G. (1995). The fusimotor system. Its role in fatigue. *Advances in Experimental Medicine and Biology, 384*, 259-270.

Halperin, I., Chapman, D. W., & Behm, D. G. (2015). Non-local muscle fatigue: effects and possible mechanisms. *European Journal of Applied Physiology, 115*(10), 2031-2048.

Halperin, I., Copithorne, D., & Behm, D. G. (2014). Unilateral isometric muscle fatigue decreases force production and activation of contralateral knee extensors but not elbow flexors. *Applied Physiology, Nutrition, and Metabolism, 39*(12), 1338-1344.

Hamada, T., Sale, D., MacDougall, J., & Tarnopolsky, M. (2003). Interaction of fibre type, potentiation and fatigue in human knee extensor muscles. *Acta Physiologica Scandinavica, 178*(2), 165-173.

Hamnegård, C. H., Sedler, M., Polkey, M. I., & Bake, B. (2004). Quadriceps strength assessed by magnetic stimulation of the femoral nerve in normal subjects. *Clinical Physiology and Functional Imaging, 24*(5), 276-280.

Harris, R., Edwards, R., Hultman, E., Nordesjö, L., Nylind, B., & Sahlin, K. (1976). The time course of phosphorylcreatine resynthesis during recovery of the quadriceps muscle in man. *Pflügers Archiv European Journal of Physiology, 367*(2), 137-142.

Harris, R., Hultman, E., & Sahlin, K. (1981). Glycolytic intermediates in human muscle after isometric contraction. *Pflügers Archiv, 389*(3), 277-282.

Hautier, C., Linossier, M., Belli, A., Lacour, J. R., & Arsac, L. M. (1996). Optimal velocity for maximal power production in non-isokinetic cycling is related to muscle fibre type composition *European Journal of Applied Occupational Physiology, 74*(1-2), 114-118.

Hautier, C. A., Arsac, L. M., Deghdegh, K., Souquet, J., Belli, A., & Lacour, J. R. (2000). Influence of fatigue on EMG/force ratio and cocontraction in cycling. *Medicine & Science in Sports & Exercise, 32*(4), 839-843.

Hayward, L., Breitbach, D., & Rymer, W. (1988). Increased inhibitory effects on close synergists during muscle fatigue in the decerebrate cat. *Brain research, 440*(1), 199-203.

Hermens, H. J., Freriks, B., Disselhorst-Klug, C., & Rau, G. (2000). Development of recommendations for SEMG sensors and sensor placement procedures. *Journal of Electromyography and Kinesiology, 10*(5), 361-374.

Hershler, C., & Milner, M. (1978). An optimality criterion for processing electromyographic (EMG) signals relating to human locomotion. *IEEE Transactions on Biomedical Engineering*(5), 413-420.

Hogan, M. C., Richardson, R. S., & Haseler, L. J. (1999). Human muscle performance and PCr hydrolysis with varied inspired oxygen fractions: a31P-MRS study. *Journal of Applied Physiology, 86*(4), 1367-1373.

Huffenus, A. F., Amarantini, D., & Forestier, N. (2006). Effects of distal and proximal arm muscles fatigue on multi-joint movement organization. *Experimental Brain Research, 170*(4), 438-447.

Hug, F., Bendahan, D., Le Fur, Y., Cozzone, P. J., & Grelot, L. (2004). Heterogeneity of muscle recruitment pattern during pedaling in professional road cyclists: a magnetic resonance imaging and electromyography study. *European Journal of Applied Physiology, 92*(3), 334-342.

Hug, F., & Dorel, S. (2009). Electromyographic analysis of pedaling: a review. *Journal of Electromyography and Kinesiology, 19*(2), 182-198.

Hug, F., Drouet, J. M., Champoux, Y., Couturier, A., & Dorel, S. (2008). Interindividual variability of electromyographic patterns and pedal force profiles in trained cyclists. *Eur J Appl Physiol, 104*(4), 667-678.

Hug, F., Turpin, N. A., Guével, A., & Dorel, S. (2010). Is interindividual variability of EMG patterns in trained cyclists related to different muscle synergies? *Journal of Applied Physiology, 108*(6), 1727-1736.

Hunter, A. M., St Clair Gibson, A., Lambert, M. I., Nobbs, L., & Noakes, T. D. (2003). Effects of supramaximal exercise on the electromyographic signal. *British Journal of Sports Medicine, 37*(4), 296-299.

Hureau, T. J., Ducrocq, G. P., & Blain, G. M. (2016). Peripheral and central fatigue development during all-out repeated cycling sprints. *Medicine & Science in Sports & Exercise, 48*(3), 391-401.

Hureau, T. J., Olivier, N., Millet, G. Y., Meste, O., & Blain, G. M. (2014). Exercise performance is regulated during repeated sprints to limit the development of peripheral fatigue beyond a critical threshold. *Experimental Physiology, 99*(7), 951-963.

Jakobsson, P., Jorfeldt, L., & Henriksson, J. (1995). Metabolic enzyme activity in the quadriceps femoris muscle in patients with severe chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine, 151*(2), 374-377.

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

Jones, D. (1996). High-and low-frequency fatigue revisited. *Acta Physiologica Scandinavica, 156*(3), 265-270.

Karelis, A. D., Marcil, M., Péronnet, F., & Gardiner, P. F. (2004). Effect of lactate infusion on M-wave characteristics and force in the rat plantaris muscle during repeated stimulation in situ. *Journal of Applied Physiology, 96*(6), 2133-2138.

Kautz, S. A., Feltner, M. E., Coyle, E. F., & Baylor, A. M. (1991). The pedaling technique of elite endurance cyclists: changes with increasing workload at constant cadence. *International Journal of Sport Biomechanics, 7*(1), 29-53.

Kawamoto, J.-E., Aboodarda, S. J., & Behm, D. G. (2014). Effect of differing intensities of fatiguing dynamic contractions on contralateral homologous muscle performance. *Journal of Sports Science & Medicine, 13*(4), 836.

Kayser, B., Narici, M., Binzoni, T., Grassi, B., & Cerretelli, P. (1994). Fatigue and exhaustion in chronic hypobaric hypoxia: influence of exercising muscle mass. *Journal of Applied Physiology, 76*(2), 634-640.

Kennedy, D. S., Fitzpatrick, S. C., Gandevia, S. C., & Taylor, J. L. (2015). Fatigue-related firing of muscle nociceptors reduces voluntary activation of ipsilateral but not contralateral lower limb muscles. *Journal of Applied Physiology, 118*(4), 408-418.

Kennedy, D. S., McNeil, C. J., Gandevia, S. C., & Taylor, J. L. (2016). Effects of fatigue on corticospinal excitability of the human knee extensors. *Experimental Physiology, 101*(12), 1552-1564.

Kernell, D., & Monster, A. (1982). Motoneurone properties and motor fatigue. *Experimental Brain Research, 46*(2), 197-204.

Kordi, M., Goodall, S., Barratt, P., Leeder, J., Rowley, N., & Howatson, G. (2017). Maximum Voluntary Isometric Torque Production for Task specific and Single-joint Muscle groups and their Relation to Peak Power Output in Sprint Cycling. *Journal of Electromyography and Kinesiology*, *35*, 95-99.

Kufel, T. J., Pineda, L. A., & Mador, M. J. (2002). Comparison of potentiated and unpotentiated twitches as an index of muscle fatigue. *Muscle & Nerve, 25*(3), 438-444.

Larsen, B., & Voigt, M. (2006). Quadriceps H-reflex modulation during pedaling. *Journal of Neurophysiology, 96*(1), 197-208.

Latash, M. L. (2012). The bliss (not the problem) of motor abundance (not redundancy). *Experimental Brain Research, 217*(1), 1-5.

Lepers, R., Maffiuletti, N. A., Rochette, L., Brugniaux, J., & Millet, G. Y. (2002). Neuromuscular fatigue during a long-duration cycling exercise*. Journal of Applied Physiology, 92*(4), 1487-1493.

Lewek, M. D., Rudolph, K. S., & Snyder-Mackler, L. (2004). Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis. *Osteoarthritis Cartilage, 12*(9), 745-751.

Maffiuletti, N. A., & Lepers, R. (2003). Quadriceps femoris torque and EMG activity in seated versus supine position. *Medicine & Science in Sports & Exercise, 35*(9), 1511-1516.

Marcora, S. M., Bosio, A., & de Morree, H. M. (2008). Locomotor muscle fatigue increases cardiorespiratory responses and reduces performance during intense cycling exercise independently from metabolic stress. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 294*(3), R874-R883.

Martin, J. C., & Brown, N. A. (2009). Joint-specific power production and fatigue during maximal cycling. *Journal of Biomechanics, 42*(4), 474-479.

Martin, J. C., Wagner, B. M., & Coyle, E. F. (1997). Inertial-load method determines maximal cycling power in a single exercise bout. *Medicine & Science in Sports & Exercise, 29*(11), 1505-1512.

Mathiassen, S. E. (1989). Influence of angular velocity and movement frequency on development of fatigue in repeated isokinetic knee extensions. *European Journal of Applied Physiology and Occupational Physiology, 59*(1-2), 80-88.

Matkowski, B., Place, N., Martin, A., & Lepers, R. (2011). Neuromuscular fatigue differs following unilateral vs bilateral sustained submaximal contractions. *Scandinavian Journal of Medicine & Science in Sports, 21*(2), 268-276.

McDaniel, J., Behjani, N. S., Elmer, S. J., Brown, N., & Martin, J. C. (2014). Joint-specific power-pedaling rate relationships during maximal cycling. *Journal of Appled Biomechanics, 30*(3), 423-430.

McDonnell, M. N., Orekhov, Y., & Ziemann, U. (2006). The role of GABAB receptors in intracortical inhibition in the human motor cortex. *Experimental Brain Research, 173*(1), 86-93.

Merletti, R., Knaflitz, M., & De Luca, C. J. (1990). Myoelectric manifestations of fatigue in voluntary and electrically elicited contractions. *Journal of Applied Physiology*(5), 1810-1820.

Millet, G. Y., Martin, V., Lattier, G., & Ballay, Y. (2003). Mechanisms contributing to knee extensor strength loss after prolonged running exercise. *Journal of Applied Physiology, 94*(1), 193-198.

Millet, G. Y., Martin, V., Martin, A., & Vergès, S. (2011). Electrical stimulation for testing neuromuscular function: from sport to pathology. *European Journal of Applied Physiology, 111*(10), 2489-2500.

Morel, B., Clemencon, M., Rota, S., Millet, G. Y., Bishop, D. J., Brosseau, O., . . . Hautier, C. A. (2014). Contraction velocity influence the magnitude and etiology of neuromuscular fatigue during repeated maximal contractions. *Scandinavian Journal of Medicine & Science in Sports, 25*(5).

Mukaka, M. M. (2012). A guide to appropriate use of correlation coefficient in medical research. *Malawi Medical Journal, 24*(3), 69-71.

O'Bryan, S. J., Brown, N. A., Billaut, F., & Rouffet, D. M. (2014). Changes in muscle coordination and power output during sprint cycling. *Neuroscience Letters, 576*, 11-16.

Pearcey, G. E. P., Murphy, J. R., Behm, D. G., Hay, D. C., Power, K. E., & Button, D. C. (2014). Neuromuscular fatigue of the knee extensors during repeated maximal intensity intermittent-sprints on a cycle ergometer. *Muscle & Nerve, 51*(4), 569-579.

Perry-Rana, S. R., Housh, T. J., Johnson, G. O., Bull, A. J., Berning, J. M., & Cramer, J. T. (2002). MMG and EMG responses during fatiguing isokinetic muscle contractions at different velocities. *Muscle & Nerve, 26*(3), 367-373.

Peveler, W. W., Pounders, J. D., & Bishop, P. A. (2007). Effects of saddle height on anaerobic power production in cycling. *The Journal of Strength & Conditioning Research, 21*(4), 1023-1027.

Place, N., Maffiuletti, N. A., Ballay, Y., & Lepers, R. (2005). Twitch potentiation is greater after a fatiguing submaximal isometric contraction performed at short vs. long quadriceps muscle length. *Journal of Applied Physiology, 98*(2), 429-436.

Place, N., Maffiuletti, N. A., Martin, A., & Lepers, R. (2007). Assessment of the reliability of central and peripheral fatigue after sustained maximal voluntary contraction of the quadriceps muscle. *Muscle & Nerve, 35*(4), 486-495.

Prieske, O., Aboodarda, S. J., Benitez Sierra, J. A., Behm, D. G., & Granacher, U. (2017). Slower but not faster unilateral fatiguing knee extensions alter contralateral limb performance without impairment of maximal torque output. *European Journal of Applied Physiology, 117*(2), 323-334.

Psek, J. A., & Cafarelli, E. (1993). Behavior of coactive muscles during fatigue. *Journal of Applied Physiology, 74*(1), 170-175.

Raasch, C. C., & Zajac, F. E. (1999). Locomotor strategy for pedaling: muscle groups and biomechanical functions. *Journal of Neurophysiology, 82*(2), 515-525.

Raasch, C. C., Zajac, F. E., Ma, B., & Levine, W. S. (1997). Muscle coordination of maximum-speed pedaling. *Journal of Biomechanics, 30*(6), 595-602.

Rasmussen, J., Hanel, B., Diamant, B., & Secher, N. H. (1991). Muscle mass effect on arterial desaturation after maximal exercise. *Medicine and Science in Sports and Exercise, 23*(12), 1349-1352.

Rasmussen, P., Dawson, E. A., Nybo, L., Van Lieshout, J. J., Secher, N. H., & Gjedde, A. (2007). Capillary-oxygenation-level-dependent near-infrared spectrometry in frontal lobe of humans. *Journal of Cerebral Blood Flow & Metabolism, 27*(5), 1082-1093.

Remaud, A., Cornu, C., & Guével, A. (2009). Agonist muscle activity and antagonist muscle co-activity levels during standardized isotonic and isokinetic knee extensions. *Journal of Electromyography and Kinesiology, 19*(3), 449.

Richardson, R., Frank, L., & Haseler, L. (1998). Dynamic knee-extensor and cycle exercise: functional MRI of muscular activity. *International Journal of Sports Medicine, 19*(03), 182-187.

Rochette, L., Hunter, S. K., Place, N., & Lepers, R. (2003). Activation varies among the knee extensor muscles during a submaximal fatiguing contraction in the seated and supine postures. *Journal of Applied Physiology, 95*(4), 1515-1522.

Rodriguez-Falces, J., Duchateau, J., Muraoka, Y., & Baudry, S. (2015). M-wave potentiation after voluntary contractions of different durations and intensities in the tibialis anterior. *Journal of Applied Physiology, 118*(8), 953-964.

Rodriguez-Falces, J., Maffiuletti, N. A., & Place, N. (2013). Twitch and M-wave potentiation induced by intermittent maximal voluntary quadriceps contractions: differences between direct quadriceps and femoral nerve stimulation. *Muscle Nerve, 48*(6), 920-929.

Rodriguez-Falces, J., Maffiuletti, N. A., & Place, N. (2013). Twitch and M-wave potentiation induced by intermittent maximal voluntary quadriceps contractions: Differences between direct quadriceps and femoral nerve stimulation. *Muscle & Nerve, 48*(6), 920-929.

Rossman, M. J., Garten, R. S., Venturelli, M., Amann, M., & Richardson, R. S. (2014). The role of active muscle mass in determining the magnitude of peripheral fatigue during dynamic

exercise. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology, 306*(12), R934-R940.

Rouffet, D. M., & Hautier, C. A. (2008). EMG normalization to study muscle activation in cycling. *Journal of Electromyography and Kinesiology, 18*(5), 866-878.

Rupp, T., & Perrey, S. (2008). Prefrontal cortex oxygenation and neuromuscular responses to exhaustive exercise. *European Journal of Applied Physiology, 102*(2), 153-163.

Ryan, M. M., & Gregor, R. J. (1992). EMG profiles of lower extremity muscles during cycling at constant workload and cadence. *Journal of Electromyography and Kinesiology, 2*(2), 69-80.

Sacco, P., Newberry, R., McFadden, L., Brown, T., & McComas, A. J. (1997). Depression of human electromyographic activity by fatigue of a synergistic muscle. *Muscle & Nerve, 20*(6), 710-717.

Sahlin, K., & Ren, J. (1989). Relationship of contraction capacity to metabolic changes during recovery from a fatiguing contraction. *Journal of Applied Physiology, 67*(2), 648-654.

Samozino, P., Horvais, N., & Hintzy, F. (2007). Why does power output decrease at high pedaling rates during sprint cycling? *Medicine & Science in Sports & Exercise, 39*(4), 680.

Sanderson, D. J., & Black, A. (2003). The effect of prolonged cycling on pedal forces. *Journal of Sports Sciences, 21*(3), 191-199.

Sargeant, A., & Dolan, P. (1987). Effect of prior exercise on maximal short-term power output in humans. *Journal of Applied Physiology, 63*(4), 1475-1480.

Selen, L., Beek, P., & Van Dieën, J. (2007). Fatigue-induced changes of impedance and performance in target tracking. *Experimental Brain Research, 181*(1), 99-108.

Shephard, R., Bouhlel, E., Vandewalle, H., & Monod, H. (1988). Muscle mass as a factor limiting physical work. *Journal of Applied Physiology, 64*(4), 1472-1479.

Sidhu, S. K., Hoffman, B. W., Cresswell, A. G., & Carroll, T. J. (2012). Corticospinal contributions to lower limb muscle activity during cycling in humans. *Journal of Neurophysiology, 107*(1), 306-314.

Sidhu, S. K., Weavil, J. C., Venturelli, M., Garten, R. S., Rossman, M. J., Richardson, R. S., . . . Amann, M. (2014). Spinal μ-opioid receptor-sensitive lower limb muscle afferents determine corticospinal responsiveness and promote central fatigue in upper limb muscle. *The Journal of Physiology, 592*(22), 5011-5024.

Singh, T., Varadhan, Zatsiorsky, V. M., & Latash, M. L. (2010). Fatigue and Motor Redundancy: Adaptive Increase in Finger Force Variance in Multi-Finger Tasks. *Journal of Neurophysiology, 103*(6), 2990-3000.

Smirmaul, B. P., Dantas, J. L., Fontes, E. B., Altimari, L. R., Okano, A. H., & de Moraes, A. C. (2009). Comparison of electromyography fatigue threshold in lower limb muscles in trained and untrained men. *Electromyography Clinical Neurophysiology*, *49*, 000-000.

Spielmann, J., Laouris, Y., Nordstrom, M., Robinson, G., Reinking, R., & Stuart, D. (1993). Adaptation of cat motoneurons to sustained and intermittent extracellular activation. *The Journal of Physiology, 464*, 75.

Stewart, R., Duhamel, T., Foley, K., Ouyang, J., Smith, I., & Green, H. (2007). Protection of muscle membrane excitability during prolonged cycle exercise with glucose supplementation. *Journal of Applied Physiology, 103*(1), 331-339.

Taylor, A., Bronks, R., Smith, P., & Humphries, B. (1997). Myoelectric evidence of peripheral muscle fatigue during exercise in severe hypoxia: some references to m. vastus lateralis

myosin heavy chain composition. *European Journal of Applied Physiology and Occupational Physiology, 75*(2), 151-159.

Taylor, J., Amann, M., Duchateau, J., Meeusen, R., & Rice, C. (2016). Neural Contributions to Muscle Fatigue: From the Brain to the Muscle and Back Again. *Medicine & Science in Sports & Exercise, 48*(11), 2294-2306.

Taylor, J. L., Butler, J. E., & Gandevia, S. (2000). Changes in muscle afferents, motoneurons and motor drive during muscle fatigue. *European Journal of Applied Physiology, 83*(2-3), 106-115.

Taylor, J. L., De Haan, A., Gerrits, K. H. L., & De Ruiter, C. J. (2009). Point:Counterpoint: The interpolated twitch does/does not provide a valid measure of the voluntary activation of muscle. *Journal of Applied Physiology, 107*(1), 354-357.

Taylor, J. L., & Gandevia, S. C. (2001). Transcranial magnetic stimulation and human muscle fatigue. *Muscle & Nerve, 24*(1), 18-29.

Taylor, J. L., & Gandevia, S. C. (2008). A comparison of central aspects of fatigue in submaximal and maximal voluntary contractions. *Journal of Applied Physiology, 104*(2), 542-550.

Thomas, K., Goodall, S., Stone, M., Howatson, G., Gibson, A. S., & Ansley, L. (2014). Central and Peripheral Fatigue in Male Cyclists after 4-, 20-, and 40-km Time Trials. *Medicine & Science in Sports & Exercise*.

Todd, G., Gorman, R. B., & Gandevia, S. C. (2004). Measurement and reproducibility of strength and voluntary activation of lower-limb muscles. *Muscle & Nerve, 29*(6), 834-842.

Tomas, A., Ross, E. Z., & Martin, J. C. (2010). Fatigue during maximal sprint cycling: unique role of cumulative contraction cycles. *Medicine & Science in Sports & Exercise, 42*(7), 1364-1369.

Tomazin, K., Morin, J.-B., & Millet, G. Y. (2016). Neuromuscular Fatigue Aetiology After Repeated Sprints Depends on Exercise Modality. *International Journal of Sports Physiology and Performance*, 1-28.

Tsiokanos, A., Kellis, E., Jamurtas, A., & Kellis, S. (2002). The relationship between jumping performance and isokinetic strength of hip and knee extensors and ankle plantar flexors. *Isokinetics and Exercise Science, 10*(2), 107-115.

Van Ingen Schenau, G., Boots, P., De Groot, G., Snackers, R., & Van Woensel, W. (1992). The constrained control of force and position in multi-joint movements. *Neuroscience, 46*(1), 197-207.

Van Ingen Schenau, G. J. (1989). From rotation to translation: constraints on multi-joint movements and the unique action of bi-articular muscles. *Human Movement Science, 8*(4), 301-337.

Verges, S., Maffiuletti, N. A., Kerherve, H., Decorte, N., Wuyam, B., & Millet, G. Y. (2009). Comparison of electrical and magnetic stimulations to assess quadriceps muscle function. *Journal of Applied Physiology, 106*(2), 701-710.

Westerblad, H., Allen, D. G., & Lannergren, J. (2002). Muscle fatigue: lactic acid or inorganic phosphate the major cause? *News in Physiological Sciences, 17*, 17-21.

Westerblad, H., Bruton, J. D., & Katz, A. (2010). Skeletal muscle: energy metabolism, fiber types, fatigue and adaptability. *Experimental Cell Research, 316*(18), 3093-3099.

Willigenburg, N. W., McNally, M. P., & Hewett, T. E. (2014). Quadriceps and hamstrings strength in athletes, (pp. 15-28): Springer. Boston, MA.

Wüst, R. C. I., Morse, C. I., De Haan, A., Jones, D. A., & Degens, H. (2008). Sex differences in contractile properties and fatigue resistance of human skeletal muscle. *Experimental Physiology, 93*(7), 843-850.

Yeo, B. K., Rouffet, D. M., & Bonanno, D. R. (2016). Foot orthoses do not affect crank power output during maximal exercise on a cycle-ergometer. *Journal of Science and Medicine in Sport, 19*(5), 368-372.

Zajac, F. E., Neptune, R. R., & Kautz, S. A. (2002). Biomechanics and muscle coordination of human walking. Part I: introduction to concepts, power transfer, dynamics and simulations. *Gait Posture, 16*(3), 215-232.

Zehr, P. E. (2002). Considerations for use of the Hoffmann reflex in exercise studies. *European Journal of Applied Physiology, 86*(6), 455-468.

APPENDICES

Appendix A - Study one

Information to participants

You are invited to participate

You are invited to participate in a research project entitled **Locomotor muscle fatigue and the regulation of sprint cycling performance**. This project is being conducted by a student researcher, Mr Steven O'Bryan, as part of a study at Victoria University under the supervision of Dr. Francois Billaut and Dr. David Rouffet from the School of Exercise Sport Science at Victoria University.

Project explanation

Competitive pacing strategies involve the conscious and/or subconscious variation of workload over the duration of an exercise in order to limit premature fatigue and, thereby, increase the likelihood of winning an event. Traditional exercise physiology has explained the decline in performance during fatiguing exercise via the development of neuromuscular fatigue, *i.e.,* a decrease in muscle power output due to 'negative' changes occurring within the 'periphery' (anything outside of the central nervous system). These peripheral components include changes in energy provision, muscle metabolism and the cardiovascular, respiratory, thermoregulatory and endocrine systems. Essentially, one or more of these systems is unable to cope with the excessive demand placed on them, and exercise is ceased to maintain homeostasis and prevent excessive harm to the individual. However, activation of the muscle by the central nervous system (CNS) initiates the cascade of events involved in muscular contraction and, consequently, force and power production. The mass of skeletal muscle recruited via the CNS during exercise would subsequently be regulated to 'adjust' the amount of mechanical output and thus exercise intensity (i.e. pacing). This occurs presumably to avoid potentially long-lasting damage to the individual by regulating the amount of end-exercise peripheral fatigue (i.e. decline in the producible force of the muscles independent of the CNS). A failure in voluntary activation during maximal efforts means that the level of muscle recruitment is less than optimal; the motor units within the muscle are either not all recruited voluntarily or they are discharging at rates that are not high enough to produce full fusion of force. A failure to activate fully the contracting musculature can theoretically reduce force and power production and alter exercise capacity.

This proposed research project will investigate how the amount of pre-exercise peripheral fatigue alters participants' performance throughout an 'all out' 30 second cycle sprint. This has previously been investigated in endurance cycling; however it is yet to be investigated during sprint cycling.

What will I be asked to do?

If you choose to volunteer in this study, you will be required to attend the Victoria University Footscray Park campus on 4 different occasions throughout May and June 2012: one familiarisation session (~1.5 hrs) and 3 testing sessions (~1hr each). Each session will involve a number of high intensity sprint efforts and a number of neuromuscular tests (i.e. peripheral magnetic stimulation and a maximal voluntary contraction test). In the 24 hours prior to each session, you will be asked to refrain from vigorous activity and the ingestion of caffeine, alcohol or other drugs.

Session One – Pre-Screening, Familiarisation and Torque-Velocity Test (~1.5hrs)

In this session, you will complete the VU Cardiovascular Risk Questionnaire and will be requested to give Informed Consent to volunteer in the study. For inclusion, you must meet all inclusion criteria as identified on the Cardiovascular risk questionnaire. If you do not meet any of the exclusion criteria as identified in the Cardiovascular risk questionnaire you will not be included in this study. You will also be given the opportunity to ask any questions about the study. You will be pre-screened via these questionnaires for overall health, injury, bleeding disorders and neuromuscular or cardiovascular diseases. The principal investigator will then assess your suitability for participation in the study.

Upon clearance, you will be introduced to the Lode cycle ergometer, where you will complete two 30 second cycle sprints separated by 5 to 10 minutes of recovery so you can become accustomed to producing a maximal effort. You will also be required to perform a Torque-Velocity test that involves performing 5 maximal sprints of a duration of 4 s on the cycle ergometer with different resistances, and interpsersed with 5 min of passive recovery between each sprint. From this test your maximal power output and optimal cycling cadence can be determined.

During this familiarisation session you will be familiarised with electromyography recording, the peripheral magnetic stimulation technique (PMS) and the maximal voluntary contraction test (MVC) (see procedures below) as many times needed to become confident and familiar with these techniques.

Session 2, 3, and 4 – Main protocol (~ 1hr each)

These session will all occur in sperate days, at least 4 days apart to allow for full recovery from previous testing sessions.

In every session, particpants will be fitted with the appropriate equipment. The neuromuscular function test (MVC and PMS; see procedures below) will be performed to record resting data. After a 5-min self-paced warm-up on the cycle ergometer, you will perform a pre-fatigue protocol. A neuromuscular function test will then be performed immediately to evaluate the degree of muscle fatigue. This will take ~3 min, after which each participant will perform an all-out, 30-s sprint with the cadence fixed at your optimal level. The cycle ergometer will be equipped with toe-clips to prevent feet from slipping. You will be asked to remain seated during the sprint. Following the test, all instrumentation will be removed and you will then perform a self-paced cool down.

The pre-fatigue protocol will include a moderately-fatiguing exercise (10-min cycling at ~60% of your maximal power), a severely-fatiguing exercise (10-min cycling at ~85% of your maximal power) and a control condition (10 min resting on the cycle ergometer). The percentage of your maximal power is obtained from the T-V test performed on the familiarisation day.

Brief description of the main procedures to be used:

All investigators are fully experienced in using these techniques.

- **Maximal voluntary isometric contraction test (MVC):** this test will determine the maximal isometric strength of the quadriceps muscle. You will lie supine on a bench, with the knee flexed at 90° (0° = knee fully extended) over the end of the bench. The upper body, hips, thigh and ankle will be braced to reduce body movement. You will then be asked to perform two 4-s maximal knee extensions before and immediately after the pre-fatigue protocol and after the sprint exercise.
- **Electromyography (EMG) recording (non-invasive):** small, self-adhesive surface electrodes will be attached to the skin over the belly of 10 different muscles of your dominant lower limb. This will not affect pedalling movements in any significant way, but may require the area to be shaved of hair and cleaned before attaching the electrodes. There is no discomfort associated with the application, wearing, or removal of the EMG electrodes. Measurement of electrical activity of muscles during exercise is a routine procedure in most physiology and biomechanics laboratories worldwide. EMG signals will be recorded during the MVCs and the sprint exercise to estimate muscle recruitment strategies.
- **Peripheral magnetic stimulation (PMS, non-invasive)**: Magnetic stimulation is usually painless. In some cases, participants may get the sensation of muscle cramping. A thorough preliminary session to get accustomed to the stimulation will be performed during familiarisation. While lying supine with legs off bench to assess maximal strength, a series of percutaneous magnetic stimulations of the quadriceps will be used at rest and during MVCs to measure the muscle function properties. This procedure is used in many exercise physiology laboratories around the world
- **Responses to exercise:** Heart rate will be continuously (5-s intervals) recorded via a wireless Polar monitoring system. A measure of the rate of perceived exertion (RPE) will also be obtained immediately after the pre fatigue trial and the 30 second sprint based on the 6-20 Borg scale, with participants rating how hard the exercise “felt”.

What will I gain from participating?

The equipment and methods will be cutting edge, which are normally reserved for elite professional athletes. The 30 second cycle sprint/Anaerobic Wingate test is a worldwide testing method, where you can determine you anaerobic capacity/fitness. Additionally, the Torque Velocity test allows you to find out your optimal cycling cadence for maximal power production during cycling, which can be used to refine your personal training. We cannot guarantee that you will receive any direct benefit from your participation, however you will gain a better understanding of the regulation of sprint exercise, which may improve your current or future training regimes.

How will the information I give be used?

The information you provide to the researchers will be kept strictly confidential. Only group data will be reported and presented via written publications and potential conference presentations. Data collected from your performance testing, along with other participants, will be used to investigate whether the central nervous system anticipates the physiological demands associated with sprint cycling, and alters its response to avoid critically-high levels of peripheral fatigue.

What are the potential risks of participating in this project?

Although it is highly unlikely, all high-intensity exercise has a risk of sudden death and also a risk of vasovagal episode (**faint**). While vasovagal episodes are not uncommon, they are reversed quickly when employing vasovagal management plan, and long-term risks are minimal. These vasovagal episodes are experience regularly by athletes during training sessions and competition.

- All participants will be required to complete the standard Victoria University Risk Factor Assessment Questionnaire which will identify those with suspected cardiovascular complications, ventilatory restrictions and/or musculoskeletal conditions or injuries. This questionnaire will help to minimise the risk of physical complications

Furthermore, the pre-fatigue trials, the 30-second cycle sprint and the knee extensor MVCs carry the risk of muscle stiffness, soreness and potential soft tissue injury. Once again, these are uncommon and regularly experienced by any person involved in hard training.

The 30 second cycle sprint, the severe fatigue trial and the T-V have to be performed at high intensity. Participants will undertake a warm-up whose purpose is to prepare the body to exercise, which will reduce the risk of muscle soreness. Furthermore, exercise bouts will be very brief and you will be able to stop exercising at any time if any of the following criteria are present:

- You wish to stop;
- You experience chest pain, severe shortness of breath or any other pain related to, or caused by exercise;
- You wish to continue, but there are abnormal signs of metabolic or cardio-respiratory distress (e.g., facial pallor);

All participants will be informed about the possibility of experiencing discomfort or pain during magnetic stimulation or MVC prior to consenting to participate in the study. Any pain or discomfort experienced as a result of magnetic stimulation will be quickly reversed following the absence of stimulation. You will be thoroughly familiarised with these techniques during the familiarization sessions and if participants experience pain or discomfort they can choose to withdrawal at any stage of the project.

How will this project be conducted?

7-12 physically active male participants between the ages of 18-35 will participate in this study. Participants will be required to attend the Victoria University Footscray Park campus on four different occasions during June/July 2012. Participants will be required to attend each session at the same time of day for all 4 sessions, separated by at least 4 days to allow full recovery. This consistent time will be arranged in conjunction with the participant. Please refer to the “What will I be asked to do” section above for more details.

Who is conducting the study?

This study is being conducted by Victoria University, Faculty of Arts, Education and Human Development, School of Sport and Exercise Science.

For further information please contact the Chief Investigator Dr. Francois Billaut, Exercise Physiologist, School of Sport and Exercise Science/ Institute of Sport, Exercise and Active Living, Victoria University, Wk: 99199451, Email: francois.billaut@vu.edu.au

Additionally, information may also be obtained from the Associative Investigator Dr. David Rouffet, Exercise Physiologist, School of Sport and Exercise Science/Institute of Sport, Exercise and Active Living, Victoria University, WK: 99191116, Email: david.rouffet@vu.edu.au

More information can also be obtained from the Student investigator, Mr. Steven J O'Bryan, Mob: 0421744428, Email: steven.obryan@live.vu.edu.au

Any queries about your participation in this project may be directed to the Chief Investigator listed above.

If you have any queries or complaints about the way you have been treated, you may contact the Research Ethics and Biosafety Manager, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 or phone (03) 9919 4148.

Risk factor questionnaire

In order to be eligible to participate in the experiment investigating: "Regulation of locomotor muscle fatigue during repeated sprints." you are required to complete the following questionnaire which is designed to assess the risk of you having a cardiovascular event occurring during an exhaustive exercise bout.

Name: _____Date: _____

Age: _____ years Weight: _____ kg Height: _____ cm Gender: M F

Give a brief description of your average activity pattern in the past 2 months:

_____
_____
_____

Circle the appropriate response to the following questions.

Are you overweight?	Yes	No	Don't know
Do you smoke?	Yes	No	Social
Are you an asthmatic?	Yes	No	Don't Know
Are you a diabetic?	Yes	No	Don't Know
Does your family have a history of diabetes?	Yes	No	Don't Know
Do you have a thyroid disorder?	Yes	No	Don't Know
Does your family have a history of thyroid disorders?	Yes	No	Don't Know
Do you have a pituitary disorder?	Yes	No	Don't Know
Does your family have a history of pituitary disorders?	Yes	No	Don't Know
Do you have a heart rhythm disturbance?	Yes	No	Don't Know
Do you have a high blood cholesterol level?	Yes	No	Don't Know
Do you have elevated blood pressure?	Yes	No	Don't Know
Are you being treated with diuretics?		Yes	No
Are you on any other medications?	Yes	No	

List all medications? (Including vitamin supplements, antioxidants and oral contraceptives)

_____

Do you think you have any medical complaint or any other reason which you know of which you think may prevent you from participating in strenuous exercise? Yes No

If Yes, please elaborate_____

Have you had any musculoskeletal problems that have required medical treatment (e.g., broken bones, joint reconstruction etc)? Yes No

If Yes, please provide details (including dates) _____

Does your family have a history of premature cardiovascular problems (e.g. heart attack, stroke)? Yes No Don't Know

Have you had any neuromuscular problems that have required medical treatment (e.g., muscle soreness, muscle spasms, loss of muscular control, muscle rigidness etc)? Yes No

If Yes, please provide details (including dates)
_____

I, _____, believe that the answers to these questions are true and correct.

Signed: _____ Date: _____

Consent form for participants involved in research

INFORMATION TO PARTICIPANTS:
We would like to invite you to be a part of a study investigating the effects of peripheral locomotor fatigue on central motor drive during a 30 second cycle sprint.

The aim of this research project is to investigate whether the central nervous system anticipates the physiological demands associated with sprint cycling and alters its response to avoid critically-high levels of peripheral fatigue (decline in muscle producible force independent of the central nervous system).

If you choose to volunteer in this study, you will be required to attend the Victoria University Footscray Park campus on 4 different occasions throughout May and June 2012 at the same time of day that is convenient for you. Each session will involve a number of high intensity sprint efforts and a number of neuromuscular tests (i.e. magnetic stimulation and maximal voluntary contraction test of the quadriceps muscle). In the 24 hours prior to each session, you will be asked to refrain from vigorous activity and the ingestion of caffeine, alcohol or other drugs.

Although it is highly unlikely, all high-intensity exercise has a risk of i) sudden death and ii) faint While fainting is not uncommon, it is reversed quickly when employing vasovagal management plan, and long-term risks are minimal. All maximal exercise (sprint and maximal contractions) also carries the risk of muscle soreness, stiffness and the potential for soft tissue injury. The leg ischemia could be slightly uncomfortable for some.

- *All participants will be required to complete the standard Victoria University Risk Factor Assessment Questionnaire which will identify those with suspected cardiovascular complications, ventilatory restrictions and/or musculoskeletal conditions or injuries. This questionnaire will help to minimise the risk of physical complications. For inclusion, you must meet all inclusion criteria as identified on the cardiovascular risk questionnaire. If you do not meet any of the exclusion criteria as identified in the cardiovascular risk questionnaire you will not be included in this study.*

There is also a slight chance you will experience pain or discomfort during magnetic stimulation. If you feel at any stage that the discomfort associated with any technique is intolerable you can choose to withdrawal from the research.

CERTIFICATION BY SUBJECT

I, _____

Of_____

Certify that I am at least 18 years old* and that I am voluntarily giving my consent to participate in the study:

"Locomotor muscle fatigue and the regulation of sprint cycling performance in men" being conducted at Victoria University by: Dr. Francois Billaut

I certify that the objectives of the study, together with any risks and safeguards associated with the procedures listed hereunder to be carried out in the research, have been fully explained to me by:

Mr. Steven J O'Bryan

and that I freely consent to participation involving the below mentioned procedures:

- **Mechanical data :** The Torque-Velocity test, pre-fatigue trials and the 'all out' 30 second cycle sprints will take place on a Lode cycle ergometer that will record peak power output, mean power output, total work and torque developed at the crank. The cadence will be kept constant throughout each sprint
- **Maximal voluntary contraction (MVC) test:** this test will determine the maximal isometric torque of the dominant quadriceps muscles. While lying supine on a bench, with the knee flexed at 90° (0° = knee fully extended) over the end of the bench, your upper body, hips and thigh will be strapped on the bench to reduce body movement. The axis of a strain gauge will be aligned with the knee flexion-extension axis and attached to the shank with a strap. You will then be asked to perform a series of maximal knee extensions of 4 s (see 'Peripheral magnetic stimulation' section below for details).
- **Peripheral magnetic stimulation (non-invasive):** while lying on a bench to assess your maximal strength, a series of magnetic stimulations of the quadriceps will be used at rest and during the contractions to measure muscle function properties and voluntary activation. Magnetic stimulation is usually painless; however some participants may experience a slight sensation of muscle cramping. A thorough preliminary session to get accustomed to the stimulation will be performed in session 1 and any participant who does not wish to undergo the stimulation can be excluded from testing.
- **Electromyography recording (non-invasive):** small, self-adhesive surface electrodes will be attached to the skin over the belly of 10 muscles of the dominant lower limb. This will not affect pedalling movements in any significant way, but may require the area to be shaved of hair and cleaned before attaching the electrodes.

I certify that I have had the opportunity to have any questions answered and that I understand that I can withdraw from this study at any time and that this withdrawal will not jeopardise me in any way.

I have been informed that the information I provide will be kept confidential.

Signed: _____

Date:
Any queries about your participation in this project may be directed to the researcher

Dr. Francois Billaut francois.billaut@vu.edu.au
9919 9451

If you have any queries or complaints about the way you have been treated, you may contact the Research Ethics and Biosafety Manager, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 or phone (03) 9919 4148.

Appendix B - Study two

VICTORIA UNIVERSITY
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Information to participants involved in research

You are invited to participate in a research project:

Fatigue and alterations of the neuromuscular system during maximal knee extension and cycling exercises

This project is being conducted by Dr. David Rouffet, Mr. Steven O'Bryan, Ms Rosie Bourke and Professor David Bishop as part of a study at Victoria University, College of Sport and Exercise Science/ISEAL.

Project explanation

During maximal physical exercises, fatigue is generally caused by alterations of the properties of the neuromuscular system at both peripheral (muscle) and central (central nervous system, CNS) levels. Very limited studies have investigated the alterations of the neuromuscular system occurring during maximal dynamic exercise requiring a large contribution of the lower limb muscles and causing high levels of fatigue.

Previous literature has shown that when no fatigue is present during isolated slow contractions of the knee extensor muscles (20°/s), the output from the CNS is reduced. However, it is currently unknown how fatigue development during repeated intermittent knee extension exercise affects the central and peripheral levels of the neuromuscular system and how this ultimately influences voluntary force production.

Unlike isolated knee extension exercise, reductions in power output during whole body cycling exercise may further be associated with alterations in muscle coordination. During maximal cycling exercise, the knee extensor muscles have been identified as the primary power producing muscles. However it is currently unknown if reductions in power output during maximal cycling exercise are associated with changes in the neuromuscular function of the knee extensor muscles. Furthermore, it is unknown how knee extensor fatigue influences maximal sprint cycling performance and the muscle coordination pattern.

Therefore, the aim of this study is to apply advanced techniques to investigate the central and peripheral levels of the neuromuscular system during and immediately following maximal intermittent knee extensor contractions and maximal sprint cycling. We will also investigate how knee extensor fatigue influences maximal sprint cycling performance through the evaluation of muscle coordination and pedal forces.

What will I be asked to do?

Time Commitment

You will be asked to attend 4/5 sessions, with two **~3-4 hrs to complete** and the other two/three **ranging from 1.5-2.5 hrs**. This will include a familiarisation session, a torque velocity test session (based on your previous experience) and 3 main testing sessions.

Pre-Screening and Familiarisation session

In this session, you will complete the VU Cardiovascular Risk and Safe Use of Transcranial Magnetic Stimulation Questionnaires and will be requested to give Informed Consent to volunteer in the study. For inclusion, you must meet all inclusion criteria as identified on these questionnaires. You will also be given the opportunity to ask any questions about the study. You will be pre-screened via these questionnaires for overall health, injury, bleeding disorders and neuromuscular or cardiovascular diseases. The principal investigator will then assess your suitability for participation in the study.

Upon clearance, you will be introduced the procedures involved in applying surface electrodes over the lower muscles. This procedure requires shaving hair, lightly abrading and cleaning with alcohol swab the area of placement. Following this, you will be familiarised the Digitimer electrical and Magstim magnetic stimulators. This will be used separately, to deliver an electrical impulse to the femoral nerve and to generate a magnetic current in your motor cortex (i.e. motor area of the brain) which will both result in a 'twitch' response.

For the electrical stimulation, the twitch response will be localized to your knee extensor muscles. We will start with the intensity of the stimulus low and then progressively increase to the required intensity. Electrical stimulation may induce moderate levels of pain at high intensities, however the progressive increase from low to high intensities will allow you give feedback on your discomfort levels. If the level of discomfort is too great, we will not apply any further stimulation. This technique has been used extensively in exercise research to monitor changes in muscle and central nervous system fatigue

TMS is a non-invasive and painless tool, which uses magnetic fields to stimulate cells in the brain through a magnetic coil held above the scalp. The coil is held over the scalp by the investigator and a brief current pulse flows through the coil. This in turn generates a magnetic field that activates the brain tissue beneath the coil. From your perspective, all you will notice is possibly a light tap on the head (not all participants report this) and an audible click sound. Although we can identify the area over the scalp that corresponds to the greatest twitch response in your knee extensor muscles, we are unable to localize this twitch response. As a result, it is highly likely that you will also experience twitches in other areas of your body such as the upper body or the face. In healthy participants, this technique has no adverse effects although it may result in the development of a headache. The Safe Use of Transcranial Magnetic Stimulation Questionnaire will be used to assess your susceptibility to any adverse effects. For example, magnetic stimulation of the motor cortex may trigger seizures in those who suffer from neurological disorders such as epilepsy. However, no serious adverse effects of single pulse TMS (used in this study) have been shown in healthy participants. If contraindications to this procedure are identified, you may be excluded from participating in this study.

After this we will introduce you to the Cybex isokinetic dynamometer where you will a number of knee extension contractions through the range of motion and speed that is required for the maximal intermittent knee extensor exercise.

Finally, you will be introduced to the stationary bike ergometer that will be used for maximal cycling exercise. You will wear cycling shoes, so if this is new for you we will explain the correct cycling technique of pushing and pulling up on the pedals. Once you complete a short warm-up, you will complete a torque velocity test which consists of a series of 4-5 second sprints at different cadences and resistances to evaluate the fore generating capacities of your lower-limb muscles at different speeds *(Nb: If this is your first time completing this torque-velocity test, an additional session will be required at a later date in order to allow sufficient familiarisation).* After this, we will practice a 30-s maximal cycling sprint.

Main Testing sessions

For each main testing session, EMG electrodes will first be placed on the lower limbs (left and right). We will then perform the electrical stimulations of the femoral nerve and magnetic stimulations of the motor cortex to elicit a number of responses in your knee extensor muscles. This will help us to determine the intensity at which we need to simulate and the optimal location of stimulation. We will happily answer any questions you have about these responses.

The prescribed cycle warm-up will be completed and followed by one of three conditions to be performed;

1) Maximal Intermittent Knee Extensor Exercise
2) Maximal 30-s cycling sprint
3) Maximal Intermittent Knee Extensor Exercise + Maximal 30-s cycling sprint

Maximal Intermittent Knee Extensor Exercise: You will be required to complete this knee extensor exercise during two of the three main testing sessions. You will sit upright in the isokinetic dynamometer with the hip and knee angle at 90° with straps firmly fastened around the waist and shoulders to limit unnecessary upper body movement. A strap attached to a double leg lever arm of the dynamometer will be attached to your left and right ankles. You will then be required to complete sets of 30 contractions from a range of motion of 100-30 ° knee flexion (total ROM of 70°, 0°=full knee extension) and speed of 15 °/s. 1.4 seconds of recovery will separate each contraction, resulting in a maximal contraction every 6 s and a work to rest ratio of 4.6:1.4 s. 45 s will separate each set in order to allow sufficient time to assess the neuromuscular system. You will complete as many sets as necessary to reduce your maximal knee extensor force to 40% of maximum. Muscle activity and force will be monitored during the exercise.

Maximal 30-s cycling sprint: The 30-s cycle sprint will be performed in isolation during a single experimental session or immediately following the fatiguing knee extensor task. You will be instructed to place the right crank angle at 45° before receiving a verbal 3-s countdown to start the sprint. Gear selection will be pre-determined during familiarisation and you will be instructed to remain seated during the sprint. Muscle activity will be recorded from the lower-limb muscles and the crank angle, cadence and torque values will be continuously recorded for the sprint and power values will be calculated post processing. During the sprint, a pulse will be sent to the electrical stimulator when the right pedal crosses 180°. This pulse will be set to trigger the electrical stimulator and deliver three consecutive single stimuli to your femoral nerve during the initial (0-3 s), middle (13.5-16.5 s) and final (27-30 s) periods of the sprint. This will permit us to track changes occurring at the peripheral level of the neuromuscular system during the sprint (i.e. M-wave).

What will I gain from participating?

The equipment and methods used during these testing sessions will be state-of-the-art, which are normally reserved for elite professional athletes. The 30 second cycle sprint is a worldwide testing method, where you can determine you maximal anaerobic power production. We are confident that you will gain a better understanding of how the Central Nervous System adjust the activation of the lower limb muscles during fatiguing exercises. Surface Electromyography allows you to see your muscles 'activated by the Central Nervous System' in real time.

How will the information I give be used?

All of the information gathered in this study is highly confidential and will be coded and stored under secure conditions. Only group data will be reported and presented via written publications and potential conference presentations.

The data gathered from this study may be used for related research studies. If you do not want your data to be used for additional studies please tick the check box on the consent form "I agree to the information collected from this study being used for related research purposes". If you agree to your data being used for related research purposes it will be done so anonymously.

During testing we might ask your permission to take photos or video footage of the experimental set up (electrode placement etc). This will only be done with your prior permission, with all images made anonymous to maintain your privacy. However, anonymity cannot be guaranteed if videoing magnetic stimulation over the head. The images may be used in research presentations or scientific publications and the video may be used for research presentations only.

What are the potential risks of participating in this project?

- Although highly unlikely, all high-intensity exercise has a risk of sudden death and stroke.
- Further, vasovagal episodes may happen, i.e. Faint. Signs and symptoms of a vasovagal episode may include precipitous drop in heart rate during recovery (common) or exercise (rare), facial pallor,

fixed facial expression, pupils constricted, volunteer becomes uncommunicative or slurring of words, restless and irritability, sweating, respiratory distress, fatigue (if exercising).

- The maximal 30-s cycling sprint and intermittent knee extensor exercise might result in some localised muscle soreness and fatigue, however this will subside completely within a couple of days.
- Electrical stimulation can induce discomfort in some participants. If your discomfort levels are exceeded, we will stop immediately.
- Magnetic stimulation is painless when delivered to the motor cortex, however in some cases and after continued stimulations this may generate a headache. In this case, over the counter pain medication can be supplied on request
- Some participants may become stressed or anxious whilst undertaking the study due to either exercise stress (the high intensity nature of the study) or environmental stress (the procedures being conducted upon them). We will endeavour to minimise these risks by explaining the procedure in full beforehand.
- Some participants may feel uncomfortable with the researcher placing surface electromyography electrodes on the muscles and the electrical stimulating electrode on the femoral nerve (groin region). We will ensure your privacy during these procedures and actively seek feedback to ensure that you feel comfortable.

If you need any psychological counselling during the study, please contact: Dr Janet Young (03 9919 4762).

How will this project be conducted?

All volunteers will be screened for cardiovascular risk factors, contraindications to transcranial magnetic stimulation and any health issues that prevent them from participating in this study. After explanation of the testing procedures by the researcher and when you feel you fully understand the requirements of the research, you will be asked to sign an informed consent document. All data will be collected at Victoria University Footscray Park Campus.

Who is conducting the study?

College of Sport and Exercise Science/ISEAL, Victoria University

Chief Investigator	**Associate Investigator**	**Student Investigator**	**Student Investigator**
Dr. David Rouffet	Dr. David Bishop	Mr. Steven O'Bryan	Ms. Rosie Bourke
Tel: (03) 9919 4384		Tel: 03 9919 4066	Tel: 03 9919 4066
Email: david.rouffet@vu.edu.au	Email: david.bishop@vu.edu.au	Email: steven.obryan@live.vu.edu.au	Email: rosie.bourke@live.vu.edu.au

Any queries about your participation in this project may be directed to the Chief Investigator listed above. If you have any queries or complaints about the way you have been treated, you may contact:

Research Ethics and Biosafety Manager
Victoria University Human Research Ethics Committee
Victoria University
PO Box 14428
Melbourne, VIC, 8001
Tel: (03) 9919 4148.

VICTORIA UNIVERSITY
MELBOURNE AUSTRALIA

Risk factor questionnaire

Investigators: Dr. David Rouffet

Mr. Steven O'Bryan

Ms. Rosie Bourke

Prof. David Bishop

In order to be eligible to participate in the experiment investigating:

Fatigue and alterations of the neuromuscular system during maximal knee extension and cycling exercises

you are required to complete the following questionnaire, which is designed to assess the risk of you having a cardiovascular event during an exhaustive exercise bout. If you have any queries regarding any of the questions please ask one of the investigators before answering it

NAME:

_____ DOB: _____

ADDRESS:

_____ SEX M / F

_____ **Postcode:** **AGE** _____ **YRS**

TELEPHONE:

_____ **WEIGHT** _____ **KG**

EMAIL:

_____ **HEIGHT** _____ **CM**

MEDICAL HISTORY

In the past have you ever had (tick No or Yes):

Medical Condition	**NO**	**YES**	**Medical Condition**	**NO**	**YES**
Heart Attack	❑	❑	Congenital Heart Disease	❑	❑
Chest Pain (angina)	❑	❑	Disease of Arteries/Veins	❑	❑
Heart Murmur	❑	❑	Asthma	❑	❑
Heart Rhythm Disturbance	❑	❑	Lung Disease (e.g. emphysema)	❑	❑
Heart Valve Disease	❑	❑	Epilepsy	❑	❑

Stroke	❑	❑	Injuries to back, knees, ankles	❑	❑

Please list any prescribed medications being taken:

_____

_____

List any lower-limb musculoskeletal injuries in your past medical history and date of injury

_____

_____

SYMPTOMS DURING OR AFTER EXERCISE

As a result of exercise, have you ever experienced any of the following (tick No or Yes):

Symptom during exercise	**NO**	**YES**	**Symptom during exercise**	**NO**	**YES**
Pain or discomfort in the chest, back, arm, or jaw	❑	❑	Palpitations (heart rhythm disturbance)	❑	❑
Severe shortness of breath or problems with breathing during mild exertion	❑	❑	Pain in the legs during mild exertion	❑	❑
Dizziness, nausea, or fainting	❑	❑	Severe heat exhaustion	❑	❑

CARDIOVASCULAR RISK FACTORS

Do you have (tick NO, YES or circle ? for DON'T KNOW)

Cardiovascular Risk Factors	**NO**	**YES**	**DON'T KNOW**	
High Blood Pressure	❑	❑	**?**	
High Blood Cholesterol/Triglycerides	❑	❑	**?**	
Diabetes	❑	❑	**?**	
Current Smoker	❑	❑	Average/day =	
Ex-smoker	❑	❑	Average/day =	
Do you drink alcohol regularly?	❑	❑	Average/day =	drinks

	NO	**YES**

Do you know of any other reason why you should not undergo physical activity? This might include severe asthma, diabetes, a current or recent sports injury, or serious illness.	❑	❑

I, _____ declare that the above information is correct at the time of completing this questionnaire

Date ……/……/…….

Please Note: If your health changes so that you can then answer YES to any of the above questions, tell one of the experimenters.

Volunteer

Signed _____

Print _____ (BLOCK CAPITALS)

VICTORIA UNIVERSITY
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Transcranial magnetic stimulation safety screening questionnaire (TASS)

(Rossi et al. 2011; Keel et al. 2001)

NAME: _____

ADDRESS: _____

_____ **Postcode:** _____

TELEPHONE: _____

EMAIL: _____

1. Have you ever undergone Magnetic Brain Stimulation (TMS) in the past? Y / N
- If you answered Yes, were there any adverse reactions or problems?

_____

2. Do you suffer from epilepsy or have you ever experienced a convulsion or seizure? Y / N

3. Do you have a family history of epilepsy? Y / N

4. Have you ever suffered from a stroke? Y / N

5. Have you ever had a serious head injury such as concussion and was this associated with any loss of consciousness? Y / N
- If you answered Yes, how long ago did this occur?

_____

6. Do you have any hearing problems or ringing in your ears? Y / N

7. Do you have cochlear implants? Y / N

8. Do you have any metal in your head such as shrapnel, surgical clips or fragments from metal or metal work? Y / N

9. Do you have any implanted devices such as a cardiac pacemakers, medical pumps or intracardiac lines? Y / N

10. Do you suffer from frequent and/or severe headaches or migraines? Y / N
- If you answered yes, please state on a scale from 1 to 10 **the severity** (with 1= very mild to little discomfort and 10 = unbearable pain and discomfort) and your **most recent episode**.

_____

11. Have you ever had any other brain related medical condition? Y / N
- If you answered Yes, what condition?

_____

12. Have you ever had a serious illness that caused brain injury? Y / N
- If you answered Yes, what condition?

_____

13. Are you currently taking any medication? Y / N
- If so, please list current medication and dose

_____

14. Are you currently pregnant or is there any chance that you might be? Y / N

15. Do you require any further explanation about the use of TMS and the associated risks? Y / N
- If so, please speak to the current investigator now

I, _____ declare that the above information is correct at the time of completing this questionnaire

Date ……/……/…….

Please Note: If your health changes so that you can then answer YES to any of the above questions, tell one of the experimenters.

Signed _____

Print _____ (BLOCK CAPITALS)

VICTORIA UNIVERSITY
MELBOURNE AUSTRALIA

Consent form for participants involved in research

We would like to invite you to take part in the study: **Fatigue and alterations of the .neuromuscular system during maximal knee extension and cycling exercises**

CERTIFICATION BY SUBJECT

I, _____ of_____ (address)

certify that I am at least 18 years old and that I am voluntarily giving my consent to participate in the study: **'Fatigue and alterations of the neuromuscular system during maximal knee extension and cycling exercises'** being conducted at Victoria University by Dr. David Rouffet, Mr. Steven O'Bryan, Ms. Rosie Bourke and Professor David Bishop

I certify that the objectives of the study, together with any risks and safeguards associated with the procedures listed hereunder to be carried out in the research, have been fully explained to me by Dr. David Rouffet (Principal Investigator) or Mr. Steven O'Bryan and that I freely consent to participation involving the below mentioned procedures:

- Sprint maximally on a bike ergometer for 30 seconds
- Repeat a series of maximal voluntary Knee Extension Exercise on an Isokinetic Dynamometer
- Have the activity of your lower limb muscles recorded via electrodes that attach to the skin
- Have the femoral nerve of your lower limb electrically stimulated via a surface electrode attached to the skin
- Have the motor area of your brain (i.e. motor cortex) magnetically stimulated via a coil placed over the head

I certify that I have had the opportunity to have any questions answered and that I understand that I can withdraw from this study at any time and that this withdrawal will not jeopardise me in any way.

I have been informed that the information I provide will be kept confidential.

If you need any psychological counselling during the study, please contact: Dr Janet Young (03 9919 4762).

☐ I agree that the information collected from this study can be used for related research purposes (e.g. effect of fatigue in other muscles on the regulation of muscle coordination by the central nervous system during cycling exercise).

☐ I give permission for photos or video footage of the experimental set up to be taken while I am participating in the study (e.g. me receiving electrical/magnetic stimulation or pedalling on the bike ergometer). I understand that all images will be made anonymous to maintain my privacy. I also understand that although a concerted effort will be made to make all video unidentifiable, this cannot be guaranteed if videoing magnetic stimulation over the head.
The images may be used in research presentations or scientific publications and the video may be used for research presentations only.

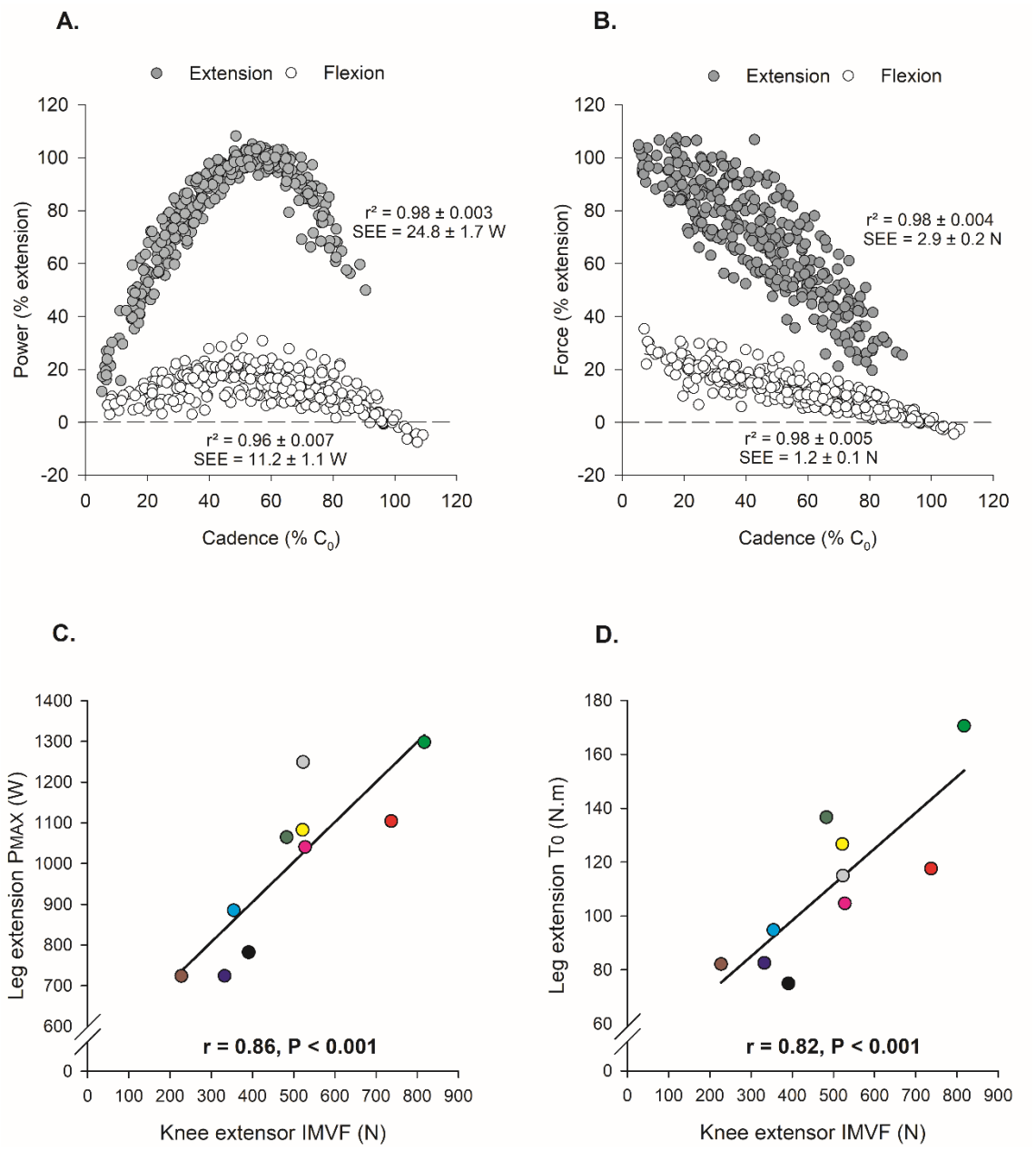
Signed: _____ Date: _____

Any queries about your participation in this project may be directed to a researcher:

Chief Investigator	**Associate Investigator**	**Student Investigator**	**Student Investigator**
Dr. David Rouffet	Dr. David Bishop	Mr. Steven O'Bryan	Ms. Rosie Bourke
Tel: (03) 9919 4384		Tel: 03 9919 4066	Tel: 03 9919 4066
Email: david.rouffet@vu.edu.au	Email: david.bishop@vu.edu.au	Email: steven.obryan@live.vu.edu.au	Email: rosie.bourke@live.vu.edu.au

If you have any queries or complaints about the way you have been treated, you may contact the Research Ethics and Biosafety Manager, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 or phone (03) 9919 4148.

Force-velocity test results



Study two F-V test results. Pooled data for maximal lower-limb power (**A**) and tangential crank force (**B**) in relation to maximal cadence during the F-V tests. Data are averaged over the leg extension phase (grey circles) and leg flexion phases (white circles). The mean R^2 represents the average of the individual R^2 values obtained (N = 10). Power and torque data is relative to the maximum achieved during the leg extension phase, whereas cadence is relative to maximum pedalling rate (i.e. C0). Relationship between the apex of the maximal power-cadence relationship (P_{MAX}) (**C**) and the Y-intercept of the maximal force-cadence relationship (T0) (**D**) with maximal isometric force of the knee extensors (IMVF).

Appendix C - Study three

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Information to participants involved in research

You are invited to participate in a research project:

Fatigue related changes in electromyographic signals during maximal exercises

This project is being conducted by Dr. David Rouffet and Mr. Steven O'Bryan as part of a study at Victoria University, College of Sport and Exercise Science/ISEAL.

Project explanation

During maximal cycling exercise, changes in central (central nervous system) and peripheral (muscle) fatigue may be reflected in the surface electromyography signal (EMG) which records the muscle activity via electrodes placed over the skin. By comparing changes in EMG measured during voluntary contraction with changes in EMG responses induced by external stimulation of the peripheral nerve (termed the M wave), it is possible to identify if changes in EMG are due to the occurrence of fatigue, but also to determine the origin of fatigue (e.g. central or peripheral).

Studies investigating EMG and M wave changes during maximal cycling indicate that changes in EMG may be caused by central fatigue as no changes in M wave are observed. However, methodological limitations in assessment of M wave exist in previous research; namely the large time delay between end of exercise and obtainment of M waves as well as differences in body position, joint angle and activation level adopted for M wave assessment and EMG during cycling. The aim of the study is therefore to determine if comparable levels of peripheral and central fatigue are obtained between a maximal modified cycling exercise, and maximal single-joint exercise, performed at a similar range of motion, joint angular velocity and muscle activation level. In this way, we will be able to overcome many of the methodological limitations associated with previous research and permit a more accurate assessment of the central and peripheral fatigue mechanisms leading to reductions in power output during maximal cycling exercise.

What will I be asked to do?

Time Commitment
You will be asked to attend three sessions at a similar time of the day, each lasting ~2-3 hrs. The sessions will be completed in a randomized order.

Trial 1 – Familiarisation Session

In this session, you will complete the VU Cardiovascular Risk Assessment Questionnaire and be requested to give Informed Consent to volunteer in the study. For inclusion, you must meet all inclusion criteria as identified on these questionnaires.

You will be given the opportunity to ask any questions about the study. You will be pre-screened via these questionnaires for overall health, injury, bleeding disorders and neuromuscular or cardiovascular diseases. The principal investigator will then assess your suitability for participation in the study.

Upon clearance, you will be introduced to the procedures involved in applying surface EMG electrodes over the lower muscles and goniometers (to measure joint angle) over your knee joint. This procedure requires shaving hair, lightly abrading and cleaning with alcohol swab the area of placement. After this we will introduce you to the Cybex isokinetic dynamometer where you will perform a number of contractions of your thigh muscles.

Following this, you will be familiarised the electrical stimulator whilst seated. This will be used to deliver an electrical pulse to the femoral nerve which will result in a 'twitch' response. For the electrical stimulation, the twitch response will be localized to your knee extensor/quadriceps muscles. We will start with the intensity of the stimulus low and then progressively increase to the required intensity. Electrical stimulation may induce moderate levels of discomfort at high intensities, however the progressive increase from low to high intensities will allow you give feedback on your discomfort levels. If the level of discomfort is too great, we will not apply any further stimulation and cease the experiment. This technique has been used extensively in exercise research to monitor changes in muscle and central nervous system fatigue without any adverse or long-lasting side effects.

Following this, we will practice neuromuscular testing. This procedure allows us to measure the reduction in the force produced by the knee extensors due to peripheral and central fatigue. For this, you will be asked to perform a maximal contraction of the knee extensors for 4 seconds, with a strap secured around one ankle, connected to a fixed resistance. An electrical stimulus will be given during the maximal contraction, after which you will be asked to completely relax, and two additional stimuli will then be given to the relaxed muscles.

After the practice neuromuscular testing, you will move to the cycle ergometer and perform a brief warm-up. We will then run through the modified cycling movement, which requires a maximal downstroke on the left side only. For this, we will practice ten downstrokes, six separate times (total of sixty contractions) and we will give you 60-s of rest between each set of ten contractions. During the last three downstrokes of each set, a pulse will be sent to the electrical stimulator when the left pedal crosses a pre-defined crank angle. This pulse will be set to trigger the electrical stimulator and deliver a single electrical stimulus to your femoral nerve. This will permit us to track changes occurring at the peripheral level of the neuromuscular system during the exercise (i.e. M-wave). The ergometer will restrict your maximal cadence to 40 revolutions per minute.

Following this, we will move to the isokinetic dynamometer. The set-up of the dynamometer will restrict the actions of the knee joint to what was observed during cycling exercise. Similar to cycling exercise, we will practice ten contractions, six separate times (total of sixty contractions) and we will give you 60-s of rest between each set of ten contractions. During the last three contractions of each set, a pulse will be sent to the electrical stimulator when your knee angle is the same as when stimulations were applied during cycling.

Trial 2 – Maximal modified cycling exercise

EMG electrodes and goniometer will first be attached to the left leg, followed by determination of the optimal intensity required for electrical stimulation. Then the cycling warm-up will be completed, followed by three separate neuromuscular testings to obtain a baseline measurement (1 min rest between each one). Then following 2 min of rest, the left leg will fixed to the left pedal of the ergometer via a cleat/pedal arrangement (Shimano SPD SL cleat with no float), whilst the right foot will rest passively on the right pedal. This will ensure that the exercise will be isolated to left knee extension, and eliminate the assistance of right pedal. You will be instructed to remain seated with hands in the lower portion of the handlebars, and to focus solely on producing a maximal effort during left knee extension only (i.e. downstroke phase of pedal cycle = 0-180° crank angle). You will be asked to complete a total of 60 maximal downstrokes (lasting 90 seconds), with electrical stimulation applied for contractions 1-3, 29-31 and 58-60. Manual assistance will be provided to the right pedal during left knee flexion (i.e. upstroke phase of pedal cycle = 180-360° crank angle) to ensure relaxation of hamstring muscles. Following the exercise, you will be required to get off the ergometer

and move to the dynamometer as quickly as possible for neuromuscular testing. This will be completed at 60s, 90s, 120s, 180s, 240s, 360s, 480s and 600s following the exercise.

Trial 3 – Maximal isokinetic knee extension exercise

This session will replicate the actions of your knee joint observed during cycling exercise but whilst seated. First, EMG electrodes and the goniometer will be placed on the lower limb muscles. We will then perform electrical stimulations of the femoral nerve to elicit a number of responses in your knee extensor muscles. This will help us to determine the intensity at which we need to simulate your nerve during the exercise. The cycling warm-up will then be completed, followed by three baseline neuromuscular testings (1 minute between each one). After 2 min of rest, you will complete the same number of maximal contractions of your thigh muscles that were completed during the modified cycling (i.e. 60). The dynamometer will restrict the range of motion and speed at which your knee joint angle changes to match that seen during the modified cycling exercise. In the same manner as trial 2, the electrical stimulator will deliver three consecutive single stimuli to your femoral nerve during contractions 1-3, 29-31 and 58-60. This will permit us to track changes occurring at the peripheral level of the neuromuscular system during the exercise (i.e. M-wave). Following exercise, neuromuscular testing will be completed at 0-s, 60s, 90s, 120s, 180s, 240s, 360s, 480s and 600s.

What will I gain from participating?

The equipment and methods used during these testing sessions will be state-of-the-art. You will gain a better understanding of the central and peripheral mechanisms causing fatigue during maximal exercises. Surface Electromyography also allows you to see your muscles activated by the central nervous system in real time. Upon completion, we will also be able to provide you with the following information;

1) The maximum strength capacity of your knee extensor muscles
2) The ability of your central nervous system (brain and spinal cord) to fully activate your knee extensor muscles

How will the information I give be used?

All of the information gathered in this study is highly confidential and will be coded and stored under secure conditions. Only group data will be reported and presented via written publications and potential conference presentations.

The data gathered from this study may be used for related research studies. If you do not want your data to be used for additional studies please tick the check box on the consent form “I agree to the information collected from this study being used for related research purposes”. If you agree to your data being used for related research purposes it will be done so anonymously.

During testing we might ask your permission to take photos or video footage of the experimental set up (electrode placement etc). This will only be done with your prior permission, with all images made anonymous to maintain your privacy. The images may be used in research presentations or scientific publications and the video may be used for research presentations only.

What are the potential risks of participating in this project?

- Although highly unlikely, all high-intensity exercise has a risk of sudden death and stroke.
- Further, vasovagal episodes may happen, i.e. Faint. Signs and symptoms of a vasovagal episode may include precipitous drop in heart rate during recovery (common) or exercise (rare), facial pallor, fixed facial expression, pupils constricted, volunteer becomes uncommunicative or slurring of words, restless and irritability, sweating, respiratory distress, fatigue (if exercising).
- Electrical stimulation can induce discomfort in some participants. If your discomfort levels are exceeded, we will stop immediately.
- Some participants may become stressed or anxious whilst undertaking the study due to either exercise stress (the high intensity nature of the study) or environmental stress (the procedures being conducted upon them). We will endeavour to minimise these risks by explaining the procedure in full beforehand.

- Some participants may become stressed or anxious whilst undertaking the study due to the anticipation of receiving electrical stimulation. We will endeavour to minimise these risks by explaining the procedure in full beforehand.
- Some participants may feel uncomfortable with the researcher placing surface electromyography electrodes/joint sensors on the muscles/joints and the electrical stimulating electrode on the femoral nerve (groin region). We will ensure your privacy during these procedures and actively seek feedback to ensure that you feel comfortable at all times.

If you need any psychological counselling during the study, please contact: Dr Janet Young (03 9919 4762).

How will this project be conducted?

All volunteers will be screened for cardiovascular risk factors and any health issues that prevent them from participating in this study. After explanation of the testing procedures by the researcher and when you feel you fully understand the requirements of the research, you will be asked to sign an informed consent document. All data will be collected at Victoria University Footscray Park Campus.

Who is conducting the study?

College of Sport and Exercise Science/ISEAL, Victoria University

Chief Investigator	Student Investigator(s)
Dr. David Rouffet Tel: (03) 9919 4384 Email: david.rouffet@vu.edu.au	Mr. Steven O'Bryan Tel: 03 9919 4066 Email: steven.obryan@live.vu.edu.au

Any queries about your participation in this project may be directed to the Chief Investigator listed above.

If you have any queries or complaints about the way you have been treated, you may contact:

Research Ethics and Biosafety Manager
Victoria University Human Research Ethics Committee
Victoria University
PO Box 14428
Melbourne, VIC, 8001
Tel: (03) 9919 4148.

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Risk factor questionnaire

Investigators: Dr. David Rouffet
Mr. Steven O'Bryan

In order to be eligible to participate in the experiment investigating:
Fatigue related changes in electromyographic signals during maximal exercises you are required to complete the following questionnaire, which is designed to assess the risk of you having a cardiovascular event during an exhaustive exercise bout. If you have any queries regarding any of the questions please ask one of the investigators before answering it.

NAME:

_____ DOB: _____

ADDRESS:

_____ SEX M / F

_____ **Postcode:** **AGE** _____ **YRS**

TELEPHONE:
_____ **WEIGHT** _____ **KG**

EMAIL:
_____ **HEIGHT** _____ **CM**

MEDICAL HISTORY
In the past have you ever had (tick No or Yes):

Medical Condition	**NO**	**YES**	**Medical Condition**	**NO**	**YES**
Heart Attack	❑	❑	Congenital Heart Disease	❑	❑
Chest Pain (angina)	❑	❑	Disease of Arteries/Veins	❑	❑
Heart Murmur	❑	❑	Asthma	❑	❑
Heart Rhythm Disturbance	❑	❑	Lung Disease (e.g. emphysema)	❑	❑
Heart Valve Disease	❑	❑	Epilepsy	❑	❑
Stroke	❑	❑	Injuries to back, knees, ankles	❑	❑

Please list any prescribed medications being taken:

_____

_____

List any lower-limb musculoskeletal injuries in your past medical history and date of injury

_____

SYMPTOMS DURING OR AFTER EXERCISE

As a result of exercise, have you ever experienced any of the following (tick No or Yes):

Symptom during exercise	NO	YES	Symptom during exercise	NO	YES
Pain or discomfort in the chest, back, arm, or jaw	❑	❑	Palpitations (heart rhythm disturbance)	❑	❑
Severe shortness of breath or problems with breathing during mild exertion	❑	❑	Pain in the legs during mild exertion	❑	❑
Dizziness, nausea, or fainting	❑	❑	Severe heat exhaustion	❑	❑

CARDIOVASCULAR RISK FACTORS

Do you have (tick NO, YES or circle ? for DON'T KNOW)

Cardiovascular Risk Factors	NO	YES	DON'T KNOW	
High Blood Pressure	❑	❑	?	
High Blood Cholesterol/Triglycerides	❑	❑	?	
Diabetes	❑	❑	?	
Current Smoker	❑	❑	Average/day =	
Ex-smoker	❑	❑	Average/day =	
Do you drink alcohol regularly?	❑	❑	Average/day =	drinks

	NO	YES
Do you know of any other reason why you should not undergo physical activity? This might include severe asthma, diabetes, a current or recent sports injury, or serious illness.	❑	❑

I, _____ declare that the above information is correct at the time of completing this questionnaire Date ……/……/…….

Please Note: If your health changes so that you can then answer YES to any of the above questions, tell one of the experimenters.

Volunteer

Signed _____

Print _____(BLOCK CAPITALS)

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Consent form for participants involved in research

We would like to invite you to take part in the study **Fatigue related changes in electromyographic signals during maximal cycling exercises**

CERTIFICATION BY SUBJECT

I,……of…….....(address)

certify that I am at least 18 years old and that I am voluntarily giving my consent to participate in the study: **'Fatigue related changes in electromyographic signals during maximal cycling exercise'** being conducted at Victoria University by Dr. David Rouffet and Mr. Steven O'Bryan

I certify that the objectives of the study, together with any risks and safeguards associated with the procedures listed hereunder to be carried out in the research, have been fully explained to me by Dr. David Rouffet (Principal Investigator) or Mr. Steven O'Bryan and that I freely consent to participation involving the below mentioned procedures:

- Perform a maximal 2 minute effort on a cycle ergometer
- Perform maximal contractions of the thigh muscles
- Have the activity of your lower limb muscles recorded via electrodes that attach to the skin
- Have the joint angle of your knee recorded via sensors placed on the skin
- Have the femoral nerve of your lower limb electrically stimulated via a surface electrode attached to the skin

I certify that I have had the opportunity to have any questions answered and that I understand that I can withdraw from this study at any time and that this withdrawal will not jeopardise me in any way.

I have been informed that the information I provide will be kept confidential.

If you need any advice during the study, please contact Dr Janet Young, a registered psychologist at Victoria University (03 9919 4762).

☐ I give permission for photos or video footage of the experimental set up to be taken while I am participating in the study (e.g. me receiving electrical stimulation or pedalling on the bike ergometer). I understand that all images will be made anonymous to maintain my privacy. I also understand that a concerted effort will be made to make all video unidentifiable. The images may be used in research presentations or scientific publications and the video may be used for research presentations only.

Signed: _____ Date: _____

Any queries about your participation in this project may be directed to a researcher:

Dr. David Rouffet
Tel: (03) 9919 4384
Email: david.rouffet@vu.edu.au

Mr. Steven O'Bryan
Tel: 03 9919 4066
Email: steven.obryan@live.vu.edu.au

If you have any queries or complaints about the way you have been treated, you may contact the Research Ethics and Biosafety Manager, Victoria University Human Research Ethics Committee, Victoria University, PO Box 14428, Melbourne, VIC, 8001 or phone (03) 9919 4148.

Appendix 4 - Conference abstracts

O'Bryan S.J[1 2]**,** Bourke R[1 2], Rouffet D.M[1 2]. Magnitude and origin of fatigue changes during repeated maximal knee extensions. European College of Sports Science (ECSS), Malmo, Sweden, 2015

[1] Institute of Sport, Exercise and Active Living (ISEAL), Victoria University, Victoria, Melbourne, Australia

[2] College of Sport and Exercise Science, Victoria University, Victoria, Melbourne, Australia

Introduction: Many sports require athletes to produce repeated maximal contractions. Previous results suggest that maximal contractions completed at high velocities lead to a rapid and higher level of peripheral fatigue, whereas at low contraction velocities central fatigue develops progressively (Morel et al. 2014; Babault et al. 2006). This study investigated changes in the magnitude and origin of fatigue observed during the repetition of maximal knee extensions (K_{EXT}) performed at a very low contraction velocity (15°/s) and with a large work to rest ratio (4.6s/1.4s).

Methods: Seven active subjects performed 120 K_{EXT} on an isokinetic dynamometer. Electromyography activity was recorded from *vastus lateralis* muscle. Torque, electromyography amplitude (EMG), median frequency (MF) and EMG/torque ratio were extracted every 30 repetitions (R_1-R_{30}-R_{60}-R_{90}-R_{120}). Neuromuscular testing (NMT) was administered at baseline and immediately following each 30 repetitions to extract maximal voluntary torque (MVT), voluntary activation (VA), potentiated quadriceps twitch (Q_{tw}), maximal M-wave amplitude (M_{MAX}), and EMG/M_{MAX}. One-way ANOVA evaluated the effect of repetition on changes in K_{EXT} and NMT variables ($P \leq 0.05$).

Results: MF decreased (R_1: 62 ± 7; R_{30}: 56 ± 6 Hz) and EMG/torque increased (R_1: 0.6 ± 0.2; R_{30}: 1.1 ± 0.4) at R_{30}; torque (R_{30}: 53 ± 8; R_{60}: 60 ± 7; R_{90}: 62 ± 9 %) and EMG (R_{30}: 22 ± 5; R_{60}: 27 ± 8; R_{90}: 33 ± 7 %) decreased until R_{90} (all $P \leq 0.05$). MVT was lower after each 30 repetitions (R_{30}: 28 ± 16; R_{60}: 37 ± 25; R_{90}: 41 ± 25; R_{120}: 48 ± 26 %; $P \leq 0.05$). Q_{tw} reduced at R_{30} (41 ± 21 %); VA decreased after R_{60} (R_{60}: 22 ± 18; R_{90}: 29 ± 17; R_{120}: 38 ± 21 %; $P \leq 0.05$); EMG/M_{MAX} was lower after R_{30} and R_{120} (R_1: 0.06 ± 0.02; R_{30}: 0.044 ± 0.01; R_{120}: 0.037 ± 0.01) (all $P \leq 0.05$). M_{MAX} did not change ($P = 0.7$).

Discussion: We observed faster and more pronounced reductions in knee extensor torque during K_{EXT} which was associated with greater variations in peripheral and central fatigue indicators when compared to previously reported results for comparable exercise protocols (Morel et al. 2014; Babault et al. 2006). An early development of peripheral fatigue was evidenced by a reduction in Q_{tw} and MF, associated to an increase in EMG/torque; presumably in response to an increase in metabolic perturbations caused by the repetition of maximal contractions.

Conclusion: A delayed onset of central fatigue was identified by a decrease in VA, likely resulting from peripheral fatigue and an increase in group III/IV afferent feedback leading to reduced neural drive and motoneuron excitability (Amann et al. 2013), as suggested by the decreases in EMG and EMG/M_{MAX}.

O'Bryan S.J[1 2]**,** Rouffet D.M[1 2]. Effect of isolated fatigue in the knee extensors on muscle activation and crank power during maximal cycling. Exercise Sport Science Australia (ESSA), Melbourne, Australia, 2016

[1] Institute of Sport, Exercise and Active Living (ISEAL), Victoria University, Victoria, Melbourne, Australia

[2] College of Sport and Exercise Science, Victoria University, Victoria, Melbourne, Australia

Introduction & Aims: Isolated muscle fatigue and/or pain can reduce the force capacity and activation level of synergistic and antagonist muscles of the lower-limb during monoarticular exercises [1, 2]. Our aim was to investigate the effect of isolated knee extensor muscle fatigue on crank power and electromyography (EMG) signals of 6 lower-limb muscles during maximal cycling.

Methods: 10 healthy subjects performed a 30-s cycle sprint in a control condition (SPRCTL) and after 120 maximal isokinetic knee extensions (SPRKEXT). Crank power and EMG amplitude for vastus lateralis, vastus medialis, rectus femoris, gastrocnemius, gluteus maximus and biceps femoris was continuously recorded. Knee extensor fatigue was assessed via maximal voluntary force (MVF), evoked twitch (Qtw) and voluntary activation (VA). Mean difference ± SD reported.

Results: MVF (-52 ± 22%), Qtw (-46 ± 18%) and VA (-36 ± 21%) were reduced prior to SPRKEXT ($P \leq 0.05$). Crank power (-16 ± 8%) and EMG for all muscles were lower for SPRKEXT ($P \leq 0.05$), especially biceps femoris (-20 ± 10%) and rectus femoris (-14 ± 12%). MVF (-31 ± 10%) Qtw (-26 ± 6%) and VA (-20 ± 12%) were lower post SPRKEXT than post SPRCTL ($P \leq 0.05$).

Conclusion: Isolated fatigue of the knee extensors evidenced via large reductions in contractile properties and activation level of this muscle group led to decreased activation level of all lower-limb muscles, despite the fact that the contractile properties of these muscles were presumably not reduced. This phenomenon most likely further reduced the ability of participants to produce crank power during maximal cycling.

O'Bryan S.J[1 2], Taylor J.L[3], Rouffet D.M[1 2]. Effect of bilateral fatigue in the knee extensors on crank power during sprint cycling. International Society of Electrophysiology and Kinesiology (ISEK), Chicago, United States of America, 2016

[1] Institute of Sport, Exercise and Active Living (ISEAL), Victoria University, Victoria, Melbourne, Australia

[2] College of Sport and Exercise Science, Victoria University, Victoria, Melbourne, Australia

[3] Neuroscience Research Australia, Sydney, Australia

Introduction: The ability to produce maximal crank power during sprint cycling is influenced by the force-generating capacity and activation level of the lower-limb muscles. It is often assumed that a reduction in the force-generating capacity of the knee extensor muscles is largely responsible for decreases in crank power during maximal cycling (Fernandez del Olmo et al. 2013), even if the direct contribution of the work produced by the knee extensors to crank power is limited (Zajac et al. 2002). The aim of this study was to investigate the effect of repeated maximal bilateral knee extensions on crank power and activation level of the lower-limb muscles during sprint cycling.

Methods: 10 subjects performed a maximal 30-s cycling sprint immediately after 120 maximal bilateral knee extensions and in a control condition. Maximal voluntary force (MVF), twitch force (Q_{tw}) and voluntary activation (VA) of the knee extensors were measured prior to maximal knee extensions as well as prior to and after the cycling sprints. Average crank power, cadence and EMG amplitude for *vastus lateralis* (VL), *rectus femoris* (RF), *biceps femoris* (HAM), *gastrocnemius* (GAS) and *gluteus maximus* (GMAX) were calculated during the 30-s cycling sprints. Mean ± SD values are reported.

Results: MVF (218 ± 109 N vs. 507 ± 193 N), Q_{tw} (77 ± 26 N vs. 137 ± 41 N) and VA (59 ± 19% vs. 90 ± 6%) were all lower following maximal knee extensions compared to control ($P \leq 0.05$). Crank power (541 ± 132 W vs. 654 ± 160 W), cadence (88 ± 5 rpm vs. 95 ± 4 rpm), knee extensor EMG (RF: -16 ± 12%, VL: -9 ± 10%) and EMG of HAM (-21 ± 8%), GMAX (-14 ± 13%) and GAS (-12 ± 13%) were lower during the cycling sprint performed after maximal knee extensions compared to the control sprint ($P \leq 0.05$). MVF (283 ± 86 N vs. 460 ± 157 N), Q_{tw} (60 ± 20 N vs. 89 ± 27 N) and VA (75 ± 11% vs. 94 ± 3%) remained lower after the sprint performed following maximal knee extensions compared to the control sprint ($P \leq 0.05$).

Conclusion: Completion of maximal bilateral knee extensions resulted in substantial levels of peripheral and central fatigue in the knee extensor muscles which decreased crank power during the subsequent sprint. However, reductions in the activity levels of GMAX, HAM and GAS during the sprint are also likely to have contributed to decreased crank power. Therefore, large reductions in the force-generating capacity of the knee extensor muscles (-52 ± 22%) may have a relatively small contribution to decreases in crank power (-17 ± 8%) during sprint cycling.

Effect of bilateral fatigue in the knee extensor muscles on crank power during sprint cycling

Steven J O'Bryan[1], Janet L Taylor[2] and David M Rouffet[1]

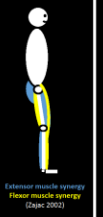
[1] Institute of Sport Exercise and Active Living (ISEAL), Victoria University, Melbourne, Australia

[2] Neuroscience Research Australia, Sydney, Australia

XXI ISEK CONGRESS
July 5-8, 2016
Chicago, IL, USA

INTRODUCTION

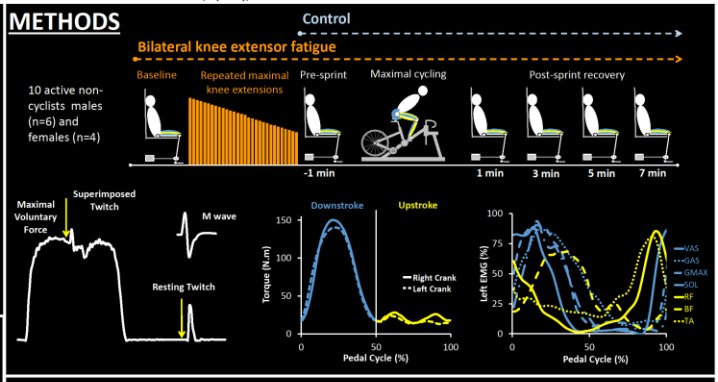
- During maximal cycling the majority of crank power is generated during the downstroke phase of the pedal cycle, with a large contribution from knee extension joint power (~40%) [Elmer, 2011] obtained via maximal activation of the vastii muscles [Rouffet and Hautier 2008].
- During prolonged maximal cycling (i.e. 30-s), large reductions in crank power are commonly associated with high levels of knee extensor fatigue [Martin and Brown, 2009; Gardner et al. 2009]. However, large reductions in the power generated at other lower-limb joints has also been observed [Martin and Brown, 2009].
- The impact of an isolated reduction in the force-generating capacity of the knee extensors on crank power production is unknown.



AIM

- To investigate the effect of repeated maximal bilateral knee extensions on crank power production and activation level of eight lower-limb muscles during a maximal 30-s cycling sprint.

METHODS

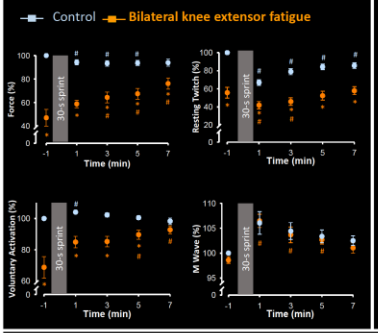


STATISTICS

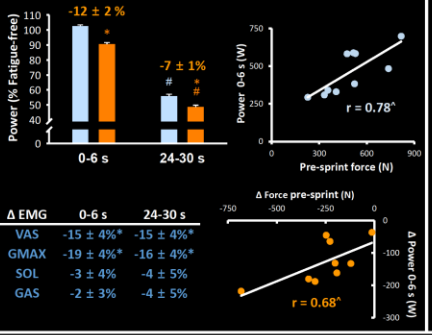
Two-way repeated measures ANOVA (condition x time) and Pearson's r correlations. Significance level $P < 0.05$. Mean change ± SEM reported. * Significantly different from control; # Significantly different from pre-sprint/0-6 s values; ^ Significant correlation

RESULTS

Isometric Knee Extension

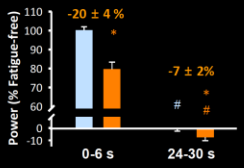


Cycling sprint - Downstroke



Δ EMG	0-6 s	24-30 s
VAS	-15 ± 4%*	-15 ± 4%*
GMAX	-19 ± 4%*	-16 ± 4%*
SOL	-3 ± 4%	-4 ± 5%
GAS	-2 ± 3%	-4 ± 5%

Cycling sprint - Upstroke



Δ EMG	0-6 s	24-30 s
RF	-13 ± 4%*	-11 ± 3%*
BF	-24 ± 5%*	-18 ± 4%*
TA	-9 ± 5%	-11 ± 4%*

CONCLUSION

- Repeated maximal bilateral knee extensions resulted in high levels of peripheral fatigue (-44 ± 6% in resting twitch) and central fatigue (-31 ± 7% in voluntary activation) in the knee extensors.
- High levels of knee extensor fatigue following the bilateral knee extension exercise (-270 ± 52 N in force) were associated with reductions in crank power during maximal cycling over the downstroke (-98 ± 26 W) and upstroke phases (-26 ± 9 W).
- The reduction in EMG activity of gluteus maximus, biceps femoris and tibialis anterior muscles observed during maximal cycling may have also contributed to the decrease in crank power during both downstroke and upstroke phases.

REFERENCES: Elmer et al., Med Sci Sports Exerc., 2011; Rouffet and Hautier, J Electromyogr Kinesiol., 2008; Martin and Brown., J Biomech., 2009; Zajac et al., Gait Posture., 2002; Gardner et al., Med Sci Sports Exerc., 2009

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